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## **ABSTRACT BOOK**

**WORLD CONFERENCE  
ON LUNG HEALTH 2023 OF THE  
INTERNATIONAL UNION AGAINST  
TUBERCULOSIS AND LUNG DISEASE  
(THE UNION)**

**PARIS, FRANCE  
15 – 18 NOVEMBER 2023**

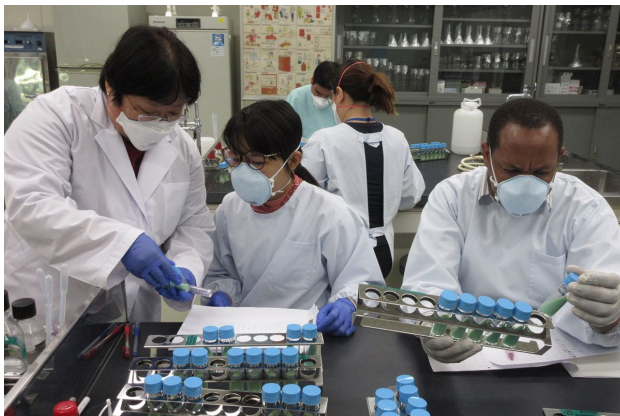
Since its foundation in 1939, the mission of the Research Institute of Tuberculosis, Japan Anti-Tuberculosis (RIT/JATA) has been to contribute to domestic and global tuberculosis control by conducting various studies, providing technical support as well as performing activities for international cooperation and collaboration.

## Our Vision

➔ A world where no one suffers from tuberculosis

## Our Mission

➔ Our mission is to eliminate TB suffering through development and implementation of comprehensive TB control strategies.



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- S2 SP02 Undernutrition and TB - people deserve better
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- S4 SP04 Higher ambitions for a gender-transformative response to TB for improving health, social and economic outcomes
- S5 SP05 Yes, we can end TB, but not without social protection. Here's the evidence: what are we waiting for? (Coordinated by Dr Tom Wingfield, LSTM)
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# The International Journal of Tuberculosis and Lung Disease (IJTLD)

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## AIMS AND SCOPE

*The International Journal of Tuberculosis and Lung Disease* is an official journal of The Union. The Journal's main aim is the continuing education of physicians and other health personnel, and the dissemination of the most up-to-date information in the field of TB and lung health. It publishes original articles and commissioned reviews not only on the clinical and biological and epidemiological aspects, but also on community aspects: fundamental research and assessment of field projects and action programmes for TB control and the promotion of lung health. The Journal welcomes articles submitted on all aspects of lung health, including cost-benefit analysis, legislation, epidemiology, intervention studies and health systems research.

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# 53rd World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union) Paris, France, November 15 – 18 2023

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## **SYMPOSIA: WEDNESDAY 15 NOVEMBER 2023**

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### **SP01 Innovation to guide practice in MDR/RR-TB treatment: efficacy and safety results of the endTB trial**

#### **endTB trial: Design and baseline characteristics of participants in a study of five all-oral, shortened regimens for MDR/RR-TB**

C Mitnick,<sup>1</sup> <sup>1</sup>Harvard Medical School, Boston, United States.  
e-mail: carole\_mitnick@hms.harvard.edu

This presentation will describe the study rationale, design, and baseline characteristics of study participants. We will report on site and regimen selection, trial inclusion and exclusion criteria, participation and monitoring schedule, and the functioning of the Bayesian response-adapted randomization.

We will introduce efficacy and safety endpoints, analysis populations, assumptions, analysis methods, selected adverse events of special interest and the MSF severity scale used to grade adverse events. We will describe the baseline characteristics of study participants by treatment arm. These include: demographics, medical history and comorbidities, prior TB treatment, and extent of TB disease (microbiological and radiographic).

#### **endTB trial: Efficacy results in a study of five all-oral, shortened regimens for MDR/RR-TB**

U Khan,<sup>1</sup> <sup>1</sup>IRD Global, Montreal, Canada.  
e-mail: uzma.khan@ird.global

This presentation will report primary, secondary, and selected exploratory efficacy results. We will report crude and adjusted analyses of the primary efficacy objective: comparison of the proportion of participants with

favorable outcomes at 73 weeks post-randomization between each experimental arm and the control arm. Secondary objectives include the same comparison at 104 weeks post-randomization (including between-arm comparisons). Subgroup analyses will also be presented.

#### **endTB trial: Safety results in a study of five shortened, all-oral regimens for MDR/RR-TB**

L Guglielmetti,<sup>1</sup> <sup>1</sup>Médecins Sans Frontières, Paris, France.  
e-mail: lorenzo.guglielmetti@paris.msf.org

This presentation will report main safety results. These include comparisons at 73 weeks and 104 weeks post-randomization between each experimental arm and the control of the following outcomes: the proportion of participants who experience grade 3 or higher adverse events, adverse events of special interest (defined as: Grade 3 or higher “electrocardiogram QT corrected interval prolonged”; Grade 3 or higher leukopenia, anemia or thrombocytopenia; Grade 3 or higher peripheral neuropathy; Grade 3 or higher optic neuritis; Grade 3 or higher increase in alanine aminotransferase or aspartate aminotransferase), serious adverse events, and death.

#### **endTB trial sub-studies: Evidence on resistance and pharmacokinetics/ pharmacodynamics to inform practice**

G Velásquez,<sup>1</sup> <sup>1</sup>University of California, San Francisco, San Francisco, United States.  
e-mail: gustavo.velasquez@ucsf.edu

This presentation will provide an overview of findings and design of substudies nested in the endTB trial to extend the knowledge acquired through the trial. Substudies include:

1. Linezolid dose optimization substudy, comparing safety and efficacy across two dose-reduction strategies to which participants were randomized;
2. PandrTB pharmacokinetic/pharmacodynamic and pharmacogenomic substudies exploring relationships among plasma concentrations of new and repurposed drugs, presence of single nucleotide polymorphisms in the host, efficacy, and toxicity;

3. DeepMTB, examining heteroresistance to bedaquiline and fluoroquinolones in sputum specimens and in *M. tuberculosis* strains;
4. Effect of resistance to pyrazinamide on treatment outcomes.

### **endTB trial: Perspective of the Global Tuberculosis Community Advisory Board (TB-CAB) on a study of five all-oral, shortened regimens for MDR/RR-TB**

P Agbassi,<sup>1</sup> <sup>1</sup>Global TB CAB, Abidjan, Cote D'Ivoire.  
e-mail: ayjpatrick@gmail.com

This presentation will provide a critical reading and interpretation of the (Bayesian response-adaptive) design, safety, efficacy, and substudy results presented during the symposium, from a patient/research-activist perspective. This will include consideration of the duration, pill burden and tolerability.

The possible impact and implications will be discussed in light of the current standard of care and international recommendations for RR/MDR-TB, and in the framework of the global clinical research landscape. The experience of the Global TB-CAB advising clinical researchers on design and implementation of trials will also be described.

### **SP02 Undernutrition and TB - people deserve better**

#### **When will we stop neglecting the role of undernutrition in TB? A TB survivor's perspective**

P Tisile,<sup>1</sup> <sup>1</sup>TB Proof, South Africa.  
e-mail: ptisile@gmail.com

It was impossible for me to eat during the first two months of treatment at least. It was hard to have an appetite in the first place, which affected my nutrition during my treatment journey.

Here I will discuss the support I received during treatment, compared to what I really needed, drawing on my own experience and that of others.

### **How undernutrition affects risk of TB: A meta-analysis**

P Cegielski,<sup>1</sup> <sup>1</sup>Emory University Rollins School of Public Health, Atlanta, Georgia, United States.  
e-mail: peter.cegielski@emory.edu

Published risk ratios for TB due to undernutrition are likely underestimates. Moreover, a mechanism by which undernutrition affects TB risk has not been advanced that is supported by direct evidence. This talk will critique published risk ratios, provide more realistic estimates, and propose a mechanism that may lead to more effective interventions

### **The impact of addressing patient undernutrition on TB treatment outcomes: A prospective cohort analysis**

M Bhargava,<sup>1</sup> <sup>1</sup>Yenepoya University, Yenepoya Medical College, Mangalore, India.  
e-mail: madhavibhargava4@gmail.com

Despite high prevalence and severity of undernutrition in patients with TB in high burden countries, there is a paucity of evidence of the impact of addressing it in treatment outcomes. RATIONS is a cluster RCT of household contacts of 2800 microbiologically confirmed patients with PTB in Jharkhand, India. The patient cohort nested in the RCT received locally evolved dry food-ration basket during the treatment period.

We discuss the improvement in clinical outcomes (lower case-fatality ratio), programmatic outcomes (lower rates of treatment interruption), and patient centered outcomes (weight gain and functional recovery) compared to cohorts without this nutritional support.

### **How changes in undernutrition affect the TB burden: A modelling study**

F McQuaid,<sup>1</sup> <sup>1</sup>London School of Hygiene and Tropical Medicine, London, United Kingdom.  
e-mail: finn.mcquaid@lshtm.ac.uk

Estimating the impact of humanitarian crises on TB often centres on health service disruptions, which consequently drives the focus of recovery efforts. The concomitant increase in vulnerability to TB due to worsening social determinants is largely neglected. We developed a mathematical model of TB in India to estimate the impact of changes to population nutritional status. We compare a baseline with no change in BMI, to a reduction in BMI as a result of major disruption to nutrition. We show that estimates of the impact on TB burden are likely to significantly underestimate change if vulnerability to TB is not considered.

## What we can do to integrate nutrition into TB therapy: A roadmap

P Sinha,<sup>1</sup> <sup>1</sup>Boston University Chobanian & Avedisian School of Medicine, Boston, United States.  
e-mail: psinha@bu.edu

Undernutrition is the leading risk factor for TB. Year after year, we see that the population attributable fraction for undernutrition far exceeds that of other leading comorbidities. And yet action remains anemic. If we are to eliminate TB, undernutrition cannot be ignored.

In this talk, we will outline a vision of integrating care for undernutrition and tuberculosis. This will include priority actions that must be done now by clinicians and TB programs, the data that needs to be gathered by researchers, and the collaborations necessary to enact change at the level of individual patients and populations.

## SP03 From neglect to child-friendly options: Assisting countries implement improved TB treatment for children and adolescents

### Challenges faced by children taking anti-TB medication

C Goslett,<sup>1</sup> <sup>1</sup>Desmond Tutu TB Centre, Stellenbosch University, Cape Town, South Africa.  
e-mail: cgoslett@sun.ac.za

I was 11 years old when I contracted MDR-TB from a family member. I needed to take 17 tablets and a painful injection every day. The tablets were not child-friendly, some were very big to swallow, some had a very bad taste and some caused nausea and discomfort with itchy skin and discolouration of my complexion, resulting in stigma and name-calling.

Today I still have vivid flashbacks about that period and I struggle to take any form of medication. I advocate for child-friendly formulations of TB medicines to be available for all children with TB.

### WHO dosing guidance for children and adolescents with MDR/RR-TB

T Masini,<sup>1</sup> <sup>1</sup>World Health Organization Global Tuberculosis Programme, Lucca, Italy.  
e-mail: tmasini@who.int

Revised WHO TB dosing guidance for children and adolescents with MDR/RR-TB includes dosing for bedaquiline and delamanid in children of all ages, in line with latest WHO recommendations. The guidance includes

dosing for all second-line TB drugs for infants weighing 3 to <5 kg with both child-friendly and adult formulations. Information notes to provide practical guidance on administration of bedaquiline and delamanid in children were developed.

A dosing application is available on the WHO Knowledge Sharing Platform to facilitate implementation. As part of the Paediatric Anti-TB Drug Optimization exercise, WHO will review appropriateness of TB formulations.

### Availability and uptake of child-friendly formulations of second-line TB drugs: Lessons learnt and future opportunities

B Kaiser,<sup>1</sup> <sup>1</sup>Stop TB Partnership Global Drug Facility, Geneva, Switzerland.  
e-mail: brian@stoptb.org

The Global Drug Facility's approach to TB commodities ensures end-to-end product life-cycle management. GDF uses multiple mechanisms, including partner coordination and alignment, prioritization, de-risking activities and supply chain technical assistance, to bring new products to the TB market and to support early adoption and scale-up. This approach has brought 11 child-friendly formulations to market to treat drug-resistant TB in children.

This session will review the approach used to support these formulations, detail practical information for programmes on availability and price of the formulations and regimens, and describe lessons learned that could be applicable to future formulations and regimens.

### Programmatic experience of treating children with adult and child-friendly TB medicines

V Rouzier,<sup>1</sup> <sup>1</sup>Weill Cornell Medical College, New York and Centres GHESKIO, Haiti, Haiti.  
e-mail: vrouzier@gheskio.org

Pediatric MDRTB treatment can be extremely challenging because of lack of health infrastructure support, trained clinical staff, social support and availability of parents and caregivers. Accessing child-friendly TB medicines has been limited or slow and managing pediatric patients with adult formulation difficult.

We will present challenges and successes of the pediatric MDRTB program in Haiti using adult and child-friendly medicines.

### **Additional research in improving TB drug administration in children**

A Garcia-Prats,<sup>1</sup> <sup>1</sup>University of Wisconsin, Madison, United States.  
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The availability of dispersible tablet formulations of second-line TB drugs is a welcome advance; however, important knowledge gaps remain. Substantial formulation effects on drugs' pharmacokinetics have been observed, especially comparing dispersible tablets to manipulated adult formulations. Taste masking may be suboptimal and improvements in palatability may still be needed. Some children still do not have access to child-friendly formulations.

In these settings, evidence is needed to inform use of adult formulations through manipulation by crushing or dispersing adult tablets, including the use of extemporaneous formulations.

This presentation will discuss ongoing research to improve administration of TB drugs for children.

### **SP04 Higher ambitions for a gender-transformative response to TB for improving health, social and economic outcomes**

#### **Transitioning to a gender-transformative response to TB**

H Lim,<sup>1</sup> <sup>1</sup>The Global Fund for AIDS Tuberculosis and Malaria, Geneva, Switzerland.  
e-mail: Hyeyoung.Lim@theglobalfund.org

The Global Fund supports programs and approaches to promote health equity, gender equality and human rights as explicitly noted in its Strategic Framework 2023-2028. These programs include community dialogues on gender-norm change, 'know-your rights' programs with TB communities, and TB Champion programs.

In India, the Global Fund supports transgender women to become TB Champions - not only raising awareness on TB within their communities but also acting change agents.

The presentation will discuss the Global Fund's commitment to advancing gender equality and human rights and share exciting case studies of gender transformative approaches and programs in TB.

### **Evidence-informed decision-making to achieve Nigeria's commitments to end TB**

O Chijioke-Akaniro,<sup>1</sup> <sup>1</sup>National tuberculosis Programme, Nigeria, Abuja, Nigeria.  
e-mail: oakaniro@gmail.com

The use of evidence in decision-making in health is key for informed development efforts. There are a wide range of actors and factors that influence public policy decisions and facilitators and barriers to evidence use in these decisions. Evidence informed decision-making remains sub-optimal due to bottlenecks that operate at individual, system, and institutional levels.

Here we highlight the importance of strengthening relationships between decision-makers and producers of evidence to co-create research questions, package and deliver timely and relevant evidence and ensure use among decision-makers through a case study on gender-equitable access to TB care and prevention.

### **Relationship between perceptions of gender-equitable norms and TB care-seeking in Malawi**

E Di Giacomo,<sup>1</sup> <sup>1</sup>London School of Hygiene and Tropical Medicine / The Hospital for Sick Children, Toronto, Canada.  
e-mail: digiacomo.elizabeth@gmail.com

This presentation shares results from a secondary data analysis investigating the relationship between perceived gender equitable norms and self-reported tuberculosis testing behaviours. Data were collected as part of the Sustainable Community Action for Lung hEalth (SCALE) Trial in Blantyre, Malawi, and have been analysed using a multivariable binomial regression model with a factor analysis and random effects.

Better understanding of perceptions around gender equitable norms and their relationship to tuberculosis testing may be used to support the design of gender-transformative strategies to improve testing uptake and end TB.

### **Changing gender norms to involve both women and men in TB care for male patients**

J Daniels,<sup>1</sup> <sup>1</sup>Arizona State University, Phoenix, United States.  
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Identifying men's and women's roles in caregiving for men with tuberculosis provides insights to develop strategies to reduce associated burden and improve treatment outcomes.

Through our qualitative study with caregivers, we found that women provided meals, health monitoring, emotional support, clinic appointment reminders, and treatment encouragement, while men provided appointment

reminders and treatment encouragement. Both men and women discussed challenges in caregiving for combative family members during their illness and treatment, but women described this most often.

Coordinated caregiving between men and women may be an opportunity to shift norms by redistributing responsibilities, which may in turn improve treatment outcomes.

### **Creating a gender-transformative agenda to address contextualised TB risk and care access for men**

J Chikovore,<sup>1</sup> <sup>1</sup>Human Sciences Research Council, Durban, South Africa.  
e-mail: jchikovore@hsrc.ac.za

Tuberculosis affects economically fragile people and settings, and men generally fare worse than women in key indicators. Current conversations place emphasis nearly exclusively on low- and middle-income countries, emphasising so-called key populations within those settings.

While crucial, this can miss vulnerable communities and groups in other settings, including within higher-income countries. A gender-transformative approach needs to unravel contextualised vulnerabilities across the world, and simultaneously pay attention to diverse socioeconomic variables, rather than treat categories as uniform. This will help avoid having hidden populations affected by tuberculosis that grapple silently with stigma, disease, and worsening precarity.

### **SP05 Yes, we can end TB, but not without social protection. Here's the evidence: what are we waiting for? (Coordinated by Dr Tom Wingfield, LSTM)**

#### **Community randomised evaluation of socioeconomic intervention to prevent TB (CRESIPT)**

C Evans,<sup>1</sup> <sup>1</sup>IFHAD: Innovation for Health And Development, Lima, Peru.  
e-mail: carlton.evans@ifhad.org

The Community randomised evaluation of socioeconomic intervention to prevent TB (CRESIPT) controlled trial has evaluated an integrated socio-economic support package offered to all households in which someone was diagnosed with TB disease in 32 communities in northern Lima, Peru. Impacts will be presented for the primary outcomes improving patient cure and preventing subsequent TB in these household members and also for secondary outcomes including preventing catastrophic costs due to TB.

### **Addressing the social determinants and consequences of TB in Nepal: the ASCOT implementation trial**

B Rai,<sup>1</sup> <sup>1</sup>Birat Nepal Medical Trust, Kathmandu, Nepal.  
e-mail: bholarai19@gmail.com

Since 2018, we have worked to generate evidence on the suitability of socioeconomic support for TB-affected households in Nepal, a low-income high TB burden country.

First, we identified barriers to accessing TB services in Nepal including TB knowledge, stigma, and high travel costs to receive care.

Second, we collaborated with key stakeholders including people with TB, WHO, and the National TB Control Center (NTCC) on the "ASCOT" implementation trial to co-design, implement, and refine a socioeconomic support package (cash transfers, peer support) for 128 TB-affected households in Nepal. The package was feasible, acceptable, and is ready for large-scale effectiveness evaluation.

### **Differentiated social protection measures for people with TB in Viet Nam**

R Forse,<sup>1</sup> <sup>1</sup>Friends for International TB Relief (FIT), Ho Chi Minh City, Vietnam.  
e-mail: rachel.forse@tbhelp.org

In Viet Nam, approximately 63% of households with TB suffer from catastrophic costs. Social protection mechanisms are needed to support vulnerable households. However, it has been found that providing financial support to economically vulnerable households is more acceptable than to all people with TB.

A predictive model for catastrophic cost incurrence was developed into a risk assessment tool, allowing for the identification and stratification of socioeconomic risk at TB treatment initiation. Over 4,500 individuals were screened with this tool and over 800 received differentiated social protection packages. Results of this programmatic implementation and its effectiveness will be presented.

### **Improving the quality of TB diagnostic evaluation in Uganda using cash transfers: the ExaCT TB Study**

P Shete,<sup>1</sup> <sup>1</sup>University of California San Francisco, San Francisco, United States.  
e-mail: priya.shete@ucsf.edu

Mitigating financial barriers to tuberculosis (TB) diagnosis and treatment is a core priority of the global TB agenda. We evaluated the impact of a cash transfer (CT) intervention on completion of TB testing and treatment initiation in Uganda. We conducted a pragmatic stepped-wedge randomized trial of a one-time uncon-

ditional CT intervention at ten health centers (HC) between September 2019-March 2020. More people were referred for TB testing (aRR=2.60, 95% CI: 1.86-3.62) and completed TB testing (aRR=3.22, 95% CI: 1.37-7.60) per National TB Guidelines.

This study adds new evidence on effects of social protection on TB-related outcomes.

### **Guidance on social protection for people affected by TB: 'know how' for TB programmes**

E Jaramillo,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: jaramilloe@who.int

Less than half of high TB burden counties currently include social protection in their response to TB. Increasing awareness and understanding about the value of mainstreaming social protection into the fight against TB will help to meet the critical gaps on how to best plan and implement effective social protection programmes for people affected by TB.

This talk will explain how the WHO guidance on social protection for people affected by TB aims to address these gaps and support TB programmes to test the extent to which social protection interventions remain feasible and effective under programmatic conditions.

### **SP06 Progress and innovation in developing shorter treatment regimens for people with TB**

#### **TRUNCATE-TB: 8-week regimens in the context of a strategy trial**

N Paton,<sup>1</sup> <sup>1</sup>National University of Singapore, Singapore, Singapore.  
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The TRUNCATE-TB trial aimed to evaluate the efficacy of a novel treatment strategy for drug-susceptible TB comprising initial treatment with one of four 8-week boosted treatment regimens, followed by monitoring and re-treatment for the minority that relapse.

The presentation will talk about the approach taken in the TRUNCATE-TB trial to evaluate these regimens and the resulting evidence supporting the potential for marked reduction of time on treatment in the context of the TRUNCATE strategy.

### **Integrated data: Uncovering the potential for treatment shortening**

R Savic,<sup>1</sup> <sup>1</sup>University of California, San Francisco, San Francisco, United States.  
e-mail: rada.savic@ucsf.edu

Many of the new regimens being studied in clinical trials have also been evaluated in mouse studies to assess their treatment shortening potential. Furthermore, we now have increasing data from late phase clinical trials both for shorter regimens that have and have not been shown to be equivalent to the standard of care.

In this presentation, Prof. Savic will talk about integrated analyses addressing the data evidence to support the potential for treatment shortening.

### **The stratified medicine approach to treatment shortening: Case studies in SPECTRA-TB and PRISM**

P Phillips,<sup>1</sup> <sup>1</sup>University of California, San Francisco, San Francisco, United States.  
e-mail: patrick.phillips@ucsf.edu

The "one-size fits all" model of care is a disservice to persons with TB as it results in the undertreatment of those with severe disease and the overtreatment of the majority with less extensive disease. A stratified medicine approach, where persons with TB are assigned to a treatment duration commensurate with their disease severity, may be one avenue to treatment shortening for the majority.

In this presentation, Dr. Phillips will discuss the opportunity for treatment shortening with stratified medicine trials drawing from work informing two planned trials SPECTRA-TB and PRISM for treatments for drug-sensitive and drug-resistant TB respectively.

### **Duration-ranging in Phase 2 trials: UNITE4TB and the MAMS-ROCI Design**

A Crook,<sup>1</sup> <sup>1</sup>University College London, London, United Kingdom.  
e-mail: angela.crook@ucl.ac.uk

The goal of the UNITE4TB consortium is to deliver novel Phase 2 clinical trials that accelerate the development of better-tolerated drug regimens of shorter duration. Applying the novel MAMS-ROCI framework in a Phase 2C setting, UNITE4TB aims to take a unique approach to identifying and advancing an optimal duration for the novel regimens considered for further evaluation in Phase 3.

### **Left in the dust: How we can leverage cutting-edge dose-ranging research to improve duration-ranging studies**

S Dufault,<sup>1</sup> <sup>1</sup>University of California, San Francisco, San Francisco, United States.  
e-mail: suzanne.dufault@ucsf.edu

Many of the challenges in duration-ranging have parallels and proposed solutions in the field of dose-ranging where the literature is substantially more established and where the traditions of qualitative, pairwise comparison studies have been replaced with model-based approaches. Such methods are more efficient and allow for extrapolation beyond the doses observed. Research on efficient study designs and methods for duration-ranging, while similarly attempting to capture a monotonic response relationship, has only just accelerated in earnest over the last two decades.

This work examines the utility of cutting-edge dose-finding methods (such as MCP-Mod) for the purposes of duration-ranging of TB treatments.

### **SP07 Improving treatment for persons with tuberculosis and substance use**

#### **Substance use disorders in people with TB in the Western Cape, South Africa: Influence on outcomes and suggestions for identification, intervention and linkage to care**

T Carney,<sup>1</sup> <sup>1</sup>South African Medical Research Council, South Africa.  
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Alcohol use is prevalent among people with TB in South Africa, but less is known about the use of other drugs. People who use substances are increasingly important to reach in this setting, as they are often excluded from healthcare and face a number of additional health concerns, including high HIV rates.

In this presentation, we highlight the prevalence of substance use disorders in our observational studies and explore recommendations for the uniform identification of substance use, interventions for addressing the dual burden of TB and substance use, and suggestions for linkage to care.

### **The impact of substance use on unsuccessful TB treatment outcomes in Brazil: results from a national multicentre cohort study**

F Ridolfi,<sup>1</sup> <sup>1</sup>Clinical Research Laboratory on Mycobacteria, Evandro Chagas National Institute of Infectious Disease, Fiocruz, Rio de Janeiro, Brazil.  
e-mail: felipe.ridolfi@ini.fiocruz.br

In this presentation we will discuss the impact of substance use on unsuccessful TB treatment outcomes in Brazil.

Our study was conducted using data from a multicenter cohort study of pulmonary TB participants that is representative of the Brazilian population: the Regional Prospective Observational Research in TB (RePORT)-Brazil. The group used the updated World Health Organization definitions for TB treatment outcomes, and found that substance use (alcohol, tobacco and other drugs) were associated with loss-to-follow-up.

### **Intervention models for people with tuberculosis who inject drugs in Vietnam**

N Nagot,<sup>1</sup> <sup>1</sup>University of Montpellier, Montpellier, France.  
e-mail: n-nagot@chu-montpellier.fr

People who inject drugs (PWID) represent a high-risk group for TB in Vietnam. In this presentation, we summarize our research with PWID and present a model for intervention. TB prevalence has been found to be estimated at 2.1% of participants living without HIV and 2.3% among 855 participants living with HIV screened for TB in Hai Phong.

These findings prompted a multifaceted interventional project aiming at managing TB among PWID at the citywide level, which is scheduled to begin in late 2023. We will build on community-based strategies that have proved highly efficacious for the management of other epidemics.

### **Hybrid trial for alcohol reduction among people with TB and HIV/TB in India (HATHI): Intervention adaptation and implementation**

G Chander,<sup>1</sup> <sup>1</sup>University of Washington School of Medicine, Seattle, United States.  
e-mail: gchander@medicine.washington.edu

Unhealthy alcohol use is prevalent among people with TB in India. Biological and behavioral effects of alcohol use combined with structural and social drivers of health increase vulnerability to TB.

Further, alcohol consumption in this population results in poorer treatment outcomes, including increased loss to follow up and mortality. Given these poorer treatment outcomes, strategies addressing alcohol use in TB clinical settings are essential.

In this presentation, we describe the adaption and implementation of a four-session evidence-based behavioral alcohol reduction intervention (HATHI) into TB clinical settings in Pune, India.

## **SP08 Promoting equity in the fight against TB: transforming words into action**

### **Persistent TB practices : dismantling the DOT dogma**

B Citro,<sup>1</sup> <sup>1</sup>Independent Researcher, Chicago, United States.  
e-mail: brcitro@gmail.com

The essence of directly observed therapy, “watching patients take their medicines”, remains the dominant TB treatment strategy. DOT is a WHO recommendation even for new, shorter TB regimens.

Although DOT is less strictly practiced than when first implemented, a growing consensus recognizes that its harms outweigh its benefits. Digital DOT, while sold as people-centered, reproduces DOT’s paternalistic paradigm and poses new risks.

This talk will explore DOT’s history, evidence, and criticisms and apply a human rights lens to chart a more equitable way forward. (It will be delivered jointly by Brian Citro and TB survivor, Rhea Lobo.)

### **Persistent TB practices : dismantling the DOT dogma**

R Lobo,<sup>1</sup> <sup>1</sup>Community Delegation - Stop TB Partnership, Copenhagen, Denmark.  
e-mail: rhea.lobo@theunion.org

DOTS continues to be a widely acceptable practice, while it is a severe human rights violation in every way.

### **From the discomfort of clinics to the comfort of community : people and family centred TB care**

Y Lin,<sup>1</sup> <sup>1</sup>Burnet Institute, Balaclava, Australia.  
e-mail: Dani.lin@burnet.edu.au

This talk discusses how community based care, family supported treatment, health literacy models involving peer counselors and empowerment of TB survivors are helping to address deep seated inequities among people affected by TB in Papua New Guinea. Drawing on examples of recent projects, the effectiveness and feasibility of non conventional approaches to TB treatment including community and family centered care - that support the agenda for equity - are described.

### **(Re)designing interventions and implementation science: research with a commitment to equity**

M Armstrong-Hough,<sup>1</sup> <sup>1</sup>New York University, New York, United States.  
e-mail: mah842@nyu.edu

Equity is often framed as an overarching goal of TB interventions. It is less often appreciated as a goal of the intervention process. Using examples of implementation science studies to improve delivery of contact investigation, evaluation, and treatment initiation for TB in Uganda, this talk will introduce steps that can be taken by research teams to operationalize a commitment to equity within the design and execution of interventions and clinical trials using tools such as participatory design and nominal group technique.

### **Changing the narrative: The role of inclusive and empowering language in infectious disease policy texts**

B Umana,<sup>1</sup> <sup>1</sup>York University, Toronto, Canada.  
e-mail: umanahappy@gmail.com

The words used to describe disease, people at risk of disease, events related to the disease, and methods to manage it can fuel a discourse that is inclusive of people affected by TB, or exclusionary and othering.

This talk will juxtapose the language used in TB, COVID-19 and HIV policy documents to highlight how inclusive and empowering language choices and framings can help to ensure an equity orientation gets embedded into TB guidance documents.

## **SP09 A human rights approach to TB among people deprived of liberty (PDL)**

### **TB in incarcerated populations: Ethical solutions for unique challenges**

M Dara,<sup>1</sup> <sup>1</sup>Otsuka Novel Products Group GmbH, Sweden.  
e-mail: MDara@otsuka-onpg.com

While the issues surrounding TB among PDL have been recognized world-wide by leading organizations such as WHO and the Stop TB Partnership, there are still many challenges in TB management and care for this group.

In this talk, Dr. Masoud Dara from The Queen Mary University of London, will provide an overview of this topic based on his extensive experiences working with and for TB-affected PDL in Eastern Europe and Central Asia. Dr. Dara will focus on how the community is addressing these challenges under an ethical framework.



### **The rights of TB-affected people deprived of liberty (PDL)**

B Citro,<sup>1</sup> <sup>1</sup>Independent Researcher, Chicago, United States.  
e-mail: briticro@gmail.com

Traditional biomedical approaches alone, such as TB testing and treatment, are not enough to address the unique situations, demographics, and problems of PDL affected by TB. Components of the larger constellation of concerns, rights, entitlements for TB affected people deprived of liberty must be considered. Brian Citro has dedicated much of his career to researching and documenting the relationship between health and human rights.

In this session, he will discuss his work on the intersection of TB and human rights, with a focus on legal and ethical issues that TB-affected PDL face.

### **TB among people deprived of liberty in Colombian prisons**

Z Rueda,<sup>1</sup> <sup>1</sup>University of Manitoba, Winnipeg, Canada.  
e-mail: Zulma.Rueda@umanitoba.ca

Many persons deprived of liberty (PDL) struggle to receive tuberculosis prevention and care, especially in prison settings. PDL are at increased risk of both tuberculosis infection and tuberculosis disease when recently incarcerated and during ongoing incarceration. This highlights the need for active case finding to manage disease as well as to break transmission. Dr. Rueda will provide an overview of the incidence and prevalence of tuberculosis among PDL in Colombian prisons as well as her perspectives as a physician and researcher.

Her talk will recommend people-centered programming and evidence-based interventions to mitigate transmission among PDL and to destigmatize PDL.

### **SP10 Providing people-centred TB care for vulnerable populations**

#### **Promoting people-centred tuberculosis care for vulnerable and at-risk populations**

K Viney,<sup>1</sup> <sup>1</sup>World Health Organization, Vetzraz Monthoux, France.  
e-mail: vineyk@who.int

A number of population groups are vulnerable to developing TB, having limited access to health services, having poor outcomes or being stigmatised or facing human rights barriers due to TB.

In this presentation, the WHO Global TB Programme's work on TB and vulnerable populations will be present-

ed and specific interventions and efforts to further promote equitable access to people centred care for those at risk of TB or with TB disease will be discussed. The ethical and human rights imperatives to sensitively address TB related vulnerability as a key part of the TB response will be a focus.

### **The global burden of tuberculosis in incarcerated populations**

L Martinez,<sup>1</sup> <sup>1</sup>Boston University School of Public Health, Boston, United States.  
e-mail: leomarti@bu.edu

Approximately 11 million people are incarcerated globally and considered at high risk of developing tuberculosis; however, the global tuberculosis burden among this population has never been quantified.

In this presentation, we describe our methods and attempts to estimate the annual regional and global incidence of tuberculosis among incarcerated populations from 2000-2019.

### **Substance use and tuberculosis**

A Versfeld,<sup>1</sup> <sup>1</sup>University of Cape Town, Cape Town, South Africa.  
e-mail: annaversfeld@gmail.com

Substance use (drug and alcohol) sets the conditions for increased risk of tuberculosis infection and disease and decreased likelihood of treatment completion. Yet there has been surprisingly little focus in TB programming on recognising this intersection and developing positive, supportive responses for people affected.

This presentation draws on over ten years of social research in South Africa to highlight how this intersection has been overlooked and misrepresented, the consequences of this, and how a better response can be developed.

### **Drug-resistant TB case-finding and TB care among the nomadic San communities in Namibia**

N Ruswa,<sup>1</sup> <sup>1</sup>Ministry of Health and Social Services Namibia, Windhoek, Namibia.  
e-mail: ncruswa@gmail.com

The San people in Namibia have been disproportionately affected by drug-resistant TB. Tsumkwe constituency, homeland to various San communities, reports the highest number of drug-resistant TB in the country.

We present the situation, approaches and unique challenges faced in the control of TB among these communities.

## **SYMPOSIA: THURSDAY 16 NOVEMBER 2023**

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### **SP11 Using community, rights and gender (CRG) as an innovative approach to reach missing patients with TB: Country experiences and the way forward**

#### **Digital CLM: Evolution and Insights from Country Implementation**

S Das,<sup>1</sup> <sup>1</sup>Dure Technologies, Switzerland.  
e-mail: sabyasachi@duretechnologies.com

Join us to explore the evolution of Digital CLM, delve into the CLM Digital Model, and discover the transformative potential of Digital CLM Clinics in revolutionising TB care delivery

#### **CRG implementation in Nigeria: Successes, challenges and lessons learnt**

S John,<sup>1</sup> <sup>1</sup>Janna Health Foundation, Yola, Nigeria.  
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This presentation examines the implementation of community-based and community-led interventions for tuberculosis (TB) control in Nigeria, highlighting the critical role of community engagement, human rights, and gender responsiveness in achieving success. The presentation showcases the positive outcomes achieved through these interventions, including increased access to TB screening and treatment services and reduced stigma associated with TB. Additionally, the presentation shares valuable insights on lessons learned from these interventions, which can be replicated in other countries with similar contexts.

#### **Joining forces to end TB: Harnessing the power of community, rights and gender**

K Eman,<sup>1</sup> <sup>1</sup>Dopasi Foundation, Islamabad, Pakistan.  
e-mail: kinza\_kz@yahoo.com

This presentation focuses on experiences from Pakistan and elaborates on how to systematically identify and overcome barriers to access for CRG by using OneImpact.

The presentation highlights the importance of collaboration with affected communities to overcome barriers to TB care and control. It emphasizes the need for community engagement throughout the entire cascade

of care, ensuring that care and support services are accessible and of high quality for all, particularly Key and Vulnerable Populations. The presentation stresses the importance of empowering TB-affected people and KVPs to participate in leadership and decision-making processes, ensuring that their voices are heard.

#### **A framework for effective CRG implementation - tools, community-led monitoring and size estimations**

C Smyth,<sup>1</sup> <sup>1</sup>Stop TB Partnership, Geneva, Switzerland.  
e-mail: caoimhes@stoptb.org

This presentation focuses on providing a comprehensive framework for effective implementation of Community, Rights, and Gender (CRG) interventions. The presenter will introduce various tools developed by Stop TB Partnership that can be used to support CRG implementation, including community-led monitoring and size estimations.

The presentation will highlight the importance of community engagement throughout the implementation process to ensure access to high-quality TB care and support services for Key and Vulnerable Populations (KVPs). The presenter will also discuss the significance of incorporating human rights and gender-responsive approaches in TB programming.

#### **SP12 Mtb antigen-based skin tests (TBSTs) – new class of tests for the detection of TB infection**

#### **WHO-consolidated guidelines on tuberculosis. Module 3: Diagnosis. Tests for tuberculosis infection**

A Korobitsyn,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
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In 2022 WHO has issued a consolidated guidelines for the diagnosis of TB infection. The guidelines include update of the earlier recommendations, focused on the two classes of tests – interferon-gamma release assays (IGRAs) and the tuberculin skin test (TST).

In addition, the update includes the recommendations on a new class of TB infection tests, the *Mtb* antigen-based skin tests (TBSTs). This class of tests is based on specific *Mtb* antigens and combine the simpler skin-test platform with the specificity of IGRAs.

### Using new approaches to implement the new Mtb antigen-based skin tests – from local to the national level

D Menzies,<sup>1</sup> <sup>1</sup>McGill International TB Centre. Montreal Chest Institute, Montreal, Canada.  
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Successful implementation of the new TB skin tests will require novel approaches at several levels. At the individual level, novel digital tools will help to ensure high quality and facilitate test administration, reading (the mTST), recording and reporting (digital apps) of results. At the health centre, re-organization to provide person-centred care, i.e. coordinating test reading, excluding TB disease, and decision to offer TPT in the same time and place.

Finally, at national level, a new multi-disciplinary evaluation method is used to evaluate the costs, cost-effectiveness, benefits, and harms as the program expands.

### Cost-effectiveness and preparedness for TBST implementation in Brazil and other LMICs

A Trajman,<sup>1</sup> <sup>1</sup>Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil.  
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In order to implement new TB diagnostic technologies, several steps are needed, including planning and budgeting, preparation guidelines, regulatory approval, supply chain, recording and reporting of new tests, among others. An essential step for TBST incorporation and implementation is training and quality control of health care providers for intradermal injection and induration reading.

We will discuss simplified protocols for training for skin testing and how to conduct cost-effectiveness and budget impact analyses for TBST implementation.

### TBST experience in South africa: Scenarios and expected challenges in implementation

S Charalambous,<sup>1</sup> <sup>1</sup>The Aurum Institute, Johannesburg, South Africa.  
e-mail: scharalambous@auruminstitute.org

The new specific skin test opens the possibility of reintroducing TB infection testing in South Africa. We conducted a desktop review and key informant interviews to determine the usability of TB skin tests in South Africa. We will review current guidance, possible use cases and the challenges anticipated in the implementation of TBSTs.

### Experiences from the field with the Cy-TB test in India

S Mannan,<sup>1</sup> <sup>1</sup>Clinton Health Access Initiative, New Delhi, India.  
e-mail: smannan@clintonhealthaccess.org

India has the highest estimated burden of tuberculosis infection (TBI) globally, with nearly 400 million people having TBI, of which 2.6 million are estimated to develop tuberculosis (TB) disease annually. Prevention of TB disease is a critical component of the National Strategic Plan 2017-25 for Ending TB in India by 2025.

This plan proposes a Detect-Treat-Prevent-Build approach and scaling up TPT would be a key to hasten the rate of decline in TB incidence from present 2.5% to 10% required annually. Experiences and learnings from using Cy-TB in one of the districts from December 2022 will be shared.

### SP13 Flipping the script: Community perspectives on TB treatment and vaccines research

#### Is shorter always better? Balancing toxicity and duration considerations in the treatment of drug-susceptible TB

O Rucsineanu,<sup>1</sup> <sup>1</sup>Global TB Community Advisory Board (TB CAB), Moldova National Association of TB Patients "SMIT", Balti, Moldova.  
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Treatment shortening is a driving force behind many ongoing and planned clinical trials. Although duration is one challenging component of TB therapy, pill burden, side effects, and management of co-morbid conditions are also important considerations. When thinking about priorities for optimizing TB regimens, these considerations may be weighed differently by affected communities than they are by clinicians, programs, researchers, and funders.

This perspective will discuss how members of affected communities and people with lived experience with TB treatment weigh these considerations, and whether the risks of certain drug-related toxicities are worth the potential treatment shortening benefits, and under what conditions.

## Meeting the needs of people with XDR-TB through research and pre-approval access to new drugs

J Stillo,<sup>1</sup> <sup>1</sup>Wayne State University, Global TB Community Advisory Board (TB CAB), Detroit, United States.  
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Three new drugs for TB were introduced in the last decade. Even before approval, these drugs and early access offered hope to people with drug-resistant TB with few treatment options.

As the next generation of new TB drugs make their way through the pipeline, and as resistance to bedaquiline emerges, it's essential that people with XDR-TB have early access to new drugs.

This perspective will describe existing XDR-TB treatment regimens, new TB drugs in development, lessons from pre-approval access programs established for bedaquiline, delamanid, and pretomanid, and make the case for how to meet the needs of people with XDR-TB.

## One size does not fit all: Choices for TB prevention and treatment

A Makone,<sup>1</sup> <sup>1</sup>Global TB Community Advisory Board (TB CAB), Harare, Zimbabwe.  
e-mail: albertmako@gmail.com

There have been several successful trials recently for the treatment and prevention of TB, but these studies have largely compared newer regimens with now older standards of care. This means there are multiple new options for treating and preventing TB included in WHO guidelines and national programs, but limited understanding of how these new regimens compare. Also missing is the preferences of communities affected by TB regarding different treatment options.

This perspective will describe the "choices" that exist for TB prevention and treatment and how differentiated models of care could replace outdated approaches to offering the same regimens to all.

## Addressing TB preventive treatment and prior history of TB in vaccines studies

P Agbassi,<sup>1</sup> <sup>1</sup>Global TB CAB, Abidjan, Cote D'Ivoire.  
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Multiple TB vaccines are entering phase III trials. Collectively, these trials will enroll 75,000 people from a dozen countries, including diverse populations such as people living with HIV. However, key groups are missing, including people with prior history of TB.

This perspective will explore the merits of justifications provided for exclusion of this population despite their increased risk of recurrent TB. It will also explore community perspectives on the incorporation of proven effective preventive interventions such as TPT in light

of trial design considerations and the ethical duty to provide study participants with access to the available "standard of care/prevention."

## The earlier inclusion of pregnant persons in TB treatment and vaccines research

A Herna Sari,<sup>1</sup> <sup>1</sup>Global TB Community Advisory Board (TB CAB), Surabaya, Indonesia.  
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Pregnant people are excluded from most TB research. Because there are no well-controlled studies to inform the dose and safety of new treatment regimens in pregnant persons, they receive more toxic and less effective regimens. Pregnant persons are excluded entirely from the TB vaccines research agenda, which will delay access for a population already at greater risk for TB.

This perspective will share outcomes of a workshop convened by the USAID-supported SMART4TB Consortium regarding the inclusion of pregnant people in TB research, including key takeaways, differences in perspectives between scientific and community experts, and the final community consensus statement.

## SP14 Promoting lung health in resource-limited settings: Donald A Enarson Memorial Symposium

### Access to essential asthma medicines: Asthma Drug Facility and beyond

K Bissell,<sup>1</sup> <sup>1</sup>School of Population Health, University of Auckland, Auckland, New Zealand.  
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To address the challenges of accessibility and affordability of essential asthma medicines, The Union established an Asthma Drug Facility (ADF), based on the experience of the Global Drug Facility (GDF) for tuberculosis. In Benin and El Salvador, ADF was able to halve the cost of treatment for severe asthma using quality-assured inhalers.

The most recent global survey assessing national capacity for the prevention and control of noncommunicable diseases reported that inhaled corticosteroid was available in only 19% of low-income countries and 33% of lower middle-income countries. It is time to revitalise efforts to improve access to essential asthma medicines.

### **Smoking cessation in TB patients and smoke-free environment: scaling up The Union's pilot project**

T Bam,<sup>1</sup> <sup>1</sup>International Union Against Tuberculosis and Lung Disease, Singapore, Singapore.  
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Smoking is associated with an increased risk of active tuberculosis (TB). Passive exposure to tobacco smoke has been reported to be associated with both active TB and latent TB infection. Smoking is significantly associated with positive smear and cavitory pulmonary TB thus may promote transmission of TB.

Studies have reported that smoking is associated with delayed sputum conversion, unfavorable treatment outcomes of TB, and increased risk of recurrent TB. Smoking cessation intervention in TB treatment has been implemented in several settings and was found to be feasible, resulting in abstinence in a substantial proportion of smokers.

### **Severe pneumonia in children: Improving care in resource-limited settings**

S Graham,<sup>1</sup> <sup>1</sup>University of Melbourne and Burnet Institute, Melbourne, Australia.  
e-mail: Steve.Graham@rch.org.au

Pneumonia is still a major cause of mortality and of hospitalisation in children globally. The Union's Malawi Child Lung Health Project adapted the model of care of tuberculosis to improve the management of severe and very severe pneumonia in children admitted to secondary care level (district) hospitals in Malawi. Implementation in all 25 district hospitals was associated with excellent adherence to WHO case-management guidelines and a marked reduction in inpatient case-fatality rate. This presentation will provide an update on more recent progress and current issues to further reduce the morbidity and mortality caused by severe pneumonia in children.

### **Comprehensive lung health project in Sudan: lessons learnt on asthma management and the way forward**

A ElSony,<sup>1</sup> <sup>1</sup>International Union Against Tuberculosis and Lung Disease, Khartoum, Sudan.  
e-mail: asmaelsony@gmail.com

A comprehensive lung health project funded by the World Bank and implemented by the International Union Against Tuberculosis and Lung Disease (The Union) and partners, aimed to reduce the burden of lung disease by improving comprehensive case management of priority cases. Standard case management of asthma, together with smoking cessation among tuberculosis (TB) patients and standard case management

of pneumonia in children, was implemented in Benin, China, and Sudan. Experiences and lessons learned in the implementation of the comprehensive lung health project may be helpful for addressing the challenges in improving lung health in resource limited settings.

### **SP15 Optimising the TRUNCATE Strategy for improved outcomes in the two-month treatment regimen for rifampicin-susceptible tuberculosis**

#### **Summary of the main TRUNCATE-TB trial results and outstanding questions**

E Burhan,<sup>1</sup> <sup>1</sup>Faculty of Medicine, Universitas Indonesia and Persahabatan General Hospital, Jakarta, East Jakarta, Indonesia.  
e-mail: erlina\_burhan@yahoo.com

This presentation will describe the rationale and main findings from this treatment strategy trial and describing the areas in which the strategy might be modified to improve outcomes

#### **TRUNCATE-TB: Optimising outcomes - drug exposure (PK/PD) considerations**

C Cousins,<sup>1</sup> <sup>1</sup>National University of Singapore, Singapore, Singapore.  
e-mail: christopher.cousins@ucl.ac.uk

This presentation will describe the relationship between exposures of key drugs in the novel regimens and measures of bacterial killing in order to determine the optimal doses of drugs used in the initial 8-week treatment period.

#### **TRUNCATE-TB: Optimising outcomes – biomarker considerations**

N Paton,<sup>1</sup> <sup>1</sup>National University of Singapore, Singapore, Singapore.  
e-mail: nick\_paton@nus.edu.sg

This presentation will describe analyses of standard clinical biomarker measurements (such as chest radiograph and sputum smear) as well as specific research biomarker measurements and their potential to discriminate between participants who can stop treatment at 8 weeks with a low risk of relapse; and participants who require an extension of initial treatment.

### **TRUNCATE-TB: Optimising outcomes – health economics**

E Schaffer,<sup>1</sup> <sup>1</sup>National University of Singapore, Singapore, Singapore.  
e-mail: elisabeth.schaffer@nus.edu.sg

This presentation will examine how the implementation parameters of the TRUNCATE strategy affect the overall costs and cost-effectiveness of the strategy; and will determine which of the potential variations of the approach might represent the best balance, from a health system perspective, for wider implementation of this approach in TB programme settings.

### **Operational research studies to explore effectiveness of the TRUNCATE Strategy in treatment programmes**

C Sekaggya-Wiltshire,<sup>1</sup> <sup>1</sup>Infectious Diseases Institute, Kampala, Uganda, Kampala, Uganda.  
e-mail: csekaggya@idi.co.ug

This presentation will describe planned and ongoing operational research studies that are exploring the effectiveness of the TRUNCATE strategy in TB treatment programme settings.

### **SP16 Advancing multisectoral action and accountability to end TB: Leadership and opportunities**

#### **The WHO Multisectoral Accountability Framework (MAF-TB): current progress in adaptation and implementation at global, regional and country levels**

L Oganezova,<sup>1</sup> <sup>1</sup>World Health Organization, Moscow, Russian Federation.  
e-mail: oganezoval@who.int

Since 2019, countries have been supported in systematically adapting and implementing the WHO MAF-TB by the WHO and partners.

The presentation describes key activities recently undertaken to support countries in MAF-TB operationalization, including development of documents, strengthening the engagement of the private sector, advocating for scaling up the MAF-TB through different events and forums, facilitating information-sharing among Member States through the MAF-TB virtual network. Liana will also provide statistics on MAF-TB core indicators collected by WHO from countries for the last 3 years.

### **Multi-sectoral agenda for TB response: the Brazilian experience**

T Arakawa,<sup>1</sup> <sup>1</sup>Ministry of Health, Brazil, Brasília, Brazil.  
e-mail: tiemi.a@gmail.com

Brazil presents measurable results of multisectoral actions being a part of the Brazilian Plan to End TB. In early 2023, the Brazilian government launched an Inter-ministerial Committee for elimination of TB and other diseases with social determinants.

The Ministry of Health committed to end TB by 2030. This became possible with continued awareness-raising among partners about TB. Brazil shares valuable experience of cooperation agreements as an effective tool to involve other ministries in TB response. Guide to promote social protection for people affected by TB was one of the major outcomes of the agreement with the Ministry of Social Development.

### **Multi-sectoral collaboration to promote the End TB Action Plan in China**

C Zhong Dan,<sup>1</sup> <sup>1</sup>World Health Organisation China, China.  
e-mail: chenzho@who.int

China recognizes the importance of taking a multisectoral approach to translate commitments into action. Dr Chen will share country's experience on how to establish an effective multidepartmental collaborative working mechanism to coordinate the prevention and control of major diseases under high-level leadership, how to create the multisectoral system with participation from multiple ministries and agencies (including Ministries of Education, Science and Technology, Finance, Civil Affairs, the State Council Leading Group Office of Poverty Alleviation and Development among others) who carry out their work according to assigned responsibilities, as well as how to monitor and review the work in progress.

### **India's experience in developing a national multisectoral action framework for TB**

R Joshi,<sup>1</sup> <sup>1</sup>Ministry of Health and Family Welfare of India, Delhi, India.  
e-mail: ywang@who.int

India shares the experience of development of a national multisectoral action framework for TB. This strategic document makes a strong case for transforming India's TB elimination efforts from a health sector struggle to a whole-of-society responsibility. The framework is a guide for policy-makers and a call to action for communities, civil society, the private sector, and other partners and stakeholders. It highlights the six key strategic areas for integrated action and defines the list of government ministries and other stakeholders, and the strategic scope of collaboration with each of them.

### **Meaningful engagement of civil society and TB-affected communities in undertaking a MAF-TB baseline assessment in Francophone Africa**

B Kampoer,<sup>1</sup> <sup>1</sup>DRAF TB, Yaounde, Cameroon.  
e-mail: kampoer@gmail.com

The Dynamics of the Response of Francophone Africa on TB (DRAF TB), a Regional civil society Network that is focused on empowering communities and TB survivors to participate in the TB response, enabled TB-affected communities to measure progress made in the implementation of the UNHLM on TB using the MAF-TB Checklist and conducted a baseline analysis of the implementation of the MAF-TB in each of the 12 Francophone West and Central Africa countries. Bertrand will share main findings and challenges of the exercise performed.

### **SP17 Access to TB care and prevention: Leveraging the 5S to overcome structural barriers and provide solutions**

#### **Staff: Investing in staff to stabilise systems**

M Luma,<sup>1</sup> <sup>1</sup>Partners In Health, Liberia, Monrovia, Liberia.  
e-mail: mluma@pih.org

Staffing is key to effectively delivering integrated, community- and facility-based TB prevention and care. This presentation will explore how public sector accompaniment and system strengthening contribute toward TB elimination.

It will advocate for investments in health workforce (“staff”) that build the next generation of social medicine practitioners, while championing fair pay and safe working environments, ensuring coverage in rural and urban communities, and promoting professional development and retention at all levels.

It will argue that investing in staff is how to transition from system strengthening to stabilization.

#### **Stuff: Securing access to essential medicines and diagnostics to achieve 1/4/6x24**

D Branigan,<sup>1</sup> <sup>1</sup>Treatment Action Group, New York, United States.  
e-mail: david.branigan@treatmentactiongroup.org

Access to medications for TB prevention and treatment, diagnostic tests and corresponding consumables, imaging technologies, and other equipment are essential for delivering effective TB care. This talk will highlight the 1/4/6x24 campaign to scale up access to shorter, safer regimens for TB prevention and treatment, along with

the diagnostics required to close diagnostic gaps for TB and drug-resistant TB, to identify strategies and pathways to provide better access for all.

### **Space: Delivering dignified person-centred TB care at all levels of the health system**

R Matji,<sup>1</sup> <sup>1</sup>AQUITY Innovations, Pretoria, South Africa.  
e-mail: refiloem@aquity.org

Appropriate, dignified care facilities for patients within a clinic, hospital, or community care setting are necessary for delivering person-centered TB care.

This talk will address learnings from the COVID-19 pandemic and how to improve access to TB care in health facilities at all levels of the health system, with a focus on improving decentralized community-based care for TB and DR-TB.

### **Support: Expanding support for people with TB to improve the quality of TB care**

N Venkatesan,<sup>1</sup> <sup>1</sup>Independent, Mumbai, India.  
e-mail: nandita.venky@gmail.com

Quality person-centered TB care involves more than just access to diagnosis and treatment. It also includes support or accompaniments for people with TB to get better, such as food, housing, counseling, and other psychosocial services.

This talk will discuss what country programs can and should be doing to better support people with TB to fully recover from the disease and to not only survive but to thrive physically, economically, and psychosocially.

## **SP18 Urgent need for coordinated action to accelerate TB vaccine access**

### **WHO-led initiatives to prepare for new TB vaccines**

**B Giersing**,<sup>1</sup> <sup>1</sup>Department of Immunization, Vaccines & Biologicals, WHO, Geneva, Switzerland.  
e-mail: giersingb@who.int

The speaker will provide a review of recent WHO-led initiatives to prepare for the introduction of new TB vaccines, including the Evidence Considerations for Vaccine Policy initiative, which outlines the evidence that will be required for WHO to adopt ECVP a new TB vaccine into policy; and, the Global Framework to prepare for country introduction of New TB Vaccines for adults and adolescents, which provides a framework for how countries can prepare for introduction of a TB vaccine for use in adults and adolescents at the national level, once a licensed vaccine is available in country.

### **Understanding the TB vaccine market: Demand considerations and implications for supply planning**

**G Gomez**,<sup>1</sup> <sup>1</sup>IAVI, Amsterdam, Netherlands.  
e-mail: ggomez@iavi.org

A clear understanding of the demand for new TB vaccines is a key priority for commercial manufacturer engagement in TB vaccine development and to support accurate planning for manufacturing scale up.

Understanding the TB vaccine market is also an important input in defining global access and volume-based pricing strategies and informing financing decisions to sustain potentially fragile TB vaccine markets.

This presentation will evaluate the TB vaccine market in both high and low burden countries, outlining demand considerations and implications for supply planning.

### **State of TB vaccine readiness: a gap assessment**

**P Pelzer**,<sup>1</sup> <sup>1</sup>KNCV, The Hague, Netherlands.  
e-mail: puck.pelzer@kncvtbc.org

In order to guide global TB vaccine policy and practice effectively, it is crucial to assess TB vaccine readiness and implementation research and provide concise summaries of key findings while identifying priority areas for future TB vaccine research.

The speaker will present a summary of a recent survey and literature review, evaluating the current state of research on implementing new TB vaccines in low- and middle-income countries (LMICs).

The presentation aims to identify knowledge gaps, and provide insights on TB vaccine implementation research, covering aspects such as feasibility, impact, acceptability, and cost-effectiveness. This research is part of the SMART4TB consortium.

## **SP19 The 2nd International Post-Tuberculosis Symposium: results and recommendations**

### **Patient perspectives, advocacy and stakeholder engagement**

**I Schoeman**,<sup>1</sup> <sup>1</sup>TB Proof, Pretoria, South Africa.  
e-mail: ingrid.tbproof@gmail.com

In this talk I will discuss the current perspectives of TB survivors and stakeholders around the topic of post-TB sequelae. I will provide recommendations for future stakeholder engagement in research, clinical care, and policymaking.

### **Post-TB sequelae: pulmonary, neurological, skeletal and cardiovascular complications**

**J Meghji**,<sup>1</sup> <sup>1</sup>Imperial College London, London, United Kingdom.  
e-mail: J.meghji@imperial.ac.uk

We will discuss the current evidence, knowledge gaps and recommendations from the plenaries and workshops examining post-TB clinical outcomes. Topics include post-TB lung disease, neuromuscular and skeletal, and cardio and pulmonary vascular disease.

### **Post TB pathogenesis, epidemiology, prevention and treatment**

**A Byrne**,<sup>1</sup> <sup>1</sup>University of New South Wales, Sydney, Australia.  
e-mail: Anthony.Byrne@svha.org.au

I will summarise the current evidence, knowledge gaps, and recommendations from plenaries and workshops from the 2nd International post TB symposium held in Stellenbosch South Africa in April this year. This relates to the pathogenesis, epidemiology, prevention & treatment of Post TB lung disease.



## Post-TB sequelae in paediatric populations and economic impacts

M Van der Zalm,<sup>1</sup> <sup>1</sup>Stellenbosch University, Cape Town, South Africa.  
e-mail: mariekevdzalm@sun.ac.za

I will be summarize the current evidence, knowledge gaps, and recommendations from plenaries and workshops on Paediatric post-TB disease. I will also review the evidence, knowledge gaps and recommendations for understanding the economic impacts of post-TB disease.

## Post-TB lung disease: modelling and next steps

B Allwood,<sup>1</sup> <sup>1</sup>Stellenbosch University, Cape Town, South Africa.  
e-mail: brianallwood@sun.ac.za

In this talk I will summarize the current evidence, knowledge gaps and recommendations for modelling post-TB sequelae. I will also summarize the symposium and discuss important next steps for the field of post-TB, including research and advocacy priorities, as well as the future of the symposium.

## SP20 Normalising TB conversations: power of the people's movement in ending TB

### Community radio intervention: Taking TB conversations closer home

A Bhardwaj,<sup>1</sup> <sup>1</sup>International Union Against Tuberculosis and Lung Disease, South East Asia Office, New Delhi, India.  
e-mail: ashish.bhardwaj@theunion.org

Effectiveness of Community Radio Stations (CRS) for health programmes is well documented in India. The objective of engaging CRS for TB is to normalise TB conversations through a hyper local medium that belongs to, has a connect with and can influence poorer rural communities within its territorial footprint. This intervention follows a multi-pronged approach - develop and broadcast TB messaging and conduct on-ground community outreach interventions.

This engagement with CRS Radio Jockeys has resulted in catalysing conversations on TB, people sharing their TB experiences, motivating people to get screened and tested and connecting the local TB Cells with the communities.

## Engaging TB survivors in TB programme implementation

N Kumar,<sup>1</sup> <sup>1</sup>Ministry of Health and Family Welfare, New Delhi, India.  
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Persons with TB (PwTB) experience significant stigma and discrimination, creating barriers for TB diagnosis and treatment completion.

However, when a TB Survivor shares his/her personal experience of TB, it is often well accepted. They represent the challenges faced by PwTB in an effective way, liaise with communities, implementers and policy makers. Hence, India's TB Program trained consenting TB survivors to become 'TB Champions' who would liaise with local TB program, move across communities encouraging them to seek health care, support treatment and counselling. Nearly 30,000 TB survivors were trained till date, with many of them actively supporting the program.

## Empowering grassroot-level elected leaders to support TB elimination efforts in India

R Sankar,<sup>1</sup> <sup>1</sup>Global Health Strategies, New Delhi, India.  
e-mail: rsankar@globalhealthstrategies.com

The presentation will provide an overview of the Indian Ministry of Health's collaboration with the Ministry of Panchayati Raj (managing rural local elected bodies) to enlist the support of 250,000 village-level elected leaders across the country in the TB elimination response.

The strategy is based on demonstrative pilot programs that showed that elected community leaders, when provided with accurate information and assistive tools, are well placed to build community participation and increase accountability toward a health issue, monitor service quality and availability, and act as a feedback mechanism to relay challenges to higher authorities and ensure their resolution.

## Digital storytelling – an innovative approach to TB elimination

K Sagili,<sup>1</sup> <sup>1</sup>International Union Against Tuberculosis and Lung Disease, South East Asia office, India.  
e-mail: ksagili@theunion.org

Real, reliable, relatable content is important for people to make right decisions and actions. Sharing personal stories of TB is a powerful tool and is used across the globe. Agencies like WHO, CDC and TAG have shared stories and tools. In India also, several groups, have made efforts in this angle.

We implemented an innovative approach of 'mobile story telling' wherein TB survivors and health workers were trained to record their own stories on their mobile phones and disseminate through social media.

Initial results showed large viewership on social media and empowerment of individuals in telling their own stories digitally.

### **SP21 Accelerating paediatric investigations of next-generation new TB drugs for children**

#### **Innovative approaches to expedite the evaluation of new TB drugs in children**

P Howell,<sup>1</sup> <sup>1</sup>University of the Witwatersrand, Johannesburg, South Africa.  
e-mail: phowell@witshealth.co.za

Pediatric investigations of new TB drugs have all been substantially delayed. Without the investment of new resources and application of innovative approaches, this will persist for the generation of new TB drugs. This presentation will discuss the causes of these long delays and highlight the implications for TB treatment in children.

Here we describe a new initiative called, CHEETA (Chasing Expedited and Equitable Treatment Access for Children with TB) that aims to accelerate pediatric TB drug development through earlier initiation and more rapid implementation of pediatric trials of new TB compounds, and the development of an innovative platform trial approach.

#### **Collaboration and trial site capacity-building for equitable and enhanced site participation**

N Montañez,<sup>1</sup> <sup>1</sup>University of Wisconsin-Madison, School of Medicine and Public Health, Los Angeles, United States.  
e-mail: nmontanez@wisc.edu

Pediatric TB clinical trial site experience and capacity are rate limiting factors to accelerating investigations of TB drugs in children. A site mapping exercise was performed to identify sites in middle-and high-TB burden countries with experience conducting TB clinical trials and/or potential or known access to pediatric populations affected by TB. A survey was created to assess the identified sites' experience and capacity needs to feasibly perform regulatory TB clinical trials in children.

During this session we will discuss the process for and outcomes of the site mapping exercise and capacity survey, and how to address the identified capacity gaps.

### **GlaxoSmithKline development portfolio and strategies for accelerating paediatric investigations of TB drugs**

S Tiberi,<sup>1</sup> <sup>1</sup>GSK, London, United Kingdom.  
e-mail: simon.x.tiberi@gsk.com

Children have the lowest treatment rates for drug resistant TB and some of the worst outcomes, new drug regimens are sorely needed. However, developing drugs for children after adult therapies have been approved is currently the norm though this means several years of delay.

In this presentation an overview on GSK's TB drug pipeline and progress for paediatric development will be given. Current challenges on trying to bring forward paediatric development will be shared and a perspective on how a platform like CHEETA could help get new drugs to children will be discussed.

### **Ludwig Maximilian University development portfolio and strategies for accelerating paediatric investigations of TB drugs**

N Heinrich,<sup>1</sup> <sup>1</sup>LMU Munich, Munich, Germany.  
e-mail: heinrich@lrz.uni-muenchen.de

Ludwig Maximilian University (LMU) in Munich is the sponsor of a new TB drug called BTZ-043, which has a novel mechanism of action that inhibits DprE1, an important enzyme for cell wall synthesis.

This presentation will provide an overview of the development of BTZ-043, including plans for advancing phase II studies in adults through a new public-private TB regimen development consortium called UNITE4TB. The presentation will also discuss early thinking around pediatric investigations of BTZ-043 in children and how innovative approaches might help to expedite research and access to new drugs like BTZ-043 for children.

### **A community perspective on accelerating access to new TB drugs for children**

G Kerubo Moses,<sup>1</sup> <sup>1</sup>Amref Health Africa/Global TB CAB/CHEETA Taskforce, Nairobi, Kenya.  
e-mail: mosesgloriah96@gmail.com

Children are typically among the last populations to enjoy the benefits of scientific progress in TB. Communities observe and must deal directly with the adverse impacts of these delays, namely unnecessary morbidity, mortality, and suffering.

This presentation will discuss how children have been slow to benefit from access to short-course regimens for TB prevention and treatment of drug-sensitive and drug-resistant TB, and how accelerating pediatric investigations of new drugs in children will help to address the needs of this population too often underprioritized or left out entirely of TB research and program initiatives.

## **SP22 Building state-of-the-art training systems to address rapidly evolving needs to end TB in TB programmes**

### **Training TB programme personnel in Indonesia**

I Eka Putra,<sup>1</sup> <sup>1</sup>School of Public Health, Faculty of Medicine, Universitas Udayana, Denpasar, Indonesia.  
e-mail: gedartawan@unud.ac.id

Indonesia has been working to accelerate progress toward TB elimination to achieve the targets of END TB strategy. The national TB program is implementing a variety of capacity building efforts to translate these policies into action across the country in all sectors. The presentation describes the capacity building methods and processes adopted and related learnings and challenges.

### **Capacity-building through international courses**

L Garrido-Herrero,<sup>1</sup> <sup>1</sup>The Union, Sydney, Australia.  
e-mail: lara.garrido@theunion.org

The Union provides support to develop clinical expertise, management skills and the ability to discover solutions through research and advocacy. The Union has a series of international courses designed for staff of national TB programmes, clinicians and technical partners working in tuberculosis care and prevention in low-and middle-income countries.

The presentation will share the recent modernisation of Union Courses, which now offer a hybrid learning environment model: online asynchronous courses, online synchronous courses and face to face field visits.

### **Developing global public goods for training**

M Easow Mathew,<sup>1</sup> <sup>1</sup>The Union, New Delhi, India.  
e-mail: manu.mathew@theunion.org

The presentation will focus on how training material, content, processes and systems/ tools can be open sourced through creative commons licenses and be made available as a global public good. This would make available, free of cost, a common pool of training material, resources and tools, to experts, organizations and TB programs around the world.

This will also enable higher levels of collaboration and co-operation, which in-turn will result in continuous improvement and expansion of a repository of technical resources in the area of training and capacity building.

## **Global public goods: uptake of digital training tools by national TB programmes**

S A Nair,<sup>1</sup> <sup>1</sup>Stop TB Partnership- Secretariat, Geneva, Switzerland.  
e-mail: sreenivasn@stoptb.org

The presentation will focus on the development of fast paced tools, strategies, approaches and policies in TB care and prevention and the need for digital technology supported approaches for quick and cost effective capacity building approaches.

The presentation will highlight global experience is e-learning opportunities and strategies to make free to use technical resources on training and capacity building as global public goods.

## **SP23 Introducing and scaling up shorter TB treatment regimens for children and adolescents: how do we move from policy to practice?**

### **Ensuring children also benefit from treatment shortening: Latest global policies and guidelines**

S Verkuijl,<sup>1</sup> <sup>1</sup>WHO, Global TB Programme, Geneva, Switzerland.  
e-mail: verkuijls@who.int

The WHO consolidated guidelines on the management of tuberculosis in children and adolescents and on drug-susceptible TB treatment contain recommendations on shorter treatment regimens for non-severe drug-susceptible TB and for TB meningitis in children and adolescents and on the 4-month HPMZ regimen in  $\geq 12$  years. The use of bedaquiline is now also recommended in  $< 6$  years. Children of all ages are therefore eligible for the subsequently recommended 9-month all oral regimens for MDR/RR-TB. WHO also recommends programmatic use of BPALM in adolescents  $\geq 14$  years. This presentation provides an overview of WHO recommendations and practical implementation guidance on shorter treatment regimens

### **Implementation of shorter-course regimens for TB treatment in children and adolescents in Kenya: key steps and practical considerations**

E Maleche-Obimbo,<sup>1</sup> <sup>1</sup>University of Nairobi, Nairobi, Kenya.  
e-mail: lisaobimbo@gmail.com

Following the release of the new 2022 WHO guidelines, the NTLP worked together with the Kenyan Childhood TB Committee of Experts (CoE) who led a step-wise process of in-depth review of new recommendations and of supporting evidence by experts from relevant disciplines and sectors.

A decision was made to adopt the shorter 4-month TB regimen. Field-tools, training material and guidelines were adapted to guide health-workers on how to identify which child was eligible for short-course TB treatment. A roadmap for roll out included sensitization, training and dissemination to stakeholders and implementers, piloting in selected counties, and national implementation by mid-2023

### **Implementing the oral shorter regimen for the treatment of drug-resistant TB in children and adolescents in Tajikistan**

W Mulanda,<sup>1</sup> <sup>1</sup>Médecins Sans Frontières, Dushanbe, Tajikistan.  
e-mail: tajikistan-medco@oca.msf.org

MSF is treating children and adolescents with drug resistant TB (DR-TB) in Tajikistan since 2012. In 2016, in collaboration with the National TB program, MSF introduced pediatric formulations for second-line drugs as well as the use of shorter, all oral regimen.

The package of care supported by MSF includes improved access to laboratory-based diagnosis and drug resistant testing, strengthening of contact investigation interventions and implementation of Family-DOT approach to improve access to TB care and enhance treatment adherence.

Key lessons learned on the effect and feasibility of implementation of this package of care will be reviewed and discussed

### **Procurement and supply considerations to ensure smooth uptake of new, shorter regimens for the treatment of drug-susceptible and drug-resistant TB in children**

M Kavtaradze,<sup>1</sup> <sup>1</sup>Global Drug Facility (Stop TB Partnership), Geneva 1218, Switzerland.  
e-mail: mayak@stoptb.org

Great strides have been made in shortening tuberculosis treatment duration using WHO-recommended child-friendly formulations of medicines.

This presentation will focus on the peculiarities of TB treatment in children that require special attention to ensure that the right medicines are available in the correct quantity at the right place and time.

Based on the experience of TB programs that have already started new, shorter regimens for drug-susceptible and drug-resistant TB treatment in children, we will also share challenges and ways forward and explain why procurement and supply considerations are essential to ensure a smooth transition to new regimens.

### **Looking ahead: Future options for shortening treatment of drug-susceptible and drug-resistant TB in children and adolescents**

N Salazar-Austin,<sup>1</sup> <sup>1</sup>Johns Hopkins, Baltimore, United States.  
e-mail: nsalaza1@jhmi.edu

The last few years, there have seen significant advances in the treatment of drug-sensitive and drug-resistant TB among adults, including HPMZ and BPALM. Translating those results to children should not only consider safety and matching drug exposures, but should also address the differences in the pathophysiology of child versus adult TB disease.

We will review ongoing and planned trials from SMART4TB, IMPAACT and the CDC's Tuberculosis Trials Consortium to assess these and other treatment advances in infants, children and adolescent

## SYMPOSIA: FRIDAY 17 NOVEMBER 2023

### SP24 Raising quality of data from observational MDR/RR-TB treatment cohorts: novel methods and best practices

#### Estimating TB recurrence post MDR/RR-TB treatment among patients with and without HIV: the impact of assumptions about death and missing follow-up

S Sauer,<sup>1</sup> <sup>1</sup>Harvard Medical School, Cambridge, United States.

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Quantification of recurrence risk following successful treatment is crucial to evaluating regimens for multi-drug- or rifampicin-resistant (MDR/RR) tuberculosis (TB). Such analyses are complicated, however, when some patients die or become lost during post-treatment-follow-up.

We will report estimates of six-month post-treatment TB recurrence risk and compare this risk by HIV status among patients who successfully completed a longer MDR/RR-TB regimen containing bedaquiline and/or delamanid. In doing so, we will compare five approaches for handling post-treatment deaths and demonstrate the impact of potential selection bias from excluding patients with missing follow-up data.

#### Risk factor analyses in MDR/RR-TB treatment cohorts - beware of the Table 2 fallacy

P Khan,<sup>1</sup> <sup>1</sup>London School of Hygiene and Tropical Medicine, London, United Kingdom.

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Risk factor analyses (i.e., those that present multiple adjusted effect estimates from a single multivariable regression model) are a popular approach for studying determinants of treatment success.

However, effect estimates from these models are at high risk of bias and misinterpretation. Using an illustrative example of an analysis of risk factors for unsuccessful treatment outcomes among patients receiving treatment for MDR/RR-TB, we demonstrate how bias may occur and why model estimates are often misinterpreted.

We will compare estimates to an alternative approach focused on the impact of a single exposure, HIV-infection, on treatment outcome and propose best practice modelling strategies.

### To adjust or not to adjust? Considering causal structure in estimating the effects of hepatitis C on unfavourable MDR/RR-TB treatment outcomes

A LaHood,<sup>1</sup> <sup>1</sup>Harvard Medical School, Boston, United States.

e-mail: Allison\_Lahood@hms.harvard.edu

Hepatitis C has been shown to be associated with unfavourable treatment outcomes in patients who have initiated MDR/RR-TB treatment; however, the reasons (i.e., mediating pathways) for this association are unclear. Possible explanations range from increased risk of liver injury to limited TB treatment options to confounding by substance use.

We leverage data from the endTB Observational Study cohort to estimate the effect of hepatitis C on unfavourable outcomes, using causal structure to guide confounder adjustment. We then estimate the extent to which treatment adherence, adverse events, and regimen composition, versus alternative pathways, explain the observed association.

### Target trial emulation in action: estimating the effect of bedaquiline use beyond six months on end-of-treatment outcome

L Trevisi,<sup>1</sup> <sup>1</sup>Harvard Medical School, Boston, United States.

e-mail: letizia\_trevisi@hms.harvard.edu

Target trial emulation to guide statistical analyses can facilitate articulation of clear research questions, increase transparency, and reduce bias. We will present an example of target trial emulation for the study of the relative effectiveness of longer bedaquiline durations (7-12 months; >12 months) as compared to six months of bedaquiline, with regard to treatment success.

We will describe the target trial and a three-step analytic strategy (consisting of cloning, censoring, and weighting) to emulate the target trial.

### Benchmarking to extend causal inferences from clinical trials to real-world evidence

U Khan,<sup>1</sup> <sup>1</sup>IRD Global, Montreal, Canada.

e-mail: uzma.khan@ird.global

One approach to increase the confidence in results from observational studies is through benchmarking the observational study results against those from a randomized trial before using observational analyses to answer questions beyond those of the trial.

In this presentation, we explore key assumptions for a causal framework to benchmark observational data using target trial emulation and provide an example based on the endTB Observational Study and endTB Clinical Trial.

## **SP25 CAD for kids: Advances in adapting computer-aided chest X-ray readings to support TB diagnosis in children**

### **The implementation of chest X-ray in primary care settings and the role of CAD for childhood TB**

O Marcy,<sup>1</sup> <sup>1</sup>University of Bordeaux/IRD, Bordeaux, France.  
e-mail: olivier.marcy@u-bordeaux.fr

Chest radiography (CXR) is an important component of tuberculosis diagnosis in children. However, poor access to good quality CXR, lack of appropriate reading skills and poor inter-reader reproducibility restrict its impact in diagnostic algorithms, notably at lower levels of healthcare.

This presentation will bring new evidence from the TB-Speed studies on decentralizing simplified CXR reading at the primary healthcare level and use of CXR in specific algorithms for children with HIV-infection or malnutrition. This will highlight the added value and the performance of CXR in diagnosing childhood TB and potential role of CAD to support the evaluation.

### **The performance of CAD4TB for paediatric TB in South Africa**

M Palmer,<sup>1</sup> <sup>1</sup>Desmond Tutu TB Centre, Stellenbosch University, Cape Town, South Africa.  
e-mail: meganpalmer@sun.ac.za

Current CAD algorithms for TB have not been trained or evaluated for children under 5 years old. In this session, we will present the accuracy of the CAD4TB system (Delft) for interpreting chest X-rays (CXR) from young children who were evaluated for pulmonary TB in Cape Town, South Africa.

We will then describe the results after re-training the algorithm with paediatric CXR data, and review the requirements and processes needed to fine-tune CAD algorithms for childhood TB.

### **The experience of developing CAD for paediatric TB in Spain and Mozambique**

M Ledesma-Carbayo,<sup>1</sup> <sup>1</sup>Universidad Politécnica de Madrid, Madrid, Spain.  
e-mail: mj.ledesma@upm.es

Universidad Politécnica de Madrid in collaboration with ISGlobal and the Spanish network for paediatric TB (pTBRed) have developed a telemedicine platform and artificial intelligent (AI) methodologies to support paediatric TB diagnosis in low resource countries using CXR and clinical data from two cohorts. The telemedicine platform facilitates the reading and CXR labelling

of radiological findings. Different AI models have been built using convolutional neuronal networks for TB vs non-TB classification and relevant areas segmentation, including methods merging image and basic clinical information. Performance comparison of these models will be presented with respect to expert radiologists readings as reference standard.

### **The CAPTURE Consortium: Catalysing artificial intelligence for paediatric TB research**

D Jaganath,<sup>1</sup> <sup>1</sup>University of California, San Francisco, United States.  
e-mail: devan.jaganath@ucsf.edu

To improve training and validation of CAD solutions for paediatric TB, we need to a large image repository from diverse, well-characterized cohorts of children with and without TB.

The CAPTURE consortium is a multi-country initiative to develop a paediatric TB CXR repository with expert CXR reads, corresponding clinical data, and standardized TB definitions. This will support independent evaluation of CAD algorithms for paediatric TB, and provide developers a critical resource to fine-tune and build new CAD algorithms for children.

In reviewing the data available, we will also outline the essential needs for a child-specific CAD algorithm and considerations for analysis.

### **Adapting CAD implementation for children**

H Sohn,<sup>1</sup> <sup>1</sup>Seoul National University College of Medicine, Seoul, Korea, Republic of.  
e-mail: hsohn@snu.ac.kr

There is limited documentation of real-world implementation issues and end-user needs, which are important factors to consider in the development and assessment of TB-CAD for paediatric populations.

We will discuss results of our initial systematic search of end-users of TB-CAD in low-resource settings and describe strategies to develop a database to collate and update TB-CAD use case, including their early use in paediatric populations. We will also describe current available paediatric TB-CAD products and propose key priority features for CAD in children that can serve as benchmark in the development and evaluation of next generation of TB-CAD for paediatric populations.

## **SP26 Challenging the use of digital technologies for TB diagnosis: global vision and experiences from Ethiopia, Nigeria, Vietnam and the Latin American and Caribbean region**

### **AI and radiology technology in TB: Global policies, advances, innovations and research**

Z Qin,<sup>1</sup> <sup>1</sup>Stop TB Partnership, Geneva, Switzerland.  
e-mail: zhizhenq@stoptb.org

This presentation will offer a comprehensive review of the most recent advancements in digital radiology and AI/CAD technology, and their significance in combating TB. We will delve into the fundamental AI/CAD principles, and explore the array of products available. Additionally, we will address radiation safety concerns and discuss global efforts to pilot and expand the use of these tools.

The presentation will also incorporate a qualitative study and survey findings, providing insights into initial user experiences and key lessons derived from the use of ultra-portable digital X-ray and CAD products.

### **Portable digital X-ray with AI to strengthen TB case-finding among key populations in Nigeria: an innovative public-private partnership scale-up model**

S Useni,<sup>1</sup> <sup>1</sup>KNCV Nigeria, Abuja, Nigeria.  
e-mail: suseni@kncvnigeria.org

Between September 2020-Dec 2022, we partnered with a private company that produces portable digital X-rays to pilot the use of portable X-rays with AI for active case finding in hard-to-reach communities, riverine areas, prisons, and TB hotspot areas. Of 15,905 people screened in prisons, 7% had presumptive TB, and 25% of those tested were diagnosed with TB. During expansion to other key populations, 118,027 people were screened, 9% of whom had presumptive TB, and 23% of those with presumptive TB were diagnosed with TB. About 94-98% of those diagnosed were immediately linked to treatment.

### **AI-supported digital chest X-rays for TB case-finding: The experience in Latin America and the Caribbean region**

P Jimenez,<sup>1</sup> <sup>1</sup>Pan American Health Organization, Washington DC, United States.  
e-mail: avedillop@paho.org

In 2021, the WHO recommended using chest X-rays and computer-aided detection (CAD) software as highly sensitive screening tools in persons at higher risk of TB,

which can detect TB prior to the onset of symptoms. In the Americas, countries such as Peru, Paraguay, Colombia, and Ecuador among others, have begun implementing these tools for TB screening in vulnerable populations such as persons deprived of liberty, Indigenous Peoples, and urban areas with a high TB burden using mobile units.

We aim to share experiences of those countries.

## **SP27 TB in conflict: Digital health and data exchange systems for linkage to care for displaced Ukrainians**

### **Implementation research in support of the use of innovative digital technologies in TB care**

D Falzon,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: falzond@who.int

This talk will highlight the potential of digital technologies when used to support people with TB and health-care systems and the role implementation research plays in assessing the effectiveness and sustainability of such interventions.

### **Addressing barriers to the optimisation of digital treatment adherence in TB-affected persons in Ukraine**

I Yeleneva,<sup>1</sup> <sup>1</sup>Labor and Health Social Initiatives, Kyiv, Ukraine.  
e-mail: ilona@lhsi.org.ua

This talk will address the use of digital adherence technologies (DATs) and the challenges present for both persons on TB treatment and providers. Participants can expect to learn about the factors that act as barriers to continuous monitoring and follow-up for TB-affected persons within a conflict setting.

Participants will leave with a more comprehensive understanding of how to identify the psychological, social, financial, and physical barriers and methods to address these challenges to increase successful applications of DATs.

### **Addressing barriers to the optimisation of digital treatment adherence in TB-affected persons in Ukraine**

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### **Applying digital technologies to support treatment in Ukrainian persons affected by TB**

N Deyanova,<sup>1</sup> <sup>1</sup>OATH, Kyiv, Ukraine.  
e-mail: ndeyanova@oath.org.ua

This talk will focus on the application of digital technologies to support TB diagnosis and treatment in Ukraine both before Russia's invasion and how this prolonged conflict has affected the country's practices. Participants can expect to learn about the specific technologies utilized, such as smart pill boxes, that have become an essential part of supporting the continuation of care in TB affected persons who have been displaced and are unable to travel to clinics due to safety concerns. Participants should expect to leave with several strategies for application of the diverse technological methods to support TB treatment.

### **The role of eHealth in TB clinical management of displaced populations**

I Margineanu,<sup>1</sup> <sup>1</sup>University Medical Center Groningen, Groningen, Netherlands.  
e-mail: i.s.margineanu@umcg.nl

This talk will give a comprehensive overview of eHealth services' capabilities for tuberculosis clinical management for displaced populations both within the conflict zone and host countries. Participants can expect to learn about telemedicine technologies and mobile health apps used to facilitate the delivery of TB healthcare services in ways that in-person services currently cannot provide under the current conditions. Participants will be provided insights into the processes behind delivering timely care at a greater level of affordability through eHealth services by strengthening the eHealth infrastructure for refugees and internally displaced peoples.

### **SP28 An International Consensus on Early TB (ICE-TB) - the path to programmatic impact**

#### **An International Consensus for Early TB (ICE-TB): Results from the 1st Early TB Symposium**

A Zaidi,<sup>1</sup> <sup>1</sup>University College London & National University of Medical Sciences, London & Rawalpindi, Pakistan.  
e-mail: Syed.zaidi.22@ucl.ac.uk

This talk will summarize the process and key outcomes of the 1st International Symposium for Early TB. For the first time in over half a century, a revised framework and nomenclature describing TB states has been developed. This was achieved through a consensus-driven process with multiple Delphi rounds and input from participants with wide geographical and discipline representation. The presentation will also cover key considerations that led to the development of the framework encompassing Mtb infection, subclinical and clinical TB. Research priorities will be outlined which were identified as crucial to translate the consensus into policy and practice.

#### **Inside or outside the lung: Where do EPTB and paediatric TB fit in?**

J Seddon,<sup>1</sup> <sup>1</sup>Stellenbosch University, Cape Town, South Africa.  
e-mail: james.seddon@imperial.ac.uk

Compared to adults with pulmonary TB, the pathophysiology of both TB in children and also adults with extrapulmonary TB is different, as dissemination is usually required. Applying a framework that has primarily been developed for adult pulmonary TB to children and individuals with extrapulmonary TB has challenges and limitations, but these may be outweighed by the benefits of developing an inclusive approach. This talk will discuss differences in pathogenesis as well as challenges and benefits of mapping TB in children and extrapulmonary TB into the overall framework of early TB.

#### **Diagnostics for early TB: Where do we begin without reference standards?**

M Kohli,<sup>1</sup> <sup>1</sup>FIND, Geneva, Switzerland.  
e-mail: Mikashmi.Kohli@finddx.org

Detection of individuals with subclinical TB is a challenge as no tests have been formally evaluated for subclinical TB. A major caveat in developing such diagnostics is the absence of reference standards to confidently categorize people into having infectious and non-infectious subclinical TB.



This challenge also opens up opportunities to develop composite standards and diagnostic criteria using current tools, clinical assessments to correctly categorize patients in these clinical studies.

This presentation will explore key issues around diagnostic tools, study designs, reference standards and propose some potential solutions as we find the path from research to programmatic impact around subclinical TB.

### **Interventions for early TB: Developing interventions for a new framework**

H Esmail,<sup>1</sup> <sup>1</sup>University College London, United Kingdom.  
e-mail: h.esmail@ucl.ac.uk

The majority of TB drug trials over the last 30 years have focussed narrowly on evaluating intervention for the two ends of the infection and disease spectrum. Trials typically either included those with symptomatic smear positive pulmonary tuberculosis or alternatively included asymptomatic participants diagnosed with latent TB with no evidence of disease. As a result there is an evidence gap around the management of subclinical TB and clinical TB which is bacteriologically negative. This presentation will explore the importance, opportunities and challenges around developing interventions for Early TB.

### **From research to programme implementation: What is the direction of travel for NTPs?**

R Fatima,<sup>1</sup> <sup>1</sup>The common management unit to manage TB HIV AIDS and Malaria, Pakistan, Islamabad, Pakistan.  
e-mail: drraziafatima@gmail.com

While a framework for early TB is not immediately available for clinical and programmatic application, developing and further validating the framework should target this ultimate objective. Significant historical and programmatic data already exists to support quantification of many of these features of clinical and subclinical TB.

This joint presentation between Dr Razia Fatima (NTP - Pakistan) and Prof Justin Denholm (Victoria NTP - Australia) will explore how current data and populations fit with the framework, and where adjustments are needed, combining the perspectives of high-resource, low burden and low-resource, high burden National TB programmes.

### **SP29 Multi-testing for TB and other diseases with WHO-recommended rapid molecular diagnostics and clinical monitoring: perspectives from high TB burden settings**

#### **Multi-disease testing using GeneXpert® equipment: The Ethiopian experience**

E Mengesha,<sup>1</sup> <sup>1</sup>KNCV TB Plus Foundation, Addis Ababa, Ethiopia.  
e-mail: endalemengesha@gmail.com

The Ethiopian Public Health Institute, TB/HIV control programs with partner support organize a network of 503 GeneXpert® Instruments from which 151 perform multi-disease testing. EID and viral load service increased from 19 to 139 with no additional cost for specimen referral and no result delays. However, ART sites have high load for presumptive TB clients and overload the machines. Therefore, viral load GeneXpert service expansion is slow compared with EID testing. Based on a study, TB and HIV programs agreed to expand multi-disease testing with GeneXpert with lower utilization. This increased the utilization of GeneXpert and shortened the TAT.

#### **Implementation of multi-testing on the GeneXpert platform in Kyrgyzstan**

K Ismailovna,<sup>1</sup> <sup>1</sup>Kyrgyzstan TB National Reference Laboratory (NRL), Kyrgyzstan.  
e-mail: gulmira.kalmambetova@gmail.com

Kyrgyzstan has 39 GeneXpert platforms: 26 for TB services, 12 for HIV services, and 4 for the Department of Infectious Disease Prevention. GeneXpert can test nosocomial infections, dangerous diseases, reproductive health, viral infections, oncology, and genetic diseases. In Kyrgyzstan, GeneXpert instruments were provided by donors for vertical programs-used internally: TB, HIV and CoV-2. So, the GeneXpert potential is not fully utilized. TB and HIV services have considered joint use of GeneXpert platforms.

During COVID-19, the health care system did not completely cover testing needs, relying on private providers, while TB and HIV services only partially used GeneXpert capacity.

### Experiences with GeneXpert multi-testing in Tanzania

A Kingalu,<sup>1</sup> <sup>1</sup>Central Tuberculosis Reference Laboratory -Tanzania, Tanzania.  
e-mail: info@ntlp.go.tz

In 2012, Tanzania adopted GeneXpert. As of 2022, 336 GeneXpert instruments across the country were used as the initial TB diagnostic test with 4 dedicated to management of MDR/XDR. 51% of GeneXpert sites are multi-testing for TB and HIV.

Testing for HIV viral load has increased dramatically as a result and integrated sample referral has been simplified with cost effective multi-testing. Quality management has been fortified with combined TB and HIV program resources. Delays for uptake of other test menus remain. Competition for prioritization of testing between TB and HIV remain. Revised service level agreements reduced downtime.

### Molecular Multi disease testing platform till the periphery with WHO endorsed Rapid molecular testing (TrueNAAT) - fully domestic funded initiative from India

C Joseph,<sup>1</sup> <sup>1</sup>KNCV TB Plus, The Hague, Netherlands.  
e-mail: carel.joseph@kncvtbc.org

The Government of Andhra Pradesh in 2018 replaced sputum smear microscopy testing with GeneXpert alternative technology Truenat in 225 PHCs/CHCs reaching a coverage of 88% for offering upfront molecular testing for all presumptive TB patients. (Locally funded initiative 1st in the country to do so).

During Covid pandemic for covid testing, NTP diverted 45 machines without stopping TB testing efforts. The Covid testing increased from 20% to 85% (11.8 million 2020, 31 million 2021 and 3.13 million 2022). Purchased additional 165 Truenat machines in 2021. Molecular multi-disease testing platform at the peripheral level is achieved for TB, Hepatitis C testing

### Implementation of multi-testing on the GeneXpert platform across Nigeria

F Ajiboye,<sup>1</sup> <sup>1</sup>KNCV TB Plus Foundation, Abuja, Nigeria.  
e-mail: prisca.ajiboye@kncvtbc.org

GeneXpert use in Nigeria is largely for tuberculosis diagnosis. However, the instrument is capable of testing for about 30 more diseases of public health importance.

Multi-testing using GeneXpert might have been incriminated in the low case detection for TB as the program made efforts to improve the process without losses in case detection. Since testing for HIV-EID, a 60% reduction has been observed in turn-around-time for patient treatment.

A 30% reduction in the costs was observed for Hepatitis B and C viral load testing. It would be good practice to have operational guidance prioritizing testing to minimize program losses.

### SP30 Closing the gap: Evidence-based approaches to CAD software for equitable paediatric TB screening

#### Chest X-ray as a screening and diagnostic tool for child TB and integration of CAD into a paediatric TB study

A Kay,<sup>1</sup> <sup>1</sup>Baylor College of Medicine, Houston, United States.  
e-mail: alexander.kay@bcm.edu

This presentation will review the role of chest X-rays (CXR) as a screening and diagnostic tool for children being evaluated for tuberculosis and will conclude with the integration of computer-aided detection (CAD) assessments into studies of childhood TB. This includes the TB GAPS project, which will enroll 5,850 participants, comprising 878 presumptive TB children and adolescents living with HIV in Eswatini, Lesotho, Malawi, Tanzania, and Uganda.

#### Developing a multi-country dataset of paediatric images for AI-based evaluation using START4ALL

J Creswell,<sup>1</sup> <sup>1</sup>Stop TB Partnership, Geneva, Switzerland.  
e-mail: jacobc@stoptb.org

The START4ALL project will operate in Cameroon, Nigeria, and Vietnam to assess new tools and approaches, including ultra-portable X-ray technology with AI, to bring TB diagnostics closer to the point of need for more people. The prospective enrollment of over 2,000 children, along with supplementary clinical information, will contribute to developing the evidence base for the potential expansion of global guidance on using AI to interpret childhood TB X-rays.

### **The CAPTURE Consortium: Developing a large image repository to support CAD evaluation and development for childhood TB**

M Palmer,<sup>1</sup> <sup>1</sup>Desmond Tutu TB Centre, Stellenbosch University, Cape Town, South Africa.  
e-mail: meganpalmer@sun.ac.za

A large, diverse repository of well-characterised chest X-rays from children with and without TB is critical to support validation of existing algorithms and development of child-specific CAD algorithms. The Catalyzing Artificial intelligence for Paediatric TB Research (CAPTURE) consortium is a multi-country initiative to build a large CXR repository from high-quality TB diagnostic studies, with expert CXR reads, full clinical evaluation, and NIH child TB classifications.

We will describe its current status and the process to validate existing algorithms and support new CAD algorithms for children. We will also review the essential needs for a child-specific CAD algorithm and analytical considerations.

### **Assessing the performance of CAD software in detecting TB in children attending TB screening centres in Bangladesh**

S Zaidi,<sup>1</sup> <sup>1</sup>Stop TB Partnership, London, United Kingdom.  
e-mail: sarahz@stoptb.org

Approximately 50-65% of children with TB go undetected and CAD holds promise for detecting these missing children, yet there is a lack of impartial evidence on its effectiveness in this age group.

This presentation will discuss results from our evaluation of two CAD products - Delft's imaging's CAD4TB and Qure.AI's qXR - on a case-control sample of 586 children aged 5-15 who attended TB screening and treatment centres in Bangladesh. It will also discuss difficulties with an imperfect reference standard, in this case GeneXpert, due to the lack of a gold standard for children's diagnosis.

### **Performance of CAD systems in children aged 5-14 years in Lusaka, Zambia**

M Muyoyeta,<sup>1</sup> <sup>1</sup>Centre for Infectious Diseases Research in Zambia, Lusaka, Zambia.  
e-mail: Monde.Muyoyeta@cidrz.org

Diagnosis of TB in children is challenging. It is largely dependent on a clinical diagnosis due to its paucibacillary nature that results in low sensitivity of current diagnostic tools. Chest x-ray (CXR) thus has an important role in the diagnostic work up of children.

However, CXRs of children are difficult to interpret (read), especially for non-expert readers and CAD may assist.

There is an urgent need to validate the performance of CAD systems in children. We will present data on evaluation of two CAD systems in Lusaka Zambia.

### **SP31 Reaching agreement on the inclusion of pregnant and lactating persons in TB research**

#### **Community perspective on earlier inclusion of pregnant persons in TB therapeutics and vaccine research**

A Herna Sari,<sup>1</sup> <sup>1</sup>Global TB Community Advisory Board (TB CAB), Surabaya, Indonesia.  
e-mail: anihernasari@gmail.com

The lack of TB therapeutics and vaccines research has largely moved the risk out of the controlled research space and onto the patients and providers.

This talk will describe one survivor's experience with DR-TB treatment in pregnancy, her continued role as an advocate for improved TB research among pregnant persons and key takeaways from the USAID-supported SMART4TB pregnancy consensus building workshop, differences in perspective and position between scientific and community experts, and key aspects of the final community consensus statement.

#### **How to ensure safe, evidence-based TB treatment for pregnant people**

N Salazar-Austin,<sup>1</sup> <sup>1</sup>Johns Hopkins, Baltimore, United States.  
e-mail: nsalaza1@jhmi.edu

Risk and liability concerns have paralyzed our ability to evaluate TB regimens in pregnancy thereby limiting safe, evidence-based treatment for this population.

Optimal inclusion of pregnant and lactating women in TB drug trials involves a careful risk-benefit assessment, both in relation to pregnant persons and their offspring. Their inclusion in TB clinical trials is not just a research gap, but an important public health and ethical imperative.

This talk will describe the TB community's consensus on approaching evaluation of new TB drugs in pregnancy and will use BPALM and HPMZ as case studies to showcase optimal study designs.

### **Maternal vaccination: It's time for a TB vaccine**

L Cranmer,<sup>1</sup> <sup>1</sup>Emory University, Atlanta, United States.  
e-mail: lisa.marie.cranmer@emory.edu

Maternal vaccination has been an effective public health strategy to reduce maternal and infant morbidity and mortality from a variety of infectious pathogens, including tetanus, pertussis and influenza.

Yet systematic exclusion of pregnant women from trials of new vaccine products results in inequitable delays in access of pregnant people to the potential benefits of novel vaccines.

We will discuss lessons learned from use of recent COVID and RSV vaccines among pregnant people to infer practical applications for TB vaccine development.

### **Tracking TB in pregnant people: the importance of surveillance**

A Hesseling,<sup>1</sup> <sup>1</sup>Stellenbosch University, Cape Town, South Africa.  
e-mail: annekeh@sun.ac.za

Lack of strong epidemiologic data has hindered our understanding of the devastating effects of TB among pregnant persons, and the benefits and risks associated with use of new TB therapeutic agents during pregnancy. Ongoing surveillance of pregnant people and their infants is critical to inform clinical management of DS and DR TB in pregnant populations.

This talk will discuss recent efforts to develop a global registry to monitor clinical outcomes of pregnant patients receiving MDR-TB therapy, and establishing commitments from strategic global partners to advance global surveillance strategies.

### **The inclusion of pregnant people in TB research is possible**

F Conradie,<sup>1</sup> <sup>1</sup>Univeristy of Witwatersrand, Johannesburg, South Africa.  
e-mail: fconradie@witshealth.co.za

Despite recent marked advances in TB treatment for the general adult population after decades of stagnation, pregnant persons still receive the less effective, more toxic, longer, and less acceptable older TB treatment regimens resulting in unethical excess and preventable morbidity and mortality. BEAT-TB is one of the first clinical trials that co-enrolled adults, children and pregnant persons in a DR-TB trial.

This talk will discuss how pregnant persons were included in the protocol design, what was done to ensure their safety, and challenges faced throughout the trial.

### **SP32 Mobilising #YouthPower to fulfil pledges made by Heads of State at the 2023 UN High-Level Meeting**

#### **The role of the young in advancing the pledges by Heads of State at the 2023 UN High-Level Meeting**

R Joshi,<sup>1</sup> <sup>1</sup>Ministry of Health and Family Welfare of India, Dehli, India.  
e-mail: ywang@who.int

Recognizing the contribution and participation of young people as important stakeholders in the fight to end TB, the WHO Global TB Programme has been leading efforts to engage young people and harness their multiplier effect across the spectrum.

Yi and Anna will share the progress made in engaging youth through WHO's 1+1 youth initiative to end TB, and give an overview of diverse approaches that youth can contribute in reaching the End TB targets and in taking forward the commitments made by heads of State at the 2023 UN High Level Meeting.

#### **Mental health among young TB patients: Youth at a pivotal stage to build self-competency**

M Maftukhah,<sup>1</sup> <sup>1</sup>Indonesia Muda untuk Tuberkulosis/IMUT, Magelang, Indonesia.  
e-mail: perseus.mazida@gmail.com

It is hard to have TB, especially being young. The medication can make you feel depressed, as it happened with Mazidatun. She has experienced hard times, facing both TB and mental health issues, but she kept on fighting and advocating for Youth care and protection for those suffering from TB and mental health issues. She believes that early intervention, guidance and preventive actions are necessary to safeguard young people from being victims of the TB and mental disorders devastating effects.

Mazidatun will share more about lessons she learned on her road to recovery.

#### **What doesn't kill you, makes you stronger – personal experience sharing in combating TB and HIV**

H Sunday,<sup>1</sup> <sup>1</sup>African Network of Adolescents and Young Persons Development (ANAYD), Abuja, Nigeria.  
e-mail: harunaaronsunday@gmail.com

Aaron was diagnosed with HIV at the age of 12. It's been already four years since he got infected through the blood transfusion. Soon he found out he also had TB. Luckily for Aaron, he was receiving his treatment

at a Global Fund supported facility and met a doctor who provided him psychosocial support that was crucial for his healing. Now Aaron is dedicated to stay healthy, strong and active with the help of antiretroviral treatments, he will share his experience with us in this session.

### **The critical role of young volunteers in knowledge sharing in TB prevention and control: A case study from China**

R Zheng,<sup>1</sup> <sup>1</sup>Ningbotech University, Ningbo, China.  
e-mail: m15257425260@163.com

A national young volunteer mobilization campaign was launched in China in 2012, aimed to advance the untapped source of youth group in disseminating knowledge in TB prevention and control. In the past 10 years, with the support from multiple governmental sectors and NGOs, over 1 million volunteers engaged and played a critical role on the road to End TB in China. Ruo-nan will share 5 key models were developed and implemented in over 40 universities across China, along with the best practices those will be further promoted to more than 200 universities in the near future.

### **Reaching the last mile: Strategies for TB elimination in remote communities, lessons from Nunavik, Canada**

Y Tcholakov,<sup>1</sup> <sup>1</sup>McGill University, Montréal, Canada.  
e-mail: yassen.tcholakov@mcgill.ca

Poverty, inadequate housing, limited access to health-care, discrimination, and other risk factors can create an environment where TB can thrive. Thus, the persistence of TB as a global health threat is large, due to insufficient attention and resources allocated to tackle its determinants.

Yassen, a public health physician experienced in epidemiology, policy-making, and global health, will share his experience working in Nunavik, Canada, on TB elimination. He will offer insights for other communities facing high TB burdens and for global action.

### **SP33 The impact of digital adherence technologies on TB care: Results from ASCENT and other studies**

#### **What we know and what more is needed: synthesising evidence on digital adherence technologies for TB care**

K Fielding,<sup>1</sup> <sup>1</sup>London School of Hygiene & Tropical Medicine, London, United Kingdom.  
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In the last few years there have been a plethora of trials and observational studies reporting on digital adherence technologies, and implementation studies have generated important data on challenges on employing adherence technologies, across many countries and settings. The presentation will share the latest data on the impact of DATs on outcomes and costs, and implementation of DATs.

#### **A community perspective on the role of digital adherence technologies in TB care**

E Fekadu,<sup>1</sup> <sup>1</sup>Volunteer Health Services, Addis Ababa, Ethiopia.  
e-mail: enda.pharm@gmail.com

To ensure people affected by TB and their health providers can use a digital adherence technology intervention appropriately, engagement with patient- and health professional organizations is crucial. This will generate insights into how the DAT intervention could be adapted to the community- and patient perspectives for each specific local context.

During this session, Endalkachew Fekadu will share the perspectives of the Ethiopian community on using digital adherence technologies such as a smart pill box or medication labels.

#### **Effectiveness of digital adherence technologies in improving TB treatment: interim results from the ASCENT studies**

D Dare,<sup>1</sup> <sup>1</sup>KNCV Tuberculosis Foundation, The Hague, Netherlands.  
e-mail: degu.dare@kncvtbc.org

The Unitaaid-funded ASCENT (Adherence Support Coalition to End TB) project started in 2019. It aims to help persons affected by TB in Tanzania, South Africa, Ukraine, Ethiopia and the Philippines successfully complete treatment using DATs such as smart pill boxes, medication sleeves and video supported treatment.

In this session, Dr Degu Jerene will share the results evaluating the impact and contextual factors of medication labels and smart pillbox with a differentiated response to patient care.

### **Acceptability, feasibility and costing of video-supported treatment (VST) in Moldova**

C Celan,<sup>1</sup> <sup>1</sup>Center for Health policies and Studies (PAS Center), Chisinau, MD-2012, Moldova.  
e-mail: cristina.celan@pas.md

In Moldova, a study was conducted to assess the acceptability and feasibility of video-supported treatment (VST) on 120 person on TB treatment.

The study showed cost reductions using VST (mobile internet cost included) compared to DOT transportation costs per treatment course for DS-TB from 95.87 USD to 31.03 USD and for MDR-TB- from 191.74 USD to 62.05 USD. Other benefits included daily time savings for people on VST up to 43-64 minutes/day. Cristina Celan will share further details on the implementation experiences in Moldova.

### **SP34 Exploring sustainable models for TB vaccine development and delivery in BRICS countries**

#### **Safety and effectiveness of the M. vaccae vaccine**

J Pu,<sup>1</sup> <sup>1</sup>Chongqing Zhifei Biological Products Co.,Ltd., China.  
e-mail: pujiang@zhifeishengwu.com

Since 1998, China has been prioritized in WHO's list of high-TB burden countries to strengthen efforts in TB prevention and care. To accelerate national end-TB efforts, Anhui Zhifei Longcom developed and commercialized *Vaccae* vaccine in China for prevention of TB disease among people infected with TB in 2021.

This session will share results of safety and effectiveness of the *Vaccae* vaccine, as well as foreseen challenges and opportunities with vaccine implementation.

#### **Preparing for new TB vaccines in South Africa: Who and when to vaccinate and how?**

M Hatherill,<sup>1</sup> <sup>1</sup>South African Tuberculosis Vaccine Initiative, University of Cape Town, Cape Town, South Africa.  
e-mail: mark.hatherill@uct.ac.za

South Africa has made tremendous progress in its fight against TB but remains part of WHO's list of high-TB burden countries. To accelerate progress, public, private and philanthropy sectors are working jointly to fast-track the testing of promising TB vaccine candidates. This presentation will discuss currently ongoing TB

vaccine trials in South Africa, and the potential national implementation strategies, should one of these TB vaccine candidates be licensed. It will review the challenges, and lessons learned from other vaccine implementation efforts for adult and adolescent populations.

#### **Ending TB in Brazil: Is a vaccine necessary?**

F Dockhorn Costa Johansen,<sup>1</sup> <sup>1</sup>Ministry of Health, Brasília, Brazil.  
e-mail: fernanda.dockhorn@saude.gov.br

Brazil has a high TB and TB/HIV burden. Due to several challenges, including disruptions caused by the COVID-19 pandemic, TB related deaths have been rising since 2019.

The presentation will discuss current efforts and challenges to improve access to TB prevention and care to vulnerable people at risk of, or affected by TB such as people with HIV, indigenous peoples, and people in prisons and other places of detention. It will also discuss the opportunity effective TB vaccines can offer to strengthen the TB response, in the context of Brazil.

#### **Health and economic impact of new TB vaccines in India**

R Clark,<sup>1</sup> <sup>1</sup>London School of Hygiene and Tropical Medicine, London, United Kingdom.  
e-mail: Rebecca.Clark@lshtm.ac.uk

India has the highest tuberculosis burden globally, and safe and effective tuberculosis vaccines could play an important role in ending the epidemic. We developed and calibrated a tuberculosis vaccine model in India to estimate the potential health and economic impact of M72/AS01E and BCG-revaccination under varying delivery scenarios. M72/AS01E scenarios were predicted to avert 40% more cases and deaths by 2050 compared to BCG-revaccination scenarios.

Cost-effectiveness ratios for M72/AS01E vaccines were around seven times higher than BCG-revaccination, but nearly all scenarios were cost-effective when compared to three country-specific thresholds. Greater investment in vaccine development and delivery is needed to raise the probability of success.

### **SP35 Closing the gaps in paediatric TB – expediting TB diagnosis in children to reach High-Level Meeting targets**

#### **What is needed to reach UNHLM targets for TB in children and adolescents and how we can achieve them**

M Casenghi,<sup>1</sup> <sup>1</sup>Elizabeth Glaser Pediatric AIDS Foundation, Rome, Italy.  
e-mail: mcasenghi@pedaids.org

Despite recent advances, progress towards achieving UNHLM targets for 2022 has been slow, in particular for those related to TB prevention, diagnosis and treatment in children. The latest WHO Roadmap towards ending TB in children and adolescents reviews progress made since 2018, identifies key remaining gaps and highlights priority actions needed to deliver a coordinated response to address TB in children and adolescents.

This presentation will review practical examples and lessons learned generated by recent projects tackling TB in children and adolescents, focusing on strategies for improving TB detection, and will discuss how those can help addressing priority actions identified by the Roadmap.

#### **Scaling up stool-based Xpert testing in routine practice: Strategies to increase access and demand creation**

W Mwanza,<sup>1</sup> <sup>1</sup>Ministry of Health, Lusaka, Zambia.  
e-mail: winnie\_mwanza@yahoo.co.uk

New recommendations to improve case detection in children include use of stool as an alternative specimen for Xpert testing. Routine implementation of stool Xpert testing in Zambia has shown increased access to bacteriological testing in children and improvements in bacteriological confirmation.

This presentation will demonstrate contribution of stool to Xpert testing of pediatric samples over time and increases in pediatric case notification. The presentation will also discuss strategies to optimize stool utilization including factors for successful buy in at all levels of the health system, challenges of ensuring demand creation for stool-based testing and M&E needs for routine settings.

### **Promoting and scaling up timely diagnosis of TB infection and TB disease among children, experience from Ukraine**

G Dravniec,<sup>1</sup> <sup>1</sup>PATH, Kyiv, Ukraine.  
e-mail: gdravniec@path.org

USAID funded Support TB Control Efforts in Ukraine project (STBCEU), implemented by PATH, provides multifaceted support to advance quality of TB care among children. Project boosted LTBI diagnosis through engagement of private laboratories.

An increasing proportion of patients with positive test results are accepting TB and DR-TB preventive treatment. STBCEU supports the introduction of stool testing with Xpert® MTB/RIF Ultra cartridges for TB diagnosis.

During the first month of the war, stool testing came to an almost complete stop, but then resumed quickly demonstrating that it has been successfully included in routine practice for TB diagnosis among children.

#### **Estimating the magnitude of missing TB-HIV cases among children: Where are the gaps?**

R Briceno-Robaugh,<sup>1</sup> <sup>1</sup>USAID, Washington D.C., United States.  
e-mail: rbricenorobaugh@usaid.gov

As the largest HIV program globally, the President's Emergency Plan for AIDS Relief (PEPFAR) supports TB diagnosis and treatment to reduce TB related deaths among people living with HIV (PLHIV). Despite the efforts and policies in place, the TB positivity yield has remained below 5%.

In order to estimate the number of missed TB episodes among PLHIV, an analysis was conducted using UNAIDS, WHO and PEPFAR data.

This presentation will feature the results estimating the number of missed episodes in children living with HIV and discuss the challenges, issues with limited data availability and trends over time.

#### **Optimising treatment decision-making for children with TB using evidence-based algorithms**

M P Sekadde-Kasirye,<sup>1</sup> <sup>1</sup>National Tuberculosis and Leprosy Program (NTLP), Kampala, Uganda.  
e-mail: moorine.sekadde@gmail.com

The recent WHO recommendation to use algorithms to facilitate treatment decision-making for children being evaluated for pulmonary tuberculosis reflects a pragmatic approach to reduce the childhood tuberculosis notification gap. The treatment-decision algorithms included in the operational handbook accompanying the WHO guidelines update were produced using an evidence-based approach.

This approach can incorporate additional data—such as of novel diagnostic tools—as they become available to develop new algorithms that reflect the available resources and priorities.

This presentation will discuss the development of the algorithms included in the operational handbook as well as considerations for future algorithm development and evaluation.

### **SP36 New tests for TB screening, diagnosis and treatment monitoring: what do we need?**

#### **Target product profiles: What are they and how they are developed**

A Korobitsyn,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: korobitsyna@who.int

Screening for and diagnostics of tuberculosis have an important role in the overall TB patient care pathway ensuring that individuals receive an accurate, rapid and quality assured diagnosis thereby informing appropriate treatment.

The World Health Organization (WHO) is updating the target product profiles for new TB diagnostics, including point-of-care sputum and non-sputum-based tests, screening tools and rapid drug-susceptibility tests for TB and drug-resistant TB. The process of developing TPP include defining the scope and main components of the product assessment, establishing steering committee and TPP development group, conducting Delphi survey and public consultation and, develop and peer review the document.

#### **Simulation-based modelling to inform target product profile development for TB diagnostics and screening tests**

A De Nooy,<sup>1</sup> <sup>1</sup>Amsterdam UMC, Amsterdam, Netherlands.  
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The development of target product profiles (TPPs) is essential in guiding the development of new diagnostic tools, however TPPs often lack evidence-based information.

A simulation-based model was developed to evaluate the trade-offs between increased access to testing and varying accuracy of new diagnostics and screening tools for Kenya, South Africa, and India.

The model aims to support TPP development by providing information on public health impact of tradeoffs between access to diagnostic tools and their accuracy.

The model also provides estimation of the desired price ranges for current and prospected levels of TB detection.

#### **New tests for TB treatment monitoring and optimisation: What do we need?**

S Den Boon,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: denboons@who.int

Sputum smear microscopy and culture are the current recommended tools for treatment monitoring and for assessing cure. However, these tests have important limitations. Furthermore, changes in the tuberculosis treatment landscape requires tests, including biomarker-based tests, that can accurately predict who will achieve successful outcomes with shorter or different treatment regimens. In this presentation, the target product profiles for future tests for TB treatment monitoring and optimization are presented with minimum and optimal targets for different characteristics. Additionally, guidance is provided on how to evaluate new TB treatment monitoring tests.

#### **New tests for TB treatment monitoring: How much would they cost?**

F Marx,<sup>1</sup> <sup>1</sup>Heidelberg University Hospital, Heidelberg, Germany.  
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New tests for TB treatment monitoring and optimisation are expected to offer considerable health benefits to patients treated for TB. Understanding cost levels at which these tests could be affordable and cost-effective for TB programmes is important ahead of their implementation.

This talk will present a model-based economic evaluation of TB treatment monitoring with subsequent adherence assessment and drug-susceptibility testing conducted to guide the development of TPPs. We estimated levels of cost for treatment monitoring at which new tests could be cost-effective at different levels of willingness to pay, using conventional smear-microscopy-based monitoring as a reference.

#### **Patient-pathway analysis of TB treatment monitoring**

A Gupta-Wright,<sup>1</sup> <sup>1</sup>University College London, London, United Kingdom.  
e-mail: ankurgw@outlook.com

Integrating new technologies and diagnostics into care pathways is complex. Mapping and understanding care pathways can inform the best fit for new technologies, and identify opportunities for improvement, cost savings and more efficient processes.



Care pathway analysis has been cited as a way of improving downstream impact of possible new tests on patient outcomes.

In this presentation we present the current TB care pathway based on a review of TB guidelines, a literature review on implementation of TB treatment monitoring, and results from an implementation survey of national TB programmes and highlight how new tests could be integrated.

### **SP37 WHO methods for estimating the global burden of TB disease**

#### **WHO Task Force on TB impact measurement and progress towards global targets**

A Dean,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: deanan@who.int

The WHO Task Force on TB Impact Measurement was established in 2006 to periodically review methods used to estimate TB disease burden and ensure robust, rigorous, and consensus-based assessment of progress towards milestones and targets for reductions in TB disease. This includes targets laid out in WHO's End TB Strategy and the UN Sustainable Development Goals for reducing TB incidence and mortality and improving TB treatment coverage. Due to the Covid-19 pandemic, progress made in recent years has stalled or reversed, and global targets are now off-track.

#### **Overview of WHO methods for estimating TB incidence and mortality**

M Bastard,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: bastardm@who.int

Methods used to estimate TB incidence vary depending on data availability and TB epidemiology. They can be informed by results from TB prevalence surveys; case notifications with adjustments to account for under-reporting, underdiagnosis and/or presumed underlying trends; national inventory studies; and mathematical models for countries that experienced significant Covid-related disruptions.

To estimate TB mortality, the main methods are direct measurements of mortality from vital registration systems; indirect estimation derived by applying case fatality ratios to TB incidence estimates; and mathematical models.

### **The impact of COVID-19 on the burden of TB disease**

N Arinaminpathy,<sup>1</sup> <sup>1</sup>Imperial College London, London, United Kingdom.  
e-mail: nim.pathy@imperial.ac.uk

Disruptions to TB services during COVID-19 have posed challenges in the estimation of TB incidence and mortality. Mathematical modelling can help to address these challenges, by systematically incorporating data for the depth and duration of disruptions in different countries. We present results from this modelling, that have informed WHO's estimation of TB incidence and mortality since 2021. Based on monthly and quarterly notifications from countries, modelling has been used for the 25 countries that accounted for over 95% of the global drop in notifications, compared to 2019. We also discuss approaches for refining these estimates in future years.

### **Disaggregation of TB incidence and mortality by age and sex**

P Dodd,<sup>1</sup> <sup>1</sup>University of Sheffield, Sheffield, United Kingdom.  
e-mail: p.j.dodd@sheffield.ac.uk

Methods developed to disaggregate WHO estimates of TB incidence and mortality for each country by sex and age will be presented. Incidence is disaggregated following notification patterns in countries with <1000 tuberculosis notifications or case detection ratio over 0.85. Otherwise, patterns are based on samples from a prior conditioned by case notifications. Mortality is disaggregated proportional to patterns in vital registration data, or where these data are lacking, using case fatality ratios applied to estimated incidence. Areas where additional data or analysis could improve this approach will be discussed.

### **Improving data availability and quality to inform disease burden estimation in the post-COVID era**

C Sismanidis,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: sismanidisc@who.int

Improving the availability and quality of data in countries is critical to improving the robustness of TB disease burden estimates, particularly in view of greater uncertainty around these estimates due to the Covid-19 pandemic. There is an urgent need to strengthen TB surveillance systems to ensure systematic and continuous collection, analysis, reporting and use of data related to TB infection and disease in countries. In certain settings, these efforts should be supported by specific surveys and studies to measure under-reporting and/or under-diagnosis of TB as well as mortality due to TB.

## **SP38 Shorter vs. safer – different perspectives on regimen duration**

### **Treatment shortening as a key research priority**

S Dorman,<sup>1</sup> <sup>1</sup>Medical University of South Carolina, Charleston, United States.  
e-mail: dorman@muscc.edu

This talk will review recent and historical progress in shortening the duration of treatment for latent tuberculosis infection and drug-susceptible tuberculosis. Advantages of shortening treatment and rationale for treatment shortening as a primary clinical trial goal will be discussed.

This will be a review of all the advantages for short regimens for TPT, DSTB and MDRTB – from programme and individual perspectives.

### **Treatment shortening: safer and better-tolerated regimens should be our primary research focus**

B Burman,<sup>1</sup> <sup>1</sup>Public Health Institute at Denver Health, Denver, United States.  
e-mail: bill.burman@dhha.org

Clinical trials of treatment of drug-susceptible TB disease have focused almost exclusively on treatment shortening. However, it is not clear that treatment duration is the key barrier to cure of drug-susceptible TB.

Toxicity and intolerability to currently used medications are common, especially among older patients; these represent major barriers to treatment completion and cure. Furthermore, the strategies used to shorten treatment such as higher dose rifamycins and the addition of other agents, such as moxifloxacin, are likely decrease to tolerability. It is time to make the identification of safer and better tolerated regimens the primary focus of TB trials.

### **Shorter MDR-TB treatment regimens - yes, but can we make them safer?**

B Nyang'wa,<sup>1</sup> <sup>1</sup>Médecins Sans Frontières, United Kingdom.  
e-mail: bern.nyangwa@london.msf.org

WHO has recommended BPALM regimen, a shorter, safer and more effective treatment for Rifampicin-Resistant tuberculosis.

The presentation will cover: Safety insights as well as pharmacokinetics and pharmacodynamics of the BPAL, BPALM and BPALC regimens from the TB-PRACTECAL trial. Reflection on the trade-offs of efficacy vs safety in the TB-PRACTECAL trial regimens on oxazolidinone choice, dose and duration. Will discuss potential av-

enues of optimising short RR-TB regimens, and make a case that the route to optimising the performance of short regimens is to improve their safety.

### **Shorter vs. safer treatment regimens – giving people with drug-resistant TB a voice in the debate**

A Daftary,<sup>1</sup> <sup>1</sup>York University, Toronto, Canada.  
e-mail: adaftary@yorku.ca

As TB service providers and program managers work hard to dispel incorrect community assumptions and myths about TB treatment, they would be served well to reflect on the incorrect assumptions and myths they might hold about the treatment values, preferences and priorities of people affected by TB.

This talk will draw on qualitative research with TB survivors in four TB-affected regions (Africa, Americas, Asia, Europe) to show how acceptability towards shorter regimens and a lower pill burden are balanced against perceived treatment safety and particular side effects, including those with differential clinical relevance.

### **Shorter vs. safer treatment regimens – the Global TB Community Advisory Board's perspective**

O Rucsineanu,<sup>1</sup> <sup>1</sup>Global TB Community Advisory Board (TB CAB), Moldova National Association of TB Patients "SMIT", Balti, Moldova.  
e-mail: oxana\_rucs@yahoo.com

Treatment shortening is a major driving force behind many ongoing and planned clinical trials. Although treatment duration is one challenging component of TB therapy, pill burden, side effects, and management of comorbid conditions are also important considerations. In considering optimal TB treatment regimens, these considerations may be weighed differently by affected communities than they are by clinicians, programs, researchers, and research funders.

This perspective will discuss how members of TB affected communities and people with lived experience with TB treatment weigh these considerations, and whether the risks of drug-related toxicities are worth the benefits of treatment shortening, under what conditions.

### SP39 Another cursed duet of afflictions—tuberculosis and severe acute malnutrition in children

#### Research gaps in co-prevalent TB and severe acute malnutrition

**B Vonasek**,<sup>1</sup> <sup>1</sup>University of Wisconsin School of Medicine and Public Health, Madison, United States.  
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This presentation will describe key research areas related to the interplay between tuberculosis and SAM, particularly for children under the age of five. Priority areas for improved programmatic implementation and future research include:

1. Better understanding the epidemiologic connections between child tuberculosis and SAM,
2. Improving case finding of tuberculosis in children with SAM,
3. Assessing unique treatment considerations for tuberculosis when children also have SAM, and;
4. Ensuring tuberculosis and SAM are strongly addressed in decentralized, integrated models of providing primary healthcare to children.

#### Optimising treatment of TB in children with severe acute malnutrition

**B Perez Solans**,<sup>1</sup> <sup>1</sup>University of California San Francisco, San Francisco, United States.  
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Undernutrition leads to pathophysiologic changes that may affect a drug's pharmacokinetic characteristics. Body mass is a key driver of drug clearance, and among well-nourished children, drug clearance and body mass correlate allometrically.

However, whether this relationship is maintained in undernourished children is unclear. Since undernourished children weigh less than well-nourished children of the same age, relating clearance to body weight assumes slower clearance in undernourished children. This may underestimate an undernourished child's capacity to eliminate a drug, resulting in sub-therapeutic drug exposure.

This presentation will provide examples of drugs for which malnutrition impacts their treatment exposure and optimal dosing proposals.

### Hospitalised children with pneumonia and severe acute malnutrition – a key group for TB case-finding

**C Chabala**,<sup>1</sup> <sup>1</sup>University of Zambia, School of Medicine, Lusaka, Zambia.  
e-mail: cchabala@gmail.com

Hospitalised children with severe pneumonia and severe acute malnutrition (SAM) are key risk groups for tuberculosis. Prompt diagnosis and treatment is cardinal in reducing tuberculosis-associated mortality in these vulnerable groups.

We conducted two prospective multicenter studies in under-5 children with severe pneumonia and SAM.

The aims were to:

- i. Evaluate the impact of systematic screening on mortality from pneumonia;
- ii. Prevalence and mortality of TB in children with SAM.

We report on the burden of tuberculosis in hospitalized children with severe pneumonia and SAM, the impact of SAM on mortality in both groups.

### One-year mortality in children hospitalised for severe acute malnutrition – role for TB preventive therapy or targeted interventions for vulnerable groups

**M Bwakura-Dangarembizi**,<sup>1</sup> <sup>1</sup>University of Zimbabwe, Harare, Zimbabwe.  
e-mail: dangas@zol.co.zw

The presentation will focus on the HOPE SAM study, an observational cohort in Zimbabwe and Zambia whose aim was to characterize 1-year clinical and nutritional outcomes in children who were hospitalised for SAM.

The study identified the major risk factors for poor outcomes, and the continued vulnerability of children discharged from hospital following treatment of complicated SAM.

The presentation will discuss the evidence of morbidity and mortality from TB in this population. Our upcoming Co-SAM study, aiming to test a package of multi-modal interventions including TB preventive therapy to improve outcomes for children with SAM, will also be introduced.

### Screening to identify presumptive TB requiring full diagnostic assessment among children hospitalised with severe acute malnutrition

**O Marcy**,<sup>1</sup> <sup>1</sup>University of Bordeaux/IRD, Bordeaux, France.  
e-mail: olivier.marcy@u-bordeaux.fr

TB diagnosis is challenging in children with SAM, which further fuels mortality in children with both diseases. Treatment decision algorithms (TDAs), recently recommended by the WHO for childhood TB diagnosis could

enhance case detection in this vulnerable population. Screening is key to identify children with presumptive TB requiring thorough diagnostic assessment. The TB-Speed SAM study assessed the added value of symptoms and simple biomarkers, the monocyte-lymphocyte ratio, haemoglobin count, C-reactive protein, and QuantiFERON-TB Gold In-Tube assay for TB screening in children hospitalized with SAM. Resulting screening and diagnosis TDA performances and implication for public health will be presented.

### **SP40 Towards sustainable tobacco control: Strategies and practices for a healthier future**

#### **Towards sustainable tobacco control: Experiences from the Asia Pacific Region**

T Bam,<sup>1</sup> <sup>1</sup>International Union Against Tuberculosis and Lung Disease, Singapore, Singapore.  
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The Asia Pacific region is home to some of the world's largest tobacco markets and faces unique challenges in implementing effective tobacco control policies. However, the region has also made significant strides in developing sustainable approaches to tobacco control that not only reduce tobacco use but also address social, economic, and environmental factors that contribute to tobacco use.

With a focus on sustainability, the session will explore the intersection of tobacco control with environmental, social, and economic issues; sharing experiences and best practices in implementing sustainable tobacco control policies and programs, in the Asia Pacific region.

#### **Building effective partnerships for sustainable tobacco control: Advocacy and policy change**

S Goel,<sup>1</sup> <sup>1</sup>Post Graduate Institute of Medical Education & Research (PGIMER Chandigarh), Chandigarh, India.  
e-mail: sonugoel007@yahoo.co.in

In order to address the complex challenges associated with tobacco control, it is critical to engage a wide range of stakeholders across departments and institutions. This session would emphasize the importance of setting shared goals and objectives, and utilizing one another's resources and strengths, & bringing together diverse perspectives and expertise; contributing to the development of a stronger advocacy movement and raising the possibility of effective policy change.

#### **Collaborating for a tobacco-free future: The role of government and global interagency organisations in advancing the UN Sustainable Development Goals**

A Yadav,<sup>1</sup> <sup>1</sup>The International Union Against Tuberculosis and Lung Disease, New Delhi, India.  
e-mail: Amit.Yadav@theunion.org

Integrating tobacco control into advancing Sustainable Development Goals (SDGs) is crucial, as it can significantly contribute to achieving several SDGs related to good health and well-being, reducing inequality, and promoting sustainable cities and communities. To achieve SDGs, it is essential to have a coordinated effort between governments and interagency organizations. The session would highlight how collaboration and partnership, between governments and interagency organizations could lead to a tobacco-free world that promotes health, equity, and sustainable development.

## **SYMPOSIA: SATURDAY 18 NOVEMBER 2023**

### **SP41 Ending TB-related stigma through evidence-based interventions and policies: the time is now! (Coordinated by Dr Tom Wingfield, LSTM)**

#### **Analysing interventions to reduce TB-related stigma - findings from a scoping review**

R Nathavitharana,<sup>1</sup> <sup>1</sup>Harvard Medical School and TB Proof, Boston, United States.  
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Dr. Nathavitharana will discuss findings of a scoping review using the Health Stigma and Discrimination framework to characterize TB stigma reduction interventions categorized by socio-ecological level, then sub-categorized by the stigma driver or manifestation targeted. Data from nine studies comprised: interventions at the individual or interpersonal level including support clubs or household counselling, interventions at the health facility or organizational level including educational workshops or participatory theatre with health workers, and community interventions including an educational campaign. Policy interventions were absent. Key research and reporting gaps include the need for consistent stigma definitions, measurement approaches, and implementation outcome assessment.

#### **The social outcomes of the community randomised evaluation of socioeconomic intervention to prevent TB (CRESIPT) trial**

S Datta,<sup>1</sup> <sup>1</sup>Liverpool School of Tropical Medicine, Liverpool, United Kingdom.  
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The Community Randomised Evaluation of Socioeconomic Intervention to Prevent TB (CRESIPT) trial has evaluated an integrated socio-economic support package offered to all households in which someone was diagnosed with TB disease in 32 communities in northern Lima, Peru. Although the primary outcomes were patient cure and TB prevention in household contacts; secondary social outcomes such as TB-related stigma, social capital, depression and wellbeing were also expected to be impacted by the intervention and the results will be presented.

### **Evaluating the psychosocial impact of TB and co-developing a community-based peer-led psychosocial support intervention for people affected by TB in Indonesia**

A Fuady,<sup>1</sup> <sup>1</sup>Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia.  
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TB-Stigma is associated with other psychosocial consequences of TB including mental illness and reduced quality of life (QoL). In a primary health facility-based survey in seven provinces of Indonesia, we found that there is a sizeable and intersecting burden of TB-Stigma and depression among adults with TB in Indonesia, which is associated with lower QoL. Participants reported a substantial unmet need for psychosocial support including peer-led mutual support groups. Based on these findings, we are working with TB-affected people and key multisectoral stakeholders to co-develop a community-based peer-led psychosocial support intervention to defray the psychosocial impact of TB in Indonesia.

### **SP41 Ending TB-related stigma through evidence-based interventions and policies: the time is now! (Coordinated by Dr Tom Wingfield, LSTM)**

#### **Barriers to TB testing in Cameroon: TB stigma in context**

E Mitchell,<sup>1</sup> <sup>1</sup>Institute for Tropical Medicine, Antwerp, Belgium, Antwerp, Belgium.  
e-mail: emitchell@itg.be

It is often assumed that TB stigma is a major barrier to TB case seeking. However as understanding of TB epidemiology has shifted to acknowledge asymptomatic transmission and disease, it is timely to revisit the question of whether anticipated stigma does inhibit test acceptance.

A unique case-control design recruited 958 (testers) and 114 (non-testers) from passively and actively referred clients from 6 regions of Cameroon. Anticipated TB stigma and stigmatizing attitudes were assessed as potential drivers of testing behavior in the context of access, acceptability, and affordability measures. When analyzed comprehensively, gender and stigmatizing views remain barriers to TB testing.

## **Translating the evidence on TB stigma to shape policies and practices**

A Daftary,<sup>1</sup> <sup>1</sup>York University, Toronto, Canada.  
e-mail: adaftary@yorku.ca

There is increasing evidence on the drivers, manifestations, and impacts of TB stigma on TB and related social and mental health outcomes. Destigmatizing TB demands the rapid translation of these data to changes in health and social policy and practice. Initiatives from South Africa, India, and Canada, among other countries, are exemplifying how community and civil society leadership, reoriented policy framings and service delivery processes, and multisectoral actions can combat TB stigma. The creation of indicators and targets to support stigma elimination can help to galvanize funding and commitment to move this agenda forward.

## **SP42 Tackling TB in crisis: threats and opportunities**

### **Innovative, person-centred model of care delivery to improve treatment outcomes for RR-TB: Experience from Kandahar, Afghanistan**

A Mesic,<sup>1</sup> <sup>1</sup>Médecins Sans Frontières, Amsterdam, Netherlands.  
e-mail: anitamesic@gmail.com

Since 2016, Médecins Sans Frontières has been providing care for people with rifampicin-resistant tuberculosis (RR-TB) in Kandahar, Afghanistan. Conventional, centralized healthcare approaches have proven to limit access to care, particularly in challenging settings where they have visibly augmented access barriers.

To overcome these challenges, we implemented innovative models of care with strengthened contingency planning, short all-oral regimens for RR-TB, delivered through person-centered care that emphasized patients' autonomy. This approach proved to be feasible and significantly improved treatment outcomes, despite adverse circumstances due to instability and the COVID-19 pandemic.

## **Building resilience against TB and climate change: Overcoming challenges in the aftermath of Pakistan's devastating floods**

U Khan,<sup>1</sup> <sup>1</sup>IRD Global, Montreal, Canada.  
e-mail: uzma.khan@ird.global

The 2022 floods in Pakistan caused immense devastation, claiming numerous lives, displacing millions, and crippling the health system. It was one of the worst humanitarian crises in the country's history, burdening TB-affected communities with dire health consequences and outbreaks. The floods rendered numerous TB diagnosis and treatment sites underwater and dysfunctional for months.

In this presentation, we share challenges in TB service delivery and the resilience of patients, communities, and health workers in overcoming them. It is our hope that this will spur much-needed debate to take the threat of climate change seriously and develop strategies to mitigate future risks.

## **Navigating the challenges of TB management in conflict areas: Insights from North Kivu Province, DRC**

R Biya Nkizinkiko,<sup>1</sup> <sup>1</sup>Goma University, Goma, Congo (Democratic Republic).  
e-mail: biyarobert1@gmail.com

This presentation will cover the Coordination Provinciale Leprosy and Tuberculosis (CPLT) mapping, providing insight into the existing infrastructure for TB management in the region.

We will share the latest trends in TB case notifications, including paediatric TB, from 2018 to 2022, as well as the burden of TB/HIV co-infection, MDR-TB, and their impact on TB treatment outcomes in conflict-affected areas. We will use images to illustrate the challenges faced and lessons learned in implementing TB services in these areas. Additionally, we will discuss future opportunities for use of innovative approaches to improve TB management in North Kivu Province.

## **TB and conflict in Ukraine: Understanding the impact of the war on TB-affected people and communities**

O Klymenko,<sup>1</sup> <sup>1</sup>TBpeople Ukraine, Ukraine.  
e-mail: olyaklymenko2910@gmail.com

The conflict in Ukraine has resulted in a severe humanitarian crisis, with significant implications for tuberculosis (TB) services.

This presentation will focus on the impact of the conflict on TB care, highlighting the challenges of accessing services, widening health disparities, and increasing discrimination. Real-world examples will showcase how the conflict has jeopardized efforts in TB response, em-

phasizing the urgent need for innovative, locally driven mechanisms that engage affected communities in addressing inequitable practices that impede healthcare access. The audience will gain deeper understanding of the critical role of community engagement in promoting equitable and effective TB care in crisis settings.

### **Breaking the silence: The urgent need for international action on TB in crisis settings**

T Abdullaev,<sup>1</sup> TBpeople Global, Tashkent, Uzbekistan.  
e-mail: abdullaev@gmail.com

Humanitarian crisis settings create a complex patient pathway, hindering access to TB services and imposing a significant burden on affected individuals. There continues to be unrealistic expectation from governments and affected individuals to mobilize domestic resources or procure life-saving TB medicines and diagnostics on their own. This demonstrates a lack of ownership by the international community for those affected by TB in crisis settings.

This presentation will feature examples, personal stories of people affected by TB, and insights from those working in crisis settings and engage the audience in reflecting on their role in effectively advocating for affected communities everywhere.

### **SP43 The BPaLM accelerator for scaling up the newly recommended 6-month treatment regimen for drug-resistant TB**

#### **A call to action and the accelerator platform for scaling up of the 6-month BPaLM regimen**

F Mirzayev,<sup>1</sup> Global Tuberculosis Programme, World Health Organization, Baku, Azerbaijan.  
e-mail: mirzayevf@who.int

This presentation will describe the Call to Action on the scale up of the newly recommended 6-month regimen for treatment of drug-resistant TB, and a recently established WHO BPaLM Accelerator Platform for technical discussions on rolling out of the BPaLM regimen. These two initiatives are to support the implementation of the new shorter and effective regimen for treatment of drug-resistant tuberculosis as recommended by WHO in the updated consolidated guidelines on tuberculosis treatment.

### **BPaLM: Global Drug Facility update on market-shaping and scale-up**

B Waning,<sup>1</sup> Global Drug Facility, Stop TB Partnership, Geneva, Switzerland.  
e-mail: brendaw@stoptb.org

This presentation will describe the size, structure, and composition of markets for medicines used in the BPaLM regimen. Details will be provided to facilitate national procurement and planning, including trends in medicine supplier base, formulation development, regulatory and registration status, price, and forecasts. Updates, projections, and timelines of BPaLM scale-up at national level will also be provided, together with lessons learned for early adoption.

### **Promoting access to shorter regimens for everyone, everywhere as a human right: The 1/4/6x24 Campaign**

L McKenna,<sup>1</sup> Treatment Action Group, New York, United States.  
e-mail: Lindsay.McKenna@treatmentactiongroup.org

Shorter, safer, more effective TB prevention and treatment regimens are the result of the last two decades of investments in TB research and development. We can now prevent TB using one month or once weekly regimens, and treat TB in as few as four months for drug-sensitive TB and six-months for drug-resistant TB using evidence-based, WHO-recommended regimens. Yet, very few communities affected by TB globally have access to these important innovations.

This presentation will describe the 1/4/6x24 Campaign, progress, continued challenges, and actions necessary for everyone, everywhere to benefit from access to shorter regimens.

### **Integration of DS-TB and DR-TB treatment using BPaLM in South Africa**

N Ndjeka,<sup>1</sup> National Department of Health, South Africa.  
e-mail: norbert.ndjeka@health.gov.za

South Africa is a high burden TB, HIV and MDR-TB country. Primary health care (PHC) is the vehicle for service provision. Integration and decentralization of services play key roles in this context. All health care facilities, including 3500 + PHC sites diagnose and treat DS-TB and HIV. While DR-TB may be diagnosed from any facility in the country, there are only 658 treatment sites that treat DR-TB.

This paper discusses the introduction of BPaLM, a shorter, all-oral, less complex regimen as an opportunity to strengthen integration of DS-TB and DR-TB care in South Africa.

### **Demand on rolling out of new shorter regimens for TB treatment**

O Khuat,<sup>1</sup> <sup>1</sup>Center for Supporting Community Development Initiatives (SCDI), Ha Noi, Vietnam.  
e-mail: oanhkhuat@scdi.org.vn

The presentation will present the needs for speedy scale-up of new recommended shorter regimens such as the 6-month BPaLM regimen for drug-resistant TB treatment or 4-month regimens for treatment of drug-susceptible TB, as a community demand and for benefits of people with TB. This is to call for all the countries, funders, and technical partners to join forces in rolling out of the shorter regimens to benefit people who suffer from the TB disease in reducing treatment duration, achieving high efficacy and safety, and saving resources for health systems as well as individual patients and families.

### **SP44 Addressing methodological challenges in analysis and interpretation of TB data from observational studies**

#### **Reliable data management in large population based studies: Challenges and opportunities**

H Timime,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
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As someone once said, “Garbage in, Garbage out” can accurately reflect the key principles of good data management. If data are not accurately managed, there is only so much data analysis that can be done to provide reliable results.

In this presentation, examples of best and worst practices from large population-based studies will be described; and arguments for investing in skilled people and taking the time to develop methods to manage massive amounts of data.

#### **Multiple imputation and best practices to handle missing data in TB observational studies**

M Bastard,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: bastardm@who.int

Missing data are common in most of observational studies and is a complex process often ignored during data analysis. The absence of reporting and handling missing data can lead to misinterpretation of the results, bias estimates of the statistics of interest and artificially narrow confidence intervals.

In this presentation, we will present the different processes of missing data encountered in TB observational studies, provide guidance on best practices to handle missing data during data analysis and to report study findings and illustrate the application of the methodology presented using data from a national TB prevalence survey.

#### **Target trial emulation to estimate the comparative effectiveness of treatment strategies for patients in whom a fluoroquinolone is unlikely to be effective.**

M Franke,<sup>1</sup> <sup>1</sup>Harvard Medical School, Boston, United States.  
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This presentation will provide an example of target trial emulation for the design of analyses on optimal treatment for RR/MDR-TB.

We will describe a target trial to estimate the relative effectiveness of five strategies for reinforcing a core regimen of bedaquiline, linezolid, and clofazimine for patients in whom a fluoroquinolone is unlikely to be effective.

We will also describe a three-step analytic strategy (consisting of cloning, censoring, and weighting) to emulate the target trial.

#### **Marginal structural models for addressing selection bias, confounding and irregular treatment initiation times in observational studies**

D Benkeser,<sup>1</sup> <sup>1</sup>Emory University Rollins School of Public Health, Atlanta, United States.  
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Randomized controlled trials are the gold standard for establishing efficacy of interventions. To learn about effectiveness of an intervention, we typically rely on observational data.

Nevertheless, it is often constructive to describe a hypothetical randomized controlled trial (target trial) that the analysis of an observational study is attempting to emulate. We motivate this approach using the example of using electronic health records to evaluate the effectiveness of TB preventive treatment.

We will also describe how marginal structural models can be used to define analyses that mimic standard clinical trials analyses, such as those based on Cox proportional hazards regression models.



### **Targeted maximum likelihood estimation for network meta-analysis of individual participant data**

M Schnitzer,<sup>1</sup> <sup>1</sup>Université de Montréal, Montréal, Canada.  
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Treatment of multidrug-resistant or rifampicin-resistant tuberculosis involves taking several effective antimicrobials over a prolonged period of time. It is important to define and estimate the relative effectiveness of specific regimens for the treatment of the disease.

We will discuss the use of targeted maximum likelihood estimation for individual patient data network meta-analysis with the Highly-Adaptive LASSO to investigate the contributions of bedaquiline to favorable clinical outcomes.

We will also describe how to incorporate the targeted trial approach of “treatment strategies” to determine causal differences between relevant regimens that include and exclude a particular drug.

### **SP45 OneImpact: A community-led monitoring (CLM) platform for people affected by TB**

#### **Innovations in community-led monitoring to maximise reach among people affected by TB**

V Dutta,<sup>1</sup> <sup>1</sup>Dure Technologies, Mumbai, India.  
e-mail: viplove.dutta@duretechnologies.com

OneImpact is a comprehensive digital platform made up of three tools that work together to provide a comprehensive community empowerment, community engagement and community-led monitoring solution that puts people at the heart of the TB response.

This presentation would aim to introduce all the tools, modules, and technical framework of the platform.

#### **Educating, engaging and empowering communities for accountable health response in Nigeria**

D Ikeh,<sup>1</sup> <sup>1</sup>Debriche Health Development Center (DHDC), Abuja, Nigeria.  
e-mail: deborah@dhdc.org.ng

A success story of OneImpact Nigeria on how digital CLM is improving awareness around TB prevention, TB care, TB support services, and the rights of people affected by TB, supporting to strengthen accountable health response from the health facility to national level programmatic change.

### **Sharing experiences and learnings from CLM implementation in the DRC**

M Lunga,<sup>1</sup> <sup>1</sup>Club des Amis Damien, Kinshasa, Congo (Democratic Republic).  
e-mail: maxilunga@yahoo.fr

In DRC the fight against TB is hampered by several challenges. However, one of the biggest issues is the lack of any systematic data collection system, not only does it hinder TB care accessibility, particularly for people who experience human rights violations and stigma at facilities, but it also impacts health system response and accountability.

This presentation would cover, how implementing the OneImpact DRC helped to address the gaps identified and highlighted by the communities.

### **SP46 Digital chest X-ray and computer-aided detection (d-CXR/CAD) – accelerating adoption to find the missing people with TB**

#### **d-CXR/CAD: A valuable tool for finding and serving people with TB**

D Falzon,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
e-mail: falzond@who.int

This presentation will deal with the evidence and implementation considerations behind the WHO recommendation on Computer Aided Detection (CAD) for TB screening or triage

#### **Top considerations in selecting d-CXR/CAD technologies**

S Kik,<sup>1</sup> <sup>1</sup>FIND, Geneva, Switzerland.  
e-mail: sandra.kik@finddx.org

This presentation will offer a taxonomy of d-CXR and CAD technologies and an overview of top considerations when selecting technology to build or scale up a TB detection program.

This presentation will include how to define the TB program’s requirements to help ensure successful implementation in the health system, and will discuss setting detection thresholds.

Finally, the presentation will outline available information resources that allow TB program managers to compare attributes of CAD technologies.

### **Closing gaps in active TB case-finding using digital X-ray and computer-aided detection (CAD) in rural Lesotho**

A Andom,<sup>1</sup> <sup>1</sup>Partners In Health, Maseru, Lesotho.  
e-mail: aandom@pih.org

This presentation will offer practical insights from d-CXR/CAD implementation in Lesotho. Lesotho has the highest TB incidence in the world- an estimated 614 cases per 100,000 population- and TB case-finding of only 32%. Partners In Health (PIH) has supported the Ministry of Health to introduce d-CXR machines and CAD systems, in hard-to-reach, rural health centers, to find more missing people with TB. The introduction of d-CXR/CAD systems resulted in a three-times increase in the number of people detected with TB during an intervention period.

The presentation will explore how d-CXR/CAD has helped health centers to reach their TB detection targets.

### **SP46 Digital chest X-ray and computer-aided detection (d-CXR/CAD) – accelerating adoption to find the missing people with TB**

#### **From idea to action: Successful d-CXR/CAD implementation for healthcare**

M Campbell,<sup>1</sup> <sup>1</sup>Clinton Health Access Initiative (CHA), Boston, United States.  
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This presentation will explore how to foster long range success of d-CXR/CAD programs for TB detection. d-CXR/CAD has great potential to increase TB case finding in low- and middle-income countries (LMICs). Uptake by Ministries of Health (MOHs) and National TB Programs (NTPs) has been slow, underscoring that WHO recommendations alone will not be sufficient to accelerate the adoption of these new tools.

The presentation will discuss building country readiness for adoption, ensuring affordable access pricing and sustainable total costs of ownership, and building operational models which fully realize the clinical and public health potential of these solutions.

### **SP47 Advancing the TB diagnostics pipeline - results from three large NIH-funded research consortia**

#### **Advancing TB diagnostics research through synergy and coordination**

C Denkinger,<sup>1</sup> <sup>1</sup>Heidelberg University, Heidelberg, Germany.  
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Several grants have been recently awarded to enable sustained advancements in TB diagnostics with the target to achieve the goals of the UN Resolution on TB from 2018.

This presentation will provide an overview of the three NIH funded Feasibility of Novel Diagnostics for TB in Endemic Countries (FEND for TB) grants: R2D2, FEND-TB and EndxTB, the consortium partners, trial networks, populations studied and use cases.

Then, we will elaborate on how the FEND grants align with programmatic grants recently funded, such as SMART4TB of USAID and DriveDxTB of UNITAID and other project-based grants.

#### **Digital and AI-based approaches to TB triage/screening**

Y Xie,<sup>1</sup> <sup>1</sup>Rutgers New Jersey Medical school, Newark, United States.  
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A robust pipeline of digital technologies with AI-based interpretations have opened key opportunities for reducing costs and enhancing efficiency of detecting TB across the spectrum.

We will review the progress and underlying concepts behind these technologies (e.g. AI-interpreted imaging and sound capture devices) and discuss their role in settings where diagnostic resources and clinical expertise are scarce.

We will also delve into the potential challenges and key opportunities of incorporating these tools into TB screening programs.

#### **Host markers for TB triage and screening in children and adults**

J Sutherland,<sup>1</sup> <sup>1</sup>MRC Unit The Gambia, Fajara, Gambia.  
e-mail: Jayne.Sutherland@lshtm.ac.uk

The ENDxTB, R2D2 and FEND project recruit participants with symptoms suggestive of TB. Adult and young children are included in the study.

In addition, treatment response is monitored at 3 time-points and progression to active TB is investigated in recent household contacts of active TB cases to evalu-

ate the utility of the novel POC tests in diagnosing TB, predicting poor treatment outcome and progression to TB. Here, we will present the promising data on triage tests in symptomatic patients.

### **Advances in swab-based molecular testing for TB diagnosis**

A Andama,<sup>1</sup> <sup>1</sup>Makerere University College of Health Sciences, Kampala, Uganda.  
e-mail: andama.alf@gmail.com

Tongue swabs are a promising alternative to sputum-based molecular testing for tuberculosis (TB), especially among populations unable to produce adequate sputum (e.g., children and PLHIV). The talk will describe the latest learnings on optimal tongue swab collection and processing methods, describe initial results from validation studies on existing diagnostic platforms (GeneXpert [Cepheid] and Truenat [Molbio]), and discuss how advances in COVID-19 diagnostics are being leveraged to further advance tongue swab-based molecular testing for TB.

### **Other promising advances in the diagnosis of pulmonary, extrapulmonary and drug-resistant TB**

C Ugarte-Gil,<sup>1</sup> <sup>1</sup>UTMB School of Public & Population Health, Galveston, United States.  
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In recent years, there have been several promising advances in the diagnosis of tuberculosis (TB), extrapulmonary TB and DR-TB. In TB diagnosis, there are more efforts to get biological samples different to sputum (such as breath-based tests), improving the accuracy for samples from extrapulmonary TB developing more accurate and rapid tests for drug-resistant strains of TB. These advances are crucial for TB prevention and care or ending TB, particularly in high burden countries with limited resources for diagnosis.

### **SP48 Right place, right time: the ECHO virtual community of practice model transforms clinical and public health evidence into practice**

#### **Training HIV teams in the management of extrapulmonary TB through e-NISCHIT in India**

U Agarwal,<sup>1</sup> <sup>1</sup>National Institute of Tuberculosis and Respiratory Diseases, New Delhi, India.  
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E NISCHIT, an ECHO distance learning clinic established in 2018, offers case-based learning to 150 government-run primary HIV clinics across 13 Indian states. In collaboration with NITRD, National TB and AIDS programs, CDC, ECHO India, and Share India, the program has improved early diagnosis and treatment of pulmonary TB in people living with HIV (PLHIV) through rapid tests and training. However, timely diagnosis of extra pulmonary TB (EPTB) remains a challenge due to its varied presentations. To address this, e-NISCHIT is focusing on real-time HIV-EPTB cases, engaging tertiary-level medical experts for in-depth case discussions and specialized skill-sharing.

#### **Ensuring quality TB and specialty care for TB patients through a strong e-learning platform during the COVID-19 pandemic in Georgia**

N Lomtadze,<sup>1</sup> <sup>1</sup>National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia.  
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COVID-19 significantly impacted Tuberculosis (TB) case detection in Georgia, resulting in a 26% decline of registered TB cases. However, quality TB treatment and care was ensured by interventions within Georgia NTP, including the TB ECHO program. Despite lock-downs and restrictions, complicated TB cases from Georgia had access to multi-disciplinary specialty care and doctors received trainings on global updates in screening, diagnosis, treatment, prevention and care through the TB-ECHO program. The program's direct impact is difficult to measure, however in parallel with other interventions, TB ECHO ensured sustained and improved treatment outcomes for MDR/RR-TB patients in Georgia during the pandemic.

### **The Ugandan CLICQ! TB continuous quality improvement initiative to close TB-HIV diagnostic gaps**

J Dawson,<sup>1</sup> <sup>1</sup>Centers for Disease Control and Prevention (CDC), Atlanta, United States.  
e-mail: kuk7@cdc.gov

The Uganda National TB/Leprosy program, supported by CDC and AFENET, recently implemented the Clinic-Laboratory Interface Continuous Quality Improvement (CLICQ!) program which included an ECHO telementoring component to address TB/HIV diagnostic gaps. By conducting patient pathway analyses and utilizing the Diagnostic Cascade Evaluation (DiCE) Toolkit, 12 clinic-laboratory pairs were enrolled. Six pairs received DiCE assessments, CLICQ! training, and virtual mentorship through Project ECHO, while the other six served as a baseline comparison, only receiving DiCE assessments. The program's impact was measured by comparing initial and follow-up DiCE assessments.

### **Nationwide expansion of the DR-TB ECHO programme to support TB elimination and capacity building of TB and HIV clinicians**

N Singla,<sup>1</sup> <sup>1</sup>National Institute of Tuberculosis and Respiratory Diseases, Sri Aurobindo Marg, New Delhi, India.  
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The DR-TB ECHO Program, initiated in 2017 by the National Institute of Tuberculosis and Respiratory Diseases (NITRD), aims to improve District TB Medical officers' management of drug-resistant tuberculosis cases through expert-led presentations and discussion of case studies.

Due to its success, India's government has incorporated it into the National Guidelines for Programmatic Management of DRTB, leading to implementation in 26 states, addressing over 300 cases, and attracting an average of 125 attendees per session. NITRD also partners with NACO for the TB-HIV co-infection ECHO program. These telementoring clinics enhance medical doctors' capacities and positively impact patients' lives.

### **SP49 Into the unknown: Drug-resistant TB in pregnancy**

#### **A case-based discussion of drug-resistant TB in pregnancy**

M Alexander,<sup>1</sup> <sup>1</sup>Byramjee Jeebhoy Medical College Clinical Trial Unit, BJ Medical College, Pune, India.  
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Pregnant people have a high risk of developing active TB, but often present with subclinical and incipient TB, complicating diagnosis and management. GeneXpert Ultra has improved sensitivity for subclinical cases but raises new questions:

Should you treat an asymptomatic pregnant person who has *M. tuberculosis* detected by Xpert Ultra?

How do you advise an asymptomatic pregnant person with drug-resistant TB?

Does management change if they are living with HIV?

In this talk, Dr. Alexander will present 3 cases of drug-resistant TB from India to highlight the challenges and research gaps for DR-TB management in pregnant people.

#### **The significance of subclinical TB - a pivotal paradox**

F Cobelens,<sup>1</sup> <sup>1</sup>Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands.  
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There is increasing recognition of the existence of a pre-clinical stage of TB with high rates of progression to active disease characterized by viable *M. tuberculosis* but no symptoms, radiographic changes, or microbiologic evidence of active TB disease (aka incipient TB). With the advent of GeneXpert Ultra and other highly sensitive diagnostics, clinicians are seeing more and more such preclinical stages, including during pregnancy, but are uncertain about what it means.

In this talk, Dr. Cobelens will review the epidemiology, definitions, diagnostic challenges, treatment and clinical outcomes of incipient TB and the implications for managing TB during pregnancy.

#### **Drug-resistant TB in pregnancy: The South African experience**

M Loveday,<sup>1</sup> <sup>1</sup>South African Medical Research Council, Durban, South Africa.  
e-mail: marian.loveday@mrc.ac.za

With newer and more effective treatments, death rates from drug-resistant TB are decreasing globally.

However, lack of drug safety data in pregnancy limits our confidence in treating drug-resistant TB in pregnancy. South Africa has one of the highest burdens of drug-

resistant TB in the world and has taken a progressive approach to treatment during pregnancy.

In this talk, Dr. Loveday will discuss the pragmatic diagnostic and management approach to DR TB in pregnancy in South Africa.

### **An ethical approach to drug-resistant TB in pregnancy**

C Waitt,<sup>1</sup> <sup>1</sup>University of Liverpool/ Infectious Diseases Institute, Liverpool/ Kampala, Uganda.  
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Everybody deserves access to evidence upon which to base clinical decisions. However, pregnant and breast-feeding people have often been excluded from clinical trials. In the absence of such evidence to treat drug-resistant TB in pregnancy, clinicians are often faced with conflicting guidance on how to treat these patients, and how to advise them about relative risks and benefits.

In this talk, Prof Waitt will provide an ethical perspective on the need for fair inclusion rather than systematic exclusion of pregnant individuals in research on drug-resistant TB, together with a framework for considering risk in specific situations.

### **SP50 Implementation of the six-month BPaL-based regimens for MDR-TB treatment**

#### **Preliminary data on safety and effectiveness of BPaL-based regimens in patients with rifampicin-resistant TB in Belarus**

N Yatskevich,<sup>1</sup> <sup>1</sup>Republican Scientific and Practical Center for Pulmonology and Tuberculosis, Minsk, Belarus.  
e-mail: yahoravanatallia@mail.ru

We will present the preliminary findings of implementing six-month, all-oral BPaL-based regimens as operational research in Belarus. A total of 330 patients were enrolled on BPaL-based regimens between February and December 2022.

We will discuss baseline characteristics, treatment outcomes and safety of these regimens under non-trial conditions. These findings will contribute to a better understanding of using these regimens in programmatic setting.

### **Programmatic Roll-out of BPaL-based Regimens for MDR-TB in Sierra Leone: Countrywide Experience**

M Mahmoud,<sup>1</sup> <sup>1</sup>National Leprosy and Tuberculosis Control Programme, Freetown, Sierra Leone.  
e-mail: manager-nltcp@mohs.gov.sl

This presentation will focus on experience of implementing BPaL-based treatment regimen for MDR-TB patients in Sierra Leone under programmatic settings. Over 100 MDR-TB patients have received the six-month regimen since its scale-up in January 2023.

We will share the lessons learned from our experience that could facilitate the programmatic rollout of the treatment in other countries.

### **Evaluating the effectiveness and safety of BPaL/BPaLM under routine programme conditions in Pakistan**

H Aslam,<sup>1</sup> <sup>1</sup>Provincial TB control Program Punjab Pakistan, Lahore, Pakistan.  
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In May 22 via rapid communication, WHO suggested programs to use Bedaquiline-Linezolid-Pretomanid and Moxifloxacin BPaL/ BpaLM. Pakistan, being a pathfinding country in programmatic implementation of DR-TB care, implemented this all-oral short regimen for treatment of DR-TB patients on selected PMDT sites in Punjab in Oct 22.

Through this presentation we will share some of the first experiences of implementation including some practical insights. We highlight some of the early challenges and successes in converting policy into practice, as well as valuable lessons learnt for scale up.

### **A feasibility study on the country-wide implementation of the 6-month MDR/RR-TB treatment in Belarus**

A Skrahina,<sup>1</sup> <sup>1</sup>The Republican Scientific and Practical Center of Pulmonology and Tuberculosis, Minsk, Belarus.  
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A feasibility assessment was conducted in Belarus to determine the health system requirements for implementation, adoption and uptake of BPaL-based 6-month all-oral treatment regimens. Since February 2022, 450 patients in Belarus have started treatment with BPaL-based regimens, accounting for 65% of all patients with RR-TB in the country who started treatment during this period.

We share the study findings and recommendations to facilitate adoption of the BPaL-based treatment regimens globally.

## **SP51 Global policy and evidence for the use of targeted next-generation sequencing for the detection of TB drug resistance**

### **Clinical evaluation of tNGS solutions for expanded resistance detection in TB - a FIND multi-country trial**

R Colman,<sup>1</sup> <sup>1</sup>FIND and University of California San Diego, San Diego, United States.  
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This talk will summarize the multi-site clinical trial of tNGS conducted by FIND. The trial enrolled patients at high risk of TB drug resistance across three clinical sites in South Africa, India and Georgia and evaluated the diagnostic accuracy of tNGS compared to phenotypic DST and whole genome sequencing. The trial also measured operational characteristics of the tNGS technologies including non-determinate rates, ease of use, and other implementation considerations.

### **Systematic review and individual patient data analysis of the diagnostic accuracy of tNGS**

T Walker,<sup>1</sup> <sup>1</sup>University of Oxford, Ho Chi Minh City, Vietnam.  
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This talk will present the methods and findings of a systematic review and individual patient data (IPD) analysis of the diagnostic accuracy of tNGS technologies that was performed to inform the GDG meeting. All tNGS platforms that met the minimum criteria for sample size and performance were included in the analysis, and pooled estimates of sensitivity, specificity, and indeterminate results rates were produced for each WHO-recommended TB drug. Certainty of the evidence was also determined for each guideline question considered.

### **Costs and cost-effectiveness of tNGS implementation in three emblematic settings**

A Zwerling,<sup>1</sup> <sup>1</sup>University of Ottawa, Ottawa, Canada.  
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This talk summarizes the results of a systematic review and cost effectiveness model that were conducted to inform the WHO guidelines on TNGS for TB. The systematic review found 10 studies providing economic data on tNGS, and no cost-effectiveness analyses were identified using tNGS from the literature. The cost effectiveness model found that tNGS was cost-effective compared to current standard of care DST practices in certain countries, using a willingness-to-pay threshold

for daily averted life years of three times the country's GDP. Under certain conditions tNGS was found to be less costly and lead to better health outcomes.

### **WHO recommendations on the use of tNGS for the detection of drug-resistant TB**

C Miller,<sup>1</sup> <sup>1</sup>World Health Organization, Geneva, Switzerland.  
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This talk will summarize the process and primary outcomes of the WHO Guideline Development Meeting to evaluate the use of targeted Next-Generation Sequencing technologies for programmatic use in diagnosis and treatment of drug-resistant TB, held in spring 2023. In addition to diagnostic accuracy, this talk will cover considerations of the technology's placement in health care systems and in patient flow pathways, as well as factors such as feasibility, acceptability, and potential impact of the technology on equitable patient care.

### **The South African experience in the use of tNGS and considerations for its implementation**

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Are we there yet? Despite the technological advances with targeted next-generation sequencing, is the tool mature enough to introduce into high-burdened countries? This talk will consider the operational aspects and infrastructural needs for introduction and scale-up of TNGS at country level.

## ABSTRACT PRESENTATIONS WEDNESDAY 15 NOVEMBER 2023

### ORAL ABSTRACT SESSION (OA)

#### OA01 Role of Immunology in the TB diagnosis

##### OA01-200-15 IGRA-on-a-chip enables rapid TB detection

**T. Hu,**<sup>1</sup> Tulane University, Biochemistry, Biomedical Engineering and Microbiology, New Orleans, United States of America. e-mail: tonyhu@tulane.edu

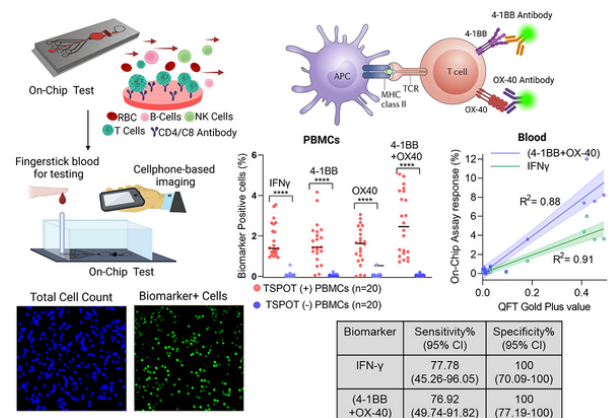
**Background:** Interferon-gamma release assays (IGRAs) are widely used to diagnose infectious diseases, particularly tuberculosis (TB) infections, by measuring pathogen-specific T-cell responses.

However, their use is limited by workflow, personnel, and instrumentation demands, making them unsuitable for point-of-care use. Moreover, a subset of immunocompetent individuals may remain negative in both Tuberculin skin tests (TST) and IGRAs despite persistent, high levels of exposure to *Mycobacterium tuberculosis* (Mtb). In TB patients with high regulatory T-cells, the Mtb-stimulated IFN- $\gamma$  levels in whole blood supernatants are also depressed, highlighting the need to explore an IFN- $\gamma$  independent biomarker for improved TB infection diagnosis.

**Design/Methods:** To address the clinical and logistic gaps associated with conventional IGRA, we aimed to develop a simple and efficient point-of-care technique for diagnosing TB infection in IFN- $\gamma$  independent manner. We investigated the expression patterns of tumor necrosis factor receptor, TNF(R) superfamily molecules (4-1BB and OX-40) on activated T cells as they are potent mediators of inflammatory responses and upregulation of 4-1BB, and OX-40 occurs on all activated T-cells phenotypes, including cytotoxic, helper, and regulatory T cells. We integrated the diagnosis process on a microchip by optimizing T-cells enrichment, surface modifications and flow rates inside the reaction chamber of the microchip making it suitable for point-of-care use.

**Results:** The new IFN- $\gamma$  independent microchip platform developed in our study allows for the rapid (6-hour sample-to-answer time) and inexpensive analysis of T-cell activation responses using fingerstick whole blood (~25  $\mu$ L) microsamples, without significant equipment or technical expertise.

We further showed that the cumulative expression of 4-1BB and OX-40 can be utilized as a new T-cell immune marker for fast and robust diagnosis of tuberculosis infection.



**Conclusions:** Our study provides a promising avenue for the development of streamlined and inexpensive assay that could also be utilized for high-throughput analyses of T-cells response in an IFN- $\gamma$  independent manner.

##### OA01-201-15 Pre-treatment metabolomic profiling of cerebrospinal fluid in tuberculous meningitis patients reveals new prognostic markers for mortality

**N. Le,**<sup>1</sup> C. Clish,<sup>2</sup> J. Avila-Pacheco,<sup>2</sup> D. Sofiati,<sup>3</sup> E. Ardiansyah,<sup>4,5</sup> H. Hoang,<sup>1</sup> V. Kumar,<sup>4</sup> R. van Crevel,<sup>4,6</sup> G. Thwaites,<sup>6,1</sup> T. Nguyen Thuy Thuong,<sup>1,6</sup> A. van Laarhoven,<sup>4</sup> ULTIMATE consortium <sup>1</sup>Oxford University Clinical Research Unit, Tuberculosis, Ho Chi Minh city, Viet Nam, <sup>2</sup>Broad Institute of MIT and Harvard, Metabolomics Platform, Cambridge, United States of America, <sup>3</sup>Universitas Padjadjaran, Department of Neurology, Bandung, Indonesia, <sup>4</sup>Radboud University Medical Center, Department of Internal Medicine and Radboud Center for Infectious Diseases, Nijmegen, Netherlands, <sup>5</sup>Universitas Indonesia, Faculty of Medicine, Jakarta, Indonesia, <sup>6</sup>University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom of Great Britain and Northern Ireland. e-mail: nhatlth@oucr.org

**Background:** Cellular metabolism plays a critical role in immune cells, which are important in the pathophysiology of tuberculous meningitis (TBM). Elevated pre-treatment cerebrospinal fluid (CSF) tryptophan have been associated to increased mortality in TBM.

We conducted a metabolome-wide association analysis to identify metabolic pathways associated with mortality in TBM, with the aim of improving prognostics and developing host-directed therapy.

**Design/Methods:** We collected pre-treatment CSF specimens and data from TBM patients in Indonesia (n=388) and Vietnam (n=679). We measured 619 metabolite abundances using untargeted liquid chromatogra-

phy-mass spectrometry. In the primary analysis, we used a Cox regression model to identify top-hit metabolites associated with mortality, adjusting for age and HIV status. In particular, we ranked the associations and selected the top-hit metabolites using the screening subset (n=194) from the Indonesia cohort. We then validated these metabolites in the within-cohort subset (n=194) from Indonesia and an external set (n=679) from Vietnam.

In the secondary analysis, we conducted stability variable selection analysis based on gradient-boosted Cox model to identify the strongest predictive metabolites among the top-hit and clinical biomarkers.

**Results:** Our primary analysis showed that in addition to *tryptophan*, eight novel metabolites (*N-carbamoyl-beta-alanine*, *hydroxyisocaproate*, *phenyllactate*, *p-hydroxyphenylacetate*, *3-hydroxyoctanoate*, *hydroxyisobutyrate*, *C4-OH-carnitine*, *N6-N6-N6-trimethyllysine*) were associated with mortality in both the screening and validation steps (as shown in Table 1). These metabolites were known to be involved in excitotoxicity and fatty acid oxidation. The variable selection analysis showed that the three highest predictors of TBM mortality were Glasgow Coma Scale, a prominent clinical biomarker, and two CSF metabolites, *3-hydroxyoctanoate* and *tryptophan*, with selection probabilities of 1, 0.94, and 0.83, respectively.

Metabolites*	HR <sup>1</sup>	Within-cohort validation (Indonesia, n=194) 95% CI <sup>2</sup> p-value		FDR <sup>3</sup>	External validation	FDR
N-carbamoyl-beta-alanine†	1.56	1.25, 1.95	<0.001	<b>0.00265</b>	1.45 (Vietnam, n=679)	<0.001 <b>0.00730</b>
Hydroxyisocaproate	1.47	1.15, 1.87	0.002	<b>0.01597</b>	1.48 95% CI <sup>1</sup> p-value	0.002 <b>0.02795</b>
Phenyllactate	1.62	1.23, 2.15	<0.001	<b>0.01035</b>	1.55 1.24, 1.94	<0.001 <b>0.00662</b>
p-hydroxyphenylacetate	1.46	1.12, 1.91	0.006	<b>0.03784</b>	1.33 1.09, 1.61	0.004 <b>0.04987</b>
3-hydroxyoctanoate	1.36	1.06, 1.74	0.014	0.05412	1.51 1.26, 1.81	<0.001 <b>0.00117</b>
Tryptophan	1.32	1.04, 1.67	0.021	0.06383	1.42 1.17, 1.72	<0.001 <b>0.00894</b>
Hydroxyisobutyrate	1.35	1.04, 1.76	0.023	0.06840	1.46 1.15, 1.86	0.002 <b>0.03301</b>
C4-OH carnitine	1.21	0.91, 1.63	0.2	0.25517	1.51 1.15, 1.99	0.003 <b>0.04546</b>
N6,N6,N6-trimethyllysine	1.83	1.40, 2.39	<0.001	<b>0.00096</b>	1.36 1.08, 1.72	0.009 <b>0.09090</b>

Table 1: Validated top-hit metabolites

**Conclusions:** Our study identified pre-treatment CSF metabolite profiles of TBM patients with poor outcomes, and the identified metabolites have the potential as prognostic markers for mortality. This work may inform the future development of host-directed therapy.

## OA01-202-15 Monocyte activation and atherosclerosis burden remain elevated post-treatment of *M. bovis* BCG infection in mice

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**Background:** Patients who recover from tuberculosis remain at increased risk of atherosclerotic cardiovascular diseases (ASCVD). We previously showed that *Mycobacterium bovis* Bacille-Calmette-Guérin (BCG) induced monocyte activation and aggravated atherosclerosis in hyperlipidemic mice.

Here, we aimed to define monocyte activation and atherosclerosis burden post-antimycobacterial treatment in infected mice.

**Design/Methods:** Twelve-week-old male and female, low-density lipoprotein receptor knockout (*Ldlr*<sup>-/-</sup>) mice were infected with BCG (0.5–2.5 x10<sup>6</sup> colony-forming units [CFU]) via the intranasal route. All mice were fed a western-type high-fat diet for 16 weeks. A group of mice were treated with Isoniazid and Rifampin (INH/RIF) between weeks 4 and 12. Age-matched uninfected *Ldlr*<sup>-/-</sup> mice served as controls. Atherosclerotic lesions in aortas were examined using Oil-Red-O staining. Lungs and spleens were cultured for CFU enumeration. Immunophenotyping profiles of monocytes and their cytokine expression upon stimulation with *M. tuberculosis* whole-cell-lysate (*Mtb-lysate*) were assessed with flow cytometry.

**Results:** INH/RIF successfully cleared BCG infection in our mice. INH/RIF treatment had no significant effects on triglycerides or cholesterol levels. Compared to uninfected mice, BCG-infected mice and post-INH/RIF-BCG-treated mice exhibited increased percentage of Ly6C<sup>low</sup> nonclassical monocytes (5.5% vs. 13.9% vs. 16.6%; *p*=0.003); increased expression of activation markers as CD36, MHC-II, CX3CR1, CD80, CD64; and production of IL-1 $\beta$  after *Mtb-lysate* stimulation. Similar results were observed in Ly6C<sup>high</sup> classical monocytes in terms of MHC-II, CD80, CD64 expression.

Compared to uninfected mice, BCG-infected mice and post-INH/RIF-BCG-treated mice displayed increased atherosclerotic lesions in aorta at 16 weeks (Area ( $\mu$ m), 295,396 vs. 444,906 vs. 429,510; *p*=0.0311). Overall, CD36 expression in nonclassical monocytes correlated with atherosclerotic plaque burden.

**Conclusions:** Monocyte activation and atherosclerosis burden remained elevated after INH/RIF treatment of BCG-infected, hyperlipidemic mice. Our results suggest that antimycobacterial treatment is not sufficient to revert infection-aggravated atherosclerosis.



Our model of post-infection atherosclerosis will allow exploring underlying mechanisms and potential AS-CVD therapeutic interventions.

### OA01-203-15 *EsxM* stop-codon Q59\* in *M. tuberculosis* reduces risk of tuberculous meningitis but enhances transmissibility of clinical strains

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**Background:** *Mycobacterium tuberculosis* (*Mtb*) typically causes pulmonary tuberculosis (PTB) but can spread to other organs resulting in extra-pulmonary TB, such as bone TB or tuberculosis meningitis (TBM). Recent studies have reported that a full-length ancestral variant of the type VII-secreted effector *EsxM* (Q59) can promote *Mtb* dissemination to the skeleton.

This study investigates associations between *EsxM* stop-codon Q59\* and two clinical phenotypes, TBM and PTB, and their respective outcomes.

**Design/Methods:** Q59\* mutation were extracted from *Mtb* whole genome sequencing data in Vietnam, comprising strains causing 631 TBM and 3361 PTB. In the primary analysis, we compared the mutation frequencies in TBM vs. PTB.

Additionally, we validated this association using an external cohort from Thailand and Indonesia with 179 TBM and 443 PTB patients. Secondary analysis assessed the impact of Q59\* on cerebrospinal fluid (CSF) parameters, severity grade and 9-month mortality of TBM patients, as well as two-month sputum conversion of PTB patients, utilizing clinical data from subsets of the Vietnam cohort.

**Results:** The Q59\* mutation was associated with reduced risk of TBM (odds ratio (OR) 0.63, (95% confidence interval 0.52, 0.76),  $p < 0.001$ ). This association was validated in external cohorts (OR=0.39 (0.24, 0.65),  $p < 0.001$ ). Notably, this mutation was present in almost all modern lineages (Lineages 2 and 4) (Table 1).

Moreover, the Q59\* mutation was associated with decreased two-month sputum conversion (OR=0.44 (0.27, 0.73),  $p = 0.001$ ) and increased unfavorable outcome (OR=2.43 (1.09, 5.42),  $p = 0.03$ ) in PTB patients.

In TBM patients, the Q59\* mutation was associated with lower CSF leukocytes ( $p < 0.001$ ), higher percentage of CSF lymphocytes ( $p = 0.02$ ), greater severity at baseline (OR=1.90 (1.17, 3.08),  $p = 0.01$ ), and slightly higher mortality (HR=1.28 (0.930, 1.773),  $p = 0.13$ ).

Lineage	Vietnam (n=3992)		Indonesia and Thailand (n=622)	
	PTB	TBM	PTB	TBM
Lineage 1 (n, %)	787 (80%)	201 (20%)	36 (54%)	31 (46%)
Lineage 2 (n, %)	2235 (85%)	390 (15%)	252 (76%)	81 (24%)
Lineage 3 (n, %)	339 (89%)	40 (11%)	154 (70%)	67 (30%)
<b>EsxM variant</b>				
full-length (L1, 100%)	777 (79%)	205 (21%)	36 (52%)	33 (48%)
truncated (L2&4, 99.6%)	2565 (86%)	425 (14%)	407 (74%)	146 (26%)
<b>OR (95% CI), p-value</b>	0.63 (0.52, 0.76), $p < 0.001$		0.39 (0.24, 0.65), $p < 0.001$	

Table 1. Association between stop codon Q59\* mutation in *EsxM* of *Mycobacterium tuberculosis* clinical strains and tuberculous meningitis.

**Conclusions:** Almost all modern lineages carry the *EsxM* Q59\* mutation with corresponding reduced risk of TB dissemination, or greater adaption to PTB and delayed sputum conversion. This potentially promotes disease transmission.

### OA01-204-15 Comparative proteomic analysis of exosomes derived from patients infected with non-tuberculous mycobacteria and *M. tuberculosis*

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**Background:** Nontuberculous mycobacterium (NTM) is a very troublesome pathogenic microorganism, placing a heavy burden on public health. At present, the pathogenesis of NTM pulmonary infection is not well-revealed, and its diagnosis is also facing challenges.

**Design/Methods:** In the present study, a comprehensive proteomics analysis of plasma exosomes derived from healthy donors, patients with rapidly growing NTM (RGM), patients with slowly growing NTM (SGM), and patients with active tuberculosis was performed.

**Results:** In these three disease states, complement and coagulation cascades were extensively and significantly activated, with a total of 24 complement and coagulation protein up-regulated, including C1R, C1S, C2, MASP2, C4B, CFI, C9, CLU, CFHR3, SERPING1, KNG1, F5, FGA, FGG, SERPINA1, SEPRINA5, SEPRND1, SEPRINF2, SEPRING1, C8B, F11, F13B, SEPRINC1, VTN, and MBL2. Most of these complement and coagulation proteins (18/24) were significantly up-regulated in RGM infected patients. 6 proteins in complement and coagulation cascades were up-regulated in patients with SGM infection and 10 proteins were up-regulated in patients with active tuberculosis. RGM infection is also related to HIF-1 signaling pathway, phagosome processes, and glycolysis. The proteins identified in these pathways are potential diagnostic and differential diagnostic markers of patients infected with NTM and *Mycobacterium tuberculosis* (*Mtb*).

**Conclusions:** This study provided a comprehensive description of the exosome proteome in the plasma of patients infected with NTM and Mtb and revealed potential diagnostic biomarkers.

### OA01-205-15 Matrix metalloproteinases as immune biomarkers for diagnosis of paediatric TB

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**Background:** Diagnosis of pediatric TB remains challenging with the current routine clinical and laboratory diagnostic tools.

There is also a lack of reliable TB diagnostic tests to be used in pediatric populations in TB endemic countries. Matrix metalloproteinases (MMPs) are known drivers of lung pathology in many diseases including TB.

Hence, we wanted to examine the plasma levels MMPs and tissue inhibitors of metalloproteinases (TIMPs) as biomarkers for diagnosis of pediatric tuberculosis.

**Design/Methods:** We conducted a prospective case control study using children with confirmed, unconfirmed and unlikely TB.

Of the 195 children screened, 167 children were recruited which includes 44 children who were microbiology positive (confirmed TB) for *M.tb*, 47 children who were microbiology negative but had clinical radiological diagnosis of TB (unconfirmed TB), 76 children with other respiratory ailments and tuberculin skin Test (TST) positive or negative as unlikely TB controls.

Multiplex assay was performed to examine the plasma MMPs (MMP1, 2, 3, 7, 8, 9, 12 and 13) and TIMPs (TIMP1, 2, 3, 4) levels.

**Results:** Baseline levels of MMP1 (P<0.001), MMP2 (P<0.001), MMP7 (P=0.005), MMP9 (P<0.001), TIMP1 (P<0.001), TIMP2 (P<0.001), TIMP3 (P=0.003) and TIMP4 (P=0.001) were significantly higher in active TB (confirmed TB and unconfirmed TB) in comparison to unlikely TB children.

Receiver operating characteristics curve (ROC) analysis revealed that MMP1, MMP2, MMP9 and TIMP-1 could act as biomarkers distinguishing confirmed or unconfirmed TB from unlikely TB with the sensitivity and specificity of more than 80%.

In addition, combiROC models offered 100% sensitivity and specificity for a three MMP signature of MMP1, MMP2 and MMP9, which can distinguish confirmed or unconfirmed TB children from unlikely TB children.

**Conclusions:** Thus, a baseline MMP signature of MMP1, MMP2 and MMP9 could serve as an accurate biomarker for the diagnosis of pediatric tuberculosis.

### OA01-206-15 Variance in *M. tuberculosis* quantification between time to positivity and colony-forming units

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**Background:** Phase II tuberculosis (TB) trials have classically used CFU as a method of manually quantifying Mtb to evaluate the efficacy of new drugs. TTP is an automated method which is increasingly used to quantify Mtb in place of CFU. CFU may miss sub-populations of Mtb, called differentially detectable Mtb (DD Mtb), which often impact TTP quantification. This may have implications for how Phase II trials are designed.

**Design/Methods:** We utilized data from three phase II studies which included patients with drug-susceptible TB who received 2 weeks of nitazoxanide followed by 6 months standard therapy; patients with drug-susceptible TB who received rifampin, isoniazid, ethambutol and pyrazinamide; and patients with multidrug/rifampin-resistant TB who received levofloxacin, bedaquiline, linezolid, clofazimine and pyrazinamide. log<sub>10</sub>CFU was determined via solid culture. TTP was determined using BACTEC MGIT 960 liquid culture system (Becton Dickinson, Franklin Lakes, USA). DD Mtb was detected using the most probable number limiting dilution assay with and without supernatant (MPNSN, MPN respectively).

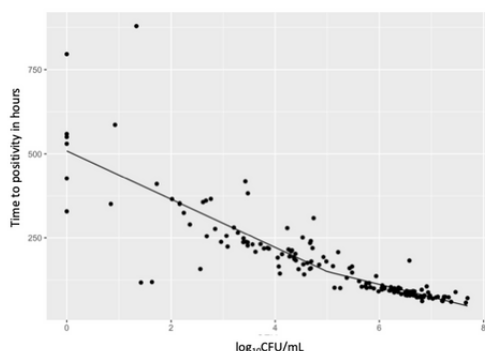
Linear regression was performed with the method of least squares; variability over time using analysis of variance.

All studies were IRB-approved.

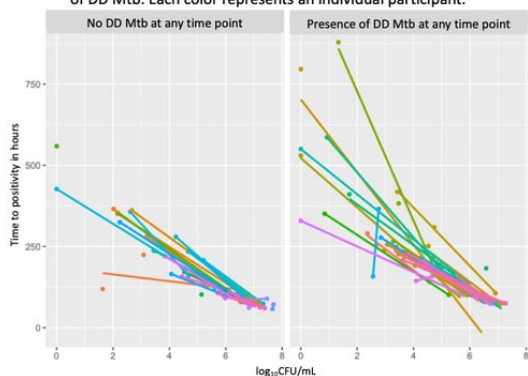
**Results:** From 2016–2020, 82 participants were enrolled with n=160 paired TTP- log<sub>10</sub>CFU samples. Paired samples are assays performed on the same sputum specimen. TTP varied with log<sub>10</sub>CFU at lower bacterial loads, with each unit increase in log<sub>10</sub>CFU associated with 72 hour decrease in TTP when log<sub>10</sub>CFU<5 (p<0.0001) and 38 hour decrease in TTP when log<sub>10</sub>CFU≥5 (p=0.004) (Figure 1A). The presence of DD Mtb increased the variability in individual participant trajectories of TTP and

$\log_{10}$ CFU over the duration of treatment (Figure 1B). There was no difference in regression lines for participants with drug-susceptible or drug-resistant TB (Figure 1C).

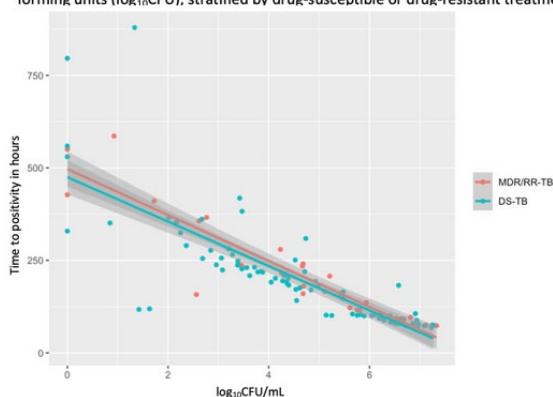
**Figure 1A.** Bilinear regression between time to positivity (TTP) in hours to colony-forming units ( $\log_{10}$ CFU).



**Figure 1B.** Trajectory of time to positivity (TTP) in hours to colony-forming units ( $\log_{10}$ CFU) in individual participants over study duration, stratified by presence of DD Mtb. Each color represents an individual participant.



**Figure 1C.** Correlation between time to positivity (TTP) in hours and colony-forming units ( $\log_{10}$ CFU), stratified by drug-susceptible or drug-resistant treatment



**Conclusions:** The variation in correlation between TTP and CFU may impact how phase II trials determine sample size and study outcomes.

## OA02 Subclinical TB: How to recognize it when you see it?

### OA02-207-15 Sub-clinical TB: A scoping review of definitions, prevalence and clinical characteristics

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**Background:** Subclinical tuberculosis (ScTB) is a disease state caused by *Mycobacterium tuberculosis*. ScTB lacks typical clinical symptoms but is detectable via radiologic abnormalities or microbiologic testing. This scoping review aimed to characterise definitions used to describe ScTB, estimate the proportion of people with ScTB in different populations and describe the clinical characteristics, natural history and treatment outcomes in the scientific literature.

**Design/Methods:** A systematic literature search was conducted using PubMed. We also reviewed national TB prevalence surveys reported up to 2022. Inclusion criteria were studies published in English between January 1990 and August 2022 that defined “subclinical” or “asymptomatic” pulmonary TB disease, regardless of age, HIV status and comorbidities. We estimated the weighted pooled proportions of people with ScTB using a random-effect model by WHO TB burden classifications, populations, and settings. We also pooled the proportion of people with ScTB by definitions described in representative prevalence surveys.

**Results:** We included 74 studies in the review. ScTB definitions inclined towards asymptomatic TB disease. The overall pooled proportion of people with ScTB was 38% (95% CI 29-47%). Higher proportions were observed in high TB burden settings, healthcare facilities, and among immunocompetent populations. Among prevalence surveys, those utilising ‘absence of cough or any duration’ versus the more stringent ‘completely asymptomatic’ threshold to initiate follow-up TB testing observed a higher proportion of ScTB. Clinical (symptomatic) cases were more likely to present radiographic evidence of TB. Disease progression varied between settings. High treatment success rates and low death rates were observed among people with ScTB.

**Conclusions:** Most published studies incompletely characterised people with ScTB. Findings were highly heterogenous between settings. ScTB prevalence varied depending on the definition used, highlighting the need for a standardised approach to characterising this phenotype. Further research is also needed to optimise case finding, screening and diagnostic modalities, and treatment options for this population.

## OA02-208-15 Characteristics of pulmonary TB patients identified using active case-finding in Indonesia

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**Background:** Active case finding (ACF) is a strategy to detect missing tuberculosis (TB) cases and start treatment early. We compared TB characteristics and treatment outcomes of cases found through ACF with those who self-presented at healthcare facilities (passive case finding [PCF]).

**Design/Methods:** Patients diagnosed with pulmonary TB in community health centres in Bandung City, Indonesia, were recruited (PCF) and their symptoms, chest X-ray (CXR), and sputum microbiology test results collected. Their household members and neighbours were screened and offered a CXR (ACF).

Anyone coughing or CXR suggestive of TB gave sputum samples for smear, Xpert® MTB/RIF, and *Mycobacterium tuberculosis* culture. Treatment outcomes data were collected from the TB information system.

Characteristics	ACF (n=57) n%	PCF (n=213) n%	P
Median age (IQR)	38 (24-50)	33 (22-50)	0.22
Coughing	39 (68.4)	211 (99.1)	<0.001
Median cough duration (IQR)	21 (7-60)	40 (21-90)	<0.001
Haemoptysis	3 (5.3)	56 (26.3)	0.001
Fever	21 (36.8)	138 (64.8)	<0.001
Weight loss	25 (43.9)	180 (84.5)	<0.001
Underweight (BMI <18.5)	21 (36.8)	122 (57.3)	0.002
Normal chest X-ray	10 (17.5)	14 (7.0)	0.14
Sputum microscopy +3	7 (13.7)	55 (25.9)	<0.001

Table 1. Characteristics of TB patients identified through active case finding compared with those identified by passive case finding

**Results:** Of 270 cases, 213 were PCF and 57 ACF patients. ACF patients were less likely to be underweight (36.8% vs 57.3%,  $p<0.001$ ), report coughing (68.4% vs 99.1%,  $p<0.001$ ), have shorter cough duration (median 21 vs 40 days,  $p<0.001$ ), less haemoptysis (5.3% vs 26.3%,  $p=0.001$ ), fever (36.8% vs 64.8%,  $p<0.001$ ), and weight loss (43.9% vs 84.5%,  $p<0.001$ ). More ACF patients had a normal CXR (17.5% vs 7.0%,  $p=0.14$ )

and fewer had a high sputum bacterial load (smear 3+ 13.7% vs 25.9%,  $p<0.001$ ). Of the 254 patients with treatment outcomes reported, slightly fewer ACF patients completed/cured treatment (76.1% vs 85.6%,  $p=0.11$ ), or failed/died (6.5% vs 7.2%,  $p=0.87$ ).

More ACF patients were lost to follow-up (17.4% vs 7.2%,  $p=0.03$ ) with reasons reported as side effects ( $n=5$ ) and feeling healthy ( $n=3$ ).

**Conclusions:** ACF patients were less symptomatic and had fewer clinical features of TB when diagnosed but were less likely (but not significant) to complete treatment. More efforts are needed to ensure adherence among ACF patients.

## OA02-209-15 Sub-clinical TB disease in household contacts of recently diagnosed TB patients

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**Background:** The recent South African National TB Prevalence Survey reported that >50% of TB cases were asymptomatic but had abnormal chest X-ray (CXR).

**Design/Methods:** The RePORT-SA-002 study consented and enrolled household contacts (HHCs) with recent significant exposure to a pulmonary TB (PTB) patient, if ≥18 years, available for 12 months follow-up, willing to be tested for HIV, and agreed to sample storage. Baseline digital CXR reviewed by radiologists, and sputum Xpert Ultra and MGIT culture were done on all participants regardless of symptoms.

**Results:** Between March 2021 and June 2022 we enrolled 450 HHCs. Microbiologically confirmed PTB was diagnosed by Xpert and/or MGIT culture positive sputa in 39 (8.6%) participants. Of participants with confirmed PTB, positive sputum Xpert Ultra and MGIT was reported in 27 (69.2%), positive MGIT alone in 4 (10.2%), and positive Xpert Ultra alone in 8 (20.5%).

An additional 6 were smear positive only. 37 (94.8%) of the 39 participants with confirmed PTB were asymptomatic by TB symptom screen, i.e. 2 of 450 HHCs had symptomatic TB (0.4%) and 37 of 450 had subclinical TB (8.2%). Of these 37 participants, 23 were male (56.1%), median age was 34 years, 6 were HIV positive (15.4%), and 15 (40.5%) had a previous history of TB one year or more prior. Twenty-seven (72.9%) were current smokers and none was diabetic. CXR was compatible with active TB in 10 of the 37 participants with subclinical TB (27.0%); with previous PTB and no evidence of reactivation in 20 (54.0%); and was normal in 7 (18.9%).

**Conclusions:** We found a 20-fold higher rate of subclinical TB among household contacts (HHC) of recently diagnosed TB patients than symptomatic TB disease. Symptom plus CXR screening would miss a considerable number of microbiologically confirmed household PTB cases unless one includes any evidence of abnormality on CXR.

**OA02-210-15 Community-wide active case-finding for the detection of sub-clinical TB disease in Vietnam: Analysis of data from a cluster randomised controlled trial**

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**Background:** Active case finding (ACF) is a key strategy in improving tuberculosis (TB) case detection. However, its effectiveness in detecting subclinical TB disease (ScTB) is uncertain. This study aimed to:

1. Evaluate the relationship between a community-wide ACF and the detection of ScTB in Vietnam and
2. Describe the microbiological and radiographic characteristics of people with ScTB.

**Design/Methods:** We conducted a cross-sectional survey comparing outcomes of passive case finding (PCF) and community-wide ACF from a cluster-randomised controlled trial conducted in Ca Mau Province, Vietnam, between 2014 and 2018. PCF participants were people with TB who self-initiated care-seeking at the public TB clinics in the control group. Community-wide ACF was conducted using chest radiography and sputum examinations in intervention sites annually.

The primary definition of ScTB was:

1. Individuals who had positive sputum tests using Xpert MTB/RIF or microscopic examination but were asymptomatic. Sensitivity analyses using alternative ScTB definitions were performed,
2. Absence of all symptoms in the WHO 4-symptom screen (W4SS),
3. Absence of at least one symptom in the W4SS, and
4. Absence of cough for  $\geq 2$  weeks. We used modified Poisson regression with a robust sandwich variance to compare the prevalence ratios of ScTB identified by ACF with PCF.

**Results:** Data from 220 PCF cases and 311 ACF cases were analysed. Compared to PCF, people with TB detected by ACF had a higher prevalence of ScTB across all four definitions,

1. Adjusted prevalence ratio 12.4, 95% CI 2.8-54.4,
2. 2.6, 1.5-4.4,
3. 1.2, 1.1-1.3, and
4. 1.9, 1.3-2.8.

The proportions of individuals with abnormal x-rays suggestive of TB and positive Xpert MTB/RIF were similar between people with ScTB and clinical TB.

**Conclusions:** A higher proportion of individuals screened using community-wide ACF had ScTB compared with standard PCF. Diagnostic testing using radiography or PCR-based diagnostics, regardless of symptoms, could increase the detection of ScTB.

**OA02-211-15 Systemic inflammation predicts infectiousness in pulmonary TB**

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**Background:** Although infectiousness among people with pulmonary tuberculosis (TB) varies greatly, the pathogenesis of infectiousness is poorly understood. Infectious aerosols from coughing were found to be better predictors of household transmission than traditional sputum-based studies. We aimed to identify factors that predict infectiousness of persons with TB.

**Design/Methods:** In a prospective study we enrolled adults newly diagnosed with pulmonary TB from outpatient clinics in Nairobi, Kenya. All participants were positive by GeneXpert and liquid culture for *M.tuberculosis* and were TB treatment naïve. Infectious aerosols were collected using a cough aerosol sampling system (CASS) with CASS-positivity defined by culture growth on any of the CASS plates. Additional interventions included chest x-ray (CXR), cough peak flow rates (CPFRs), phlebotomy, and biometric measurements. We compared characteristics by CASS status and identified the best performing multivariable logistic regression model for predicting CASS-positivity using the likelihood ratio test.

**Results:** We enrolled 133 participants (median age 34 years, interquartile range 28-45) among whom 75% were men, 10% were people with HIV, and 18% had a history of TB treatment. There were 43 CASS-positive (32%) and 90 CASS-negative (68%) participants who did not differ by gender, HIV status, body mass index, mid-upper arm circumference (MUAC), CPFR, prior TB, or sputum appearance. CASS-positive participants

were more likely (*see Table*) to be younger (32 vs. 36 years), have lower GeneXpert cycle threshold (Ct) values (16.1 vs. 19.4), higher CRP (88.3 vs. 44.6 mg/L), shorter time-to-detection in liquid culture (4 vs. 6 days), and cavitory CXRs (86% vs. 59%). The best performing model included age, GeneXpert Ct, CRP, and MUAC (AUC = 0.85).

Bivariate regression			Multivariable regression	
Variable <sup>a</sup>	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	0.95 (0.92, 0.99)	0.008	0.95 (0.91, 1.00)	0.04
Xpert cycle threshold	0.84 (0.75, 0.94)	0.002	0.84 (0.74, 0.95)	0.007
CRP (mg/L)	1.02 (1.01, 1.03)	<0.001	1.03 (1.01, 1.04)	<0.001
MUAC (cm)	1.12 (0.99, 1.28)	0.08	1.31 (1.10, 1.57)	0.002
Cavities on CXR	4.31 (1.65, 11.23)	0.003		

<sup>a</sup>Additional variables evaluated in models were: HIV status, gender, body mass index, peak expiratory flow rate, CXR finding of cavitory disease, and smoking status. Culture time to detection not included in multivariable model due to missing data.

OR – odds ratio; CI – confidence interval; MUAC – mid-upper arm circumference

*Table. Logistic regression analyses: Factors associated with M. tuberculosis growth on Cough Aerosol Sampling System (n=120).*

**Conclusions:** We identified several predictors of infectiousness, among which CRP is novel. Based on our model, the odds of CASS-positivity increase by 2% for every 1 mg/L increase in CRP. Transcriptomic studies are underway to identify specific inflammatory predictors of infectiousness.

### OA02-212-15 Integration of molecular, spatial and clinical data to understand *M. tuberculosis* transmission among people with sub-clinical TB in a rural South African population

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**Background:** In high-burden settings, most TB disease derives from recent *Mycobacterium tuberculosis* (Mtb) transmission. Subclinical TB accounts for at least half of prevalent TB but its infectiousness is unknown.

**Design/Methods:** To better understand Mtb transmission in rural KwaZulu-Natal, South Africa, we integrated molecular, spatial and clinical data from a population-based multi-disease screening study conducted from 2018-2020.

All participants over the age of 15 years were screened for TB. Participants with TB symptoms or radiological abnormality had sputum collected for liquid culture and whole genome sequencing. Genomes were assembled, annotated and clustered using published pipelines (TB profiler and MTBseq) and transmission investigations were done using TransPhylo.

**Results:** Of 18,041 participants enrolled, 106 (0.6%) were liquid culture positive. 105/106(99%) isolates were successfully whole genome sequenced and confirmed as Mtb (8/105 Lineage 1, 36/105 Lineage 2, 4/105 Lineage 3, 57/105 Lineage 4). 17/105(16%) isolates grouped into eight clusters (related closely to at least one other isolate by  $\leq 12$  single-nucleotide polymorphisms). 11/17(65%) of clustered isolates were derived from individuals who were asymptomatic (defined as reporting none of the four WHO screening symptoms - cough of any duration, fever, night sweats or weight loss). 4/8(50%) of clusters involved only people with asymptomatic TB.

Geospatial analysis demonstrated that members of one cluster resided in the same household, members of three clusters resided in different households from the same neighbourhood and members of four clusters had no discernable geospatial relationship.

**Conclusions:** One in six Mtb isolates from a cross-sectional population-based survey in rural KwaZulu-Natal clustered, consistent with high rates of recent transmission. A substantial proportion of people whose Mtb clustered were asymptomatic, suggesting that subclinical TB may contribute to transmission. To control ongoing transmission in high prevalence settings, more information about the infectiousness of subclinical TB and how it may contribute to transmission is urgently required.

### OA02-213-15 3-year outcomes in individuals with microbiologically proven sub-clinical TB detected in a population-based survey in rural KwaZulu-Natal, South Africa

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**Background:** In prevalence surveys, approximately 50% of people diagnosed with tuberculosis (TB) have sub-clinical disease. The outcomes of these individuals compared to those diagnosed with clinical TB are poorly understood.

Here we assessed the 3-year clinical, radiological and microbiological outcomes of people diagnosed with TB during a population-based survey.

**Design/Methods:** People newly diagnosed with microbiologically-confirmed TB during the baseline survey (2018-2020) were contacted for a follow-up visit approximately three years later (2021-2023).

Follow-up measures included a health questionnaire, height and weight measurements, chest radiography and sputum collection for TB culture and Xpert Mtb/RIF Ultra testing. Results were then compared by HIV status and baseline symptom status.

**Results:** Among 174 eligible participants, 143 (82%) were asymptomatic at baseline (by WHO 4-symptom screen, including cough of any duration) and 76 (44%) were people living with HIV (PLHIV). On recontact, 15/174 (9%) were confirmed to have died and 129/174 (74%) attended follow-up. Of those assessed at follow-up, 122/129 (95%) reported having initiated and completed 6 months of TB treatment.

Clinical, radiological and microbiological outcomes did not differ by baseline symptom status. Symptom status at follow-up differed by HIV status with fewer PLHIV than people without HIV reporting persistent respiratory symptoms (7% vs. 27%,  $p=0.0069$ ).

**Conclusions:** Despite very high rates of asymptomatic or subclinical disease, nearly all the people who were evaluated for 3-year follow-up after diagnosis of microbiologically-confirmed TB during a community-based survey reported linkage to care and completion of TB treatment. Only 9% of people diagnosed with community-detected TB had died – less than half of

South Africa's case fatality ratio of 19% – suggesting potential benefit from treatment of TB at an early stage. Most outcomes, including death, did not differ by HIV or baseline symptom status. Clear guidance for the detection and management of subclinical TB is required urgently.

### OA02-214-15 Benefits of diagnosing sub-clinical TB disease among people who smoke drugs

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**Background:** People who smoke illicit drugs (PWSD) are at increased risk of tuberculosis (TB) disease and may delay seeking care. Diagnosing and linking to care individuals with early TB disease may improve outcomes and reduce transmission.

**Design/Methods:** We analyzed data from 187 individuals with TB from Worcester, South Africa. Fifty-seven were recruited through respondent driven sampling, an active case finding (ACF) approach. One-hundred-thirty were diagnosed by self-referral in clinic (passive case finding (PCF)). All had microbiologically confirmed TB and screened urine positive for methamphetamine and/or methaqualone.

We compared demographics and bacterial burden using basic descriptive statistics. We obtained adjusted associations of ACF and PCF with bacterial burden using negative binomial regression for TTP and logistic regression for cavitation and smear positivity. We report the proportion initiating TB treatment and their 6-month treatment outcomes.

**Results:** Median (IQR) TTP for ACF was 12 (7,17) days compared to 7 (5, 10) for PCF. Thirty-one (54.4%) ACF participants were asymptomatic, reporting no cough, fever, night sweats, or weight loss compared to 129 (99.2%) PCF participants reporting  $\geq 1$  symptom. Fourteen (24.6%) ACF participants were smear positive compared to 96 (73.8%) PCF participants (Table 1). PCF participants were more likely to be smear positive (OR:9.1, 95%CI:4.3, 20.2), have cavitory disease (OR:2.4, 95%CI:1.2, 4.9) and have a shorter TTP (RR:0.5, 95%CI:0.5, 0.7), after adjusting for age, sex,

HIV, and tobacco use. Among ACF participants, 25/34 (73.5%) initiated treatment with 19/25 (76.0%) completed, cured, or on treatment at 6 months.

	Active case finding (N=57)	Passive case finding (N=130)
Age, years	36 (29, 41)	35 (27, 48)
Male Sex	43 (75.4%)	101 (77.7%)
HIV Positive	18 (31.6%)	40 (31.0%)
Tobacco Use	54 (94.7%)	99 (76.2%)
TTP, days	12 (7, 17)	7 (5, 10)
Smear positive	14 (24.6%)	96 (73.8%)
Cavitary Disease	22 (43.1%)	82 (63.1%)
Asymptomatic	31 (54.4%)	1 (0.8%)

Table 1. Demographics and disease burden comparison for participants newly diagnosed with TB who smoke illicit drugs from active versus passive case finding.

**Conclusions:** We found lower bacterial burden and substantial subclinical disease among PWS identified with TB through ACF compared to individuals diagnosed in clinic. Most ACF-diagnosed participants successfully initiated and completed TB treatment. Diagnosing and linking to care PWS early in disease progression when infectivity is low has strong potential to reduce transmission and improve outcomes.

## OA03 WGS for DRTB

### OA03-215-15 Development and validation of a targeted nanopore sequencing panel to personalise treatment dosing in TB patients

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**Background:** Standardized dosing of anti-tubercular (TB) drugs contributes to substantial interindividual variation in plasma drug levels, which in turn may associate with adverse drug reactions, delayed treatment response, and relapse. Mutations in genes involved in

drug metabolism influence pharmacokinetic variability; however, scalable pharmacogenomic (PGx) assays that can predict the metabolism of anti-TB drugs have been lacking.

**Design/Methods:** We developed a Nanopore PGx panel targeting 15 single nucleotide polymorphisms (SNP) in 5 genes affecting the metabolism of isoniazid (INH), rifampin (RIF), linezolid (LZD) and bedaquiline (BDQ). To validate the panel, we sequenced DNA samples (n=48) from the 1000 genomes project and compared variant calling accuracy with Illumina whole genome sequencing. We then sequenced DNA samples from patients with active TB (n=100) from South Africa on a MinION Mk1C and related pharmacokinetic measures of INH and RIF with genotypes. Data was analyzed on MinKNOW (release 22.08.4) and Epi2ME (version 4.1.3.). We compared INH and RIF clearance rates by genotype patterns using Kruskal-Wallis tests.

**Results:** The PGx panel demonstrated 100% concordance with Illumina sequencing in variant identification for the 48 samples from the 1000 Genomes Project and 20 oral swabs from healthy volunteers. In the clinical cohort, coverage was >100x for 1498/1500 (99.8%) positions across the 100 samples. One third (33/100) of participants were identified as N-acetyltransferase-2 (NAT2) slow, 47% intermediate and 20% rapid acetylators. INH clearance rates were nearly 4 times greater in rapid acetylators (42.0 L/h) compared with slow acetylators (11.1 L/h) (p<0.0001). Rifampicin clearance rates were 15% lower (21.1 L/h vs 25.0 L/h) in individuals who were homozygous for AADAC rs1803155 G>A substitutions (p=0.031).

**Conclusions:** Targeted nanopore sequencing enables highly accurate detection of polymorphisms influencing TB drug metabolism on a low-cost, portable instrument. This approach could enable personalized dosing of TB therapy, reducing toxicity risks and improving treatment outcomes.

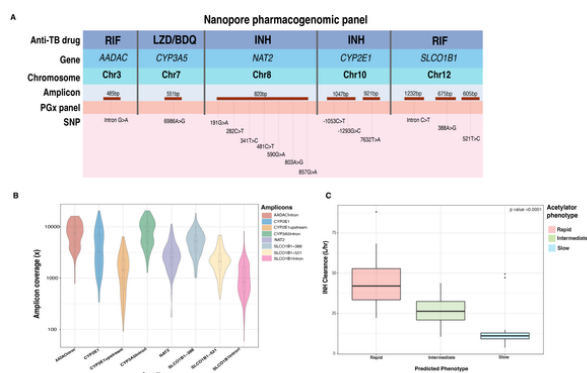


Figure: (A) Nanopore PGx panel. Top row contains a list of anti-TB drugs for which pharmacogenomic associations were identified in the literature. Genes and their corresponding chromosomes are listed in the rows two and three respectively. Amplicons are not scaled to their product length. (B) Amplicon coverage: Sequencing coverage per amplicon in samples from active TB patients (n=100) sequenced on MinION Mk1C. (C) Predicted NAT2 phenotype and INH clearance in TB patients: Predicted rapid acetylators retained INH in plasma for shorter period than predicted intermediate and slow phenotypes (p-value<0.0001).



**OA03-216-15 Performance of whole-genome sequencing and the BACTEC MGIT 960 system in the analysis of anti-TB drugs under routine conditions in Peru: A comparison**

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**Background:** Since 2018, the WHO recommended the use of Whole Genome Sequencing (WGS) to detect mutations associated with resistance in *Mycobacterium tuberculosis* (MTB).

The study aims is to evaluate the diagnostic performance of the WGS in comparison with the BACTEC MGIT 960 for the detection of drug resistance in a routine workflow in Peru.

**Design/Methods:** 100 solid cultures with genotypic resistance to isoniazid and/or rifampicin were simultaneously processed for DST through BACTEC MGIT 960 and WGS according to routine laboratory workflow. Strains were sequenced on Illumina MiSeq at the Instituto Nacional de Salud in Peru. Resistance-associated variants were identified with TBProfiler v4.1.1 using the catalogue of mutations published by the WHO. First and second line drugs were evaluated by both methodologies. Sensitivity, specificity, positive predictive value, negative predictive value, and categorical agreement of WGS were determined for different drugs using as reference phenotypic test.

Drug	WGS	BACTEC		CA (%)	Sensitivity (CI)	Specificity (CI)	PPV (CI)	NPV (CI)	Kappa
		R	S						
Rifampicin	R	2	2	94.4	1.00 (0.16, 1.00)	0.94 (0.80, 0.99)	0.50 (0.07, 0.93)	1.00 (0.89, 1.00)	0.64
	S	0	32						
Isoniazid	R	5	0	90.9	0.83 (0.36, 1.00)	1.00 (0.48, 1.00)	1.00 (0.48, 1.00)	0.83 (0.36, 1.00)	0.82
	S	1	5						
Pyrazinamide	R	31	1	94.0	0.89 (0.73, 0.97)	0.98 (0.89, 1.00)	0.97 (0.84, 1.00)	0.92 (0.81, 0.98)	0.88
	S	4	48						
Moxifloxacin	R	2	6	93.2	1.00 (0.16, 1.00)	0.93 (0.85, 0.97)	0.25 (0.03, 0.65)	1.00 (0.95, 1.00)	0.38
	S	0	80						
Levofloxacin	R	8	0	100.0	1.00 (0.63, 1.00)	1.00 (0.95, 1.00)	1.00 (0.63, 1.00)	1.00 (0.95, 1.00)	1.00
	S	0	80						
Amikacin	R	2	0	100.0	1.00 (0.16, 1.00)	1.00 (0.96, 1.00)	1.00 (0.16, 1.00)	1.00 (0.96, 1.00)	1.00
	S	0	86						
Capreomycin	R	7	0	98.9	0.88 (0.47, 1.00)	1.00 (0.95, 1.00)	1.00 (0.59, 1.00)	0.99 (0.93, 1.00)	0.93
	S	1	80						

WGS: Whole genome sequencing, CA: Categorical agreement, CI: 95% Confident interval, PPV: Positive predictive value, NPV: Negative predictive value, R: resistant, S: susceptible

Table 1. Diagnostic performance results of WGS comparing with phenotypic BACTEC MGIT in routine conditions.

**Results:** According to BACTEC MGIT 960 new or repurposed drugs only presented susceptible patterns. WGS detected 64 MDR-TB, 8 Pre-XDR-TB, 47 isoniazid-mono-resistant TB, 6 rifampicin-mono-resistant TB, 2 with additional resistance and 13 susceptible strains. Overall categorical agreement for the seven compared drugs was 96.5%.

Sensitivity had a minimum value of 0.83 (isoniazid) and a maximum of 1 (rifampicin, moxifloxacin, levofloxacin and amikacin). Specificity had a minimum of 0.93 (moxifloxacin) and a maximum of 1 (levofloxacin, isoniazid, amikacin and capreomycin).

According to kappa index isoniazid, pyrazinamide, levofloxacin, amikacin and capreomycin exhibited an almost perfect agreement, whereas rifampicin had a good agreement and moxifloxacin a medium agreement (Table 1). Regarding delamanid and linezolid, categorical agreement was 100%.

**Conclusions:** The routine use of WGS in laboratory workflows in Peru has a high diagnostic performance to detect resistance against anti-TB drugs, allowing results to be obtained through a single analysis and quickly cutting the chain of transmission of drug-resistant TB in the Peruvian community.

**OA03-217-15 Genome sequencing to resolve discrepant *M. tuberculosis* in pyrazinamide drug susceptibility results**

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**Background:** Pyrazinamide (PZA) has a unique role in current anti-TB regimens, and its application in Pyrazinamide resistant (PZA<sup>R</sup>) patients leads to treatment failure. Thus, understanding PZA<sup>R</sup> patterns would improve treatment management. Due to infrastructure and complexity, PZA susceptibility testing (DST) is not routinely performed. This study investigated diagnostic performance of phenotypic and genotypic methods for detecting prevalence of PZA<sup>R</sup> from presumptive drug resistance TB patients.

**Design/Methods:** We assessed DST among 401 *Mycobacterium tuberculosis* isolates from Chennai, India, collected during 2017-2018. We investigated phenotype by Wayne's and reduced inoculum MGIT960-DST, genotype by Sanger sequencing. The discrepancies were resolved using whole genome sequencing (WGS) to investigate WHO-listed variants and novel gene mutations. PZA<sup>R</sup> was confirmed by performing PZA-DST at various concentrations (50, 100, 200 µg/ml).

**Results:** The prevalence of phenotypic PZA<sup>R</sup> was 11.7%. Sensitivity and specificity of PZA MGIT-DST and Wayne's method were 100% and 91.2%, respectively. In Wayne's method, 8.4% showed discrepancy with MGIT and 0.5% with Sanger sequencing. Of 11.7% PZA<sup>R</sup>, 3.2% had *pncA* mutations, and 8.5% had unknown mechanisms associated with PZA<sup>R</sup> detected by

WGS. WGS data revealed four novel gene mutations with different polymorphisms in *mas*, *glpK*, *gpsI* and *lprG*. Sixteen variable mutations were found in the mentioned four newly reported genes, and two isolates had individual mutations in *mas* and *glpK* genes with wild-type *pncA*.

Mutation identified by WGS	No. of isolates with Wildtype <i>pncA</i>	§Drug Susceptibility by MGIT	Spoligotyping
<i>glpK</i>	1	PZAR (100µg/ml)	*EAI3-IND
<i>mas</i>	1	PZAR (100µg/ml) + INH	T1
*Combined Mutations in <i>clpC1</i> , <i>glpK</i> , <i>mas</i> , <i>gpsI</i> , <i>fadD2</i> and <i>lprG</i>	16	PZAR (200 µg/ml) – 3 isolates PZAR (100 µg/ml) – 2 isolates PZAR (50 µg/ml) – 2 isolates PZAR (100µg/ml) + INH - 4 isolates PZAR (50µg/ml) + INH – 1 isolate PZAR (200µg/ml) + RIF + INH - 1 isolate PZAR (100µg/ml) + RIF + INH – 1 isolate PZAR (50µg/ml) + RIF + INH – 2 isolates	*EAI3-IND- 12 EAI5- 1 EAI1-SOM- 2 Orphan strain -1
*Combined Mutations in <i>panD</i> , <i>clpC1</i> , <i>glpK</i> , <i>mas</i> and <i>gpsI</i>	2	PZAR (200µg/ml) + INH - 1 isolate PZAR (100µg/ml) + INH -1 isolate	EAI5-1 *EAI3-IND-1

**Abbreviations:** *glpK*- glycerol kinase; *mas*- Mycocerosic acid synthase; *gpsI*- bifunctional protein guanosine pentaphosphate synthetase; *lprG*- Lipoprotein; *panD*- Aspartate decarboxylase; *clpC1*- Caseinolytic protein; PZAR<sup>R</sup> -Pyrazinamide resistant; INH- Isoniazid; RIF- Rifampicin; \*- Indicate that PZA may interfere with multiple targets; §-True PZA<sup>R</sup> confirmed by different concentration (50, 100, 200 µg/ml) of PZA drug; \*-Predominantly EAI3-IND lineage was associated with PZA<sup>R</sup> in this region.

*Table. List of gene mutations identified from discrepant isolates (Wayne's negative).*

**Conclusions:** The study standardized PZA MGIT-DST using reduced inoculum protocol and found greater concordance with WGS than Wayne's method, which relies solely on PZase activity or *pncA* mutations. Performing WGS in addition to MGIT-DST to identify mutations involved in PZA<sup>R</sup> reduced the probability of getting ambiguous outcomes. The findings suggest developing new molecular techniques for the presence of PZA<sup>R</sup> variants and ensuring high-quality DST performance.

## OA03-218-15 Characterisation of *M. tuberculosis* drug resistance mutation patterns using targeted next-generation sequencing in Namibia

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**Background:** Namibia is a tuberculosis (TB) high burden country with an estimated incidence of 560 per 100,000 inhabitants. TB control is challenged by the emergence of multi drug-resistant (MDR) and extensively-drug-resistant (XDR) of *Mycobacterium tuberculosis complex* (MTBC) strains. Effective tools for drug resistance (DR) testing are essential to guide diagnostics and surveillance.

Here, we determined DR profiles of clinical MTBC strains in Namibia using targeted Next Generation Sequencing (tNGS).

**Design/Methods:** A total of 134 clinical MTBC strains obtained between January 2020-December 2022 with rifampicin resistance (RR) by GeneXpert Ultra were analysed. tNGS was performed using the Deeplex<sup>®</sup>-Myc-TB kit on the iSeq100 platform. Data were analysed on the Deeplex<sup>®</sup>-Myc-TB web application.

**Results:** Of 134 sequenced samples, 115 (86%) had complete resistance profiles across 15 anti-TB drugs evaluated by Deeplex<sup>®</sup> assay (Figure 1).

Overall, 129 (96%) strains were MDR, two (1.5%) were XDR. Further, pyrazinamide, ethambutol, and fluoroquinolone resistances were detected in 52%, 48%, and 2% of the MDR strains, respectively. Two strains had frameshift mutations in *Rv0678* (insGA, insC, delG) and were classified bedaquiline/clofazimine (BDQ/CFZ) resistant.

Interestingly, 11 strains had a Rv0678 D88G mutations with unknown implication for BDQ/CFZ resistance. Mutations *rpoB* A450L (45%), H445Q (13%), L430P (11%) were the main RR conferring mutations, mutations *katG* S315T (55%) and *inhA* C15T (27%) were the main INH resistance mutations.

Pyrazinamide and ethambutol resistance mutations were observed, with *pncA* gene mutation L35P (17%) and *embB* M306I (29%), M306V (12%) and G406S (4%) being most frequent. Mutations D94N and D94G have been found in the MTBC strains with fluoroquinolone resistance.

Antibiotic	Locus	Mutation	No. of isolates (frequency %)	Total # of mutation detected per locus
RIF	rpoB1	H445Q	18 (13)	26
		L430P	15 (11)	
		L430PIH445Q	15 (11)	
		S450L	60 (45)	
INH	katG	S315T	74 (55)	3
		S315R	1 (0,7)	
		inhA	2 (1)	
PZA	pncA	fabG1 C-15T	36 (27)	16
		D12A	9 (7)	
		L35P	23 (17)	
EMB	embB	M306I	39 (29)	9
		M306V	16 (12)	
FQ	gyrA	D94N	1 (0,7)	2
		D94G	1 (0,7)	
SM	rpsL	K43R	42 (31)	1
ETH	ethA	Y84D	23 (17)	2
BDQ-CFZ	rv0678	C46*insGA insC	1 (0,7)	3
		R134* delIG	1 (0,7)	

**Conclusions:** tNGS can provide timely and more comprehensive DR information for clinical MTBC strains in Namibia, that can be used to guide therapy and DR surveillance. In patients with RR-TB, resistance to other first line drugs is high, while fluoroquinolone and bedaquiline/clofazimine resistances are still low.

### OA03-219-15 Tuberculini: targeted sequencing that detects resistance to 12 antibiotics from TB patient sputum

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**Background:** For tuberculosis, established molecular tests are fast but only cover a small number of drugs, whereas with culture resistance to multiple drugs can be tested simultaneously but is quite slow, requiring weeks. These shortcomings are addressed by Tuberculini, a molecular diagnostic test that provides a 12-drug resistance profile within 48 hours.

**Design/Methods:** Tuberculini is a highly multiplex panel amplifying 96 targets to cover almost the entire set of mutations associated with drug-resistant tuberculosis given in the 2021 WHO mutations catalogue, and 62 lineage mutations that distinguish the 7 main lineages and 55 sublineages of *Mycobacterium tuberculosis*.

**Results:** Over the resistance mutations from the WHO mutations catalogue, Tuberculini had 99.6 % concordance with whole-genome sequencing (WGS) over 528 phenotypes from 44 *Mycobacterium tuberculosis* isolates. There was 100 % concordance over these 528 phenotypes between isolate and spiked sputa. For sputa spiked with these 44 isolates and 10 clinical samples

Tuberculini achieved accuracy of 92 % over 564 phenotypes, with accuracy of 100 % across 10 clinical samples from routine testing at a Swiss hospital. Tuberculini works directly on sputa with a limit of detection between  $C_t$  (cyclic threshold) values 33.3 and 34 (average coverage >20) and an average coverage in the thousands for  $C_t$  values between 22 and 28 (low TB load in GenXpert classification).

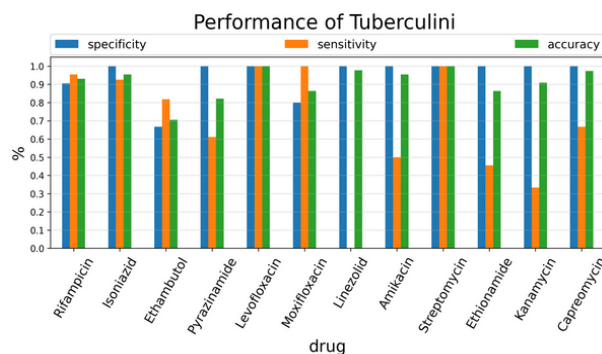


Figure. Tuberculini's specificity, sensitivity and accuracy in predicting resistance for 44 *Mycobacterium tuberculosis* isolates when spiked in sputa, taking phenotype (culture) as the ground truth.

**Conclusions:** As the first study on the newly certified Tuberculini the results are promising, showing good overall sensitivity, specificity, and accuracy over the 44 isolates carefully chosen to test the panel. The 100 % concordance between spiked sputa and isolates and 100 % performance on patient samples indicate that Tuberculini can be successfully deployed in clinical settings without the need for the cultured isolates required by WGS. This means that comprehensive drug resistance profiles can be produced within 2 days allowing bespoke treatment to begin with little delay.

### OA03-220-15 Implementation of targeted next-generation sequencing for improved diagnosis of drug-resistant TB in low-resource settings

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**Background:** Targeted next-generation sequencing (tNGS) from clinical specimens has the potential to become a comprehensive tool for routine drug-resistance (DR) prediction of *Mycobacterium tuberculosis* complex strains (MTBC), the causative agent of tuberculosis (TB).

However, TB mainly affects low- and middle-income countries, which have specific needs and challenges for implementing new technologies.

**Design/Methods:** Within the framework of the German Global Health Protection Programme, we share our experience on using a model for programmatic implementation of tNGS in Namibia, an upper-middle-income country located in Southern Africa and suffering from a high-burden of TB (460 per 100,000 population) and around 560 new multidrug-resistant TB cases per year. Our strategy for the implementation of tNGS was based on three pillars: preparation, implementation, and sustainability.

The first cycle of implementation was concluded between 2019-2022, with a total investment of approximately 418,500 USD. The local team received hands-on on-site and on-line trainings and conferences/workshops. Local wet and dry NGS lab infrastructures were developed.

**Results:** Upon completion of the practical sequencing training, in a pilot run to assess the capacity and feasibility, strains from clinical culture samples from TB patients were sequenced. 49 MTBC rifampicin-resistant (RR) samples (based on Xpert MTB/RIF Ultra) were tested, upon informed consent from participants, for tNGS after culture.

The majority (31/49, 63.3%) of the sequenced samples showed acceptable sequencing results, i.e. the quality of the sequencing data was enough to detect resistance-associated mutations with high prevalence among the reads. Only a single sample demonstrated negative (2%) sequencing result acceptability.

**Conclusions:** Despite the delays caused due to COVID-19 restrictions for construction of infrastructure, on-site trainings and deliveries, tNGS is successfully implemented in Namibia with potential for clinical application and to interrogate other emergent pathogens.

Our next steps are to introduce sequencing from direct sputum samples and programmatic adoption in clinical practice.

### OA03-221-15 Construction of whole-genome sequencing by *de novo* assembly of a *M. tuberculosis* isolate from North Korea and its comparison with H37Rv

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**Background:** WGS is a valuable tool for providing a broader genomic perspective. Although *Mycobacterium tuberculosis* (M.tb) H37Rv genome sequence is the most common reference for genetic variation analysis, numerous reports describe the limitations of its use for comparative analyses of clinical strains.

Our objective was to construct the first known WGS of a clinical M.tb strain from North Korea and compare its genetic variations with H37Rv.

**Design/Methods:** PSNK363, a M.tb isolate belonging to one of the major groups based on rep-PCR genotyping of 179 isolates from North Korea in our previous study. PSNK363 is susceptible to all anti-TB drugs by phenotypic DST in LJ medium. The genomic DNA was extracted using the CTAB method from the culture of PSNK363 grown in Middlebrook 7H9 media with 10% OADC at 37°C.

*De novo* whole genome assembly was performed by MacroGen Inc. (Seoul, South Korea). Briefly, the genomic DNA was applied for preparing SMARTbell template, and for sequencing on the PacBio Sequel II System and an Illumina MiSeq platform. The sequences were compared with Genbank data of H37Rv (NC\_000962.3).

**Results:** The total length of the complete genome sequence of PSNK363 was 4,422,110 bp, making it 10,578 bp longer than H37Rv. There were 4,079 protein-coding genes in PSNK363 compared to 4,018 in H37Rv.

Additionally, 53 tRNAs and 3 rRNA operons in PSNK363 were annotated, while 45 tRNAs in H37Rv. The majority of the genes (72.7%) were assigned putative functions, while the remaining 27.3% were annotated as hypothetical. The phylogenetic tree of PSNK363 indicated that it is closest to Hong Kong isolates.

Interestingly, assembled contigs showed that PSNK363 contained two inversion regions which were not present in H37Rv.

We found that PSNK363 was susceptible to all first-line TB drugs.

**Conclusions:** Compared to H37Rv, PSNK363 had a longer genome sequence, more protein-coding genes and two inversion regions.

### OA03-222-15 Targeted next-generation sequencing, a potential tool for detecting drug-resistant TB directly from sputum specimens: Lessons learnt from high-burden clinical settings in Bangladesh

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**Background:** Access to drug-susceptibility testing (DST) is a major challenge for drug resistant tuberculosis (DR-TB) detection. Phenotypic DST (pDST) takes long time while Xpert MTB/RIF (Xpert) and line probe assays (LPAs) can detect DR-TB directly from clinical specimens but are limited to detecting few drugs with only common mutations. Targeted next-generation sequencing (tNGS) has emerged as an alternative to existing DST which can detect resistance directly from the clinical specimens.

We aimed to investigate the potential of tNGS for detecting DR-TB directly from the clinical samples in Bangladesh.

**Design/Methods:** A total of 264 sputum samples from confirmed TB cases (102 rifampicin sensitive and 162 rifampicin resistant by Xpert) were collected and processed for pDST, LPAs and tNGS. Resistotypes of tNGS by using the Deeplex Myc-TB kit were compared with pDST. Sensitivity and specificity were measured and agreement was evaluated by Cohen's kappa coefficient.

**Results:** tNGS showed 58.0% and 50.4% resistant to rifampicin (RR) and isoniazid and 47.0% were MDR-TB. Among the RR-TB, 20.3% were also resistant to fluoroquinolones. tNGS showed higher sensitivity for rifampicin (98.5%; 95% CI, 94.6-99.8), isoniazid (96.3%; 95% CI, 91.6-98.8), and fluoroquinolones (93.3%; 95% CI, 77.9-99.2), but comparatively lower for streptomycin (69.4%), ethionamide (55.2%) and pyrazinamide (50.7%) against pDST. Semi-quantitative Xpert burdens are associated with sequence quality, samples having high burden showed high quality sequencing than low bacterial burden. It also achieved higher specificity and positive predictive value for all the drugs. The kappa values range from 0.5085 (ethionamide, pyrazinamide and streptomycin) to 1.0 (rifampicin, isoniazid and fluoroquinolones) for different drugs, indicating perfect agreement for the key drugs.

**Conclusions:** Our results suggested that tNGS is a valuable tool to identify drug resistance profiles directly from samples with faster turnaround time than pDST. The feasibility, throughput, and accuracy of tNGS lends it the potential to replace pDST in high-burden settings like Bangladesh.

### OA04 Clinical and epidemiologic aspects of post-TB lung health

#### OA04-223-15 Prevalence of TB-related symptoms and self-reported disability among adults post-TB treatment in Uganda: A retrospective study

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**Background:** There is growing evidence to suggest that post-TB related morbidity occurs but there is limited epidemiological data on the burden of symptoms and disability after TB treatment.

Our study evaluated the prevalence of TB-symptoms, self-reported disability and factors associated among individuals who recently completed TB treatment in Uganda.

**Design/Methods:** Between January and July 2022, we conducted a retrospective cohort study of adults  $\geq 18$  years who had successfully completed treatment for drug-sensitive TB in Kampala, Uganda within 6 months prior to enrollment. We collected data on current TB-related symptoms (cough, chest pain, weight loss, fever, hemoptysis and night sweats). We measured disability using 12-items adopted from the World Health Organization Disability Assessment Schedule (WHODAS 2.0). The WHODAS 2.0 captures the level of functioning in six domains including cognition, mobility, self-care, getting along, life activities and participation on a 5-point Likert scale (1=none to 5=extremely cannot do). The minimum and maximum scores are 12 and 60 respectively.

**Results:** Of the 101 participants, the mean age (SD) was 37.1 (12.1), 55 (54.5%) were female, and 26 (25.7%) were HIV-infected. The prevalence of any TB-related symptoms was 48 (47.5%). The proportion of persons self-reporting any disability was 71.3% (95% CI, 61%-80%). The median (IQR) disability score was 15 (12-20), 56% reported disability in 3-6 domains while the mo-

bility and participation domains contributed 339/777 (51.3%) of the cumulative disability score. Being female was significantly associated with self-reporting a disability in any of the domains (AOR: 2.90,  $p=0.022$ ) after adjusting for age and HIV status.

**Conclusions:** TB-related symptoms and self-reported disability were highly prevalent in the study setting suggesting that the health and wellbeing for persons who complete TB treatment remain compromised. Further evaluation and interventions to address the quality of life for survivors during the post-TB period should be considered as part of the continuum of care.

### OA04-224-15 Incidence and determinants of sub-clinical recurrence of TB among cured patients with pulmonary TB in India

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**Background:** With the global target to eliminate tuberculosis (TB) by 2030, subclinical pulmonary TB (PTB), defined as viable detectable mycobacterium TB (MTB) in absence of symptoms, has emerged as a potential contributor to continued TB transmission, impeding global efforts for ending TB.

Data are limited on subclinical TB-recurrence in high-burden settings. Using two large prospective cohorts, we assessed the incidence and determinants of subclinical TB-recurrence in India.

**Design/Methods:** Drug sensitive PTB (PTB) participants  $\geq 14$  years of age who successfully completed anti-TB treatment (ATT) (clinical response with or without microbiological evidence of cure at the end of ATT) and followed for up to 18-months post-ATT completion were included in the analysis. They underwent mycobacteriology (smear microscopy and cultures) at 6, 12, and 18-months post-ATT and suspected TB-recurrence visit. TB-recurrence was categorized as subclinical infectious (asymptomatic, positive mycobacteriology (smear and/or culture)), clinical non-infectious (TB symptoms, negative mycobacteriology) and clinical infectious TB (TB symptoms, positive mycobacteriology).

We calculated incidence of TB-recurrence and performed Cox-regression to identify its determinants. We performed sensitivity analysis in a subset with culture-confirmed cure.

**Results:** Of 1196 PTB cases enrolled, 889 (74%) were cured. Among these 889, 67 (8%) had TB-recurrence (incidence rate:7.8 (95% CI:6.0-9.9)/100 PY). The incidence for subclinical ( $n=28$ ), clinical non-infectious ( $n=9$ ) and clinical infectious TB ( $n=30$ ) was 3.3 (IQR:2.2-4.8), 1.1 (IQR:0.5-2.1), and 3.6 (IQR:2.4-5.1), per 100-PY, respectively. Median time to subclinical TB-recurrence was 208 (IQR:148-280) days post ATT-completion. Sub-clinical TB-recurrence was independently associated with 14-35 year age-group (aHR-3.3, 95% CI- 1.25-10.0,  $p=0.02$ ) and smokeless tobacco (aHR-2.3, 95% CI-1.0-5.3,  $p=0.04$ ).

Undernutrition (aHR-1.9, 95% CI-0.8-4.5,  $p=0.16$ ) showed a trend though not statistically significant. The results were similar in a subset with culture-confirmed cure (Table 1).

	Treatment complete $\pm$ evidence of microbiological cure (N= 889)		Treatment complete with evidence of culture-confirmed cure (N= 756)	
	Unadjusted HR * uHR (95% CI), p-value	Adjusted HR aHR (95% CI), p-value	Unadjusted HR * uHR (95% CI), p-value	Adjusted HR aHR (95% CI), p-value
<b>Age-group (Years)</b>				
14-35	2.5 (1.1-5.0), 0.03	3.3 (1.3-10.0), 0.02	2.6 (1.1-6.2), 0.03	3.0 (1.2-7.4), 0.02
$\geq 35$	Ref	Ref	Ref	Ref
<b>Gender</b>				
Female	0.7 (0.3-1.5), 0.34	0.8 (0.3-1.9), 0.57	0.7 (0.3-1.5), 0.36	0.8 (0.3-1.9), 0.57
Male	Ref	Ref	Ref	Ref
<b>Body mass index</b>				
Underweight	2.1 (0.9-5.0), 0.09	1.9 (0.8-4.5), 0.16	2.0 (0.9-4.1), 0.11	1.8 (0.8-4.4), 0.18
Obese	0.8 (0.1-6.6), 0.84	1.3 (0.2-10.5), 0.83	0.9 (0.1-7.4), 0.93	1.5 (0.2-12.5), 0.71
Normal	Ref	Ref	Ref	Ref
<b>Tobacco chewing</b>				
Yes	2.3 (1.1-4.8), 0.03	2.3 (1.0-5.3), 0.04	2.3 (1.1-4.8), 0.03	2.4 (1.0-5.5), 0.04
No	Ref	Ref	Ref	Ref
<b>Pre-treatment Smear</b>				
Positive	1.7 (0.7-4.3), 0.23	1.5 (0.6-3.7), 0.39	1.1 (0.4-2.5), 0.96	Not included
Negative	Ref	Ref	Ref	
<b>Diabetes mellitus</b>				
No	0.8 (0.3-1.8), 0.53	Not included	0.7 (0.3-1.6), 0.35	Not included
Yes	Ref		Ref	
<b>Treatment Regimen</b>				
Thrice Weekly	1.0 (0.4-2.6), 0.97	Not included	1 (0.4-2.5), 0.92	Not included
Daily	Ref		Ref	

\* Data not shown: Other risk factors assessed in the univariable analysis but found to be not associated with subclinical TB include- HIV infection, smoking, alcohol consumption, cavitory disease, pre-treatment chest radiographic score, regimen duration, duration of symptoms, and month 2 smear.

Table 1. Risk factor analysis for Subclinical TB-Recurrence after successful completion of anti-TB treatment.

**Conclusions:** Subclinical TB-recurrence was as common as clinical TB-recurrence among persons with cured TB in India. Our findings highlight the importance of strategies to identify and treat subclinical TB.

### OA04-225-15 Characterisation of spectrum of post-TB symptoms, lung function and imaging abnormalities: A systematic review and meta-analysis

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**Background:** Many of the approximately 8 million annual TB survivors develop post-tuberculosis lung disease (PTLD). We conducted a systematic review to characterize post-TB sequelae, specifically patterns of abnormal spirometry, unique respiratory symptoms, and distinct anatomical abnormalities in low- and middle-income countries (LMIC).

**Design/Methods:** PubMed, Embase and CINAHL were searched for studies including patients with previous pulmonary or intrathoracic TB to outline the spectrum of sequelae after TB treatment. Data were abstracted on pattern of post-TB symptoms, chest imaging abnormalities and spirometric abnormalities (by varied definitions). Results are presented as pooled prevalence where appropriate or narrative synthesis.

**Results:** We identified 29 eligible studies; 20 reported on spirometry, 13 on symptoms, and 9 on chest imaging following TB. Prevalence of persistent symptoms ranged from 14.3 to 56.0% for cough, 13.2 to 55.9% for breathlessness, 11.1 to 35.0% for sputum production, 36.1 to 56.9% for wheeze and 3.2 to 32.3% for chest pain. Prevalence of anatomic abnormalities was also high, particularly residual fibrosis (range 15.6 to 61.1%) and cavities (8.6 to 69.6%). Pooled prevalence of obstruction, defined as forced expiratory volume in 1-second (FEV1)/forced vital capacity (FVC) ratio < 0.7 was 27.3% (95% CI 7.5, 63.4) as compared to 28.1% (95% CI 18.7, 40.5,  $p = 0.93$ ) when defined as FEV1/FVC ratio < lower limit of normal (LLN). Pooled prevalence of restrictive pattern, defined as FVC < 80%, was 39.6% (95% CI 22.1, 60.3) as compared to 38.7% (95% CI 14.3, 70.4,  $p = 0.94$ ) when defined as FVC < LLN. In studies reporting on mixed obstructive and restrictive ventilatory impairment, pooled prevalence was 13.7% (95% CI 6.9, 25.2).

**Conclusions:** There is a large spectrum of respiratory symptoms, functional and structural lung abnormalities following treated TB. A detailed understanding of the clinically relevant manifestations of PTLD is important for TB care providers, particularly in LMIC settings.

### OA04-226-15 Development and validation of a simple, point-of-care, case-finding approach for post-TB lung disease

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**Background:** Tuberculosis disease (TB) is associated with impaired lung function that persists despite treatment. Spirometry, the gold standard for diagnosing lung function defects, is expensive and technically challenging. We sought to develop a simple, point-of-care, case-finding approach for post-TB lung disease (PTLD).

**Design/Methods:** We enrolled 569 adults ( $\geq 18$  years) within 60 days of successfully completing their pulmonary TB treatment in the ongoing TB Aftermath study in India. Participants underwent pre-bronchodilator spirometry and respiratory questionnaires for symptoms known to be associated with chronic lung diseases.

PTLD was defined as having airflow obstruction (FEV1:FVC < 70% or < 5<sup>th</sup> percentile for z-scores) and/or restriction (FVC < 5<sup>th</sup> percentile for z-scores) at enrolment. The database was split into training ( $n = 380$ , 67%) and validation ( $n = 189$ , 33%) sets.

We used LASSO regression to identify a minimum set of variables that predicted PTLD at enrolment, evaluated model calibration and discrimination statistics to develop a "PTLD scale", and identified its optimal cut-point using Youden's Index in the training set. Scale performance was separately evaluated in the validation set.

**Results:** Spirometry defined PTLD was detected in 291 (51%) participants. A 6-item scale comprising of three clinical variables (male sex, low body-mass index, and low peak expiratory flow rate [PEF]) and three respiratory symptoms (chest tightness, mucus production and wheezing) had an area under the receiver operating characteristic curve (AUC) of 0.77 (95% CI 0.73-0.82), sensitivity of 68% (95% CI 62-75%), and specificity of 73% (95% CI 66-79%) in the training set; we found similar results in the validation set. Lung function improved during post-TB follow-up.

In a subset of participants with PTLD detected on two separate occasions at least 6 months apart, the PTLD scale at enrolment had a 0.79 (95% CI 0.71-0.87) AUC and 78% (95% CI 63-89%) sensitivity.

Performance of the PTLD scale administered at enrolment	Spirometry defined PTLD within 60 days of TB treatment completion	Spirometry defined PTLD on two separate post-treatment visits 6 months apart
AUC	0.77 (95%CI 0.73-0.80)	0.79 (95%CI 0.71-0.87)
Sensitivity	68% (95%CI 63-74%)	78% (95%CI 63-80%)
Specificity	73% (95%CI 67-78%)	64% (95%CI 53-74%)
Positive predictive value	72% (95%CI 67-78%)	54% (95%CI 41-66%)
Negative predictive value	69% (95%CI 63-74%)	84% (95%CI 73-92%)
Odds ratio scale +ve v/s -ve	5.74 (95%CI 4.00-8.25)	6.30 (95%CI 2.74-14.48)

**Conclusions:** We developed a simple, inexpensive, 6-item scale with moderate discriminatory ability for point-of-care PTLD case-finding.

### OA04-227-15 Cardiovascular comorbidity in patients with and without post-TB lung disease

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**Background:** Cardiovascular disease is a major contributor to mortality in post-tuberculosis (TB) patients, yet studies are scarce.

This study aims to address gaps in our knowledge related to the cardiovascular comorbidity spectrum of sub-Saharan African TB patients, and how these differ among sub-groups with or without post-TB lung diseases (PTLD).

**Design/Methods:** This was a case-control study embedded in an observational TB cohort study (TB Sequel) among adult patients receiving treatment for pulmonary TB. 430 eligible participants were divided into the following groups: no/mild lung impairment defined by spirometry readings (=controls) or moderate/severe lung impairment (=cases).

Cardiovascular abnormalities were assessed with ECG, serum markers, physical exam, and symptom questionnaire at six months (V1) and 24 months (V2) after end of TB treatment. An additional echocardiography was performed at V2.

**Results:** At V1, 74.4% (291/391) had an abnormal profile of cardiac serum markers, and 60.5% (233/385) had abnormal ECG. ECG abnormalities were related to the left heart in 41.6% (160/385), whereby 34.8% (134/385) had right heart abnormalities and 18.4% (71/385) showed signs for both. Between V1 and V2 there was an increase in the proportion of abnormalities seen for all serum markers and ECG-abnormalities. At V2, the main findings in echo were left ventricular hypertrophy and valve insufficiencies. We are currently analyzing whether PTLD is a risk factor for the development of cardiac abnormalities and the role of co-risk factors (age, sex, metabolic syndrome, hypertension).

**Conclusions:** Our findings show a large burden of cardiac comorbidities that increase over time. Further research on the role of risk factors, including PTLD, is needed to tackle excess cardiac mortality after TB.

### OA04-228-15 TB and incident cardiovascular disease events before and after TB diagnosis: analysing data from two large UK and US health databases

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**Background:** Limited evidence suggests higher risks of Cardiovascular Disease (CVD) among people diagnosed with Tuberculosis (TB) disease. However, existing studies have not examined CVD incidence before TB diagnosis and also may be affected by selection biases or residual confounding.

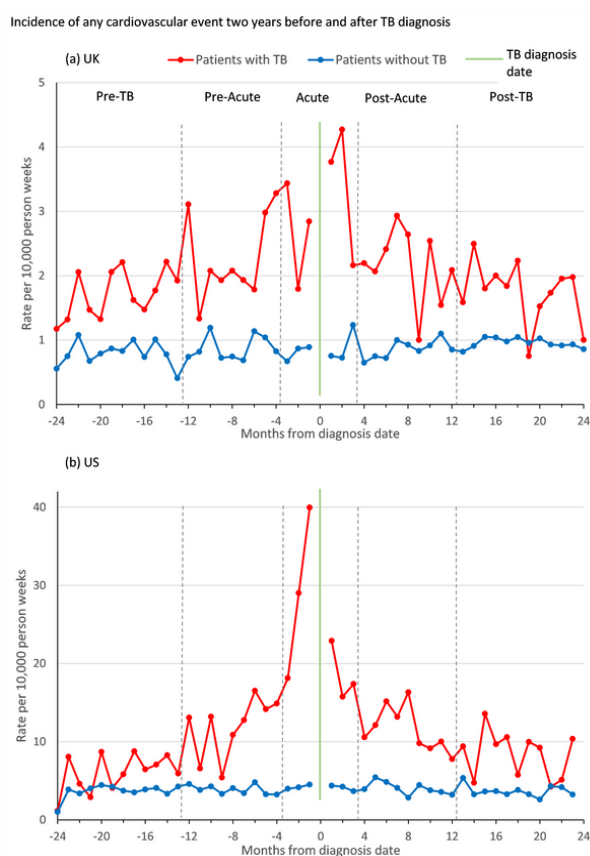
**Design/Methods:** Cohort analyses used 2000-2019 data from the United Kingdom (Clinical Practice Research Datalink) and United States (Veterans Medical Centers). Adults with incident TB (UK n=15,913; US n=4,686) were matched (age, sex, ethnicity, health-care practice) with up to 10 patients without TB.

The main outcome was incident CVD events +/- 2 years of TB diagnosis date, with +/- 90 days of this date defined as the acute period. Patients with prevalent CVD >2 years before TB diagnosis were excluded. Poisson regression models estimated incident rate ratios (IRR) for CVD events in patients with TB compared to those without TB.



**Results:** Median age of patients from the UK was 44 years and 69 years from US; most were male (52% UK and 97.5% US). In both UK and US cohorts, CVD incidence was consistently higher in patients with TB compared to patients without TB in the two years before and after TB diagnosis (Figure).

However, incidence was significantly higher for the acute period: UK IRR=4.11 (95% CI 3.30, 5.11), US IRR=6.98 (95% CI 5.97-8.15). Estimated increases in relative risks during the acute period compared to relative risk 1-2 years before TB diagnosis were UK 1.90 (95% CI 1.43, 2.53), US 4.30 (95% CI 3.37, 5.49). Risks were similar by age, sex and ethnicity.



**Conclusions:** We observed 4-7 times increased relative CVD incidence for patients with TB close to time of diagnosis, approximately 2-4 times higher when accounting for differences in baseline CVD incidence.

Whether TB disease causally increases CVD remains uncertain, however expanding TB treatment to include CVD care may provide an important opportunity to reduce new CVD events.

### OA04-229-15 Long-term consequences of TB: a longitudinal comparative analysis of 10-year medical cost and attributing disease burdens between TB and the healthy population

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**Background:** There is a limited long-term and comprehensive understanding of the epidemiology and medical costs associated with pre- and post-tuberculosis (TB) illness compared to the healthy population. We assessed the 10-year incremental medical costs and attributed diseases, using the International Classification of Disease (ICD) framework, due to TB.

**Design/Methods:** From the multi-year South Korean national TB cohort database with national health insurance claims data, a sub-set of newly reported TB patients who successfully completed treatment without recurrence were matched 1:1 with healthy controls using propensity score matching based on key patient characteristics and survival duration. Person-level quarterly total medical costs, assessed as 2020 US\$ and associated ICD-10 classification for medical service use for both TB and control groups were tracked over a 10-year (five years before and after the TB treatment initiation date) period. Pairwise differences in annual medical costs between the two cohorts were assessed using a paired t-test. A comparative interrupted time series analysis was conducted to obtain the difference-in-difference (DID) estimates for each year, 2 years prior to the treatment initiation as the index date.

**Results:** A total of 65,815 TB patients reported between 2013-2016 were matched to the healthy controls. 10-year cumulative incremental medical cost due to TB illness was US\$11,458 (95% Confidence Interval 10,792, 12,124). This estimate was three times higher for drug-resistant (DR) TB. End-stage renal and leukemia-associated diseases were the two highest attributing diseases to the incremental medical cost. The degree of cost difference was highest one year after the treatment initiation (DID estimate: 3.59 for DS-TB, 7.94 for DR-TB) and this trend continued five years after the TB treatment initiation (DID estimate: 1.87 for DS-TB, 2.06 for DR-TB).

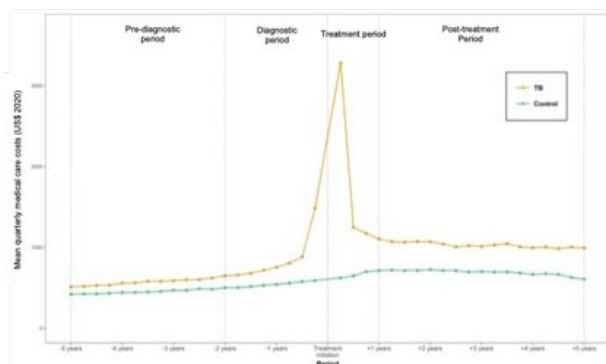


Figure A. Temporal trends in mean quarterly medical care costs (TB vs. control).

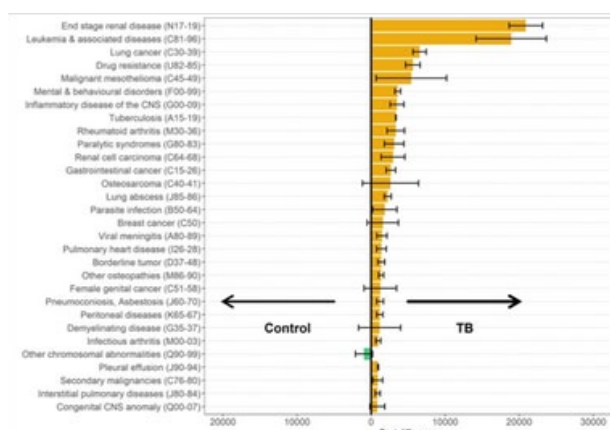


Figure B. Ten-year mean medical cost difference between TB and control and attributing diseases (ICD-10 codes).

**Conclusions:** Long-term consequences of TB illness on medical cost and associated illnesses start well prior to TB treatment and extend many years after the completion of treatment.

## OA04-230-15 TB recurrence among successfully treated patients with drug-susceptible TB: The role of hepatitis C virus coinfection

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**Background:** Patients with tuberculosis (TB) are commonly coinfecting with hepatitis C virus (HCV), but the impact of coinfection on long-term outcomes is poorly understood. In this study, we sought to assess the effect of HCV coinfection on TB recurrence.

**Design/Methods:** We conducted a population-based cohort study in the country of Georgia using nationwide electronic databases of TB and hepatitis C programs and the country's death registry. Study population included adults with newly diagnosed drug-susceptible (DS) TB disease during 2015-2019 who successfully completed their TB treatment (cure or completed treatment). The primary exposure was HCV infection status with three categories: uninfected (reference group), HCV-infected but untreated, and completed treatment for HCV infection. We calculated rates and rate ratios (RR) for the recurrence of TB disease. We generated adjusted hazards ratios (aHR) and 95% confidence intervals (CI) using subdistribution hazards model, with death as a competing event.

**Results:** A total of 5,351 patients were successfully treated for DS TB and had hepatitis C status available. After a median follow-up of 28 months, we identified 262 (4.9%) cases of TB recurrence, corresponding to a recurrence rate of 2,029 (95% CI: 1,790, 2,290) cases per 100,000 person-years. A higher recurrence rate was observed among males compared to females (RR=1.6, 95% CI: 1.2, 2.1), those with a history of incarceration (RR=2.3, 95% CI: 1.5, 3.6), and people with untreated hepatitis C (RR=2.3, 95% CI: 1.6, 3.3).

In multivariable analysis, untreated hepatitis C remained positively associated with TB recurrence (aHR= 1.6, 95% CI: 1.0, 2.4), while association of treated hepatitis C and TB recurrence is inconclusive due to low precision (aHR=0.6, 95% CI: 0.3,1.3).

CHARACTERISTICS	Total		TB recurrence				aHR* (95%CI)
	N	PY	N	% (row)	Rate per 100,000 PY (95% CI)	Incidence rate ratio (95% CI)	
<b>TOTAL COHORT</b>	5,351	12,916	262	4.9%	2,029 (1,790, 2,290)		
<b>Hepatitis C status**</b>							
Never infected	4,810	11,596	222	4.6%	1,914 (1,671, 2,184)	1	1
Infected, untreated	426	727	32	7.5%	4,403 (3,011, 6,216)	2.3 (1.6, 3.3)	1.6 (1.0, 2.4)
Infected treated	344	593	8	2.3%	1,349 (581, 2,658)	0.7 (0.3, 1.4)	0.6 (0.3, 1.3)

\*Adjusted for sex, employment status (employed, unemployed or military), place of TB diagnosis (region of residence or penitentiary system), whether a person was internally displaced from the occupied regions, and presence of HIV infection.  
 \*\*Hepatitis C status was treated as time-varying variable and some patients who were treated contributed to the person-time to both treated and untreated group, therefore, total N in this variable sums up to more than the actual total number of patients.  
**Abbreviations:** DS TB, drug-susceptible tuberculosis; PY, person-year; CI, confidence interval; aHR, adjusted hazards ratio

**Conclusions:** Patients with untreated HCV coinfection had a higher rate of TB recurrence. Timely treatment of hepatitis C among patients with TB may decrease the risk of TB recurrence, highlighting the need for coordinated efforts between TB and hepatitis C programs.

## OA05 Moving Pediatric TB Forward

### OA05-231-15 Impact of TB and other factors on mortality in children admitted with severe pneumonia in sub-Saharan Africa and South-East Asia: the TB-SPEED Pneumonia Study

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**Background:** Pneumonia is the deadliest infectious disease for young children worldwide. Tuberculosis is frequent in children with severe pneumonia yet often undetected. We sought to assess the impact of TB on mortality in children admitted with severe pneumonia.

**Design/Methods:** We did a secondary analysis of the TB-Speed Pneumonia stepped-wedge cluster randomized trial conducted in 16 hospitals from 6 countries (Ivory Coast, Cameroon, Cambodia, Uganda, Zambia, Mozambique) with high TB incidence.

Children <5 years with WHO-defined severe pneumonia received either the WHO standard of care (SOC) including large spectrum antibiotics, management of severe hypoxia and comorbidities, or the SOC with Xpert Ultra tests on nasopharyngeal aspirates and stools at admission. Children also had a complete blood count, HIV serology, chest X-ray, TB diagnosis per routine procedures if relevant and were followed-up for 12 weeks. We assessed mortality rates and association with tuberculosis and other factors using Kaplan Meier estimates and multivariate Cox model.

**Results:** Of 2570 children included - median age 11 months, 58% male, 132 (5.1%) HIV-infected, 537 (21%) with severe acute malnutrition (SAM) - 162 (6.3%) were diagnosed with tuberculosis, including 39/162 (24.1%) microbiologically confirmed. Tuberculosis was diagnosed in 92/537 (17.1%) children with SAM and 70/2033 (3.4%) children without SAM (P-value<0.0001). At 12 weeks, 210 (8.17%) children had died, 81 (3.2%) were lost to follow-up, 20 (0.8%) were withdrawn for 559.3

person-years (PY) of follow-up accrued during the study. The mortality rate was 35.9 deaths per 100 PY (CI: 32.1-40.0). 27 (16.7%) in children with tuberculosis and 174 (7.2%) without tuberculosis (Log-Rank P-Value < 0.0001).

	Reference	Adjusted hazard ratio (95% CI) (N=2512)	P-value
Age <12 months	≥ 12 months	1.48 (1.08; 2.01)	0.0135
HIV infected	HIV negative	2.67 (1.78; 4.02)	<0.0001
Haemoglobin <6 g/dL	≥6 g/dL	1.71 (1.01; 2.89)	0.0473
Severe hypoxemia (Spo2 <90%)	Spo2 ≥90%	3.014 (2.30; 4.29)	<0.0001
Severe acute malnutrition (SAM)	Non-SAM	3.68 (2.71; 5.01)	<0.0001
Tuberculosis diagnosis	Not TB	1.12 (0.72; 1.75)	0.6078
WHO SOC and Xpert Ultra	WHO SOC only	0.96 (0.72; 1.29)	0.7918

Table 1. Factors associated with mortality.

**Conclusions:** Although the mortality rate is higher among children diagnosed with tuberculosis, tuberculosis is not significantly associated with mortality in children admitted with severe pneumonia. Severe acute malnutrition, HIV infection, young age and signs of disease severity were independent predictors of death.

### OA05-232-15 High prevalence of TB infection in children and adolescence in rural Uganda

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**Background:** Much of the large latent Tuberculosis (TB) reservoir is established in childhood and adolescence. Yet, data on the prevalence and drivers of infection in children and adolescents are sparse and needed to guide prevention and case finding efforts.

**Design/Methods:** In an ongoing cohort of children and adolescents aged 1-17 years in rural Southwest Uganda, we estimated the overall and age-stratified population-level prevalence of TB infection. We defined TB infection by a positive QuantiFERON Gold-in Tube (QFT) test. Estimates were adjusted for differences between participants with and without a valid (positive/negative) QFT. We assessed predictors of prevalent TB infection, controlling for age and TB contact person. Analyses accounted for clustering by household.

**Results:** Between December 2021 and December 2022, we enrolled 3749 persons; approximately half (49%) were female and nearly 90% (3350/3749) had a QFT

completed. A household TB contact person was reported by 6.7% of participants with a positive QFT and 2.3% with a negative QFT. The estimated population-level prevalence of TB infection was 10.6% (95% CI: 9.6-11.7%) and increased with age: 10.3% among 1-5 years, 11.2% among 6-11 years, and 13.2% among 12-17 years. Predictors of prevalent TB infection included mobility, (spent ≥1 night outside of the home in the last month; adjusted risk ratio [aRR]=1.35, 95% CI: 0.95-1.92), household with ≥2 alcohol drinkers (aRR=1.48, 95% CI: 1.10-2.01), lower household wealth (aRR=1.45, 95% CI: 1.15-1.82, compared to highest tertile) and among children 1-5 years, having a caregiver with HIV (aRR=1.67, 95% CI: 0.96-2.91).

**Conclusions:** The prevalence of TB infection was high among children and adolescents. Few infections are explained by a known household exposure, suggesting undiagnosed household or community-based exposures are key drivers of TB infections.

Living with adults who drink alcohol, child mobility, having a lower household wealth and a caregiver with HIV are important risk factors for TB exposure in the household and community.

### OA05-233-15 Acceptability of a once-weekly TB preventive therapy in children: child, caregiver, and health worker perspectives

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**Background:** TBTC Study 35 trial investigates the pharmacokinetics and safety of rifapentine and isoniazid dispersible formulations given once-weekly over 12 weeks (3HP) in children 0-12-years-old. We aimed to understand the experiences and perceptions of children, caregivers and health workers using the 3HP regimen in South Africa.

**Design/Methods:** We conducted serial, in-depth qualitative interviews with 20 child-caregiver dyads and 9 health workers across two study sites between February 2021 and August 2022. Interviews were audio-recorded and detailed case descriptions were written after each interview. We analysed the data deductively, using case-descriptive analysis, guided by an acceptability framework.

**Results:** Caregivers and health workers reported that they preferred the 3HP regimen over the standard 6H regimen. Overall, children preferred the 3HP formulations' taste. Caregivers who had previously administered

6H perceived 3HP as easier to administer. A mother of a 1-year-old girl said: “because then the tablet is not once a day. [...] That everyday pill is difficult to give because I had to buy yogurt [to improve its taste] to make it easier to administer”.

Health workers described the treatment as a “big flat tablet that dissolves nicely,” smells sweet, and is easy to prepare and administer.

Both caregivers and health workers were concerned about integrating 3HP into routine care, primarily due to its once-weekly administration which could lead to forgetting doses. Some caregivers said they worried that if a child spat up a portion of a dose, it would be more impactful because they would not get more medication until the following week.

**Background and challenges to implementation:** TBTC Study 35 trial investigates the pharmacokinetics and safety of rifapentine and isoniazid dispersible formulations given once-weekly over 12 weeks (3HP) in children 0-12-years-old. We aimed to understand the experiences and perceptions of children, caregivers and health workers using the 3HP regimen in South Africa.

**Intervention or response:** We conducted serial, in-depth qualitative interviews with 20 child-caregiver dyads and 9 health workers across two study sites between February 2021 and August 2022. Interviews were audio-recorded and detailed case descriptions were written after each interview. We analysed the data deductively, using case-descriptive analysis, guided by an acceptability framework.

**Results/Impact:** Caregivers and health workers reported that they preferred 3HP regimen over the standard 6H regimen. Overall, children preferred the 3HP formulations’ taste. Caregivers who had previously administered 6H perceived 3HP as easier to administer.

A mother of a 1-year-old girl said: “because then the tablet is not once a day. [...] That everyday pill is difficult to give because I had to buy yogurt [to improve its taste] to make it easier to administer”.

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Both caregivers and health workers were concerned about integrating 3HP into routine care, primarily due to its once-weekly administration which could lead to forgetting doses. Some caregivers said they worried that if a child spat up a portion of a dose, it would be more impactful because they would not get more medication until the following week.

**Conclusions:** As new guidelines increasingly recommend shorter TPT regimens, it is important to consider the acceptability of these regimens. 3HP may reduce therapeutic burden for children and their caregivers and the formulations were clearly preferred over 6H.

However, once-weekly dosing may require additional adherence support to ensure regimen completion.

## OA05-234-15 Understanding TB care pathways and experiences in a paediatric population: A mixed-methods study in Pune, India

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**Background:** Globally, tuberculosis (TB) is among the top ten causes of mortality among children. While the focus of TB programs has largely been on adults, pediatric TB often remains a neglected area. We aimed to explore TB care pathways and experiences in pediatric population in Pune City, India.

**Design/Methods:** We conducted a cross-sectional mixed-methods study among adults and pediatric individuals (age <15 years) who had TB and registered for treatment with the National Tuberculosis Elimination Program (NTEP) during January 2018 to September 2019. Parents/guardians of children (n=35, 4 MDR-TB and 31 non-MDR-TB) underwent a structured interview followed by an in-depth interview (n=32). Qualitative analysis was carried out using a phenomenological approach.

**Results:** For the majority (26/32) of children, private provider was the first source of help seeking. Care pathways ranged from one to nine episodes of care. The majority of children received their diagnosis of TB in the public sector (29/32). The median diagnostic delay for children was 60 days (IQR 30-120) which was comparable to adults. We observed that median diagnostic delay among children with MDR-TB was 75 days (IQR 37-112) lesser than the adults (90 days IQR 60-180) though we did not have power to measure this difference. Children with extra-pulmonary TB saw a larger number of providers before receiving the diagnosis than those with pulmonary TB (5 providers vs. 3 providers, P= 0.043). In case of children with MDR-TB, parents described heavy expenses in the private sector prior to diagnosis. Parents of male children described borrowing money for their child’s treatment, while parents of female children described altering treatment plans due to the cost.

**Conclusions:** Our study shows that early referral of symptomatic children to the NTEP can help in their early TB diagnosis and reduce parents’ out of pocket costs in the private sector.

## OA05-235-15 Challenges in the management of paediatric drug-resistant TB: Experiences from India

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**Background and challenges to implementation:** Nearly a third of the children with TB globally are from India, despite an estimated detection gap of 56% reported in 2020. Further, the gap in diagnosis is wider for children with Drug-resistant tuberculosis (DR-TB). To address the challenges in current paediatric DR-TB diagnosis and care in India, FIND India through funding support from J&J is implementing a project since June 2022. This document describes the challenges in paediatric DR-TB diagnosis and treatment experienced by paediatric patients, caregivers and healthcare providers in India.

**Intervention or response:** To systematically assess and address challenges in the patient care cascade hindering the effectiveness of paediatric DR-TB services, FIND India has conducted gap analysis workshops with experts to develop road maps for addressing key bottlenecks in three states of India.

Post state specific consultations, a national level meeting was organised on 12 December 2022, to deliberate on the gaps related to management of paediatric DR-TB diagnosis and treatment in consultation with the project steering committee experts, WHO consultants and National TB programme officials.

**Results/Impact:** The challenges for paediatric DR-TB were categorized in three sections: diagnosis, treatment and post-treatment care including prevention (Figure 1).

Paediatric TB sections	List of challenges
1. At the level of Paediatric DR-TB diagnosis	<ol style="list-style-type: none"> <li>1. Need of continued capacity building of health care providers</li> <li>2. Difficulty in sample collection and transport of paediatric DR-TB samples (sputum and non-sputum)</li> <li>3. Lack of community awareness about paediatric DR-TB</li> <li>4. Poor linkage between adult and paediatric DR-TB centres for cross referral TB screening of household contacts</li> <li>5. Inadequate collaboration of public and private sector for early diagnosis (availability of newer diagnostics, trained personnel)</li> </ol>
2. At the level of Paediatric DR-TB treatment	<ol style="list-style-type: none"> <li>1. Non-accessibility of available paediatric formulations including dispersible tablets/ treatment by identifying patient load at each level.</li> <li>2. Low level of knowledge of private sector paediatricians regarding Paediatric DR-TB treatment and care</li> <li>3. Inadequate awareness about paediatric DR-TB treatment and follow up among patients and caregivers</li> <li>4. Unavailability of trained counsellors at all DR-TB centres</li> </ol>
3. At the level of Paediatric DR-TB post treatment including prevention	<ol style="list-style-type: none"> <li>1. Lack of comprehensive post TB rehabilitation programme, guiding the patients towards physical, psychological, and educational aspects of post treatment and prevention</li> <li>2. Non-availability of standardized testing (Skin test, IGRA) and TPPT provision for DRTB household contacts</li> <li>3. Poor "Airborne Infection Control" at Health centers (Paediatric wards) as well patient household level</li> </ol>

Figure 1. Challenges in paediatric DR-TB diagnosis, treatment and post-treatment, discussed in India national consultation, 2022.

Challenges in policy and programme implementation (at field and central level) were discussed (Example, need of paediatric friendly diagnostics and DRTB regimens, requirement for capacity building of healthcare providers, non-availability of paediatric focused information handbooks for patients and caregivers). The national consultation highlighted lack of collaborative efforts between patients and caregivers, healthcare providers, pharmaceutical agencies and research and development institutions towards paediatric DR-TB management.

**Conclusions:** The challenges for paediatric DR-TB diagnosis and treatment could be managed through implementation of appropriate strategies and actions at field and national level in consultation with community and relevant stakeholders collaborating towards paediatric DR-TB care.

## OA05-236-15 High treatment success rates among paediatric patients treated with new regimens for drug-resistant TB

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**Background:** Children and adolescents represent ~2.5% of all persons with rifampicin-resistant or multidrug resistant tuberculosis (MDR/RR-TB) in the country of Georgia. With the availability of the new WHO guidelines for management of TB in children, we aimed to describe final and post-treatment outcomes among children with MDR/RR-TB treated with bedaquiline, delamanid and/or linezolid containing regimens in comparison with previously used second line drugs (SLDs) regimen.

**Design/Methods:** We conducted a retrospective study of pediatric patients (≤18 years) treated for MDR/RR-TB in Georgia from 2009 to 2022. We defined "new regimen" as regimens that contained Bdq, Lzd, and/or Dlm (used between 2017 and 2022) and "traditional SLDs" as

regimens that did not contain these drugs (used between 2009 and 2016). We defined successful final treatment outcome as treatment completion or cure at the end of therapy. We defined “sustained treatment success” as being free of TB and alive at 12 months after successful treatment. We used bivariate analysis to estimate the associations between new regimens and study outcomes.

**Results:** 148 patients with MDR/RR-TB who had a treatment outcome recorded were included. Forty-seven (32%) patients received new regimens (all regimens included at least one new drug, 34 Delamanid, 18 Linezolid, 11 Bedaquiline) and 101 (68%) received traditional SLDs.

Successful final treatment outcome was reported among 46 (98%) patients who received a new regimen and 81 (80%) patients who received traditional SLDs (RR=1.23; 95% confidence interval [CI] 1.10 - 1.36). Among 127 patients with successful final treatment outcomes, sustained treatment success was reported among 46 (100%) patients who received a new regimen and 78 (96%) patients who received traditional SLDs (RR=1.04; 95% CI 1.00 - 1.08).

**Conclusions:** Among pediatric patients with MDR/RR-TB regimens with bedaquiline, delamanid, and/or linezolid, higher treatment success and relapse free post-treatment rates were observed, compared to traditional SLDs.

### OA05-237-15 TB treatment outcomes among adolescents in a high TB burden city in Metro Manila, the Philippines

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**Background and challenges to implementation:** Tuberculosis treatment outcomes among adolescents (10 -19) are understudied. This population is unique as they are more mature than those under ten but not as independent as those older than 19. Adolescents in this age group may be in or out of school. Older adolescents (15-19) are expected to participate in family or household activities and be self-sufficient in managing their TB treatment.

**Intervention or response:** To describe treatment outcomes and identify potential intervention points, we compared two groups (10 – 14 years and 15 – 19 years) among adolescent TB cases registered in Quezon city, Philippines in 2019. We analyzed data using descriptive statistics in Tableau.

**Results/Impact:** Out of 1,500 adolescents registered for TB treatment, 23.5% were in the 10-14 age group, and 76.5% were in the 15-19 age group.

Among the 10 – 14 age group, 29.7% initiated treatment within one week of diagnosis, 17.4% within one month but more than one week, and 52.2% initiated more than one-month post-diagnosis. Among the 15-19 group, 62.1% initiated within one week of diagnosis, 43.3% within one month but more than one week and 2.3% initiated more than one-month post-diagnosis.

None of the 333 (22.2%) adolescents registered in non-NTP facilities

had outcomes recorded. Among the 1,167 adolescents with outcomes, the 15-19 age group (915) had better treatment success (88.5%) than the 10-14 age group (252, 60.9%),  $p < 0.0001$ , with more cases of the younger group lost to follow-up (26.1% vs 2.3%,  $p < 0.0001$ ) or died (13.04% vs 6.9%,  $p = 0.0009$ ).

**Conclusions:** The results show the 10-14 age group had worse treatment outcomes, with significant delays in treatment initiation compared to the 15-19 age group. The study suggests that age group-specific interventions are critical to improving treatment outcomes for the 10-14 age group.

Additionally, better recording and reporting of non-NTP facilities would improve the understanding of adolescent treatment outcomes in this sector.

### OA05-238-15 Estimating the burden, mortality and morbidity of tuberculous meningitis in children – a modelling study

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**Background:** Tuberculous meningitis (TBM) in children is universally fatal if untreated and can cause life-long disability for survivors. Yet, limited surveillance data are available with no estimates of the global burden of childhood TBM.

**Design/Methods:** We carried out two distinct literature reviews and sourced routine national notification data to generate the following model parameters:

1. The risk of progression to TBM following *Mycobacterium tuberculosis* infection using pre-chemotherapy literature,

2. The proportion of notified childhood TB that is TBM and;

3. Risk ratios of TB mortality by age.

Model parameters for mortality (case fatality) and morbidity (neurological sequelae) were obtained from a published systematic review and meta-analysis.

A Bayesian model was constructed (figure) to synthesize data on expected TBM incidence following *M.tb* infection, expected notified TBM, and expected case detection ratios from WHO burden estimates across 202 countries in 2019. We also estimated TBM mortality and morbidity in children.

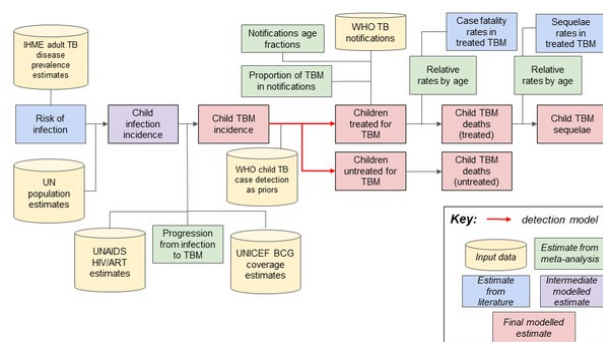


Figure: Conceptual framework of the model constructed to estimate global paediatric TBM incidence, mortality and morbidity.

**Results:** An estimated 21,300 (95% credible interval [CrI]: 15,800-28,200) children <15 years developed TBM in 2019, around 2% of the estimated TB incidence among children.

Amongst children with TBM, an estimated 14,300 (95% CrI: 10,400-18,900) died – most <5 years old. Over 80% of children who died did not receive TB treatment; 7.5% (95%CrI: 7.0-7.9) of deaths were among children living with HIV. Of the survivors, 4,700 (95% CrI: 3,400 to 6,300) suffered neurological sequelae.

**Conclusions:** These are the first estimates of childhood TBM, demonstrating high mortality and morbidity. TBM prevention strategies such as BCG vaccination and TB preventive therapy should be prioritised. Healthcare workers in high TB burden countries should have a high index of suspicion to facilitate early diagnosis and treatment.

## OA06 Safety of regimens for R-R

### OA06-239-15 A prospective description of the neuropsychiatric side effects of delamanid: a nested cohort study in the BEAT Tuberculosis randomised controlled trial

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**Background:** Delamanid is a drug used for the treatment of Rifampicin Resistant Tuberculosis (RR TB). There is, however, growing concern that it may cause neuropsychiatric side effects. This is a major concern especially in children as this could make the drug intolerable as part of a RR TB regimen.

**Design/Methods:** BEAT Tuberculosis is an ongoing randomized controlled trial conducted in two sites in South Africa. Among 309 trial participants, we conducted a Modified Mini Screen (MMS) sub-study to document the incidence of any neuropsychiatric side effects. This screen was conducted at baseline, week 12 and week 24 of treatment. The MMS comprised of questions which were used to elicit any neuropsychiatric side effects wherein further questioning and investigations done to ascertain if they were related to Delamanid and if interrupt or permanently discontinuation of the drug was indicated.

Our cohort included adults, children, pregnant women, and persons with HIV. Results were compared between those on a Delamanid containing-regimen and those not.

**Results:** Throughout the study we had 100 participants answer Yes to at least one of the MMS questions at week 0, 12 or 24. Of those, 45 of the patients were on a delamanid containing regimen and 55 were not. There was only one participant who had to have their delamanid stopped due to neuropsychiatric side effects (see table).

Age	Delamanid (Y/N)	Visit	Side effect	Causality	Outcome
10	Yes	Week 2	Insomnia, visual and auditory hallucinations	Delamanid	Resolved after stopping delamanid

Table.

**Conclusions:** On review of both groups, it was found that there was little to no difference between the groups and that the incidence of neuropsychiatric side effects was minimal and only one patient had to have their delamanid discontinued.



In conclusion, although a small number of cases of neuropsychiatric side effects were found, they were found to be clinically relatively insignificant and therefore, this should not deter the use of delamanid in the treatment of RR TB.

### OA06-240-15 Adverse events in patients on the BPaL regimen under operational research conditions in the Philippines

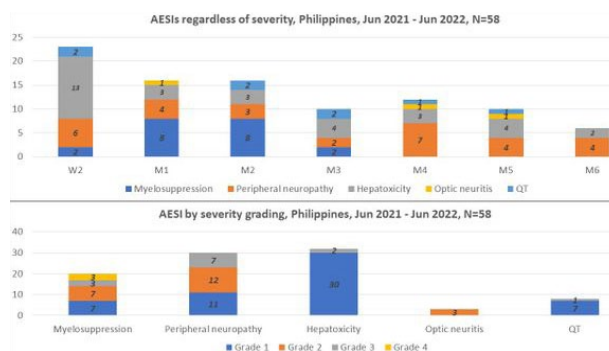
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**Background:** In 2020, WHO recommended 6 months of standardized regimen consisting of bedaquiline, pretomanid and linezolid (BPaL<sub>1200 mg/day</sub>) under operational research (OR) for eligible rifampicin-resistant TB (RR-TB) patients. Safety objectives according to the OR protocol included determination of serious adverse events (SAEs) and adverse events of special interest (AEs), namely peripheral neuropathy, myelosuppression, optic neuritis, hepatotoxicity and QT prolongation. OR site staff underwent training on active TB drug safety monitoring and management (aDSM) including the identification, and clinical management of adverse events based on severity grading. The TB Medical Advisory Committees provided clinical advice to the OR sites and the Research team did regular monitoring.

**Design/Methods:** This abstract describes the occurrence of adverse events in patients enrolled on the BPaL regimen with Linezolid initiated at 1200 mg/day. Data were obtained from REDCap and OR databases.

**Results:** Among 58 patients who finished 6 months of treatment, serious adverse events occurred in 7 (12%) patients: death (1); life threatening situation (2), hospitalization (2), and persistent or significant disability (2). There were 93 episodes of AEs of special interest among the 58 patients: hepatotoxicity (32), peripheral neuropathy (30), myelosuppression (20) and QT prolongation (8) and optic neuritis (3).

Despite the high number of AEs, majority were mild (59%) with no intervention needed, 23% moderate, 14% severe and 3% life-threatening. Majority resolved with Lzd modification.



**Conclusions:** Although AEs occurred quite frequently in patients on BPaL, majority of these AEs were mild and required no intervention. Moreover, this cohort received 1200 mg/day of Linezolid. With reduced Linezolid dose to 600 mg/day per WHO recommendation, lesser AEs are anticipated during programmatic implementation. Nonetheless, aDSM remains a crucial component in the introduction of new regimens with capacity building needed for AE identification, severity grading and appropriate and timely clinical management.

### OA06-241-15 Linezolid-containing short treatment regimens result in high risk of severe adverse events

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**Background:** All-oral bedaquiline (BDQ) and linezolid (LZD) containing regimens are recommended for rifampicin-resistant tuberculosis (RR-TB) treatment regimens by WHO. In Niger, a high cure rate was obtained in the past decade with a RR-TB treatment strategy relying on a second-line injectable drug (SLID) containing Short Treatment Regimen (STR), with linezolid replacing the SLID in patients when any grade of ototoxicity was identified on monthly audiometry. To inform national policy, we conducted the SHOORT (SHORT ORal Treatment) trial. Here we report the interim analysis for the primary safety endpoint (any grade 3-4 adverse event).

**Design/Methods:** The SHOORT study is an ongoing pragmatic randomised clinical trial (RCT), with random assignment (block randomisation, with month of diagnosis as stratifying variable) of patients diagnosed

with fluoroquinolone-susceptible RR-TB to either the Niger treatment strategy (STR with SLID) or the BDQ/LZD-containing WHO all-oral STR. We used survival statistics to estimate the association between LZD vs SLID exposure (time-dependent covariate) on having a grade 3-4 adverse event (AE).

**Results:** Between April 2021 and July 2022, 91 patients were enrolled, 46 on the Niger treatment strategy and 45 on the WHO all-oral STR. Baseline characteristics were similar between both arms. Of 46 on the Niger strategy, 19 were switched to LZD due to baseline (15) or emerging (4) low-grade ototoxicity. No patient developed grade 3-4 ototoxicity. During treatment with LZD (vs SLID), the risk of having a grade 3-4 AE was 9 times higher (HR 8.8; 95% CI:1.2-66.1)

(Figure; emerging grade 3-4 AE included anaemia, neuropathy, and hepatotoxicity).

**Conclusions:** Severe SLID-induced ototoxicity can be prevented by LZD replacement for a short duration. Long-term exposure to LZD was associated with a high risk of grade 3-4 AE. LZD is not a safe drug, as component of the WHO all-oral regimen. Final outcomes are expected by the end of 2023.

### OA06-242-15 Safety and effectiveness of the BPAL regimen: Preliminary analysis of the first multi-country operational research cohort

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**Background:** Individuals suffering from drug-resistant tuberculosis (DR-TB) have been subjected to ineffective, toxic treatment regimens for years. However, the TB Alliance's BPAL regimen, which comprises Bedaquiline, Pretomanid, and Linezolid, provides a highly effective, all-oral, six-month alternative. In June 2020, the World Health Organization (WHO) recommended using the BPAL1200 regimen under operational research (OR) conditions.

Subsequently, in the updated guideline released in December 2022, the WHO recommends the programmatic scale-up of the BPAL600 regimen.

**Design/Methods:** Indonesia, Kyrgyzstan, the Philippines, Uzbekistan, and Viet Nam introduced the BPAL regimen under OR conditions. Between May 2021 and March 2023, 319 individuals with multidrug- or rifampicin-resistant (MDR/RR-) TB with treatment intolerance, non-response, or additional fluoroquinolones resistance (pre-XDR-TB) were enrolled in the OR.

The findings of this multi-country OR will serve as essential supplementary evidence in establishing the safety and effectiveness of BPAL usage under programmatic conditions.

**Results:** The OR cohort had a median age of 40 years (IQR: 29-52), with 187 males (58.6%) out of the total. At baseline, 176 individuals (55.2%) were culture positive, and 158 individuals (89.8%) reported no growth in MGIT culture after one month of BPAL treatment. End-of-treatment outcomes were available for 146 individuals (45.8%) as of February 2023, and 138 individuals (94.5%) completed BPAL treatment successfully. Of these, 88 individuals (60.3%) reported adverse events of special interest that led to discontinuation or interruption of the full BPAL regimen or Linezolid only or permanent dose reduction of Linezolid in BPAL. Two individuals (1.4%) were classified as treatment failures due to BPAL discontinuation. Table 1 summarizes the effectiveness and safety of the BPAL regimen.

End-of-treatment outcomes	Number (%)
Cured	95 (65.1%)
Treatment completed	43 (29.4%)
Treatment failed	3 (2.1%)
Lost to follow-up	1 (0.7%)
Died	4 (2.7%)
Treatment Success (Cured and Treatment completed)	138 (94.5%)
<b>AESI leading to discontinuation or interruption of the full BPAL or Lzd only or permanent dose reduction of Lzd in BPAL</b>	
Individuals with at least one AESI	88 (60.3%)
Individuals with more than one AESI	24 (16.4%)
Individuals with Peripheral neuropathy	45 (30.8%)
Individuals with Myelosuppression	35 (24.0%)
Individuals with Optic neuritis	7 (4.8%)
Individuals with QT prolongation	2 (1.4%)
Individuals with Hepatotoxicity	1 (0.7%)

AESI, Adverse Event of Special Interest; Lzd, Linezolid

Table 1. The BPAL Regimen Effectiveness and Safety in the multi-country OR Cohort with End-of-treatment outcomes, N=146.

**Conclusions:** The treatment success rate in this multi-country OR cohort is comparable to the Nix-TB, Ze-Nix, and TB PRACTECAL studies' treatment success rates. The BPAL regimen will be programmatically scaled-up to manage eligible individuals with pre-XDR-TB in these countries and beyond.

### OA06-243-15 Predictive analyses of QT prolongation from ECG monitoring in the STREAM Stage 2 trial

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**Background:** ECG monitoring for QT prolongation in patients receiving drug-resistant tuberculosis (DR-TB) treatment remains important for clinical management. An ECG monitoring strategy developed based on STREAM Stage 1 data for the 9-month injectable-containing regimen identified participants who developed a QT or QTcF interval  $\geq 500$ ms with a high sensitivity and potentially allowed reduced frequency of ECG visits for two-thirds of patients. This strategy was tested in the same regimen in STREAM Stage 2 and in the 9-month oral bedaquiline containing regimen.

**Design/Methods:** Participants allocated the two regimens who developed, or did not develop, a prolonged QT/QTcF  $\geq 500$ ms during follow-up were identified. QT/QTcF measurements within the first month of treatment were used to find the optimal strategy.

**Results:** All 14 participants randomised to the Control regimen who developed a QT/QTcF  $\geq 500$ ms during follow-up had a 4-hour QTcF  $\geq 425$ ms. Only 53 of 183 participants who never reached 500ms were above this threshold at 4-hours, a sensitivity of 100% and specificity of 71%.

Of 7 participants randomised to the oral regimen who developed a QT/QTcF  $\geq 500$ ms, only 5 could be identified at 4-hours. The optimal sensitivity and specificity for this regimen required using two time-points and thresholds of 430ms at week 2 and 420ms at week 3 which identified all 7 participants. Only 37 of 198 participants who never reached 500ms were above this threshold, a sensitivity of 100% and specificity of 81%.

**Conclusions:** Our analysis suggests the ECG monitoring strategy developed from STREAM Stage 1 data is valid in a different population who took the injectable-containing 9-month regimen. The oral regimen required a combination of time-point cut-offs (week 2 - 430ms and week 3 - 420ms) but may permit reduced ECG monitoring in many patients without missing those at high risk.

### OA06-244-15 QT interval prolongation and cardiac safety of shorter treatment regimens for rifampicin-resistant TB: A prospective cohort study

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**Background:** Effective rifampicin-resistant tuberculosis (RR-TB) regimens contain multiple QT-prolonging agents, including bedaquiline, fluoroquinolones, clofazimine. Understanding the severity of QT interval prolongation in different regimens is critical.

**Design/Methods:** We prospectively enrolled RR-TB patients receiving three shorter regimens: the WHO injectable-containing regimen (including moxifloxacin, clofazimine), a levofloxacin-based oral regimen and a bedaquiline-based oral regimen (both containing clofazimine). Patients with baseline QTcF  $> 500$  ms were excluded. Electrocardiograms were conducted biweekly for 8 weeks and then monthly. Significant QTcF prolongation referred to QTcF  $> 500$  ms or increasing from baseline  $> 60$  ms. The severity and risk factors of significant QTcF prolongation were evaluated.

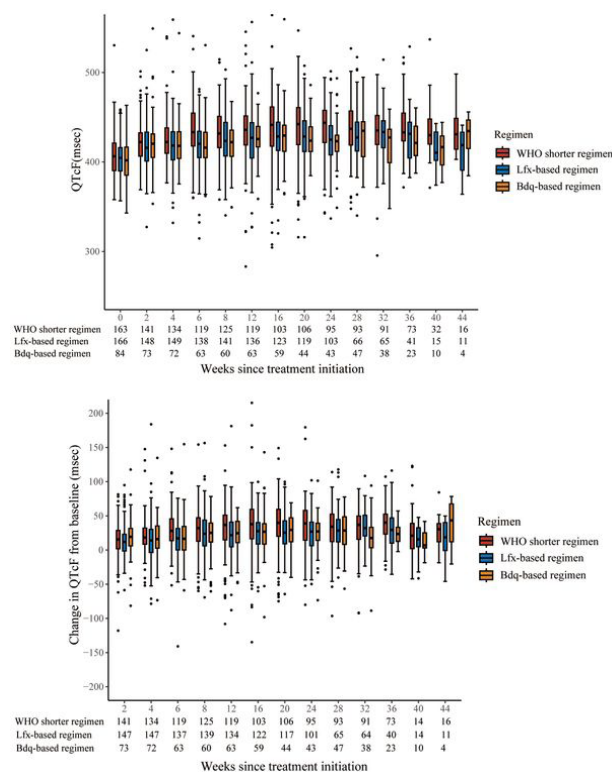


Figure 1. Boxplots of QTcF and QTcF change.

**Results:** Among 413 patients, 163 received the WHO shorter regimen, 166 received the levofloxacin-based regimen, and 84 received the bedaquiline-based regimen. QTcF  $> 500$  ms was more frequent in the WHO shorter regimen than the levofloxacin-based regimen (16.6% vs. 7.8%,  $p = 0.015$ ) and the bedaquiline-based regimen

(16.6% vs. 4.8%,  $p = 0.008$ ). More patients in the WHO shorter regimen group experienced a QTcF increase  $>60$  ms than those receiving the levofloxacin-based regimen (47.2% vs. 30.7%,  $p = 0.004$ ) and the bedaquiline-based regimen (47.2% vs. 31.0%,  $p = 0.023$ ). QTcF peaked at week 24, week 20 and week 16 in three groups and increase of QTcF peaked at week 20.

Risk of significant QTcF prolongation was reduced with the levofloxacin-based regimen (aHR 0.67; 95% CI 0.47–0.96;  $p = 0.029$ ) and the bedaquiline-based regimen (aHR 0.53; 95% CI 0.34–0.84;  $p = 0.007$ ) but increased with thyroid disease (aHR 1.98; 95% CI 1.15–3.40;  $p = 0.014$ ) and cavitation (aHR 2.18; 95% CI 1.28–3.72;  $p = 0.004$ ).

**Conclusions:** QTcF prolongation was severer in patients receiving moxifloxacin and clofazimine than those receiving concomitant clofazimine with levofloxacin or bedaquiline. Close electrocardiogram monitoring was advisable in patients with thyroid disease and cavitation.

### OA06-245-15 Hepatotoxicity of shorter treatment regimens for rifampicin-resistant TB in China: A prospective cohort study

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**Background:** Hepatotoxicity was common during tuberculosis treatment. We conducted a prospective cohort study to evaluate hepatic safety of shorter regimens for rifampicin-resistant tuberculosis (RR-TB).

**Design/Methods:** We prospectively enrolled RR-TB patients receiving three shorter regimens: the 9-month WHO injectable-containing regimen, a levofloxacin-based oral regimen (levofloxacin, linezolid, cycloserine, clofazimine and pyrazinamide) and a bedaquiline-based oral regimen (bedaquiline, linezolid, cycloserine, clofazimine and pyrazinamide).

In oral regimens, pyrazinamide-susceptible patients replaced clofazimine with pyrazinamide for 6 months, and pyrazinamide-resistant patients replaced pyrazinamide with clofazimine for 9 months.

Liver function tests (LFT) were conducted biweekly for 4 weeks and then monthly. Drug-induced liver injury (DILI) was defined according to the 2011 International DILI Expert Working Group Consensus Statement. The severity and risk factors of significant hepatotoxicity were evaluated.

**Results:** Among 430 patients, 171 received the WHO shorter regimen, 171 received the levofloxacin-based regimen and 88 received the bedaquiline-based regimen. More patients in the WHO shorter regimen group experienced alanine aminotransferase (ALT) exceeding 3 times of upper limit of normal (ULN) than the levofloxacin-based regimen group (23.4% vs. 4.1%,  $P < 0.001$ ) and the bedaquiline-based regimen group (23.4% vs.

5.7%,  $P < 0.001$ ). The median time to peak ALT was 85 (interquartile range [IQR] 29–153) days, 75 (IQR 18–148) days, and 93 (IQR 28–149) days in three regimens. The incidence of DILI was 16.4% in the WHO shorter regimen group, 3.5% in the levofloxacin-based regimen group and 3.4% in the bedaquiline-based regimen group. Compared to oral regimens, the WHO shorter regimen increased risk of ALT exceeding  $3 \times$  ULN (OR 7.24; 95% CI 3.11–16.86;  $P < 0.001$ ) and DILI (OR 7.24; 95% CI 3.11–16.86;  $P < 0.001$ ).

Characteristic, n (%)	WHO shorter regimen (N = 171)	Levofloxacin-based regimen (N = 171)	Bedaquiline-based regimen (N = 88)	P value
Age, mean $\pm$ SD, years	42.2 $\pm$ 13.6	42.0 $\pm$ 13.4	40.3 $\pm$ 13.9	0.563
Female	47 (27.5)	44 (25.7)	28 (31.8)	0.583
Alcohol abuse	8 (4.7)	6 (3.6)	1 (1.1)	0.310
History of chronic liver disease	8 (4.7)	9 (5.3)	5 (5.7)	0.936
Baseline ALT, median (IQR), $\times$ ULN	0.30 (0.19–0.48)	0.33 (0.20–0.48)	0.28 (0.20–0.47)	0.834
ALT $>3 \times$ ULN	40 (23.4)	7 (4.1)	5 (5.7)	$<0.001$
ALT or AST $>5 \times$ ULN	26 (15.2)	11 (6.4)	5 (5.7)	0.008
ALP $>2 \times$ ULN	7 (4.1)	2 (1.2)	1 (1.1)	0.178
DILI	28 (16.4)	6 (3.5)	3 (3.4)	$<0.001$

Table 1 Baseline characteristics and hepatotoxicity in three shorter regimens.

**Conclusions:** Oral shorter regimens revealed a better hepatic safety profile than the WHO shorter injectable-containing regimen and close LFT monitoring was advisable.

### OA06-246-15 High prevalence of severe adverse events identified during treatment among deaths due to drug-resistant TB in KwaZulu-Natal, South Africa, 2020

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**Background and challenges to implementation:** South Africa has been ranked among countries with the highest burden of TB, TB/HIV coinfection and DR-TB globally. It has been at the forefront of DR-TB treatment research and programmatic implementation of shortened regimens with new and repurposed drugs such as bedaquiline, linezolid and clofazimine. Despite improved treatment success rates, high mortality rates have still been observed.

**Intervention or response:** Through the USAID TB-LON programme, THINK conducted a retrospective mortality cohort review in four districts in KZN, South Africa. Files of people who commenced treatment between

January and June 2020, and died while taking DR-TB treatment, were examined. A descriptive analysis of individual demographic information, risk factors, treatment journey and mortality was performed.

Adverse Events (AEs) were identified through review of clinician notes, laboratory results and ECGs, and graded using a standardised grading scale. Grade 3 or higher were defined as Severe Adverse Events (SAEs).

**Results/Impact:** Records of 30 people were reviewed. Of these 50% were male, and the overall median age was 40 years (IQR; 31-52). There was no statistically significant difference in age by gender ( $p=0.79$ ). The file reviews revealed high rates of SAEs with 77% (23/30) experiencing a severe adverse event during their treatment.

The most frequent SAE was myelosuppression at 40% (12/30); followed by severe nausea and vomiting in 20% (6/30) and hepatitis in 10% (3/30). High rates of baseline anaemia with haemoglobin  $< 10\text{g/dL}$  in 59% (7/30), and  $< 8\text{g/dL}$  in 23% (7/30), were observed.

**Conclusions:** Whilst new regimens and repurposed drugs have been robustly demonstrated as non-inferior to traditional standards of care, these results demonstrate a high incidence of SAEs in patients who subsequently died.

This emphasises the critical importance of active drug safety monitoring, capacity building, and institutionalised clinical audits of care to ensure the safe programmatic roll-out of new shorter regimens.

### OA06-247-15 Clofazimine-induced skin pigmentation and psychiatric disorders in the treatment of multidrug-resistant TB: Longitudinal analyses of two prospective cohorts

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**Background:** Skin pigmentation due to clofazimine (Cfz), a core agent for MDR-TB treatment recommended by WHO, brings accumulating concerns and mental burden to patients. Yet, clofazimine-induced skin pigmentation (CISP) has not been well investigated.

**Design/Methods:** In two cohorts, we prospectively collected opisthenar images of MDR-TB patients before, during and 2 years after the Cfz-containing treatment from 144 participants. We employed the Multi-Scale Retinex with Color Restoration (MSRCCR) algorithm for the opisthenar image normalization, analyzed the opisthenar skin color evolution and built the corresponding evolution model. Simultaneously, depression and anxiety were compared and analyzed for the Cfz-containing and Cfz-free participants.

**Results:** Skin pigmentation is an unavoidable trend in patients of all ages, although most of patients will return to normal skin colour after about one year. The pigmentation is mainly reflected in the enhanced ability to absorb green light, while the ability to absorb blue and red light is reduced, but with different appearance phenotypes in different age groups. The built unified CISP model achieved better prediction performance with mean absolute error of 7.5/6.5, 15.6/15.3 and 15.8/10.6 for treatment/recover period in red, green and blue colour channels, respectively. The incidences of depression and anxiety in all participants were 38.36% and 44.44%. However, there is no significant difference between Cfz-containing and Cfz-free groups.

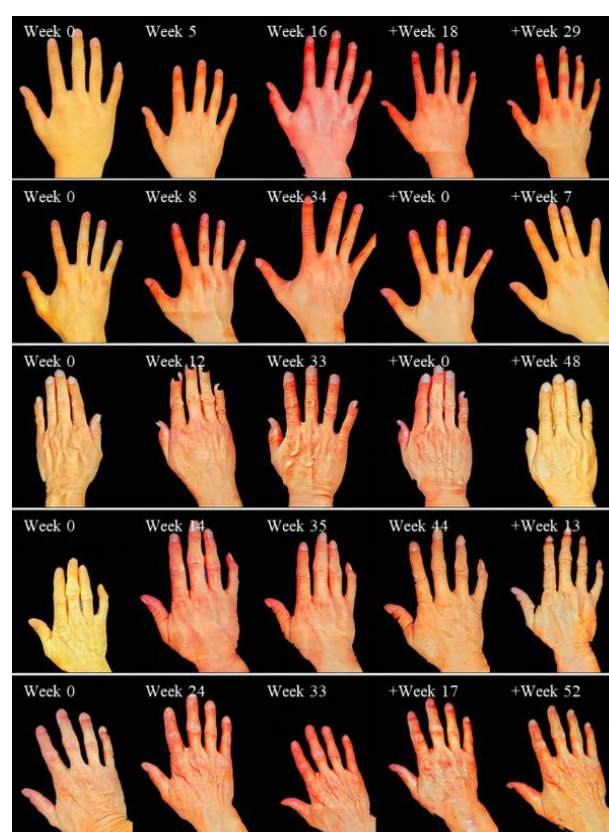


Fig 1. MSRCCR normalized opisthenar images series examples with different ages during taking Cfz and after withdrawal Cfz (+) for patients with different ages (up to down:  $< 30$ ,  $30-40$ ,  $40-50$ ,  $50-60$ ,  $\geq 60$ ), respectively.

**Conclusions:** Opisthenar skin colour of MDR-TB patients on Cfz constantly turned darker till Cfz was stopped, and return to almost normal colour 1 year after treatment completion. Cfz or the pigmentation it causes did not significantly increase the depression or anxiety.

## OA07 Treatment outcome of all oral-short course regimens for RR.TB

### OA07-248-15 All-oral short regimens provided by self-administered treatment delivery are feasible, safe and effective: experience from Kandahar, Afghanistan

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**Background:** To provide care for people with rifampicin-resistant tuberculosis (RR-TB) in unstable settings, where access to care is limited, improved treatment regimens and person-centered models of care need to be applied. In the period of 2019-2022 Médecins Sans Frontières studied safety and effectiveness of nine months all-oral short treatment regimens for RR-TB in Kandahar, Afghanistan. We describe our model of care and present 12 months post-treatment outcomes.

**Design/Methods:** A single arm clinical trial was conducted. Standardized short (9 months) regimens were designed for all population groups: all ages, pregnant women and regardless of fluoroquinolone resistance. Regimens were composed of bedaquiline, levofloxacin, linezolid, clofazimine and pyrazinamide.

Delamanid and cycloserine were used in case of age limitation for bedaquiline or fluoroquinolone resistance. Ambulatory care was provided, unless clinically indicated hospitalization. Self-administered treatment was offered to all participants in the ambulatory care.

**Results:** We enrolled 115 participants with RR-TB, 77 (67%) adults and 38 (33%) age < 19 years old. 87 (76%) originated from outside of Kandahar, requiring long travel time to reach RR-TB care. Fluoroquinolone resistance was assessed in 52/115 (45%) participants with 25/52 (36%) being infected with fluoroquinolone-resistant strain. Majority, 100/115 (87%), were treated ambulatory with self-administered treatment at home, throughout the follow up period. Treatments were in general well tolerated.

However, we observed 18 serious adverse reactions occurring among 14/115 (12.2%) participants. Treatment success was achieved in 103/115 (90%), five (4%) participants died, six (5%) failed (none was bacteriological failure) and one (1%) was lost to follow-up.

During the 12 months post-treatment period one participant died, two were lost to follow-up and among remaining 100 none was diagnosed with TB disease recurrence.

**Conclusions:** Shorter, safer all-oral regimens for RR-TB combined with innovative models of RR-TB care that emphasize person-centeredness improve access to care and treatment outcomes in the most challenging environments.

### OA07-249-15 Comparison of all-oral 39-weeks treatment regimen for rifampicin-resistant tuberculosis with bedaquiline for 24 and 39 weeks

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**Background:** Modified shorter all-oral bedaquiline-containing treatment regimens (mSTR) under operational research conditions were introduced in Belarus since 2018. Objective: To compare the initial outcomes of mSTR with bedaquiline for 24 and 39 weeks.

**Design/Methods:** This was a prospective cohort study of standardized regimen containing bedaquiline (Bdq), levofloxacin (Lfx), linezolid (Lzd), clofazimine (Cfz) and Cycloserine (Cs) with total duration of 39 weeks. Cohort I received Bdq for 24 weeks and Cohort II for 39 weeks. Study population included laboratory-confirmed pulmonary rifampicin-resistant (RR) and fluoroquinolone-sensitive patients.

**Results:** A total of 469 patients received mSTR, with significant difference between cohorts found related to age and history of alcohol abuse (Table 1). Treatment success at the end of treatment was achieved in 90% (200 out of 222) in Cohort I and 91% (225 out of 247) in Cohort II. No significant difference in the initial treatment success was identified in the multivariate analysis (aOR=1.33, 95% CI 0.70-2.51, p=0,71).

	Cohort I, n (%)	Cohort II, n (%)	P-value*
Total enrolled	222 (100%)	247 (100%)	-
Male	172 (77%)	195 (79%)	0.70
Age, mean (standard deviation)	44 (+/-13.0)	47 (+/-12.5)	0.02
Mean BMI mean (standard deviation)	21.7 (+/-3,6)	21,7 (+-3,6)	0.91
Sputum smear positive at baseline	79 (36%)	104 (42%)	0,15
HIV-positive	13 (6%)	14 (6%)	0.93
HCV-positive	23 (10%)	23 (9%)	0.70
Alcohol abuse in anamnesis	66 (30%)	110 (45%)	<0.001
Cavities	79 (35%)	89 (36%)	0,91
Monolateral	42 (19%)	59 (24%)	0,19
Bilateral	37 (17%)	30 (12%)	0,17

\*T-test used for calculation of the difference between groups

Table 1. Baseline characteristics of patients on bedaquiline-containing mSTR.

**Conclusions:** Modified shorter all-oral regimen for RR-TB significantly improves treatment success with either duration of the use of bedaquiline for 24 and 39 weeks. Further analysis of the final treatment outcomes after 12 months follow-up is needed to compare the sustained treatment success.

**OA07-250-15 All-oral, short-course regimens for patients with multidrug-resistant and pre-extensively drug-resistant TB in a high-burden country: A multicentre prospective cohort study**

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**Background:** Long, ineffective, and toxic regimens hinder the treatment of patients with multidrug-resistant tuberculosis (MDR-TB) and pre-extensively drug-resistant tuberculosis (pre-XDR-TB).

**Design/Methods:** We conducted a multicenter cohort study and prospectively evaluated the safety and efficacy of three regimens for 9 months.

Regimen A [bedaquiline (Bdq)-linezolid (Lzd)-moxifloxacin (Mfx)-cycloserine (Cs)-pyrazinamide (Pza)] and Regimen B [Lzd-Mfx-Cs-clofazimine (Cfz)-Pza] were for MDR-TB.

Regimen C [Bdq-Lzd-Cs-Cfz-Pza] was for pre-XDR-TB. The primary endpoint was the occurrence of an unfavorable outcome within 12 months after the end of treatment.

**Results:** A total of 104 patients were included in the analysis population. At 12 months after the end of treatment, 5 patients were not assessable; of the remaining 99 participants, 7 (7.1%) had an unfavorable outcome, and 92 (92.9%) had a favorable outcome. The 7 participants with unfavorable outcomes included 2 deaths, 4 with treatment failure, and 1 loss to follow-up. Culture conversion was 82.5% (80/97) at month 2 and 97.9% (94/97) at month 6. Adverse events (AEs) causing drug adjustment occurred in 69.2% (72/104) of participants, mainly due to Lzd and Pza. A QT interval prolongation of ≥ 500 ms occurred in 5.8% (6/104) of participants.

Variable	A	B	C	Total
Disposition of participants				
Underwent assignment	34	46	24	104
Were considered not assessable	1	4	0	5
Were included in primary outcome analysis	33	42	24	99
Favorable outcome	32 (97.0)	40 (95.2)	20 (83.3)	92 (92.9)
Unfavorable outcome	1 (3.0)	2 (4.8)	4 (16.7)	7 (7.1)
	Dead	0	0	2
	Failed	0	2	2
	Lost to follow-up	1	0	0
				1

**Conclusions:** For MDR-TB and pre-XDR-TB patients, three tailored short-course all-oral regimens with 5 drugs for 9 months were satisfactory in terms of the primary efficacy outcome. The majority of the AEs were manageable and reversible.

**OA07-251-15 Outcomes of short oral treatment for rifampicin-resistant TB among children aged ≤15 years in Kandahar, Afghanistan**

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**Background:** In 2018 World Health Organization recommended to pilot all-oral short regimens for treatment of rifampicin-resistant tuberculosis (RR-TB). Children are often excluded from innovative approaches until enough evidence about effectiveness and safety is gathered. Provision of RR-TB care in a context of Afghanistan requires person-centered approach for everyone, including children.

The cornerstones of this approach are all-oral, short, and safe treatment regimens delivered by family supported self-administration, as most of the participants have to travel long distances to reach RR-TB care. We describe outcomes of short oral regimens for RR-TB among children age of 15 years or younger.

**Design/Methods:** Médecins Sans Frontières conducted a one arm clinical trial to study effectiveness and safety of nine months oral regimens for RR-TB in the period of 2019-2022.

The regimens consisted of bedaquiline, levofloxacin, linezolid, clofazimine and pyrazinamide. Delamanid and cycloserine were used in case of age limitation for bedaquiline or fluoroquinolone resistance.

**Results:** We enrolled 28 children age ≤15 years, 24/28 (86%) of whom were detected by contact tracing. In 18/28 (64%) RR-TB disease was bacteriologically confirmed and 17/28 (61%) were infected with fluoroquinolone-resistant strains.

Three children were hospitalized due to severe clinical condition at baseline, 25/28 (89%) were treated ambulatory by family supported self-administered treatment delivery.

We observed 78 episodes of adverse events among 22/28 children (79%). No serious adverse reaction was reported. Treatment success was achieved by 25/28 (89%), one (3.6%) experienced clinical treatment failure and two

(7.1%) children died due to co-morbidities. Children were followed for 12 months post-treatment and none was diagnosed TB with recurrence.

**Conclusions:** Our study demonstrated that family supported self-administered treatment of short oral regimens for RR-TB was feasible, effective and safe in Afghanistan context. Children should receive the best possible care for RR-TB, which requires programmes not to delay use of innovative approaches for this specific population.

### OA07-252-15 Long-term outcomes in STREAM Stage 2: A phase 3 trial in rifampicin-resistant TB

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**Background:** STREAM Stage 2 was a randomised non-inferiority trial comparing two bedaquiline-containing regimens for rifampicin-resistant tuberculosis (RR-TB), one 9-month fully oral and one 6-month injectable-containing regimen, to a 9-month injectable-containing control.

**Design/Methods:** Primary results, 76 weeks post-randomisation, demonstrated that both intervention regimens had superior efficacy to the control. All participants were subsequently followed to 132 weeks for assessment of safety and mortality. To complete follow-up within a predetermined time scale efficacy assessments beyond 30/11/2021 were censored; the efficacy analysis reported is based on the 80% with follow-up to week 132.

A participant's long-term outcome was classified as unfavourable if they were unfavourable at Week 76, started any RR-TB treatment or died between their Week 76 and last efficacy visit, or had a positive culture from one of their two most recent specimens. A participant without a culture result at last visit, having not otherwise been classified as unfavourable, was regarded as non-assessable if their last two cultures, from specimens on separate occasions, were negative.

**Results:** Only five new unfavourable efficacy outcomes occurred; two participants received additional treatment (one Oral, one 6-month) and three died (two Oral, one Control). In the uncensored population at 132 weeks 19.9% (28/141) Oral and 32.9% (47/143) Control had an unfavourable outcome ( $p=0.013$ ), 10.7% (12/112) 6-month and 33.9% (38/112) concurrent Control ( $p<0.001$ ).

A grade 3 or higher adverse event occurred in 54% (113/211) Oral, 59% (84/143) 6-month and 57% (115/202) Control participants. Brock grade 3-4 treatment emergent hearing loss was reported in 3% Oral, 3% 6-month and 8% Control participants. All-cause mortality by 132 weeks was 5.2% Oral, 1.4% 6-month and 4.0% Control.

**Conclusions:** The bedaquiline-containing regimens maintained significantly better long-term efficacy and grade 3-4 hearing loss was less common than on Control. There was no evidence at week 132 follow-up of increased mortality in participants allocated bedaquiline.

### OA07-253-15 Treatment outcomes with a shorter all-oral regimen for rifampicin-resistant tuberculosis in a programmatic setting: interim analysis from the SHIFT-TB cohort

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**Background:** In 2018, the South African National Tuberculosis (TB) Programme introduced a modified all-oral short-course regimen (SCR) for most patients with rifampicin-resistant (RR)-TB, substituting linezolid for ethionamide in the standardised World Health Organization (WHO)-recommended 9–11-month regimen. This regimen has not been evaluated in clinical trials, and its effectiveness has not been rigorously studied.

**Design/Methods:** A prospective observational cohort study was conducted to evaluate the safety and effectiveness of the SCR in a programmatic setting. 260 consecutive patients  $\geq 15$  years old with bacteriologically-confirmed pulmonary RR-TB starting the SCR were enrolled from a TB referral facility in the Eastern Cape Province, starting January 2021. Interim results of clinical and bacteriological outcomes in participants through 12 months of follow-up are reported. Treatment outcomes were assigned using the 2020 WHO outcome definitions.

**Results:** Of 146 included participants, 60% (87) were male, 66% (96) were HIV-positive, and 18% (27) had baseline resistance to second-line agents, including 13% (19) with quinolone resistance. Treatment outcome with the SCR was unfavourable in 62% (90): 30% (43) failed treatment, 12% (17) died, 18% (27) were lost to follow-up and 2% (3) were unevaluable. Reasons for treatment failure are shown in Table 1. Of 124 (86%) participants with a positive baseline culture, the proportion with cul-



ture conversion at 30, 60, and 90 days of treatment were 58%, 90% and 94%, respectively; overall median time to culture conversion (TTCC) was 28 days (95% confidence interval (CI): 25-30). TTCC was similar between groups with and without additional baseline resistance (HR=0.60, 95% CI: 0.36-1.01; restricted mean survival time difference: 7.6 days, 95% CI: -3.2-18.4).

<b>Favourable (Treatment success)</b>	<b>56 (38.4)</b>
Cured or Treatment completed	56 (38.4)
<b>Unfavourable</b>	<b>90 (61.6)</b>
Treatment failed	43 (29.5)
Lack of culture conversion	-
Culture reversion	1/43
Additional acquired resistance	1/43
Change of ≥ 2 SCR agents or switch to a long, individualised regimen	41/43
Baseline resistance not compatible with SCR	22/41
Adverse drug reaction	5/41
Extensive lung disease on CXR	8/41
Poor clinical response	3/41
Extrapulmonary TB	2/41
Previous exposure to 2 <sup>nd</sup> -line drugs in SCR	1/41
Died	17 (11.6)
Lost to follow up	27 (18.5)
Not evaluated	3 (2.1)

Table 1: Clinical outcomes with the modified South African short course regimen.

**Conclusions:** In a programmatic setting, a third of patients starting the modified South African SCR required switching to individualised regimens. However, culture conversion was rapid and bacteriological failure was rare. A standardised regimen that is less affected by quinolone resistance is needed.

### OA07-254-15 Implementation of the BPaL regimen in Ukraine - from operational research to programmatic implementation

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**Background:** Treatment success for pre-extensively resistant (XDR)/XDR-TB with longer regimens in Ukraine is only 62,9%. In war conditions, the risk of interruption from longer treatment is much higher due to population migration, destroyed infrastructure, constant rocket attacks, the outflow of personnel, and barriers to access to medical care.

**Design/Methods:** Prospective study in one cohort of pre-XDR/XDR-TB patients to assess the effectiveness of BPaL.

**Results:** All bacteriologically confirmed rifampicin-resistant cases registered in 22 out of 25 regions of Ukraine (excluding temporarily occupied regions) during July 2022 - February 2023 were screened for inclusion in the study.

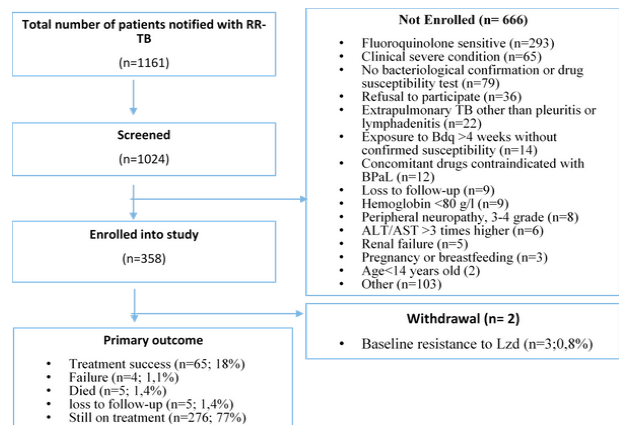


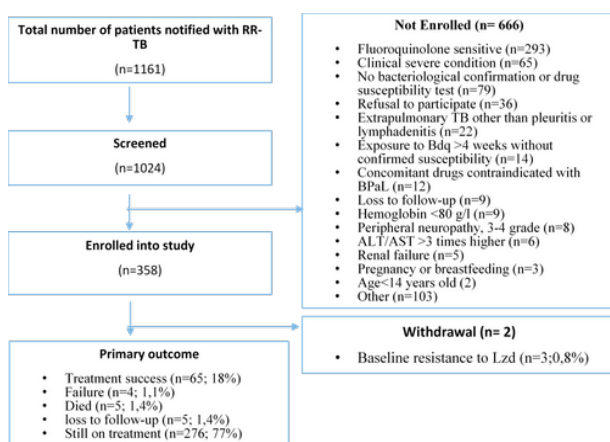
Figure 1. Enrolment flow diagram, operational research on BPaL in Ukraine, 2022 – 2023

Out of 1024 patients screened, 358 were enrolled in the study (Figure 1), 65 (18%) successfully completed treatment, 276 (77%) were still on treatment, and 5 (1,4%) lost to follow-up registered. Out of 245 patients who completed three months of treatment, 196 (80%) reached culture conversion.

**Background and challenges to implementation:** Treatment success for pre-extensively resistant (XDR)/XDR-TB with longer regimens in Ukraine is only 62,9%. In war conditions, due to population migration, destroyed infrastructure, constant rocket attacks, outflow of personnel and barriers to access to medical care, the risk of interruption from longer treatment is much higher.

**Intervention or response:** Prospective study in one cohort of pre-XDR/XDR-TB patients to assess effectiveness of BPaL.

**Results/Impact:** All bacteriologically confirmed rifampicin-resistant cases registered in 22 out of 25 regions of Ukraine (excluding temporarily occupied regions) during July 2022-February 2023 were screened for inclusion to the study. Out of 1024 patients screened 358 were enrolled in the study (Figure 1), 65 (18%) successfully completed treatment, 276 (77%) were still on treatment and 5 (1,4%) loss to follow-up registered. Out of 245 patients completed 3 months of treatment, 196 (80%) reached culture conversion.



**Conclusions:** BPaL shows high early efficacy. In January 2023, Ukraine started the programmatic implementation of BPaL based on experience from this study and WHO recommendations.

## OA07-255-15 Effectiveness and safety of varying doses of linezolid with bedaquiline and pretomanid in adults with pre-extensively drug-resistant pulmonary TB

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**Background:** The recently recommended shorter regimen of Bedaquiline(Bdq)-Pretomanid(Pa)-Linezolid(Lzd) is expected to improve the treatment outcome of highly drug-resistant tuberculosis. However, the appropriate dose and duration of Lzd, especially in co-morbidity like malnutrition, is not clear.

**Design/Methods:** A pragmatic multicentric clinical trial at nine sites in India enrolled adults with pre-extensively drug-resistant and non-responsive/intolerant multidrug-resistant pulmonary TB and randomized them to receive Bdq and Pa for 26 weeks, with daily Lzd(600mg) for 26 weeks (arm1) OR Lzd(600mg) for 9weeks then LZD(300mg) for 17 weeks (arm2) OR Lzd(600mg) for 13 weeks then Lzd(300mg) for 13 weeks (arm3).

Primary outcome of trial is relapse-free cure at 48-weeks post-treatment. We are presenting the interim analysis of efficacy and safety done after 33% of total sample size (400) completed 26 weeks of treatment.

**Results:** In preliminary report of 125 patients, 70(56%) were females with mean age of 31years and mean weight 46.9 kg. Seven were culture negative at baseline and not included in further analysis.

Of the 118 patients, 112(95%) culture converted by 26 weeks – 40/40(100%) in arm 1, 36/39(92%) in arm 2 and 36/39 (92%) arm 3.

There were two bacteriological failures in arm2; one clinical failure due to adverse event (AE) in arm3; 11 SAEs (arm1-two, arm2-five and arm3-four) including 3 deaths (arm2-one and arm3-two).

Of the 514 AE, there were 20, 12 and 12 episodes of myelosuppression and 15, 7 and 9 episodes of peripheral neuropathy in arm1, arm2 and arm3 respectively. Majority of AEs were of grade 1/2 and resolved with symptomatic management.

System	Arm 1	Arm 2	Arm 3	Total
* Investigations	108	95	108	311
Gastrointestinal	16	13	16	45
Peripheral Nervous System	15	7	9	31
General**	9	5	5	19
Musculoskeletal	8	6	4	18
Skin	5	4	6	15
Cardio Vascular system	6	2	4	12
Central Nervous System	1	3	2	6
Eye	2	2	2	6

**Conclusions:** Favourable outcome of >90% was seen with all three Bdq-Ptm-Lzd arms. Lower incidence of Lzd-associated toxicity was reported in groups that had structured reduction to 300mg after 9-13 weeks. Close monitoring to identify and treat AEs early is essential. Overall risk–benefit ratio should be evaluated before finalizing Lzd dose in shorter regimens.

## OA08 How media can shape the message

### OA08-256-15 Exploring children-friendly communication on TB with age-appropriate information products

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**Background and challenges to implementation:** Strategies for reaching children with age-appropriate information on TB have been needed for many years. This was highlighted again in the 2022 Assessment[GD1] on Children with TB needs in Ukraine conducted by people with TB, which indicated that the lack of clear, friendly, and digestible TB information for youngsters, their parents, and caregivers led to increased stigma.

**Intervention or response:** Building on the 2022 assessment findings, the STBCEU project, with the Stop TB Partnership, launched an initiative to develop creative, child-friendly, age-appropriate information products. These included a coloring book depicting a quest for learning TB basics and healthy behaviors, as well as a three-part colorful cartoon series for very young children. The project was guided by a TB specialist, psychologist, and artist. The book, to be used with guidance from a parent or nurse, has helped build trust and communicate sensitive TB-related information using entertaining, non-stigmatizing messages and images.

**Results/Impact:** After the initial coloring book was released on television and social media and distributed to 100 school libraries throughout Ukraine, the book's

popularity surged, leading to a huge demand for TB educational tools for schools, preschools, and TB and public health facilities. An additional 5000 copies were distributed to social workers and another 5000 to TB health facilities. These were used in community- and facility-based TB education sessions with children and parents. The materials were also distributed through social media (Facebook, YouTube), making them accessible throughout the country. An evaluation to assess changes in knowledge about TB among target populations is planned.



Figure. TB education sessions with children and parents.

**Conclusions:** Age-appropriate, positive learning materials motivate children to develop healthy skills, increase knowledge about TB and reduce stigma towards people affected by the disease.

### OA08-257-15 Incentives as an effective TB communication tool: A case study of KNCV Nigeria's Facebook page

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**Background:** The power of incentives is immense, and it is a hidden force that can make human beings feel appreciated and convinced to shape their behavior to a certain level.

This is a study on the usefulness of incentives in driving effective TB awareness messages on social media during a KNCV Nigeria-supported online Radio program TB Tori (Story).

**Design/Methods:** A comparative study of the reach and response to TB awareness questions and answers published by the communication team with incentives such as free airtime gifts during a Radio program titled The TB Tori, versus other TB posts published without incentives.

Responses on KNCV Nigeria's Facebook page were tracked and categorized under reach, comments, and health-seeking questions. The period reviewed was May – October 2021.

**Results:** From September to October 2021, 8 questions with a free Airtime gift to any mobile network to be given to listeners that provided accurate answers to questions on TB were published on KNCV Nigeria's Facebook page. These posts reached 5,192 persons, 155 persons liked the post, 177 comments on the answer to the TB Tori question of the day, and 5 inbox messages inquiring to get help when one dials the TB hotline 3340. From May to June 2021 10 TB posts were published on KNCV Nigeria's social media pages without an incentive, 2,428 persons were reached, and 66 people liked the posts with six (6) comments and (0) inbox messages. When incentives were used two times more people were reached.

**Conclusions:** From the results gathered from KNCV Nigeria's Facebook page interactions, incentives have been seen to be a very effective tool in improving the reach of TB awareness creation messages. This approach is recommended to increase interactions and engagement in radio programs creating awareness for TB and other diseases of public health concerns in Nigeria.

### OA08-258-15 Digital behavioural change campaign to increase TB awareness during the COVID-19 pandemic

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**Background and challenges to implementation:** Tuberculosis notifications dropped over 20 percent from 2019 to 2021 during the pandemic. Community outreach and contact investigation that enabled education about TB were disrupted.

Thus, when physical mobility was limited and a new disease with similar symptoms emerged, a digital mass campaign was needed to reach people with prolonged coughs to get checked for TB.

**Intervention or response:**

STPI implemented a digital behavioral change communications campaign in 2 high TB burden provinces targeting 15-39 years old based on a survey, FGD with the target audience, and a consultation with NTP and TB experts. The '141 Cek TBC' campaign message is "14 days of persistent cough? 1 solution, go check to the doctor immediately".

In February-August 2022, STPI developed 1 website, 54 articles, 19 advertisement banners, 1 PSA, 2 posters, 18 press releases, 1 webinar, 1 visual interactive page, 440 social media contents, and 6 contents in a Health e-Commerce.

**Results/Impact:** The campaign reached 30.6 million Indonesians, primarily in Jakarta and West Java or 10.9 percent of the population. Advertisement banners in the news contributed 48 percent and in social media contributed 32.6 percent of the total reach.

There is a significant increase (28.3%) for awareness of coughing for 14 days or more as a symptom of TB among 600 respondents. There is no significant change in the behavior to access healthcare facilities to address coughs for 14 days.

Nonetheless, a qualitative evaluation described that the campaign message was helpful for the target audience to beware of cough symptoms and encourage others with prolonged coughs to visit healthcare facilities.

**Conclusions:** Raising TB awareness massively can be done effectively and efficiently by optimizing advertisement strategies. Consistent investment for evidence-based digital campaign is promising to advance behavioral changes from awareness to appropriate action.

This strategy can support behavioral change needed to influence the uptake of TB innovations.

### OA08-259-15 Acceptance of a national multimedia TB campaign in Nigeria

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**Background and challenges to implementation:** Tuberculosis knowledge, risk perception and awareness of service provision centers remain major drivers for Nigeria's missing TB cases. A systematic Social and Behavior Change (SBC) approach was applied to understand drivers and develop a campaign to respond to the determinants contributing to missed TB cases.

**Intervention or response:** The Breakthrough ACTION-Nigeria project is funded by USAID to increase the practices of priority health behaviors in public health disease including TB. In 2020, the project brought together stakeholders including implementing partners, healthcare providers, patients and caregivers to contribute to the development and implementation of a strategic campaign to increase awareness and create demand for TB services.

The resulting multimedia and multilingual campaign, "Check Am O!", launched in 2021 to promote prompt testing of cough and amplify awareness of Nigeria's national TB hotline. The campaign's impact was monitored using data from social media analytics, mass media monitoring and data from the national TB call center.

**Results/Impact:** After 24 months of implementing the campaign, The average number of callers to the national TB call centre rose from 288 before the campaign to 11,697 after the campaign, over 70% of whom reported learning about the hotline on radio and television.

Monthly average number of callers referred for TB tests increased from 65 to 256. Over 80% of people sampled in an omnibus survey reported exposure to the "Check Am O!"

Social media posts reached 9,122,644 individuals and 1,434,782 individuals engaged with the 274 contents shared on Facebook, Instagram and Twitter.

#### Conclusions:

Applying an evidence based and systematic approach to developing a multi-channel, multi-language campaign provided an opportunity to increase awareness, knowledge, risk perception and behavioral change towards increasing demand for TB services in Nigeria.

### OA08-260-15 Applying a behavioural lens to the role of TB counselling in treatment journeys: Understanding how storytelling impacts people's behaviour

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**Background and challenges to implementation:** Tuberculosis (TB) counseling content is widely used by TB programs as an intervention to address treatment gaps. However, content is often focused solely on didactic medical information and does not examine the behavioral aspects conditioned by emotional, cultural, and social factors surrounding people's experiences. Despite the deployment of educational content, information asymmetry remains, with limited impact on people's ability to cope with their daily experience of illness.

**Intervention or response:** Data collection comprised of documenting story-telling narratives to understand the implicit factors conditioning people's behavior. A total of 356 individual micro-stories were collected documenting daily activities of TB patients and healthcare providers in Surat, Gujarat and Ranchi, Jharkhand. Data was analyzed with a behavioral design framework that examines the strength of connections between variables in order to identify conditional patterns.

**Results/Impact:** Three significant conditions affecting patient behavior were identified:

1. Emotional state: Anxiety and guilt had significant connections within treatment journey. Guilt was associated with the perception of disease as a punishment for past actions and of being a burden to the family. Anxiety was associated with a mismatch between what is an expected recovery vs. actual experience of adverse drug reactions that worsen symptoms.

2. Cognitive function: People with TB expressed confusion and an inability to make decisions throughout the treatment journey. This condition was attributed to unexpected changes in physical condition; as well as the inability to contextualize chronic TB illness with prior illnesses that needed short-term antibiotics. Resulting behavior was the substitution or supplementation of TB medication.

3. Aesthetic presentation: The experience of specific physical changes such as darkening of skin and weight loss resulted in specific behavioral patterns contributing to treatment experimentation.

**Conclusions:** TB counseling content should be transformed from treatment literacy information – to behavioral communication services delivery designed to empower the patient to cope with circumstances and therefore treatment success.

### OA08-261-15 Encouraging health-seeking behaviour by leveraging the fourth estate of democracy – (social) media

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**Background and challenges to implementation:** Health communications has experienced democratization through social media's interactive functionality and popularity. Its application to raise awareness about a major public health issue such as tuberculosis (TB) is critical; findings from India's national prevalence study suggest that 64% people with TB symptoms did not seek care, with many ignoring or not recognizing the symptoms.

**Intervention or response:** GHS leveraged India's official awareness campaign's (TB Harega Desh Jeetega) Facebook page to build knowledge about TB symptoms and the availability of services in 292 high-burden districts across 13 states in India, for a period of five weeks. GHS ran a paid campaign to promote these messages among target groups (people aged 15-49).

Information was packaged in popular formats (short videos) and disseminated; based on the analysis of engagement patterns, dissemination strategies were revised.

**Results/Impact:** The campaign reached 112 million users; 5.16 million *Thruplays* (a video watched for more than 15 seconds or to completion), and a frequency of 3.94 (average number of times users see the ad).

A majority of responses were appreciative, and shared TB-related experiences – a valuable outcome to help normalize the disease. Of the total responses, 11% were queries related to requests – for doctor referrals, for more information on TB, and requests to be contacted. Content disseminated in local languages achieved greater reach - the Hindi infographic received 31 times more responses than its English counterpart.

**Conclusions:** Paid social media campaigns (especially in local languages) help disseminate public health information to target populations. Social media analytics helps gauge target group responses, helping improve and refine content and dissemination strategies.

To convert TB awareness to an increase in presumptive TB screening, online awareness campaigns may be linked to an online database that provides information about TB, helps screen symptoms, and links people to nearby TB centers.

### OA08-262-15 Media engagement in the fight against TB: A case for Malawi

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**Background and challenges to implementation:** Ending Tuberculosis (TB) requires multi-sectoral approach. Complete and correct information on TB prevention, signs and symptoms, and treatment to people is crucial in fight against TB. Lack of knowledge creates myths and misconceptions which results in stigma against TB and ex-TB patients. Media engagement creates awareness on TB transmission, prevention, adherence to drugs, access to treatment, and availability of diagnostic equipment in health facilities, hence shaping perceptions and influencing policy makers.

From 2016, Malawi National TB and Leprosy Elimination Program (NTLEP) started to work in collaboration with both national and community, print and online (electronic) media houses for TB information dissemination.

**Intervention or response:**

**1. Media tours:** The program conducted biannual media tours to communities for material collection. The following individuals were interviewed, Directors of social and health services, TB and Ex-TB patients, local leaders, Miners and Ex-miners, District TB officers, primary school teachers and learners, TB volunteers and guardians to TB patients.

**2. Media meetings:** Reporters, camerapersons and producers from selected national and community media houses were engaged in the meetings. Participants were encouraged to air their stories and develop work plans.

**3. Media coverages** in different TB and Leprosy meetings, open days including world TB Day commemoration.

**4. Airing of jingles:** Contract signing by selected media houses for TB programs airings

**5. Programs airing:** Done by the media professionals.

**Results/Impact:** Interactions with media professionals has resulted to:

1. The number of media houses engaged with the NTLEP increased from 3 in 2016 to 35 in 2023
2. An increase in treatment adherence among TB patients
3. The number of TB stories increased from 13 in 2016 to 793 in 2022.

**Conclusions:** Engagement with the media houses has resulted in improved working relationship between NTLEP and the media fraternity. Malawi National TB and Leprosy Elimination Program needs to do the knowledge, attitude and practice survey to assess the impact of this intervention.

### OA08-263-15 Indonesia young populations and its innovations to increase public awareness: a social media approach on TB

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**Background and challenges to implementation:** Tuberculosis (TB) has been a global health problem since decades ago, and the political leaders have been committed to End TB in 2030. Based on the Global TB Report 2022 around 2.2 million young people between 15 and 34 years of age develop TB.

Moreover, adolescence is a pivotal phase of development that combines increased vulnerability to tuberculosis with distinct developmental and social traits to produce new risks for TB.

**Intervention or response:** With the TB program mostly focusing and prioritizing TB in adults, it is crucial to raise TB awareness in young people to prevent the transmission and accelerate the TB elimination. It is recognized that young people experience a challenge in accessing traditional health services and the internet offers them confidential and convenient access to health information.

One of the social media that is massively used by young people in Indonesia is TikTok. A youth TB movement organization in Indonesia (IMUT), in collaboration with NTP and TikTok Indonesia having a week-long campaign in TikTok during National Children Day in 2021. The campaign is also supported by the 13 medical doctor influencers in TikTok and targeted young men and women mostly in Java island – a high burden area for TB in Indonesia. The campaign was using TikTok algorithm and AI for a week with hashtag #LawanTBC. The algorithm filters all the content using the hashtag with the right information about TB and makes them trending for a week.

**Results/Impact:** The TikTok campaign collaboration with TikTok Indonesia resulted in 96 million user engagements. It is supported by the Ministry of Health and has engaged more micro influencers who have boosted TB awareness.

**Conclusions:** Health promotion using social media has been shown to be a successful strategy, and it can be accessible by the public, particularly young people, at any time and from any location.

### OA08-264-15 Using Instagram for social media engagement of youth and community health officers: Changing the discourse of TB in Kangra, India

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**Background and challenges to implementation:** Instagram is a photo and video sharing social networking service, it has rapidly gained popularity among youth. In fact, a local survey conducted recently in suburbs of Dharamshala, the headquarter of the hill district of Kangra, revealed that among social media users aged below 30 years of age, Instagram was the first preference among 60% users. Content in Instagram is mostly reels (short video) and the discourse is not yet on health issues.

**Intervention or response:** We took the opportunity to change the discourse on Instagram to TB Elimination. We created an Instagram handle in March 23, and shared content regularly regarding the TB Awareness campaign activity. We had a workshop with 50 youth and nodal officers of Red Ribbon Clubs and 2 workshops with 185 Community Health Officers in the month of March 2023.

We also encouraged Youth of Red Ribbon clubs and Community Health Officers to create good content on TB and post from their own handles.

**Results/Impact:** The feed which earlier used to consist predominantly of dancing videos (reels), changed to abundance of Reels with TB Harega Desh Jeetega slogans and theme of this World TB Day Campaign.

We had over 2k posts from Kangra on the TB Campaign messages. The Instagram handle of District TB Elimination Cell Kangra got 462 enthusiastic responses, with 462 followers within a month, which is higher than 303 followers of Central TB Division India- TB Mukht Bharat India.

**Conclusions:** Social media can be leveraged to take the message of TB Elimination, spread awareness, stigma mitigation, among the young population, and needs to be targeted as per local preference of the social media platform.

## OA09 Finding the missing children with TB

### OA09-265-15 High prevalence of TB among children aged <5 years hospitalised with severe acute malnutrition in Malawi

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**Background:** Children with severe acute malnutrition (SAM) are at high risk for tuberculosis (TB), but accurate TB diagnosis in this population remains elusive. The objectives of this study were to define TB prevalence in children hospitalized with SAM and to explore TB diagnostic strategies in this population.

**Design/Methods:** This was a prospective observational study of children aged 6 to 59 months admitted to Kamuzu Central Hospital (Lilongwe, Malawi) with SAM. All enrolled children were screened for TB-associated signs and symptoms, abnormal chest x-ray (CXR), and HIV infection. Those with any abnormality on screening underwent diagnostic testing with mycobacterial culture and Xpert Ultra (Ultra) on gastric aspirate specimens. Stool was collected for Ultra testing. Children were followed until discharge from the hospital. CXRs were independently interpreted by at least two reviewers. Absolute numbers and proportions of abnormal findings were reported.

**Results:** From November 2021 to May 2022, 132 children were enrolled. Their mean age was 19 months, 27% had kwashiorkor, 5% were HIV infected, and 6% were HIV exposed. In-hospital mortality was 5%. Under routine care, 11 (8%) children were started on TB treatment. At least one microbiologic test was positive for 6 (5%) children, with the Table showing these results by sample and test.

Study ID	GA AFB Smear (N=132)	GA Mycobacterial Culture (N=132)	GA Ultra (N=132)	Stool Ultra (N=131)	RIF Resistance
43	Scanty	Negative	Very low	Medium	Negative
64	2+	Positive	High	Low	Negative
104	Negative	Negative	Negative	Trace	Negative
122	Negative	Negative	Negative	Trace	Negative
130	Negative	Positive	Very low	Negative	Negative
131	Negative	Negative	Very low	Negative	Detected (GA)

Abbreviations: AFB: Acid fast bacteria. GA: gastric aspirate.

*Table. Summary of all microbiologic testing results for enrolled children with at least one positive microbiologic test.*

Urine FujiLAM testing will be done in the near future. CXRs were available and of adequate quality for remote review from 106 children. Of these, 52% were abnormal and 25% had findings suggestive of TB.

**Conclusions:** These results highlight the large burden of TB in children hospitalized with SAM in this setting and the need to focus intensive case finding efforts in this high-risk group. Results suggest an additive yield for microbiologic diagnosis with Ultra when both gastric aspirate and stool specimens are tested.

### OA09-266-15 Development of screening and treatment decision algorithms for TB diagnosis in children below 5 years hospitalised with severe acute malnutrition: A diagnostic cohort study

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**Background:** In children with severe acute malnutrition (SAM) tuberculosis is frequent, challenging to diagnose, and often fatal. We assessed tuberculosis prevalence and developed two treatment decision algorithms (TDAs) for tuberculosis in these children.

**Design/Methods:** We enrolled children aged <60 months hospitalized with SAM in Zambia and Uganda. They underwent tuberculosis screening (including contact history), chest X-ray, abdominal ultrasound, Xpert MTB/RIF Ultra and culture (respiratory and stool samples) and were followed-up for 6 months. Tuberculosis was defined using the 2015 standard case definition for children.

We used logistic regression to develop diagnostic prediction models for a one-step diagnosis and a two-step screening and diagnosis approach, excluding Xpert, chest X-ray and abdominal ultrasound from screening. We selected models on their discriminative ability (area under the receiver operating characteristics curve - AU-ROC) and parsimony. We derived scores from models using WHO-recommended thresholds for sensitivity and proposed TDAs.

**Results:** Of 603 children enrolled - median age 15 (IQR: 11-20) months, 345 (57.2%) male, and 65 (11.0%) HIV-infected, TB prevalence was 108/603 (17.9%, [CI 95% 15.5; 21.7]), 51 (8.5%) children had microbiological confirmation, and 104 (17.2%) initiated treatment at a



median of 6 (IQR: 2-10) days after inclusion. 75 (69.4%) children diagnosed with tuberculosis reported cough of any duration, 26 (24.1%) cough >3 weeks and 11 (10.2%) a TB contact history.

The one-step diagnostic model (TDA in Figure 1) had 15 predictors, including Xpert, clinical, radiographic and abdominal features, an AUROC of 0.910, and derived TDA sensitivity of 85.2% (95% CI 76.9-90.8) and specificity of 81.6% (95% CI 77.7-84.9). The two-step models had AUROCs of 0.750 and 0.912 for screening and diagnosis, respectively, and derived combined TDA sensitivity and specificity of 77.2% and 85.7%.

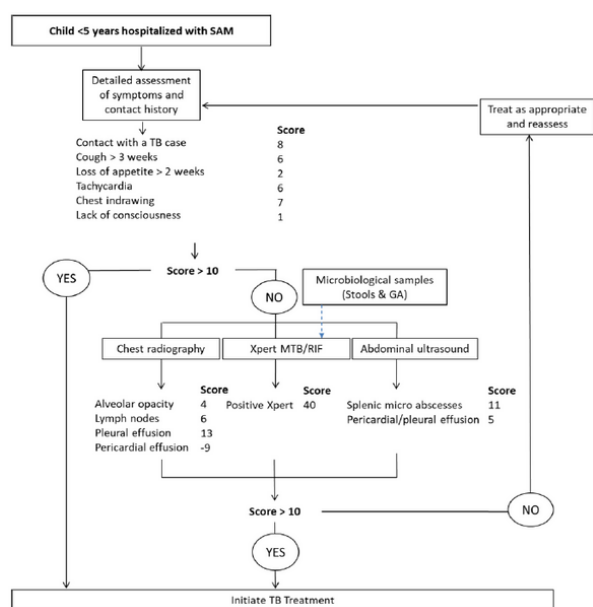


Figure 1. Proposed one-step diagnosis TDA.

**Conclusions:** Tuberculosis prevalence was high among hospitalized children with SAM. TDAs achieved satisfactory diagnostic accuracy and could be used to improve diagnosis in this vulnerable group.

### OA09-267-15 Increased detection of childhood TB through multipronged interventions: experience from Bangladesh

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**Background and challenges to implementation:** In high tuberculosis (TB) burden countries such as Bangladesh, 10% of all TB cases are estimated to occur in children aged under 15 years. However, in Bangladesh, in 2021, only 3.4% of all notified individuals with TB were children, according to WHO Global TB Report 2022. Diagnosing child TB remains a major challenge for several reasons, namely diagnostic challenges, lack of awareness among healthcare providers, lack of sensitive diagnostic tools, lack of community knowledge about TB in children, and stigma associated with the disease.

**Intervention or response:** With an aim to increase child TB detection, USAID’s Alliance for Combating TB in Bangladesh (ACTB) Activity supported the National Tuberculosis Control Programme (NTP), from February 2021, to design and implement a multipronged intervention - capacity building of healthcare providers, intensified case finding (ICF) and active case finding (ACF), use of new diagnostic tools and awareness raising activities in 8 districts of Rajshahi division- and observed a considerable increase in childhood TB detection.

**Results/Impact:** A total of 228 physicians were oriented on child TB in 8 districts of Rajshahi division to improve physicians’ diagnostic capacity and confidence. In 2022, about 0.6 million children were screened for TB symptoms in health facilities and communities through ICF and ACF approaches and 10,597 presumptive children were identified.

Among them, 699 children were detected with TB. In Rajshahi division, during July to December 2021, NTP had reported that children with TB constituted of 3.5% of all notified individuals with TB which has increased to 5.1% in the same period in 2022.

**Conclusions:** Increased attention on child TB particularly in TB-endemic areas with limited resources led to substantial increase in case detection in the intervention areas. This model is recommended for nationwide scale-up to increase TB diagnosis among children.

### OA09-268-15 Decentralising paediatric TB care in the public and private health sector across five districts from five states of India: lessons learnt

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**Background and challenges to implementation:** Pediatric TB accounts for 12% of total incident TB cases in India, but only half are notified, with the highest gap in the under-five age group.

Key challenges include underdiagnosis due to clinical characteristics, systemic gaps of non-availability of diagnostics and trained manpower to perform sample collection (SC) at sub-district facilities, and limited engagement of private sector pediatricians.

**Intervention or response:** To increase pediatric TB diagnosis, SAATHII is implementing a project to decentralise pediatric TB care in five districts across five states since May 2022, supported by the USAID-funded Tuberculosis Implementation Framework Agreement project implemented by JSI Research & Training Institute, Inc. Technical support was provided to establish 50 secondary-level facilities as pediatric TB hubs (32 public, 18 private) through:

- Onsite sensitisation and provision of SC consumables,
- Development of training manual and SOPs,
- Training of 37 mentors and 95 hub site staff,
- One round of mentorship visits.

Partnerships were established with at least one radiology/pathology lab for X-ray interpretation in each district. Service data from hubs were used to strengthen care provision.

**Results/Impact:** During Nov'22 – Mar'23, 550 pediatric presumptive-TB (PR-TB) identified; 77% of them got X-rayed, 95% had at least one sample collected of which 92% were NAAT evaluated, and 36 (6.5%) were diagnosed as TB. 36% of PR-TB and 30% of TB cases were among children under-five; 92% and 38% of hubs reported at least one pediatric PR-TB and TB case, respectively.

Sites conducting SC procedures increased by 150%. Major challenges include low confidence among providers for SC, inadequate parent counselling, and lack of community awareness initiatives.

**Conclusions:** Decentralizing pediatric TB care is feasible by establishing sub-district level hubs. Instituting coordination structures between child health programs, and

district-level pediatric TB expert teams from both public and private sectors will ensure quality of care and sustainability in each district.

### OA09-269-15 Enabling access to innovative, child-friendly TB/drug-resistant TB diagnostic methods: Introduction of stool testing in Ukraine

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**Background and challenges to implementation:** Childhood TB diagnosis is challenging, especially in children younger than five. One-fourth of new TB cases and half of retreatment cases in Ukraine have MDR-TB. Treating children under five was usually based on the spectrum of drug resistance of the source of infection. However, the infection source cannot be reliably established in all cases.

**Intervention or response:** STBCEU and the National Reference Laboratory (NRL) developed and distributed methodological recommendations to detect TB among children by testing stool samples with Xpert MTB/RIF. The project also worked with KNCV Tuberculosis Foundation and USAID to share practical experiences and develop Ukrainian-language video instructions for stool testing.

To further operationalize stool testing, including use of Xpert MTB/RIF Ultra, STBCEU experts adopted a generic USAID-developed protocol.

Stool testing using a one-step method was selected and used with current diagnostics to increase the proportion of bacteriologically confirmed TB cases among children. Project and NRL experts provided ongoing mentoring for clinical and laboratory staff in pilot regions.

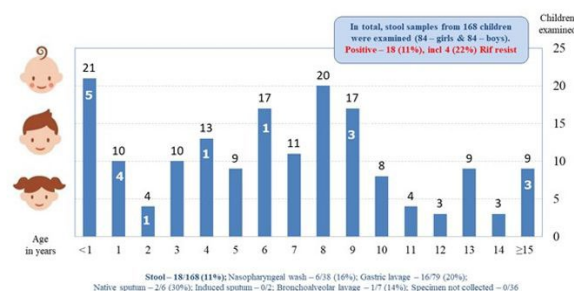


Figure 1. Age distribution of examined children from November 2021 to September 2022.

**Results/Impact:** Since the start of stool testing in November 2021, tests have been conducted in all 12 pilot regions. 168 tests were conducted, of which 18 (11%) were positive. Twenty-five (14.8%) samples from other biological materials were positive. Tuberculosis was confirmed in eight children due only to stool testing. Although children under five were prioritized, children over five (60% of tested) who could not produce sputum also were tested.

**Conclusions:** This approach avoids the need to subject children to gastric lavage to collect the diagnostic sample. Early detection of TB and its drug-resistant strains in children will allow timely adjustment to provide safer and more effective treatment and save more lives. Beginning in June 2022, based on updated WHO recommendations and learning from project's experience, Ukraine's NTP began promoting the use of stool testing throughout the country.

### OA09-270-15 Reversing the trend of low childhood TB diagnosis in Nigeria: the usefulness of stool-based Xpert testing

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**Background and challenges to implementation:** TB diagnosis in children has remained a challenge. Diagnosis being mostly sputum-based has posed a major challenge to timely diagnosis of TB in children given the difficulty in obtaining spontaneously expectorated sputum. This often necessitates the use of respiratory specimens such as gastric aspirates, induced sputum, nasopharyngeal aspirates, or bronchoalveolar lavage.

However these procedures are not only invasive but require resources and special skills and where these are unavailable, children who are unable to produce sputum are inadvertently denied access to diagnosis.

**Intervention or response:** KNCV Nigeria on the USAID funded TB LON Project introduced the stool based Xpert test for Diagnosis of TB in children. Guidelines and Standard Operating Procedures (SOPs) were developed. Laboratory Focal persons were trained on modified Simple One Step method (SOS) of stool processing, Clinicians were sensitized on the availability of Stool based Xpert test, a webinar on use of stool for childhood TB diagnosis was held for all relevant stakeholders, A you tube video demonstration of the stool test method was uploaded for country wide use.

**Results/Impact:** Stool based Xpert test was received as a diagnostic method for childhood TB among laboratory Focal persons, Clinicians and other health care workers. Across the implementation states, in the 4 quarters of 2022, a total of 27,825 stool samples were referred for

GeneXpert testing, all 27,825 (100%) were processed and a total of 1242 TB cases were diagnosed- an average TB yield of 4%. There was 18%, 58%, 69%, quarterly increase in stool samples processed and a 53%, 77% and 156% quarterly increase in Childhood TB cases diagnosed from stool compared to Q1 2022.

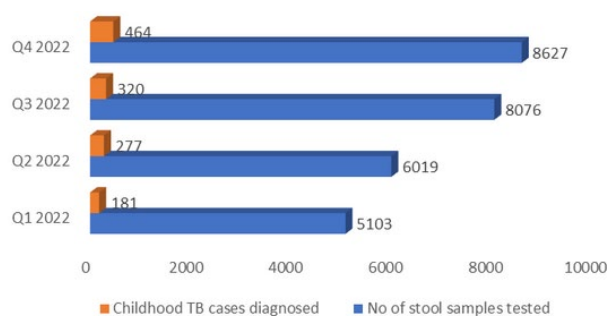


Figure. Childhood TB yield from stool based Xpert test.

**Conclusions:** The use of stool based Xpert improves childhood TB diagnosis by providing an alternative to respiratory samples which are often difficult to obtain in children. These Childhood TB cases would have been missed.

### OA09-271-15 Clinico-radiological spectrum and results of mycobacterial testing of cerebrospinal fluid in paediatric tubercular meningitis at diagnosis - findings from the SURE trial

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**Background:** Tuberculous meningitis (TBM) in children causes significant mortality and neurological disability. We describe the clinical and neuroimaging characteristics and results of CSF mycobacterial testing of a large group of children recruited in the SURE trial, an international multi-centric trial of TBM treatment.

**Design/Methods:** SURE is a factorial phase III RCT evaluating the non-inferiority for mortality of shorter intensive 6-month (high-dose rifampicin/isoniazid, pyrazinamide, levofloxacin) vs standard 12-month antituberculosis treatment and superiority of aspirin vs placebo on neurological disability. 400 children aged <18 years with TBM are being enrolled in 3 African and 2 Asian countries. The clinical features and findings of neuroimaging (as per local site reporting) and CSF mycobacterial testing at baseline are described.

**Results:** Between 3 March 2021 and 1 March 2023, 177 children (females [45%], median age 3.5 years [IQR 1.0 – 8.2]) were enrolled. Five [3%] were HIV infected. Fever was the most common symptom at presentation, seen in 92%, followed by lack of playfulness/energy (139, 79%). Seizures and focal neurological signs were pres-

ent in 83 (47%) and 72 (41%) respectively. At enrolment, 78 (44%), 70 (40%) and 29 (16%) were TBM stage I, II and III respectively. Acid fast bacilli on CSF smear were noted in 20 (11.2%). CB-NAAT of CSF detected *Mycobacterium tuberculosis* in 39/167 (23.3%) children. 18/143 (12.5%) revealed showed mycobacterial growth on MGIT. The most common neuroimaging abnormalities included pathological meningeal enhancement (56, 61%), hydrocephalus (51, 55%), infarcts (32, 35%) and tuberculomas (31,34%).

**Conclusions:** The SURE trial has recruited 177/400 children, despite diagnostic challenges and severe disruptions caused by COVID; most children were TBM stage I/II. Several sub-studies are ongoing, including evaluation of new diagnostic techniques, and follow up MRI scans at 24 weeks to evaluate the evolution of infarcts and their response to aspirin in children with TBM.

### OA09-272-15 Missed opportunities in tuberculous meningitis care for children in Cape Town, South Africa

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**Background:** Tuberculous meningitis (TBM) is the most severe form of tuberculosis (TB) in children, resulting in high mortality and life-long disability among survivors. Bacille Calmette-Guérin (BCG) vaccination and TB preventive therapy (TPT) following exposure are both effective strategies to prevent TBM. Delays in diagnosis are associated with worse outcomes.

We explored individual and health-system factors that contribute to missed opportunities for TB prevention and TBM diagnostic delay in children.

**Design/Methods:** We conducted an observational cohort study, enrolling children <13 years of age routinely diagnosed with TBM at two hospitals in Cape Town, South Africa. Data were collected through baseline in-depth interviews with caregivers and medical record reviews. BCG vaccination status was verified on Road-to-Health booklets. Quantitative data were analyzed using descriptive statistics and qualitative data using deductive thematic analysis.

**Results:** We enrolled 36 children, median age 4 years (IQR=2.0-5.8 years); 18 (50%) males and 3 (8%) living with HIV, from March 2022 to February 2023. Road-to-Health booklets were available for 32 (89%) children. Only 23/32 (72%) received BCG vaccination, all within 7

days of birth. Nineteen of 36 (53%) children had known TB exposure in the preceding year; only 1 received TPT, for two weeks only. Fourteen children (39%) had 4 or more healthcare visits in the 3 months preceding diagnosis. Qualitative data analysis found that diagnostic delay was underpinned by a lack of symptom recognition, misdiagnosis, and health system failures at different levels of care. An expeditious referral process between facilities enabled more rapid diagnosis for twelve out of 36 children (33%).

**Conclusions:** Scaling up implementation and accessibility of both BCG vaccination and TPT for children are essential and urgent in this high TB-burden setting. Health systems should be strengthened to ensure prevention, early recognition, and prompt treatment initiation of TBM to prevent unnecessary childhood TB mortality and morbidity.

### OA10 TB Infection and Improvement of TBT Uptake

#### OA10-273-15 Improving uptake of and adherence to TB preventive treatment using structured community approach: A case study in Ebonyi State, Nigeria

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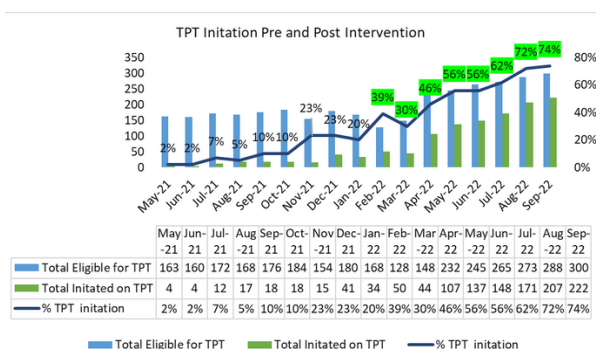
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**Background and challenges to implementation:** TPT initiation for eligible contacts has been a serious challenge in Nigeria. Ensuring adherence and completion are even more difficult. In Ebonyi State Nigeria, the PPM facilities initiated only 2% of eligible contacts on TPT in May 2021. A root cause analysis showed that one major reason for the low uptake is that most of the identified eligible contacts do not get to the referred facilities for initiation and the few that were initiated do not continue follow-up visits as they are required to visit the facilities monthly for a refill. Hence, we decided to implement a structured community-level initiation of TPT and drug refill

**Intervention or response:** We devolved TPT initiation to the community Level using the linkage coordinators (LC), who coordinate the Global Fund Public-private mix TB project (GFPPMTB) activities including Contact Tracing in the communities and Patent Medical Vendors (PMVs) who also work in the communities for TB case finding in the same Project.

A 2-day training was conducted for the LCs on TPT initiation. Weighing scales and TPT standard operating procedures were distributed to all 13 LGA LCs. Each LGA was mapped to a PPM hospital to ensure documentation, Drug supply, and reporting of activities. The PMVs were used as treatment supporters for drug refills for eligible contact in their communities while the LCs ensure updates in the facility registers. Results were collated monthly and analyzed

**Results/Impact:** This Intervention was monitored over a period of 8 months February to September 2022, compared with the 8 months pre-intervention period, TPT initiation increased from 2% to 74% of the eligible contacts in September 2022. 75% of contacts initiated collected up to month 4 refill.



**Conclusions:** Initiating TPT at the community level and using community actors for refill is very effective in increasing the uptake of TPT and adherence

**OA10-274-15 Understanding the three 'As' (acceptance, adherence and adverse drug reactions) of the 6H and 3HP regimens under programmatic conditions in India**

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**Background:** WHO has recommended multiple TB Preventive Treatment (TPT) regimens. Available literature pertaining to India mostly contains information on uptake, compliance, safety and efficacy of different regimens in research settings. Evidence from population level programmatic implementation is limited for adult household contacts of pulmonary TB patients from India.

**Design/Methods:** Joint Effort for Elimination of TB (JEET 2.0) project, funded by the Global Fund and supported by India's NTP, implements TPT amongst household contacts (HHCs) of drug sensitive pulmonary TB patients in 65 districts across 11 provinces. 3HP and 6H regimen was offered to HHCs across "Test & Treat" (6) and "Screen & Treat" (59) districts respec-

tively. Project MIS was used to capture real-time information on HHCs' acceptance (*initiated TPT with the given regimen*), adherence (*completion of treatment*) and ADR (*Adverse drug reaction*). Data was analysed using STATA 17.0

**Results:** Between Jan-22 to Feb-23, uptake of TPT did not differ significantly between the 6H and 3HP groups (OR 1.03, 95% CI 1.01-1.06). Although, individuals on 3HP had 1.9 times greater odds (95% CI 1.8-2.0) of completing treatment than those on 6H. However, the odds of ADR with 3HP were 6.9 times (95% CI 7.0-8.2) to that with 6H. The reported ADR of 3HP were non-severe in nature and includes vomiting (38%), dark colored urine (32%), nausea (25%) and persistent fatigue (23%). 19% and 16% of HHCs with ADR discontinued treatment with 3HP and 6H respectively.

Domain	Indicator	6H (%)	3HP (%)	aOR*	95% CI
Acceptance	% of HHCs initiated TPT	57.9	56.4	1.03	1.01-1.06
Adherence	% of HHCs successfully completed TPT	84.0	91.1	1.97	1.83-2.11
ADR	% of HHCs who have been initiated TPT reported any ADR	1.0	7.6	6.91	6.42-7.44

p-value<0.05, statistically significant

\*aOR- Adjusted Odds ratio of 3HP with reference to 6H

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**Conclusions:** In programmatic conditions, household contacts were more likely to complete TPT with shorter weekly regimen, although treatment uptake rate for the two regimens was similar. For Individuals on 3HP regime patient education on ADRs and regular monitoring for adverse reactions will be important for treatment completion.

### OA10-275-15 TB prevention treatment coverage at fixed health facilities and community settings in Pakistan

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**Background and challenges to implementation:** We implemented TB prevention treatment (TPT) in routine programmatic settings in cities of Peshawar and Karachi, Pakistan.

Here, we compare the TB prevention cascade when services were provided at fixed health facilities and in community settings.

**Intervention or response:** We enrolled household contacts of TB patients from January-2018 to December-2019. Household contacts underwent clinical evaluation including chest x-ray, XpertMTB/RIF (if able to produce sputum), and clinical assessment by medical officer. TB disease-free contacts were started on TPT. Contacts <2 years started 6 months of Isoniazid while ≥2 years started 3 months of Isoniazid-Rifampentine.

Clinical evaluation, TPT initiation, and follow-ups were compared across fixed health-facilities vs community settings. Final outcome was completion of TPT or TB diagnosis (TB prevention cascade).

**Results/Impact:** In Karachi, 83% (18,228/22,046) household contacts completed clinical evaluation of which 93% (2,796/3,022) were evaluated in the community and 81% (15,432/19,024) at health facilities. TB was diagnosed in 2.6% (476/18,228) contacts while TPT initiation was 58% (10,543/18,228) and 69% (7,280/10,543) contacts completed TPT.

In Peshawar, 95% (6,073/6,389) household contacts completed clinical evaluation of which 99% (718/720) were evaluated in community and 94% (5,355/5,669) at health facilities. TB was diagnosed in 2.2% (136/6,073) contacts while TPT initiation was 64% (3,888/6,073) and 93% (3,598/3,888) contacts completed TPT.

In multivariable analysis, contacts were 5% more likely to complete TB prevention cascade in community settings than in health facilities (RR:1.05; 95% CI:1.03-1.06) after adjusting for city, index patients' age, gender and TB type, and contacts' age and gender. Contacts in Peshawar were 15% more likely to complete the cascade than in Karachi (RR:1.15; 95% CI:1.13-1.16).

Characteristics	Unadjusted			Adjusted		
	Risk Ratio (RR)	95% Confidence Interval	p-value	Risk Ratio (RR)	95% Confidence Interval	p-value
<b>Screening Location</b>						
Health facility	1.00	-	-	1.00	-	-
Community	1.03	1.02 – 1.05	<0.001	1.05	1.03 – 1.06	<0.001
<b>City</b>						
Karachi	1.00	-	-	1.00	-	-
Peshawar	1.17	1.16 – 1.18	<0.001	1.15	1.13 – 1.16	<0.001
<b>Contact Gender</b>						
Males	1.00	-	-	1.00	-	-
Females	0.99	0.98 – 1.00	0.541	1.00	0.99 – 1.01	0.622
<b>Contact Age Group</b>						
<5 years	1.00	-	-	1.00	-	-
5-9 years	1.08	1.05 – 1.10	<0.001	1.05	1.02 – 1.08	<0.001
10-14 years	1.09	1.07 – 1.12	<0.001	1.06	1.03 – 1.08	<0.001
15-19 years	1.09	1.07 – 1.12	<0.001	1.06	1.04 – 1.09	<0.001
≥20 years	1.03	1.01 – 1.05	0.001	1.01	0.98 – 1.03	0.316
<b>Index Gender</b>						
Males	1.00	-	-	1.00	-	-
Females	0.99	0.98 – 1.00	0.400	0.98	0.97 – 0.99	0.008
<b>Index Age Group</b>						
<5 years	1.00	-	-	1.00	-	-
5-9 years	1.00	0.98 – 1.03	0.528	1.00	0.97 – 1.03	0.768
10-14 years	1.03	1.00 – 1.05	0.018	1.02	0.99 – 1.05	0.070
15-19 years	1.05	1.03 – 1.08	<0.001	1.02	1.00 – 1.05	0.048
≥20 years	1.01	0.99 – 1.04	0.181	0.97	0.95 – 1.00	0.099
<b>Index TB Type</b>						
PTBP	1.00	-	-	1.00	-	-
PTBN	0.94	0.93 – 0.95	<0.001	0.97	0.96 – 0.98	<0.001
EPTB	0.89	0.87 – 0.90	<0.001	0.90	0.89 – 0.91	<0.001

Figure 1. Risk ratios for completing TB prevention cascade in fixed health facilities versus community settings. Adjusted risk ratios calculated after adjusting for city, age and gender of contacts, age and gender of index TB patient and type of TB in index patient.

**Conclusions:** We observed improved uptake of TB prevention treatment services among household contacts of TB index patients in the community settings compared to health facilities. We suggest a decentralized model of TB care services in high TB burden settings, closer to the patients to improve the uptake of TB screening, diagnosis, and prevention.

### OA10-276-15 Community-based initiation and delivery of TB preventive treatment refills for household contact persons below 5 years through integrated community case management in Uganda

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**Background:** In 2019, only 31% of household TB contact persons aged <5 years initiated TB preventive treatment (TPT) in Kyegegwa district. More than 40% of those eligible for TPT are unable to access a health facility, contributing to the low TPT uptake. We integrated TPT delivery into the existing integrated community case management (iCCM), to improve TPT initiation and completion rates among household contacts persons aged <5 years.

**Design/Methods:** We conducted an implementation science project from February 2021 to January 2022 in ten Ugandan TB diagnostic and treatment units. Contact persons aged <5 years were screened for TB symptoms during household TB contact tracing home visits. Children without TB symptoms initiated TPT at home; a clinician prescribed TPT and monitored the contacts for TPT side effects, TB symptoms, and TPT completion. The caretakers collected TPT refills from iCCM community health workers' homes. Children with TB symptoms were referred to the nearest health facility for clinical evaluation.

The primary outcome was the percentage of contact persons who initiated TPT within the iCCM approach, as recorded in routine facility TPT registers.

**Results:** More than half (75.8%, 263/347) of identified contact persons <5 years initiated TPT, and 82% (216/263) of these initiated and received TPT refills within iCCM. Majority (97%, 210/216) who received refills through iCCM completed the six-month TPT regimen.

Hospitalisation due to severe malaria with anaemia (1/216, 0.5%) was the only identified serious adverse event. Breakthrough TB disease was diagnosed in one child (1/216, 0.5%), and TPT discontinued in one contact of a multi-drug resistant TB (MDR-TB) patient (1/216, 0.5%). No TPT-related deaths occurred.

**Conclusions:** Community-based TPT initiation and refills within iCCM is feasible, and improves TPT initiation and completion among child TB contact persons. This approach may be considered to deliver integrated person-centered care towards the End-TB target of 90% TPT uptake among high-risk groups.

### OA10-277-15 The implementation of systematic prescription of TB preventive treatment based on QuantiFERON®-TB Gold test results in Ukraine

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**Background and challenges to implementation:** To achieve TB elimination, treating LTBI before it turns into active disease. Before the USAID-financed STBCEU project, use of tuberculin skin testing among children was unsystematic, and access to LTBI testing using the QuantiFERON®-TB Gold (QFT-Gold) test was not widely established.

**Intervention or response:** To scale up access to QFT-Gold test for LTBI testing, STBCEU collaborated with two private laboratories and conducted training and mentoring meetings for regional specialists in 12 regions on improving TB case detection, rationalizing patient selection, explaining the benefits of short TPT regimens, following the TPT referral algorithms, tracking test results, and analyzing clinical management. Then, in late 2021, STBCEU conducted clinical mentoring on interpreting QFT results, determining patient management tactics, and establishing rational TPT prescription protocols, especially regarding use of TPT in QFT-negative persons older than five.

**Results/Impact:** From October 2021 to March 2023, 4,029 people were identified through index patients and received QFT-Gold testing. Index patient profiles included 52% with DS-TB, 34% with DR-TB, and 14% with unknown resistance.

Contact-tracing identified 62 cases of active TB (1.5%). QFT testing was provided to 3,317 people, with LTBI detected in 665 (20%). Among all tested, 485 courses were prescribed for (+) QFT (73% 485/665) and 251 for (-) QFT (10% 251/2652).

The percentage of (-) QFT patients over five receiving TPT declined from 18% to 0.4%, increasing to 4.3% due to testing initiation in 5 new regions.

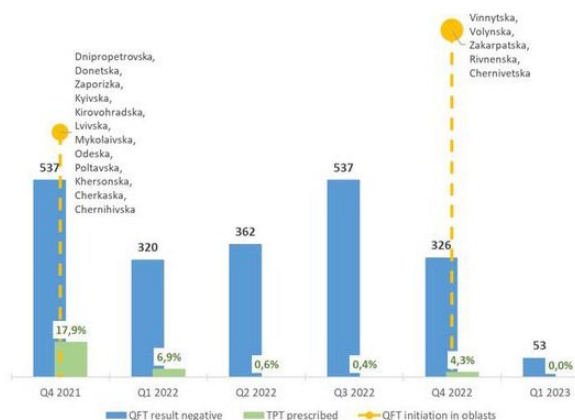


Figure. Percentage for TPT prescription for persons above 5 years old with (-) QFT test.

**Conclusions:** The STBCEU pilot strengthened access to QFT-Gold testing and improved clinical management by identifying priority groups for TPT. PATH's clinical mentoring contributed to capacity-building of medical specialists, improving service quality and strengthening management of LTBI+ persons. Due to STBCEU technical assistance, the proportion of preventive treatment prescribed to (-) QFT persons older than five was significantly reduced. PATH is now supporting national expansion of QFT-Gold testing.

### OA10-278-15 Latent TB infection study in South African hospitals using interferon-gamma release assays

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**Background:** Healthcare workers (HCWs) in high burden countries are at a greater risk of acquiring tuberculosis (TB) than the general population. Knowing the status of latent TB infection (LTBI) is important to protect both health workers and the patients to whom they provide health care. TB infection status is important to protect both the HCWs and patients to whom they provide healthcare. We aimed to determine the prevalence and incidence of LTBI as well as associated factors among HCWs in South Africa.

**Design/Methods:** We recruited all HCWs from three hospitals between 2018 and 2022. They were screened for TB symptoms, sputum Gene Xpert testing/Chest

X-rays were done and they completed a questionnaire capturing demographic data, medical history and risk factors. Blood samples were drawn to screen for LTBI using the QFT-Plus assay.

**Results:** Of the 939 participants (male=222; female=717), 476 (53%) were LTBI positive. Females had 76% LTBI positivity (362/476).

Factors associated with higher IGRA positivity were age $\geq$ 40-49 (157=51%), smokers (53=74%), TB history (40=59%) and were household contacts (41=58%). Those who had worked in healthcare for more than 15 years had the highest prevalence of LTBI (55%).

At month 24, 6% of the cohort had converted from a negative to positive IGRA. The prevalence of microbiologically confirmed TB was low at baseline and follow-up (0.5%). Overall, a low indeterminate rate was observed in this study (3.7%).

**Conclusions:** HCWs had a 53% prevalence of LTBI and a low prevalence (0.5%) of microbiologically confirmed TB disease during the study period. This demonstrates a need to prioritise the implementation of infection control strategies to reduce the risk of acquiring TB infection. TPT is also recommended for HCWs with LTBI to prevent progression to TB.

### OA10-279-15 M. tuberculosis infection burden, IGRA conversion and reversion among healthcare workers in a high TB-HIV burden country - groundwork for TB vaccine trials in Nigeria

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**Background:** Nigeria remains among the 14 high burden countries for TB, MDR TB and TB/HIV co-infection and also among the 8 countries accounting for over 60% of the global TB estimates. Unfortunately, among the several TB vaccine trials being conducted globally, none has been conducted in Nigeria despite its huge burden. As a groundwork towards pushing for TB vaccine trials in Nigeria, we describe the burden of Mycobacterium tuberculosis Infection (MTBI) IGRA conversion and reversion rates among healthcare workers (HWs) at-risk of TB.

**Design/Methods:** We conducted a 2-year prospective cohort study and enrolled consented HWs in HIV care and treatment clinics over a 4-month period after obtaining ethical clearance. We administered a standardized questionnaire to assess risk factors for MTBI and screened using quantiferon plus (QFT) over 4 time points (i.e. baseline, month 6, 12 and 24).



**Results:** 1043 HWs were enrolled at baseline with a LTBI prevalence of 44.8% (400/892) after excluding indeterminate or no test results (151).

Of the 643 participants followed up (i.e. after excluding 400 IGRA positive at baseline), the serial MTBI prevalence was 24.3% (140/575) at month 6, 21% (85/402) at month 12, and 21% (84/395) at month 24 among those with valid IGRA results.

Using the previous time point as baseline (i.e. month 6 as baseline compared with month 12 and month 12 as baseline compared with month 24), the IGRA conversion and reversion rate at month 12-time point were: 9.5% (39/409) and 36.4% (51/140) and at month 24-time point were 12.1% (37/305) and 40% (34/85) respectively.

**Conclusions:** There is huge burden of MTBI and significant conversion rates among HWs in Nigeria, which project these as a potential target population for TB vaccine trials. Understanding the impact of background IGRA conversion and reversion rates are vital in the design and interpretation of future TB vaccine trials in Nigeria.

#### OA10-280-15 Annual incidence infection with *M. tuberculosis* in an African City with endemic TB

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**Background:** The incidence of infection with *M. tuberculosis* (Mtb) in the community is a useful metric of tuberculosis burden since it depicts transmission from undetected infectious persons.

In a prospective study, we estimated the annual incidence of Mtb infection among HIV infected and uninfected adults in Kampala City, Uganda.

**Design/Methods:** Between April 2019 - December 2022, 994 adults (18 – 65 years) without evidence of current Mtb infection were enrolled in a prospective cohort study in Kampala, Uganda. Participants were evaluated quarterly to identify new infections. New infections were defined as conversion of the interferon-gamma release assay (IGRA, criterion for conversion - test  $\geq$  0.35 IU/ml) or culture-confirmed tuberculosis. Incidence rates were estimated for overall follow-up and at quarterly intervals; incidence rates were stratified by sex and HIV serostatus.

**Results:** Of the 994 participants, 86 incident infections occurred over 6965 person-months of observation (pmo), giving an overall incidence rate of 1.23/100 pmo (95% CI: 1, 1.52), equivalent to an annual incidence of

13.8% (95% CI: 11.3%, 16.7%). Over the quarterly intervals, the incidence rate varied slightly from a low of 1.06/100 pmo at month 6 to a high of 1.56/100 pmo at 12 months; across all follow up visits, the confidence intervals of visit specific incidence rates overlapped.

The incidence rate was 1.33 /100 pmo (95% CI: 0.82%, 2.13%) among HIV seropositive persons and 1.24/100 pmo (95% CI: 0.98%, 1.57%) among HIV seronegative persons; the incidence rate was 1.3/100 pmo (95% CI: 0.93%, 1.82%) in males and 1.26/100 pmo (95% CI: 0.97%, 1.63%) in females.

**Conclusions:** In an African city with endemic TB disease, we found a high and stable occurrence of new infections among adults. These findings suggest that the residents of the city encounter undetected infectious cases of TB in the community.

#### OA11 Measuring treatment adherence

##### OA11-281-15 Implementation outcomes of TB digital adherence technologies: A scoping review using the RE-AIM Framework

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**Background:** Tuberculosis (TB) remains a global health problem. Low adherence to TB treatment increases the risk of poor outcomes. Digital adherence technologies (DATs), aiming to improve TB adherence and potentially outcomes, are increasingly being evaluated.

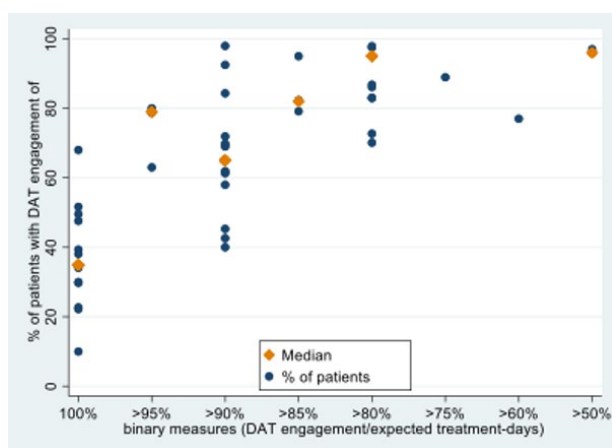
We used the RE-AIM Framework to understand the outcomes of DAT implementation.

**Design/Methods:** We conducted a scoping review (PROSPERO-CRD42022326968), including MEDLINE, Embase, CENTRAL, CINAHL, and Web of Science databases for publications from January 2000-April 2022. Articles meeting the prespecified inclusion criteria and containing data on at least one RE-AIM framework domain were included.

Here, we report on “Reach”, focusing on the proportion and representativeness (equity) of potential DAT users based on DAT eligibility, any engagement and sustained engagement, and “Implementation”.

**Results:** Of 12,906 records identified, 147 were included. DATs included SMS, phone, video, and pillboxes (interim analysis, n=76). Across a range of settings, cellphone ownership varied from 50%-100%, and 4-20% of TB patients had technology challenges (such as inability to send SMS). The proportion of TB patients who were offered a DAT and engaged at least once ranged from 73%-82%. The percentage of patients with 100%, >90%, and >80% DAT engagement over their treatment course ranged from 10-68%, 40-98%, and 70-98%, respectively (Figure).

Sustained engagement (proportion of treatment-days with DAT engagement) was similar for video (median 92%, interquartile range [IQR 84-94%]; 12 measures) and pillbox (87% [81-98%]; n=20) DATs followed by SMS (29% [24-48%]; n=5). Implementation was affected by technological issues (cellphone coverage, DAT malfunction, or difficulty of use) and provider-facing issues (failure to initiate intensified patient management following low DAT engagement).



**Conclusions:** This analysis suggests that a small proportion of patients lack cellphone access; technology issues included cellphone signal or inability to send SMS. Video and pillbox DATs appear to be generally acceptable with moderate to high levels of engagement. Implementation challenges included technological and provider-facing issues.

## OA11-282-15 The acceptability of two digital adherence technologies and differentiated model of care among TB patients in South Africa

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**Background:** As digital adherence technologies (DATs) are being introduced, factors affecting their adoption and use in high TB burden settings need to be understood.

Our objective was to evaluate the acceptability of two DATs, the smart pillbox and SMS self-report using labels. These were rolled out with a Differentiated Model of Care (DMC) based on missed doses, and consisted of automated reminder SMS's, phone calls and home visits.

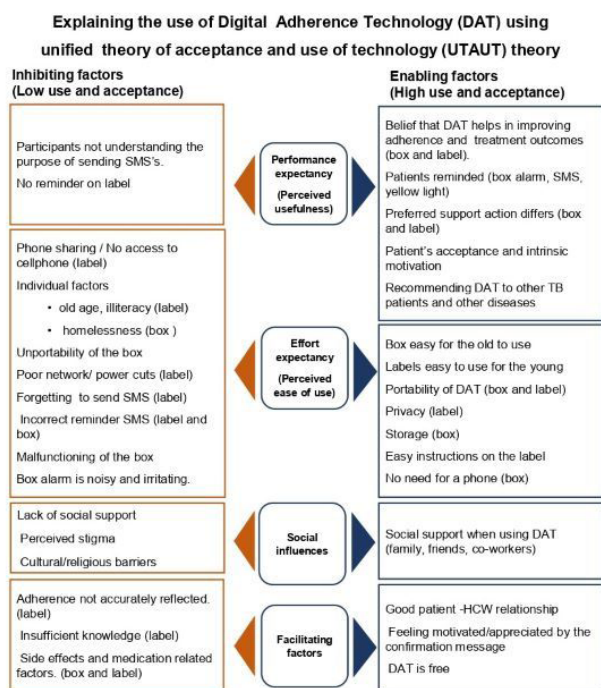
**Design/Methods:** We conducted in-depth interviews with adult drug-sensitive TB patients in two South African Provinces from May-August 2022. Interviews were conducted in local languages, audio recorded, transcribed verbatim and translated to English. Participants were purposively selected by DAT type, gender, and adherence-level.

We used inductive thematic analysis approach and unified theory of acceptance and use of technology to develop themes.

**Results:** We included 35 individuals, 20 and 15 enrolled in pillbox and labels groups respectively. Most participants reported positive attributes of the pillbox, citing the alarm reminder, storage, ease of use, not requiring a phone, social support, and portability. Others found the pillbox unportable and experienced box malfunction leading to study withdrawal.

Although some label users cited ease of use (among the young), daily confirmation message, social support and portability majority were unhappy, and some switched to the pillbox. Reasons for discontinuation included power cuts affecting network and phone battery charging, forgetting to send the SMS, old age, illiteracy, no cellphone access, and lacking understanding.

Although participants generally appreciated DMC, as they felt cared for by the Health Care Worker, there were different perceptions on the most suitable follow-up action as some felt home visits stigmatizing.



**Conclusions:** Results show that features favoring acceptability are more common among pillbox users while use of labels was challenged by structural and individual level factors. Further work is needed to make some of the DMC components less stigmatizing.

### OA11-283-15 Piloting 99DOTS: A digital tool to improve TB treatment adherence in Burkina Faso

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**Background:** 99DOTS is a mobile phone-based technology that enables real-time remote monitoring of daily intake of TB treatment. In October 2022, we implemented the 99DOTS in Burkina Faso to improve adherence to TB treatment and its success rate and to reduce patient's indirect costs.

**Design/Methods:** We conducted a before and after mixed methods study to evaluate 99DOTS impact on TB treatment adherence and outcomes in seven pilot health centers (6 urban, 1 rural). Only adults and children with drug-sensitive pulmonary TB (TB-S) were eligible. Quantitative data was prospectively collected from TB patients using 99DOTS and enrolled between

October 2022, and January 2023. Treatment outcomes of TB patients not using 99DOTS and registered 12 months earlier were retrospectively collected. The qualitative component aimed at evaluating the acceptability of the 99DOTS in patients and health staff.

**Results:** During the study period, 99DOTS was proposed to all new TB-S patients. Only one refused corresponding to a total of 257 patients, of which 196 were males (76%), 12 (4.7%) children under 15 years of age, and 13 (5.1%) people ≥ 65 years of age.

Overall treatment adherence was 90% in patients undergoing treatment and 88% in those with assigned treatment outcome.

Of the 257 patients using 99DOTS, 12 (4.7%) died and 3 (1.2%) were lost to follow-up (LTFU) compared to 7,9% death and 4,3% LTFU in the same centers in 2022. A total of 14 healthcare providers and 16 patients were interviewed after 3 months of implementation. Results showed that using 99DOTS reduced the workload for most providers (11/14) and the number of visits to the health center for all patients interviewed.

**Conclusions:** We found 99DOTS efficient and well accepted by TB patients and health providers. The NTP plans to extend its use in the insecurity's areas of Burkina Faso.

### OA11-284-15 The mediating effect of video-supported treatment (VST) on loss to follow-up in the USAID Activity sites in Uzbekistan

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**Background and challenges to implementation:** COVID-19 pandemic restrictions compounded the challenges of in-person TB treatment and increased the risk of treatment interruption. These challenges highlighted the need for digital health methods to support delivery of TB treatment.

**Intervention or response:** In 2021, Uzbekistan's National TB Program (NTP) developed guidelines for TB patient management using video-supported treatment (VST). In May 2021, the USAID Eliminating TB in Central Asia activity supported the NTP in launching VST in three pilot oblasts (Syrdarya, Ferghana, and Jizzak). Patients used the free Telegram app to submit videos of themselves taking medication and shared the videos via Telegram with a TB facility nurse. The nurse would review the video and record the results on standard Directly Observed Treatment (DOT) forms. By the end of 2021, VST was operating through three urban and three rural institutions. In 2022, following initial results in the pilot sites, VST was scaled up.

USAID ETICA provided 14 tablets for medical staff and more than 70 smartphones for patients to implement VST.

**Results/Impact:** Loss to follow-up (LTFU) was assessed in cohorts from the pilot areas that included both drug-susceptible (DS)-TB and drug-resistant (DR)-TB cases. Following an increase in LTFU cases during the pandemic compared to previous periods, since implementation of VST began in 2021, the percentage of patients lost to follow-up has gradually declined. Since VST launch, the number of patients enrolled in VST has quadrupled (Figure 1).

97.3% of VST participants had a successful treatment outcome (DS-TB 98.1%; DR-TB 91.3%) as compared to only 83.9% (DS-TB 87%; DR-TB 66%) of patients who did not receive VST.

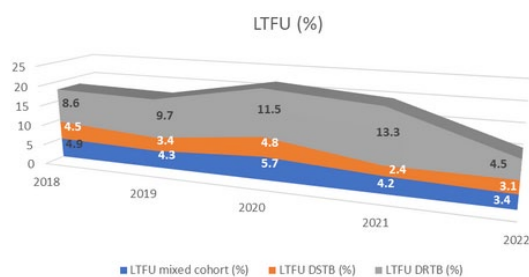


Figure 1.

**Conclusions:** LTFU gradually declined in the three pilot areas as the use of VST expanded. We can conclude that VST could be useful in reducing LTFU among both the DS TB and DR TB cohorts, and we, therefore, recommend VST for countrywide expansion.

## OA11-285-15 Promoting treatment outcomes through video-supported treatment in the country of Georgia

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**Background and challenges to implementation:** High loss-to-follow up among drug-resistant tuberculosis patients is one of the main challenges of the national tuberculosis (TB) response in Georgia. Video-supported treatment (VST) was suggested as an option providing more flexibility for patients as well as for healthcare providers.

**Intervention or response:** Georgia started using VST in 2016, and a VST mobile application was developed in 2018. At first, VST was offered to only patients with drug-resistant tuberculosis. As of now, all TB patients can be enrolled on VST, both synchronous and asynchronous modes. Synchronous VST is done using instant messaging software and asynchronous is done

using the VST application, where patient uploads the video of taking TB medication. To evaluate VST in the country, we analyzed the data among patients enrolled on VST during 2019-2022. We compared 4-year average treatment success rates by treatment type (first-line and second-line) and by VST mode (synchronous vs asynchronous).

**Results/Impact:** A total of 2697 TB treatment episodes were enrolled in VST during 2019-2022. Data for 2209 patients were matched with the national TB database and were included into the further analysis. Out of 2209 patients, 76% (n=1683) were on first-line treatment, median age was 38 (IQR=23) and 65% were male (n=1426). Out of the new and relapse TB patients who had treatment outcome assigned, treatment success rate was 94% and 83% (first-line treatment and second-line treatment, respectively).

Treatment success rate was also compared between asynchronous and synchronous VST (Figure 1). New and relapse TB patients who started TB treatment in Georgia during 2019-2022 either on DOT or VST had 86% and 79% treatment success rate (first-line treatment and second-line treatment respectively).

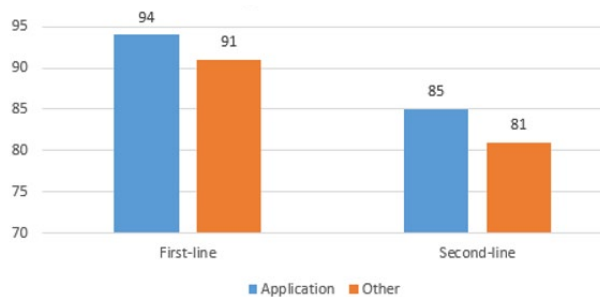


Figure 1. Treatment success rate (%) asynchronous vs synchronous.

**Conclusions:** Results show that VST is an effective tool for TB treatment. Treatment success rates were higher among patients using VST application. VST also served as a powerful tool for uninterrupted treatment during the pandemic.

**OA11-286-15 The evolution of electronic directly observed therapy in TB treatment: before, during and after the COVID-19 pandemic in Taiwan**

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**Background and challenges to implementation:** Since 2006, Taiwan’s Directly Observed Treatment, Short-course (DOTS) program has relied mainly on in-person DOT that trained workers provide care and medication to TB cases through home visits. The coverage of the DOTS program is as high as 98%. In 2015, an electronic Directly Observed Therapy (eDOT) app was developed as a complement to in-person DOT for TB patients who faced mobility, lifestyle and privacy issues. Until 2020, the eDOT usage rate remained at less than 5%. However, during the COVID-19 outbreak in 2021, due to the control regulations, a significant increase (30%) in the eDOT use was observed.

**Intervention or response:** We conducted a retrospective analysis of the use of eDOT and in-person DOT for TB patients and their contacts with latent TB infection (LTBI) who received community-based DOTS in 2021-2022. Inpatients and residents in long-term care facilities were excluded from the population. Demographic data and treatment outcomes were collected and analyzed using a multi-variate logistic regression.

**Results/Impact:** The eDOT usage rate for 5,363 DS-TB patients and 7,768 contacts collected were 33.5% and 28.4% respectively. Demographic data revealed that women had a higher eDOT usage rate than men, as well as younger population compared to their older counterparts (Table). After adjusting sex and age, the population using eDOT had significantly better treatment outcomes than their counterparts who received in-person DOT for both TB patients (OR = 1.474, p < 0.001) and LTBI contacts (OR = 2.031, p < 0.001), indicating that eDOT was effective during the pandemic.

		N	%	eDOT	%	Treatment completion			
						Treatment success	%	p value *	Adjusted Odds Ratio (95% CI)
DS-TB		5,363	100	1,796	33.5	4,551	84.9		
sex	female	1,665	31.0	619	37.2	1,450	87.1	0.012	1.24 (1.05-1.07)
	male	3,698	69.0	1,177	31.8	3,101	83.9		Ref.
age	<65 years	2,495	46.5	1,159	46.5	2,262	90.7	<0.001	2.26 (1.90-2.68)
	≥65 years	2,868	53.5	637	22.2	2,289	79.8		Ref.
DOT type	eDOT	1,796	33.5	-	-	1,609	89.6	<0.001	1.47 (1.23-1.77)
	In-person DOT	3,567	66.5	-	-	2,942	82.5		Ref.
LTBI contacts		7,768	100	2,207	28.4	6,845	88.1		
sex	female	3,802	48.9	1,116	29.4	3,347	88.0	0.999	1.0 (0.87-1.15)
	male	3,966	51.1	1,091	27.5	3,498	88.2		Ref.
age	<65 years	5,622	72.4	1,886	33.5	5,076	90.3	<0.001	1.78 (1.54-2.05)
	≥65 years	2,146	27.6	321	15.0	1,769	82.4		Ref.
DOT type	eDOT	2,207	28.4	-	-	2,060	93.3	<0.001	2.03 (1.69-2.45)
	In-person DOT	5,561	71.6	-	-	4,785	86.0		Ref.

Abbreviations: DOT = Directly Observed Therapy; eDOT = electronic Directly Observed Therapy  
\* : chi-square test

Table. Multi-variate logistic regression for treatment outcome among patients with drug-susceptible TB (DS-TB) and contacts with latent TB infection (LTBI).

**Conclusions:** eDOT was a practical solution to the challenges posed by social distancing regulations during the COVID-19 pandemic. The equal or even better treatment outcome makes it possible for this digital tool to be utilized in TB care in community in post-pandemic period. More studies to tackle-down the low uptake rate of the eDOT app are warranted.

**OA11-287-15 Adolescent, caregiver and health provider perceptions of TB treatment supervision during the COVID-19 pandemic in Lima, Peru**

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**Background:** In Peru, tuberculosis treatment is administered at a health facility under direct supervision of health providers. However, during the COVID-19 pandemic, selected patients were allowed to take treatment at home under the supervision of family members or health providers via synchronous or asynchronous videos.

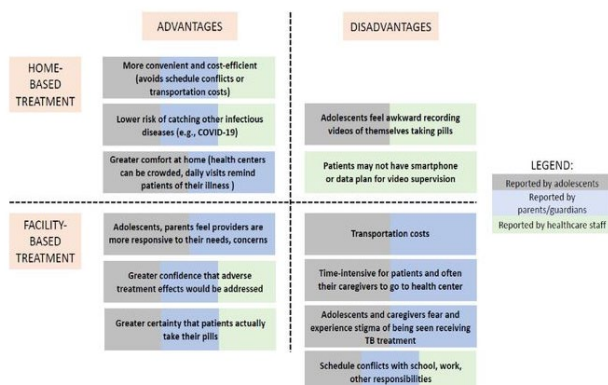
This study explored the perspectives of adolescents (10-19 years old) who completed tuberculosis treatment, their caregivers, and health providers regarding facility-based vs. home-based treatment.

**Design/Methods:** Between August-October 2022, we conducted 16 focus groups (7 of adolescents, 6 of caregivers, and 3 of health staff) using semi-structured guides. Two investigators independently developed codes, applied codes to the transcripts, and identified emerging themes. After each step, they compared results and resolved disagreements through discussion.

**Results:** Health providers explained that they allowed home-based treatment only if they perceived the patient and family to be responsible and committed to treatment completion, and if adverse treatment events were mild and infrequent. They reported that home-based treatment was reliable and effective for these selected adolescents. This was confirmed by adolescents and caregivers, all but one of whom reported good adherence with home-based treatment.

Participants explained that, unlike facility-based treatment, home-based treatment did not interfere with daily activities (e.g., studying, working, etc.) and reduced the risk of other infections, TB-related stigma (from being seen receiving TB treatment), and transportation costs. However, some adolescents lacked access to a cell phone, meaning that supervision had to be by family

member only. Because some patients did not send videos of themselves taking their medications or answer video calls at the scheduled time, health staff had to spend a lot of time following up until they received a response (see Figure).



**Conclusions:** Home-based tuberculosis treatment is feasible and reliable in selected adolescents. Home-based treatment should be strongly considered to help adolescents maintain daily routines, including schooling and work.

### OA11-288-15 99DOTS, a digital monitoring system for TB treatment adherence: experience from Bangladesh

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**Background:** The Directly Observed Treatment, Short course (DOTS) is effective for TB treatment but has significant drawbacks when applied in resource-constrained settings. It is expensive and highly burdensome on patients, providers, and health systems. New strategies that are more cost-effective, patient-friendly, and less burdensome for health system are needed for monitoring TB medicine intake. 99DOTS, a low-cost digital adherence technology (DAT), can be a potential approach.

**Design/Methods:** We implemented 99DOTS in March 2022 at 270 DOTS centers throughout four divisions of Bangladesh. TB-diagnosed individuals were counseled and enrolled upon receiving consent by service-providers. They were provided with two weeks' worth of TB medication, inserted in envelopes, revealing charge-free numbers. After taking medication, patients call the numbers, yielding high confidence that dose

has been taken. Service providers were trained on participant enrollment, monitoring the dashboard, and counseling. They monitor dashboard and follow-up any participant shown as missing doses for two successive days via phone. Moreover, participants not calling the charge-free numbers are reminded by text messages to take medicine.

**Results:** A total of 3447 participants were enrolled from April to June, 2022. Treatment outcome is available for 3068 participants. Among them 1706 were cured and 1294 were stated as treatment complete yielding 97% treatment success rate. Automated medication reminder SMS was reported to be helpful in taking medication dose on time. Service providers identified participants with poor adherence and counseled them to complete treatment according to the schedule.

**Conclusions:** 99DOTS initiative reportedly reduced patients' burden by reducing travel costs and time. It eased the monitoring process for service-providers and allowed them to have a real-time transparent view of the adherence of registered patients and response to irregularities.

Further research is required to understand the acceptance of 99DOTS among participants and service-providers, and its impact on improving health system efficiency.

## SHORT ORAL ABSTRACT SESSION (OA)

### SOA01 Treatment and treatment outcomes of DR - TB

#### SOA01-800-15 Global treatment outcomes of extensively drug-resistant TB in adults: A systematic review and meta-analysis

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**Background:** Extensively drug-resistant tuberculosis (XDR-TB) is notoriously difficult to treat and is associated with poor treatment outcomes. In this study, we investigated the proportion of individuals with XDR-TB who achieved a successful treatment outcome globally.

**Design/Methods:** We searched PubMed/MEDLINE, Scopus, Web of Science, and Embase (January 2005 to June 2022). Eligible studies reported treatment outcomes of pre-XDR- and/or XDR-TB patients according to the definitions provided by the World Health Organization, or adaptations hereof. Pooled proportions of treatment outcomes were calculated using a random-effects model. Subsequently, a series of sensitivity and subgroup analyses were performed.

**Results:** Among 4 692 studies screened, we included 86 studies from 26 different countries that reported treatment outcomes for 8 623 individuals with XDR-TB. The overall pooled proportion of successful outcomes was 43.7% (95%CI: 37.4-50.3). All sensitivity analyses yielded similar estimates. Subgroup analyses showed a

significantly lower proportion of successful outcomes in studies with more diabetics compared to studies with less (21.0% [95%CI: 14.2-29.8] vs. 35.9% [95%CI: 23.2-51.0],  $p = 0.029$ ), and in studies with more tobacco users compared to studies with less (19.2% [95%CI: 12.1-29.2] vs. 36.3% [95%CI: 22.8-52.5],  $p=0.009$ ). There was also a significant difference across subgroups based on five-year intervals of the first year of inclusion, with a tendency towards improved outcomes after 2013 ( $p<0.000$ ).

**Conclusions:** We found a success rate of 43.7% among individuals treated for XDR-TB globally, comparable to an estimate from 2010, and still discouragingly far away from the WHO's goal of a 75% success rate. This indicates that the implementation of novel drugs and treatment regimes has not yet impacted the published literature. However, reassuringly there seems to be a tendency towards better outcomes in more recent studies.

#### SOA01-801-15 All-oral multidrug-resistant TB regimens during COVID: Programme outcomes from an Ethiopian NGO-NTP partnership, 2017-2021

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**Background:** The Global Health Committee(GHC) has provided comprehensive MDR/RR-TB treatment and care at 3 sites in Ethiopia through a partnership with the National TB Program beginning in 2009. The COVID-19 pandemic arising in 2020 introduced substantial barriers to access to diagnosis and treatment of MDR/RR-TB, coinciding with increased availability of all-oral treatment regimens. We evaluated outcomes of the GHC-NTP collaborative program immediately before and after 2020.

**Design/Methods:** Cohort study with two cohorts: persons initiating MDR/RR-TB treatment pre-COVID (2017-2019) and post-COVID (2020-2021). Logistic regression compared successful treatment outcomes (cured or completed) by time period, adjusting for HIV status, age, and gender.

**Results:** GHC initiated 570 persons on MDR/RR-TB treatment (383 (68%) injectable (INJ)-containing regimens) between 2017-2019 and 159 (3 (2%) INJ) between 2020-2021. All GHC/NTP program participants re-

ceived travel and nutritional support, side effect management and community outreach worker support. Population characteristics were similar in both pre- and post-COVID cohorts (median age 30, IQR 23-39; 59% male, median BMI 17.5 (missing for N=175/792), IQR 15.6-19.5; 8% extrapulmonary TB), except pre-COVID, a higher proportion of persons initiating treatment had HIV (28% vs. 17% post-COVID,  $p=0.007$ ). The proportion of favorable treatment outcomes was similar in pre- and post-COVID periods (403 (71%) vs. 121 (76%),  $p=0.18$ ). Across both time periods, all-oral regimens were associated with a favorable treatment outcome compared to INJ (OR 1.47, 95% CI 1.06-2.05).

Odds of treatment success pre-COVID were similar to post-Covid, adjusting for age, gender, and HIV status (aOR 0.76, 95% CI 0.50-1.15). People with HIV had decreased odds of treatment success (aOR 0.59, 95% CI 0.41-0.84).

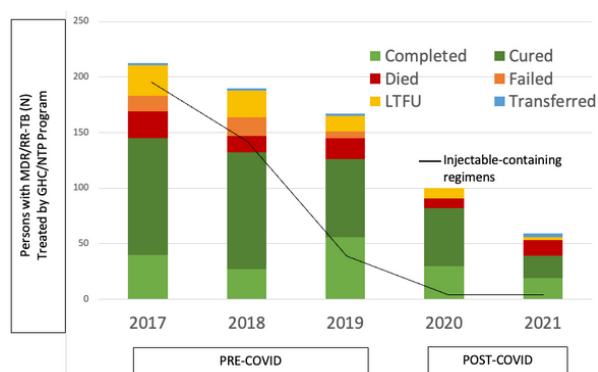


Figure. MDR/RR-TB treatment outcomes by year.

**Conclusions:** High rates of MDR-TB treatment success were maintained with a near-complete transition to all-oral regimens during the COVID-19 pandemic. Although fewer people initiated treatment for MDR/RR-TB in the post-2020 period, potentially reflecting challenges accessing MDR-TB diagnosis, equally high successful outcomes were achieved as pre-pandemic in this NGO/NTP collaboration.

## SOA01-802-15 Effectiveness of a 9-month all-oral regimen for multidrug/rifampicin-resistant TB in Lesotho, a high HIV burden setting

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**Background:** Since 2019, World Health Organization has called for operational research on shortened all-oral regimens for multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB). We report treatment outcomes of the first 100 patients who received a nine-month all-oral regimen containing bedaquiline (BDQ), linezolid (LZD), levofloxacin (LFX), delamanid (DLM), and clofazamine (CFZ) in Lesotho, a setting with a high prevalence of HIV-infection.

**Design/Methods:** Beginning in 2020, we conducted a prospective cohort study among patients with bacteriologic evidence of MDR/RR-TB who initiated the regimen under routine program conditions. Patients with a strain of *Mycobacterium tuberculosis* resistant to fluoroquinolones at the time of treatment initiation were withdrawn from the study and treated with a longer regimen. Treatment could be extended up to twelve months in patients with delayed treatment response.

**Results:** Of the 100 patients, 76% were men, median age was 41 years (interquartile range [IQR]: 34-58), 39% had a body mass index less than 18.5, and 62% were living with HIV (median CD4 cell count: 275; IQR: 77 to 607). The frequency of treatment success was 82% (95% confidence interval [CI]: 73 to 89). Of those who did not have documented treatment success, nine died, three were failed by treatment, one was lost to follow-up, two were withdrawn, and three were not evaluated.

**Conclusions:** The frequency of treatment success with an all-oral nine-month regimen compared favorably with that observed among patients who were treated with longer regimens primarily composed of new and repurposed drugs in Lesotho between 2015 and 2018. High rates of success at the end of treatment underscore the urgent need to scale-up shortened regimens containing new and repurposed drugs, including among patients living with HIV.



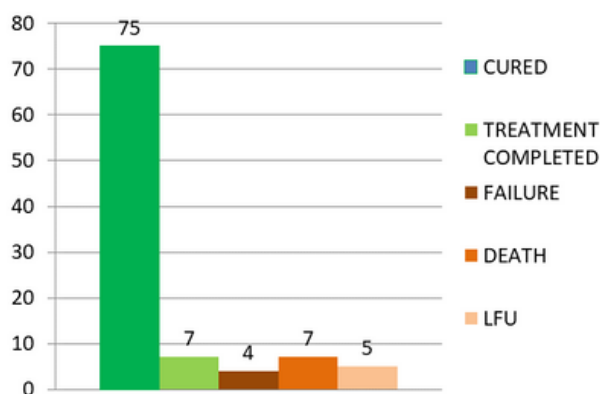
### SOA01-803-15 Outcome of isoniazid-mono-resistant TB with a new regimen under programmatic management of drug-resistant TB in India

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**Background:** Isoniazid (INH) is a very important first line drug in designing anti-Tuberculosis (TB) treatment. National drug resistance survey from India has reported INH mono-resistance in 11.96 % of new cases and 22.54 of retreatment cases. We aimed to study treatment outcomes of INH mono resistant TB under programmatic conditions in India.

**Design/Methods:** A retrospective record-based study from 1 January 2018 to 30 December 2021. People with INH mono-resistant TB who received daily treatment regime of six months of INH, rifampicin, pyrazinamide and levofloxacin (6RZE Lfx) under programmatic management of drug resistant TB in India, were included in the study.

**Results:** Treatment outcomes of 98 patients were declared out of which 56 were males and 42 were females. 82(83.6%) had favourable outcome and 16 (16.4 %) had unfavourable outcome. 71.8% of patients aged <50 years, and 83.33 % of patients aged >50 years had favourable treatment outcomes respectively. 100 % of EPTB patients had favourable outcome and 80.6 % of pulmonary TB patients had a favourable outcome. Males had a relatively more proportion of unfavourable outcomes (14/42 (33.33%)) as compared to females (2/40 (5%)) (p<0.005).



82(83.6 %) Favourable ,  
16( 16.4%) Unfavourable outcome

Figure 1: Treatment outcomes of INH mono resistant TB in India under programmatic conditions.

Outcome was favourable in 80% patients with InhA resistance and 94% had favourable outcome with KatG resistance (p<0.05). Age, Type of TB (pulmonary/extrapulmonary), or HIV status did not significantly affect the treatment outcomes.

**Conclusions:** 6 RZE Lfx is an effective regimen with 83.6% cure rate in cases of INH mono-resistance even in field conditions and when overall resistance is ruled out by 2<sup>nd</sup> line LPA. It is important to rule out drug resistance atleast to INH, Rifampicin, and fluoroquinolones while determining the treatment regime. inhA mutation is associated with unfavourable treatment outcome and these patients require close monitoring.

### SOA01-804-15 TB recurrence among people treated with all-oral, short standardised regimens

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**Background:** World Health Organization (WHO) recommends the use of all-oral short, standardized regimens for the treatment of rifampicin-resistant tuberculosis (RR-TB), with a duration from six to nine months. The frequency of recurrence depends on regimen composition and treatment duration. The evidence for the new recommendations comes from clinical trials and programmatic data. We aimed to synthesize evidence on the frequency of tuberculosis disease recurrence among people treated with short oral regimens for RR-TB.

**Design/Methods:** A systematic review was conducted to summarize findings related to the proportion of recurrence among people treated with all-oral short standardized regimens for RR-TB.

**Results:** We identified seven studies with a total of 1512 participants: six clinical trials (n=824) and one retrospective cohort study (n=688). Three studied bedaquiline-pretomanid-linezolid-based regimens and four studies reported outcomes of non-BPaL regimens (based on WHO guidelines 2018-2020). In all studies, participants were followed up after treatment, with a post-treatment follow-up duration of between six and 30 months. Six studies reported recurrence of TB disease in 0.2-5.3% of their participants and only one study did not report recurrence in any of their participants.

**Conclusions:** Short all-oral regimens are effective and result in improved treatment outcomes. The proportion of people experiencing a recurrence of TB disease post-treatment is low however, the duration of post-treatment follow-up time in included studies was short. Longer-term evidence from the programmatic experience is necessary to define if currently recommended short regimens for RR-TB are associated with an increased risk of TB disease recurrence.

## SOA01-805-15 BPAL regimen modifications under operational research conditions in the Philippines

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**Background:** In 2020, WHO recommended 6 months of standardized regimen consisting of bedaquiline, pretomanid and linezolid (BPAL<sub>1200 mg/day</sub>) under operational research (OR) for eligible rifampicin-resistant TB patients. In 2021, the BPAL OR protocol and Clinical Guide were developed under LIFT-TB.

In case of toxicity, modifications are allowed including:  
 a. BPAL regimen interruption during the first 4 weeks of treatment for  $\leq 14$  days, and  $\leq 35$  days thereafter, with missed doses made up at end of treatment;  
 b. Linezolid modification through dose reduction, interruption or discontinuation after 4 weeks of Linezolid 1200 mg/day, or after 9 weeks of 600 mg/day.

**Design/Methods:** This abstract describes the occurrence of protocol modifications on the BPAL(1200 mg/d) regimen under OR in the Philippines from June 2021-December 2022. Data were obtained from REDCap and OR databases.

**Results:** Among 58 patients who finished 6 months of treatment, BPAL interruption occurred in 8 (14%) patients due to peripheral neuropathy (3), myelosuppression (2), QT prolongation (1), hepatotoxicity (1) and surgery of unrelated cause (1).

Interruption duration was 2-22 days at various treatment stages. Majority of AEs were resolved with no re-appearance upon re-introduction of the BPAL regimen. Among the 58 patients, Linezolid modifications occurred in 22 (38%) patients in 30 episodes: temporary interruption occurred in 21 (70%), dose reduction in 7 (23%), permanent discontinuation in 2 (7%) with AEs partially or completely resolved.

AEs included peripheral neuropathy in 13, myelosuppression in 11, optic neuritis in 1, and undocumented in 1. Treatment success remained exceptionally high at 97% despite the modifications.

**Conclusions:** WHO guidelines allow reasonable modifications to the 6-month BPAL-based regimens to ensure drug safety with no compromise to efficacy. Strengthen-

ing active drug safety monitoring and management is crucial in the introduction of the new regimens to detect and strategically manage adverse events in a timely manner.

## SOA01-806-15 A patient-centred approach to reducing pre-treatment loss to follow-up in drug-resistant TB care in Nigeria

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**Background and challenges to implementation:** Nigeria barely notifies 14% of the estimated 21,000 MDR-TB cases, yet reported a 26% pre-treatment loss to follow-up (PTLTFU) in 2021. Oyo and Akwa-Ibom States respectively ranked 3<sup>rd</sup> and 9<sup>th</sup> in DR-TB case notification with a combined PTLTFU of 44% in the same year.

Key drivers include delay in communicating diagnosis, poor documentation impeding patient tracking, poor counseling, centralized baseline investigations and treatment initiation.

Through the TB REACH wave 9 grant (Q2 2022-Q2 2023), RedAid Nigeria, implemented targeted interventions to reduce PTLTFU in these two states.

Similar states (Delta and Edo) served as control populations (CP).

**Intervention or response:** Multiple interventions along the patient-care pathway were deployed, viz:

1. Modified specimen examination form to capture extra patient's contact details and training/retraining of frontline health workers on complete documentation;
2. Single WhatsApp group for all state-wide DR-TB activities including instant notification of new cases by the GeneXpert lab personnel;
3. Introduced and trained healthcare workers on structured pre-treatment counselling with a checklist, health education video and a DR-TB survivor's lived-experience sharing;
4. Decentralized baseline investigations by engaging new pre-qualified laboratories;
5. Decentralized treatment initiation by training clusters of clinicians and local government TB Supervisors; and;
6. Engaged an ad-hoc staff to coordinate decentralization of all DR-TB diagnosis-enrollment activities.

Project interventions were conducted under routine programmatic conditions, and routine surveillance data over 3 quarters of implementation analyzed to measure outcomes.

**Results/Impact:** After three quarters (Q2-Q4, 2022) of implementation, PTLTFU decreased from 59% to 34% ( $z=6.3014$ ,  $p<0.001$ ) compared with the same preceding period (Q2-Q4, 2021). Conversely, the PTLTFU increased from 31% to 46% ( $z=-2.4398$ ,  $p=0.01468$ ) in the same period in CP.

There is significant relationship between enrolment status and intervention ( $X^2=5.63$ ,  $p=0.018$ ), with evaluation population more likely to have patients commenced on DR-TB treatment.

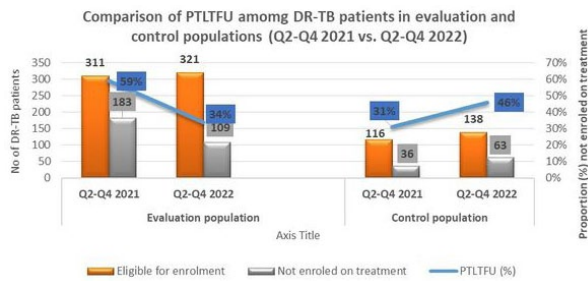


Figure. Comparison of PTLTFU among DR-TB patients in evaluation and control population (Q2-Q4 2021 vs. Q2-Q4 2022).

**Conclusions:** A multi-pronged patient-centered approach using targeted interventions is expedient to reduce diagnosis-enrollment gap in DR-TB care.

### SOA01-807-15 Impact of isoniazid mono-resistance on 2-month sputum culture conversion and survival in pulmonary TB patients: A 10-year, nationwide cohort study, Taiwan

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**Background:** Isoniazid is an early bactericidal anti-tuberculosis (TB) agent and isoniazid mono-resistance TB is the most prevalent drug resistant TB worldwide. Concerns exist regarding whether resistance to isoniazid would lead to delayed culture conversion and worse outcome.

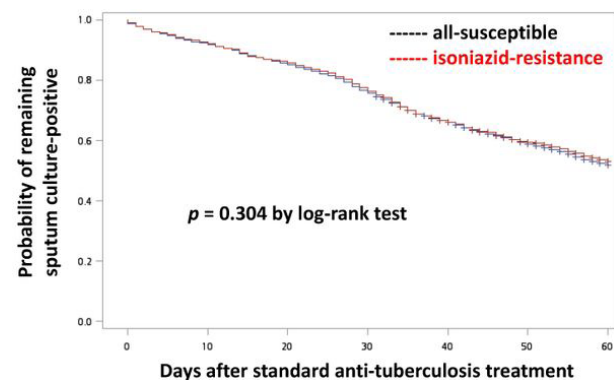
**Design/Methods:** From January 2008 to November 2017, adult culture-positive pulmonary TB patients were identified through Taiwan Center for Disease Control database. Their clinical characteristics and follow-up information until end of 2017 were also retrieved from Taiwan National Health Insurance Research Database. Primary outcome was time to culture conversion within two months. Secondary outcome included death within two months and unfavorable outcome at 2nd month.

**Results:** A total of 39742 pulmonary TB patients including 36931 drug-susceptible pulmonary TB and 2811 isoniazid-resistant TB were identified. Compared with all susceptible TB, isoniazid mono-resistance was

not associated with longer time to culture conversion within two months (HR:0.99, 95% CI: 0.93-1.04, 95% CI:0.6050), higher risk of mortality within two months (HR:1.13, 95% CI: 0.87-1.47,  $p=0.3701$ ) and unfavorable outcome at 2nd month (OR:1.03, 95% CI: 0.95-1.12,  $p=0.4285$ ).

In subgroup analysis, patients aged between 20 and 65 were less likely to achieve culture conversion (HR:0.9, 95% CI:0.84-0.98,  $p=0.0136$ ), and had higher risk for unfavorable outcome (OR:1.17, 95% CI:1.05-1.32,  $p=0.0065$ ).

Also, participants with no underlying comorbidities required longer time to achieve culture conversion (HR:0.89, 95% CI:0.81-0.98,  $p=0.0205$ ).



**Conclusions:** Our study revealed that isoniazid mono-resistant TB had comparable outcome with drug-susceptible TB at end of intensive phase. Healthy and non-elderly patients, however, were more likely to had culture persistence, which may raise the concern of disease transmission in this subgroup of patients.

## SOA02 Pediatric TB: From determinants to outcomes

### SOA02-809-15 Determinants of TB disease development in children in central Ethiopia: A matched case-control study

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**Background:** The risk factors that determine the progression of latent tuberculosis infection to tuberculosis (TB) disease such as Bacillus Calmette Guerin (BCG) vaccination and smoking are the subject of heated debate.

The objective of this study was to identify determinants of TB disease development in general and in relation to the effect of BCG vaccination over time in children in central Ethiopia.

**Design/Methods:** The characteristics of children who developed TB (cases) and those who did not (controls) were compared using a 1:1 age matched case-control design. The information was gathered between February 8, 2022 and June 24, 2022 in healthcare facilities in Addis Ababa city, Adama, and Bishoftu towns. We studied 256 matched case-control pairs in total. A bivariate conditional logistic regression analysis was performed first to select variables with p-values less than or equal to 0.20 for the multivariable model.

Finally, variables with a p-value less than 0.05 for matched adjusted odds ratio (mORadj) were reported as significant determinants of TB disease development.

**Results:** Being unvaccinated for BCG at birth or within two weeks following birth was found to be more than twice as common (mORadj = 2.11, 95% CI = 1.28-3.48) among TB patients as it was in children who had never had TB.

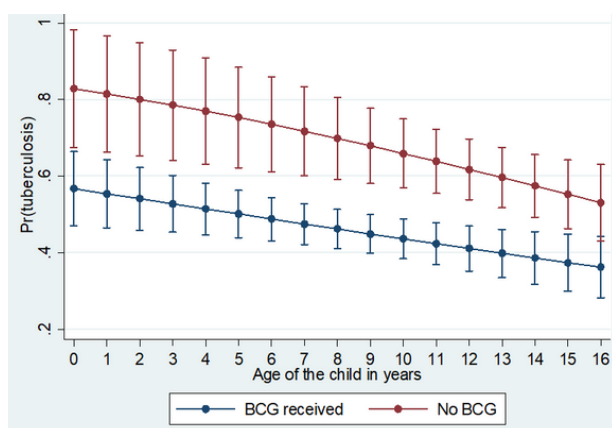


Figure. Predictive margins of BCG with 95% CIs.

Children who ever lived with a TB-sick family member (mORadj = 4.28, 95% CI = 1.95–9.39), smoking family members (mORadj = 3.15, 95% CI = 1.07–9.27), and HIV-infected children (mORadj = 8.71, 95% CI = 1.96–38.66) were more likely to develop TB disease. BCG vaccination was found to be protective of TB disease development to the age of 15 years.

**Conclusions:** Being BCG-unvaccinated, having TB patient contact in the household, having a smoker in the household, and having HIV infection were found to be determinants of TB disease development in children.

### SOA02-811-15 Closing the TB case detection gap among children: Early lessons from a paediatric TB intervention in India

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**Background and challenges to implementation:** Significant gap of ~50% exists between estimated pediatric tuberculosis (TB) incidence and case notifications in India. Contributors to this include lack of trained healthcare providers (HCP) to collect samples for TB detection, and sub-optimal linkage between health care facilities (HCF). To address these challenges, FIND, in collaboration with the National TB programme (NTEP), India implemented an intervention focused on children. The USAID-Tuberculosis Implementation Framework Agreement (TIFA) project funded the intervention.

**Intervention or response:** The intervention was rolled-out in four states of India covering a population of ~12million focusing on peri-urban, rural, and aboriginal geographies. Key activities included training of HCPs on non-sputum sample collection techniques, identification of tertiary HCFs that could act as mentoring institutes and linking peripheral HCFs (public and private sector) to higher centres through a hub and spoke model to decentralize sample collection. Screening camps were conducted to enhance TB case detection. Linkages were established between collection and diagnostic sites within the districts, and sample transportation was facilitated by NTEP/existing mechanisms/volunteers. Data from the first quarter of sample collection (December'22-February'23) were analysed.

**Results/Impact:** Approximately 340 HCPs were trained on non-sputum sample collection techniques (e.g., gastric lavage/aspirate(GA), induced sputum(IS), and fine needle aspiration(FNA)) through theoretical and live demonstration sessions. Linkages were established between 168 HCFs (23 hubs, 141 spokes, 4 mentoring institutes). Till February'23, 660 non-sputum samples (Figure

1) were collected from presumptive children ( $\leq 18$  years, median age=8 years, IQR:4,12), 48% females) through 42 sample collection facilities (52% private-sector) operational under the intervention and one screening camp. Among these, 12% of samples were diagnosed positive for TB (53% females, median age=14years, IQR:10,16).

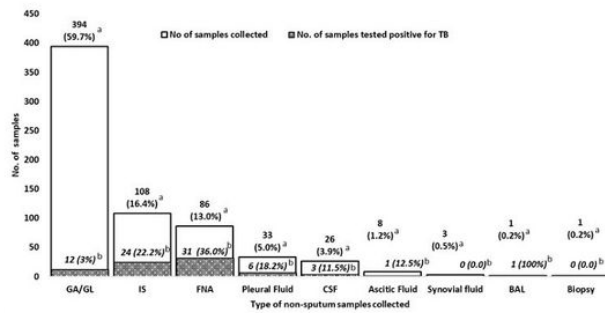


Figure 1. Distribution of non-sputum samples collected and TB positive cases diagnosed: Dec '22 - Feb '23, Pediatric TIFA project, FIND.

GA/GL: Gastric aspirate/lavage, IS: Induced sputum; FNA: Fine needle aspirate, CSF: Cerebrospinal fluid, BAL: Bronchioalveolar lavage

<sup>a</sup>Percentage shown for 'No. of samples collected' is the percentage of a particular sample-type among all samples collected (denominator: N = 660).

<sup>b</sup>Percentage (in italics) shown for No. of samples tested positive for TB is the proportion of a particular type of sample identified positive for TB.

**Conclusions:** Preliminary data demonstrate the feasibility of improving pediatric TB sample collection and diagnosis significantly through mechanisms established under the project. Scale-up of the intervention may contribute substantially to decreasing the TB detection gap among this 'special group'.

## SOA02-812-15 Impact of practical demonstration of stool sample Xpert test on childhood TB case detection In Oyo State, Nigeria

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**Background and challenges to implementation:** According to the World Health Organization, there were 194,000 child TB deaths and 1 million pediatric tuberculosis infections in 2017. Children typically are unable to expectorate and produce a sample of sputum. The stool collection method was adopted since obtaining a specimen requires invasive procedures like sputum induction, gastric induction, or gastric aspiration. Nevertheless, not every facility in TB-endemic areas has the tools and employees trained to carry out these treatments. This paper, therefore, presents the impact of practical demonstration of stool sample Xpert test on childhood TB case detection in Oyo State, Nigeria.

**Intervention or response:** This intervention was conducted among laboratory employees in ten Genexpert sites in seven Local Government Areas of Oyo State, Nigeria. The participants were provided with continuous stool sample testing training using Genexpert in 2020 and 2021.

Supportive supervision was also provided, and the linkage coordinators were asked to prioritize immediate stool sample movement to the laboratories to maintain the samples' efficacy. In 2022, the trained personnel were asked to practically demonstrate what they have learned in the previous years without any supervision to evaluate the efficacy of the intervention and retainers of knowledge.

**Results/Impact:** During the 3 years implementing period (2020-2022), 807,188 children were eligible for the stool sample Xpert test, of which 85.6% (690,885) were screened. 2.08% (14,389) of the children screened were presumptive, and 99.1% (14,254) of the presumptive were evaluated. Of the presumptive evaluated, 5.7% (809) were diagnosed with childhood TB.

**Conclusions:** Practical demonstration, training, and supportive supervision of laboratory personnel are effective and contribute to childhood TB case detection

in the state. Therefore, this intervention recommends scaling up to the remaining 26 local governments in Oyo State, Nigeria.

### SOA02-813-15 Testing stool specimens using Xpert MTB/RIF Ultra: A gamechanger in TB detection among children

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**Background and challenges to implementation:** Child tuberculosis (Ch-TB) is under-diagnosed in Bangladesh (3% vs estimated 8%). Major reasons for misdiagnosis are specimen collection difficulties and negative test result for paucibacillary nature of disease. World Health Organization recommended stool testing by Xpert MTB/RIF Ultra (Ultra) assay to minimize diagnostic gap of child pulmonary TB (Ch-PTB).

Here we evaluated usefulness of stool testing by Ultra for Ch-PTB diagnosis in programmatic approach.

**Intervention or response:** USAID's Alliance for Combating TB in Bangladesh (ACTB) Activity is supporting the National Tuberculosis Control Programme (NTP) to identify missing Ch-TB through Intensified Case Finding approach. To increase Ch-PTB diagnosis, stool-based diagnostic approach was introduced in June 2021 and expanded to 41 healthcare facilities throughout Bangladesh. Physicians advised stool test by Ultra for presumptive Ch-PTB (<15 years of age) as part of routine TB diagnostics.

Collected stool specimens were transported and tested at divisional level testing facilities. TB diagnosis were made by physicians and treatment was provided as per national guideline.

**Results/Impact:** Between January and December 2022, stool from 7485 Ch-PTB presumptive were tested by Ultra with mean ( $\pm$ SD) age 5.3 ( $\pm$ 3.7) years. Among tested, 343 (4.6%) were positive for *Mycobacterium tuberculosis*, of which 256 (74.6%) showed 'trace detected' result. Positivity rate was 4.5% (162/3602) in <5 years, 3.9% (105/2660) in 5-9 years and 6.2% (76/1223) in  $\geq$ 10-year-old children.

In contrast, we found Xpert positivity rate 5.6% on induced sputum among children. Majority (297/343, 86.6%) with *Mycobacterium tuberculosis* positive on stool were diagnosed with TB and put on anti-TB treatment.

**Conclusions:** Findings demonstrated that stool testing by Ultra is helpful for Ch-PTB diagnosis. Stool can be an alternative specimen, especially for younger children,

who cannot expectorate sputum. NTP should ensure sufficient logistics and proper staff training at all level of healthcare facilities to improve Ch-PTB detection, especially under-5, to reduce childhood illness and death.

### SOA02-814-15 Evaluation of teachers' training on TB to increase case detection among school children in Nigeria

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**Background and challenges to implementation:** In Nigeria, Tuberculosis (TB) among children frequently goes undetected and untreated. Current childhood TB notification is 7% of the total TB case notification in Nigeria. As part of innovations to commemorate the 2023 World TB Day, the USAID-funded Breakthrough ACTION Nigeria (BA-N) project introduced training of school teachers on TB to increase awareness of childhood TB and strengthen referral for TB tests amongst children.

This study aims to assess the immediate effectiveness of training teachers on TB in the Federal Capital Territory, Abuja.

**Intervention or response:** BA-N conducted a pre- and immediate post-evaluation study among 44 teachers from 29 schools in the six area councils of Abuja, Nigeria. The teachers received a one-day training on TB. Topics included childhood TB, signs and symptoms, transmission, prevention, stigma, contact tracing, and its impacts on student education. The evaluation assessed the teachers' knowledge, attitude and risk perception including identification of TB signs and symptoms before and after the training using a questionnaire.

**Results/Impact:** The training significantly improved the teachers' knowledge, attitude, and risk perception on TB from  $5.5 \pm 2.6$  at pre-evaluation to  $10.2 \pm 2.6$  at post evaluation ( $P < 0.001$ ).

Overall, there was a 31% increase in the teachers' knowledge post-training evaluation, demonstrating that the program had a beneficial effect on their knowledge and abilities to recognize TB signs and symptoms among school children.

**Conclusions:** Training teachers on signs and symptoms of TB among children in Nigeria is feasible and effective in improving their knowledge, perception, attitude, and practice. Teachers can be helpful partners in TB case detection and referral among children in environments with inadequate resources, especially schools in known TB hotspots.

## SOA02-815-15 Comparison of treatment-decision algorithms for children evaluated for TB in Bangladesh

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**Background:** Treatment-decision algorithms to prompt rapid TB treatment initiation in children accompanied the latest WHO guidelines. Due to numerous included characteristics not being routinely collected, we developed a different algorithm using only programmatic data from children evaluated for TB in Pakistan (previously reported).

We aim to assess its utility in an external population in Bangladesh.

**Design/Methods:** Using data from an active patient-finding program implemented in the Mymensingh Division of Bangladesh, we attempted five applications of the Pakistan-model, which aims to predict children diagnosed with TB—either bacteriologically-confirmed or clinically diagnosed.

First, we apply it to the Bangladesh cohort using the same identified variables, risk scores, and optimal cutoff threshold.

Second, using the same variables and risk scores, we identify a data-specific cutoff value using Youden's *J*.

Third, using the same variables, we re-calculate risk scores and cutoff value.

Fourth, we derive a completely new risk-score model; fifth, we hold sensitivity at 85%.

We calculate sensitivity, specificity, positive and negative predictive values (PPV, NPV) for each.

**Results:** In Bangladesh, 8,084 children with presumed TB were further evaluated for disease; 1,783 (22.1%) were diagnosed. PPVs were low (range: 26.3-31.8%); NPVs were high (range: 87.9-91.3%). The newly derived Bangladesh-model had a sensitivity of 77.0% (95%CI: 74.9-78.9) and specificity of 47.4% (95%CI: 46.2-48.7), and included the following: age group, contact with an individual with TB, weight  $\leq 5^{\text{th}}$  percentile, cough duration, fever, night sweats, weight loss, poor appetite, family history of TB, and chest radiograph suggestive of TB. When sensitivity was held at 86.2%, specificity was 35.3% (95%CI: 34.1-36.5). See Table 1.

Model	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Pakistan-model applied to Pakistan cohort (original, for reference only)	98.2% (97.3-98.8)	89.2% (88.1-90.1)	76.9% (75.2-78.5)	99.3% (98.9-99.5)
(1) Pakistan-model: same variables, same risk scores, same cutoff score of 9	90.5% (89.0-91.8)	28.2% (27.1-29.3)	26.3% (25.8-26.7)	91.3% (90.0-92.4)
(2) Pakistan-model: same variables, same risk scores, new cutoff score of 14	79.0% (77.1-80.9)	51.1% (49.9-52.3)	31.4% (30.6-32.1)	89.6% (88.7-90.4)
(3) Pakistan-model: same variables, new risk scores, new cutoff score of 11	77.0% (75.0-78.9)	53.3% (52.1-54.5)	31.8% (31.0-32.6)	89.1% (88.2-89.9)
(4) Bangladesh-model: new variables, new risk scores, new cutoff score of 6	77.0% (74.9-78.9)	47.4% (46.2-48.7)	29.3% (28.6-30.0)	87.9% (86.9-88.8)
(5) Bangladesh-model: same as previous, but sensitivity held ~85% using cutoff score of 3	86.2% (84.5-87.8)	35.3% (34.1-36.5)	27.4% (26.9-27.9)	90.0% (88.9-91.1)

Table 1. Discriminatory Properties for Each Model.

**Conclusions:** Different predictive models including similar but varying characteristics and cutoff thresholds provided large variability in associated discriminatory properties.

External clinical algorithms should be used with caution; attempts to understand the context-specific application of such algorithms prior to implementing them can help guide clinical care.

## SOA02-816-15 Finding the missing paediatric TB cases via partnerships with the Indian Academy of Paediatrics in India

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**Background and challenges to implementation:** TB causes significant morbidity and a large number of deaths in children. A considerable number of TB cases are missing in the community; in 2022, only 135,921, approximately 38% of paediatric TB patients (0-14-year age) of estimated 3,56,000 paediatric TB cases (12% of total estimated TB cases) were notified in India.

**Intervention or response:** Annually, almost 50% of paediatric TB cases are missed being notified in India. A significant proportion of parents seek healthcare for their children in the private sector. To address the diagnostics and treatment barriers to Paediatric TB notification, The National TB Elimination Programme (NTEP) signed a Memorandum of Understanding (MoU) in partnership with the Indian Academy of Paediatrics (IAP).

The MoU aims to build capacity among the NTEP Medical Officers and the paediatricians, in both the public and private sectors, for the diagnosis, notifica-

tion, treatment and provision of public health actions for the management of paediatric TB.

**Results/Impact:** Through the partnership, the IAP has to train 18,000 paediatricians and 2,000 NTEP Medical Officers on the latest programmatic and clinical management in paediatric TB through 300 district-level Continued Medical Education (CME) workshops.

Despite the disruptions caused by the COVID-19 pandemic, the IAP has completed 148 CMEs, including 1 National, 5 Regional, and 142 District-level workshops. The collaboration has increased TB notification by the private sector. Additionally, 6,709 paediatric TB cases have been notified till 6<sup>th</sup> March 2023 by the paediatricians trained during these CMEs.

**Conclusions:** Partnerships with medical professionals have been one of the critical components of the strategic priorities towards reaching the national target to END TB by 2025.

The partnership with IAP supported the capacity building of paediatricians in the private and public sectors and decreased missed paediatric TB cases.

## SOA03 Multimorbidity Comorbidities

### SOA03-817-15 Depression in adolescents on TB treatment in Lima, Peru

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**Background:** An estimated 1.8 million adolescents develop tuberculosis (TB) disease worldwide each year. The prevalence of depression in adult TB patients is high, but the prevalence of depression among adolescents with TB is unknown.

We analyzed data from a prospective cohort study to identify the prevalence and risk factors for depression in adolescents receiving treatment for rifampicin-susceptible tuberculosis in Lima, Peru from 2020-2022.

**Design/Methods:** Between weeks 3-5 of treatment for rifampicin-susceptible TB, 249 adolescents 10-19 years old completed a self-administered survey that included demographic questions and the following scales: PHQ-9 for depression, Adverse Childhood Experiences (ACEs), Alcohol Use Disorders (AUDIT), caregiver support, TB-related stigma, and TB knowledge.

Participants with PHQ-9 score  $\geq 10$  (indicating moderate or severe depression) were referred to study psychologists for further evaluation (using a repeat PHQ-9 and psychological interviewing) and treatment, if indicated. Using regression, we identified factors associated with PHQ-9 score.

Predictors of PHQ-9 Score	Coefficient	95% CI	p-value
Female gender	1.42	0.21, 2.64	0.02
Eats <3 meals/day at least once weekly due to poverty	1.77	0.57, 2.96	0.004
ACEs score	0.77	0.49, 1.05	<0.001
Caregiver support score	-0.22	-0.38, -0.06	0.006
TB stigma score	0.27	0.19, 0.34	<0.001
Endorses current TB symptoms	2.94	1.55, 4.32	<0.001
Frequency of adverse treatment events (per day/week)	0.92	0.63, 1.22	<0.001
Illicit drug use in past 12 months	-0.32	-2.02, 1.38	0.71
AUDIT score	0.33	0.12, 0.55	0.002

**Results:** Of 249 participants, 98 (39.4%), 62 (24.9%), and 33 (13.3%) had mild, moderate, and severe depression, respectively. Depression was associated with female gender; food insecurity; higher scores on the ACEs, TB stigma, and AUDIT scales; lower caregiver support score; current TB symptoms; and more frequent adverse treatment events.

Of the 95 participants reevaluated by psychologists, 26 (27.4%) were judged to not require any intervention because they scored  $< 5$  on a psychologist-administered PHQ-9; 50 (52.6%) received psychotherapy because they scored 5-14; 17 (17.9%) were referred for urgent psychiatric care because they scored  $\geq 15$  and/or had suicidal ideation; and 2 (4.0%) were lost to follow-up and unable to be evaluated. The most common factors implicated in depression, as identified by the psychologist, were TB illness ( $n = 25$ ) and pre-existing family difficulties ( $n = 20$ ).

**Conclusions:** The high prevalence of depression that we observed underscores the importance of screening adolescents on TB treatment for depression.



### SOA03-818-15 Burden of physical, mental, social and economic multi-morbidities in patients diagnosed with TB

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**Background:** TB is a disease of poverty and patients often face other conditions or “multi-morbidities”. Most TB care is provided in vertical programs focusing on TB cure with testing for HIV and diabetes. Untreated multi-morbidities impair return to good health and can be exacerbated by TB causing long-term illbeing. Most studies characterise individual comorbidities or biomedical multi-morbidities, so the burden of broader multi-morbidities in TB is unclear.

**Design/Methods:** All patients starting TB treatment in 32 health posts in Callao, Peru were invited for interview, height and weight measurements, and sputum collection. Patients were re-visited 6 months later to confirm their health status and TB program outcomes.

During analysis morbidities were grouped as: physical (malnutrition, chronic illnesses, pregnancy, requiring surgery, significant side effects or continued symptoms); mental (depression, alcohol or substance abuse); social (hunger, homelessness, ex-incarceration, domestic violence or immigration); and economic co-morbidities.

**Results:** Between June 2016-December 2019, 2702 patients were to be treated for TB, of whom 2415 (89%) provided data. HIV co-infection had 6.6% (95%CI=5.7-7.7%) prevalence and diabetes 7.2% (95%CI=6.2-8.2%).

However, 43% (95%CI=41-45%) reported a physical co-morbidity; the most common being continued/worsened symptoms at 6 months (21% (95%CI=19-23%), 40% of whom had completed or were completing TB treatment.

Also, 38% (95%CI=36-40%) had social co-morbidities, 27% (95%CI=25-29%) had mental co-morbidities, and 21% (95%CI=19-22%) economic co-morbidity. Only 28% (95%CI=27-30%) of patients had no co-morbidities.

Morbidities overlap (see Figure) with 39% (95%CI=37-41%) of patients having multi-morbidities, i.e. co-morbidities that fell into 2 or more groups.

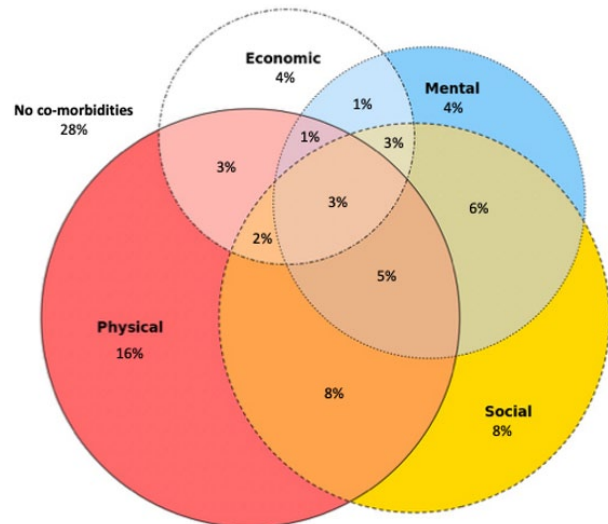


Figure. TB multi-morbidities (N=2415 patients).

Rifampicin-resistant treatment was provided to 11% (95%CI=10-13%) and was associated with 1.4-times (95%CI=1.2-1.6,  $p<0.0001$ ) higher risk of multi-morbidities with 52% (95%CI=46%-58%) patients with multi-morbidities in 2 or more groups.

**Conclusions:** Multi-morbidities with TB are extremely common. TB programs should provide patients with comprehensive care including socio-economic support aiming for symptom-free healthy survival and not just TB cure.

### SOA03-819-15 Multimorbidity in post-TB patients – a longitudinal analysis

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**Background:** TB is a major global health problem affecting millions of people every year. While TB is primarily known as a respiratory disease, it can also affect other organs. Multimorbidity, the co-occurrence of two

or more chronic conditions, is frequently observed in TB survivors. However, its progression and underlying risk factors are not yet well understood.

**Design/Methods:** The TB Sequel study recruited patients with microbiologically confirmed TB in four African countries; Tanzania, Mozambique, South Africa and Gambia. Throughout two years after treatment initiation, clinical examinations and laboratory assessments were carried out at predefined time points. A longitudinal analysis of hypertension, elevated HbA1c, obesity, malnutrition and anaemia at six and twelve months after TB diagnosis was performed. Based on a cluster analysis of the aforementioned comorbidities, multimorbidity of non-TB-associated comorbidities was modelled using a poisson regression. Covariates were integrated as predictors of multimorbidity using the stepwise AIC approach.

**Results:** 1430 subjects were included in the study. The change in proportions between month twelve and baseline  $\Delta$  was significant for all comorbidities. A decrease was seen for malnutrition ( $\Delta = 0.29$ ), anaemia ( $\Delta = 0.49$ ), and elevated HbA1c ( $\Delta = 0.09$ ) whilst an increase was seen for hypertension ( $\Delta = 0.18$ ) and obesity ( $\Delta = 0.10$ ).

The poisson regression identified sex and age to be strong predictors of morbidity. Data on the effects of further risk factors (clinical, behavioral, environmental, socio-economic) for multimorbidity after TB treatment is pending and results will be presented at the conference.

Finally, the regression indicated that the morbidity at baseline has predictive potential for morbidity at month six and twelve.

**Conclusions:** The results indicate a change in morbidity pattern at the end and after TB treatment. While possibly TB-associated malnutrition and anaemia are decreasing the proportion of other non-communicable diseases, e.g. hypertension and obesity, are increasing.

### SOA03-820-15 Association between diabetes and TB treatment outcomes: A Korean nationwide cohort study

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**Background:** Despite its significant impact on outcomes, tuberculosis (TB)-diabetes mellitus (DM) co-prevalence is yet to be fully investigated.

Therefore, we aimed to evaluate the association between DM and treatment outcomes in TB patients, with a focus on mortality.

**Design/Methods:** This retrospective nationwide cohort study included TB patients diagnosed between 2011 and 2018 in South Korea. The study population was classified into DM group and a non-DM group depending on their DM status.

**Results:** Of 239,848 patients included, 62,435 (26.0%) were included in the DM group and 177,413 (74.0%) were included in the non-DM group. Compared with non-DM group, treatment success rate was lower (76.8% vs 85.5%) and mortality was higher in DM group (14.5% vs 6.3%).

Cox proportional hazard regression analyses showed DM as an independent risk factor for TB mortality. Of the total 20,203 deaths, 11,582 (57.3%) patients died during the initial 2-month intensive phase of anti-TB treatment.

DM patients showed higher TB related death and non-TB related death ( $p < 0.001$ ) compared with non-CM group. The proportion of non-TB related death in DM group was higher than that in non-DM group ( $p = < 0.01$ ).

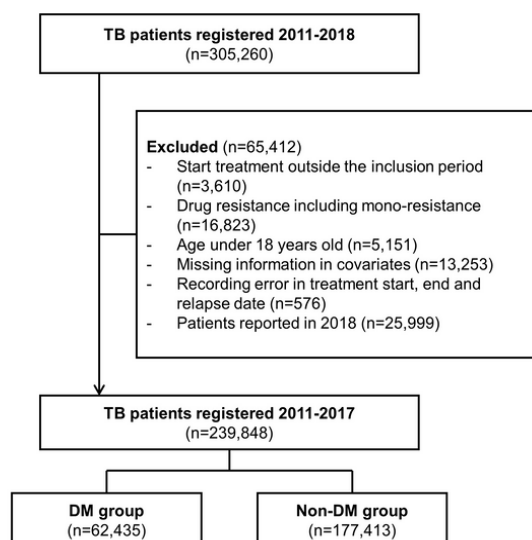


Figure 1. Flow diagram of the study population. DM: diabetes mellitus

**Conclusions:** DM is an independently associated with greater hazard of deaths among TB patients in both men and women in South Korea. More than half of deaths in DM patients occurred within the initial 2-month. DM group had higher rates of both TB and non-TB related deaths than non-DM group, but non-TB related deaths accounted for the majority.

### SOA03-821-15 Barriers to the integration of diabetes management into TB services in Eswatini

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**Background:** Tuberculosis (TB) is a major public health problem in Eswatini, a high TB/HIV burden country. Diabetes mellitus (DM) is especially prevalent among people newly diagnosed with TB and leads to suboptimal TB treatment outcomes. Exploring healthcare provider (HCP) attitudes and preferences is key when designing interventions that integrate TB/DM management.

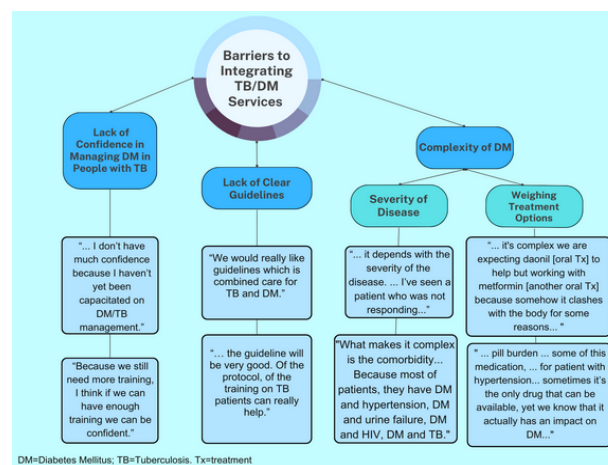
**Design/Methods:** The DETECT (Diabetes Evaluation in people with TB in Eswatini for improving TB/HIV Care and Treatment) study uses mixed-methods to assess the prevalence of DM and preDM among adults with TB and explores HCP attitudes and preferences to tailor interventions that integrate TB/DM management.

We conducted in-depth interviews (IDIs) with 20 HCPs who provide TB or DM services in 10 Ministry of Health (MoH) facilities in Manzini, Eswatini. IDIs explored barriers to TB/DM integration as well as the suitability of lifestyle management intervention strategies to facilitate TB treatment success and glycemic control.

**Results:** HCPs identified multiple barriers to integration of TB/DM services, including lack of confidence in managing TB and DM, lack of clear TB/DM guidelines, and complexity of DM management (Figure).

Some HCPs felt reported feeling ill-prepared to manage DM in people with TB. HCPs noted the lack of clear guidelines on how to co-manage the two conditions. Regarding DM management complexity, HCP mentioned concerns over different DM treatment options and how they relate to TB treatment, DM severity, and incorporating lifestyle modification interventions into DM treatment.

Suggested strategies for better service integration included capacitating HCPs to improve their counselling skills, bundling TB/DM monitoring, working with people with TB to find solutions, providing support tools, and giving transport reimbursement or increasing home/community visits to improve visit accessibility.



**Conclusions:** A multicomponent, culturally-tailored intervention strategy to support HCP who provide integrated TB/DM services in Eswatini is needed.

### SOA03-822-15 Changes in body mass index and its association with rifampicin-resistant TB treatment outcomes among STREAM Stage 1 participants

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**Background:** An active infection from pulmonary Tuberculosis (TB) is associated with weight loss and weight gain is considered an indicator of response to TB treatment. Body mass index (BMI) is a simple measure used to indicate overall nutritional status.

**Design/Methods:** This project explores BMI changes in 236 patients enrolled onto the short-regimen of STREAM Stage 1, a phase III, randomised, non-inferiority trial in participants with RR-TB. Latent Class methods, primarily Growth Mixture Models, are used to identify individuals that share a similar trajectory in how their BMI changes over the first 16 weeks of treatment. The resulting trajectories are characterized and important variables, such as key baseline characteristics, assessed for association with latent class membership. The association between class membership and TB-specific *Failure or Relapse* (FoR) outcome, defined for STREAM Stage 1, is also assessed.

**Results:** At randomisation, 28 (12%) participants were severely underweight (BMI<16kg/m<sup>2</sup>) and 77 (33%) underweight (BMI between 16 and 18.5kg/m<sup>2</sup>). Three distinct classes were found. The most common group, Group 1 (N=158) was associated with a small linear increase in BMI. Group 2 (N=61) was associated with a rapid increase in BMI which stabilised by the end of 16 weeks of treatment. The least common group, Group 3 (N=17) was associated with initial weight loss which was mostly recovered after 16 weeks of treatment. There was some evidence at the 10% level for significance that sex, age, baseline BMI, baseline culture, and whether a patient stopped the drug prothionamide were associated with latent group membership. There was no evidence that latent group was associated with FoR outcome.

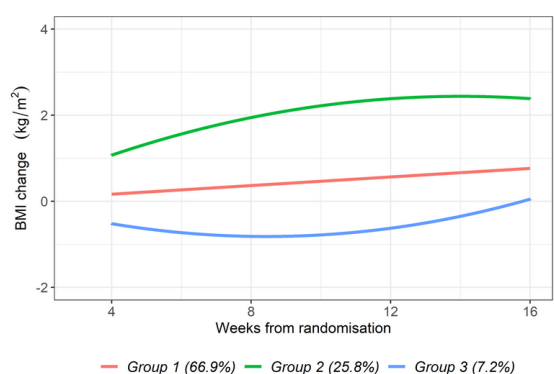


Figure. Mean trajectories of BMI change for a typical individual with mean BMI at baseline.

**Conclusions:** Although three distinct trajectories and their associations were identified, further work is needed to replicate and quantify these associations in other MDR/RR-TB populations. These could be explored in further data arising from ongoing clinical trials.

### SOA03-823-15 Pulmonary fungal pathogens among pulmonary TB patients with persisting symptoms in Uganda

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**Background:** Superimposed pulmonary fungal pathogens may complicate pulmonary tuberculosis (PTB) by causing persistence of symptoms even in the presence of optimal and effective anti-PTB therapy. Left untreated, they increase morbidity and mortality, and adversely affect the quality of life in this patient population.

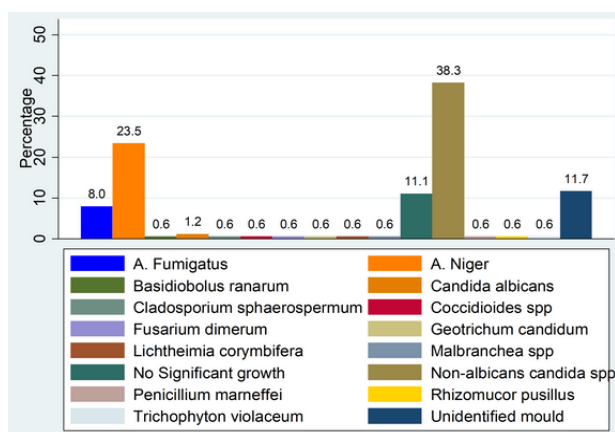
**Design/Methods:** This hospital-based cross sectional survey was a sub study of a much larger published study conducted at the Tuberculosis Treatment Centre of Mulago National Referral Hospital in Kampala, Uganda. A sputum sample was collected from each study participant. Only drug-sensitive PTB patients with persisting symptoms after 2 months of effective anti-PTB therapy were eligible for enrollment.

Fungal culture was performed using Sabouraud Dextrose Agar. Microscopic speciation of the organisms was done using lactophenol cotton blue stain (filamentous fungal growth) and Germ Tube test (yeast growths).

The following data was also available from the much larger study for use to answer our questions:

1. Chest X-rays (CXR)
2. Clinical and demographic data on; age, sex, HIV status, other co-morbidities, clinical symptoms, smoking and alcohol use, and prior history of PTB diagnosis.

**Results:** Out of 162 study participants, 144 (88.9%) grew a pulmonary fungal pathogen on sputum. The most prevalent species were: non- albicans candida species, 62 (43.1%); *Aspergillus niger*, 38 (26.4%); and *Aspergillus fumigatus*, 13 (9.0%). Growth of fungal pathogens was associated with prior history of PTB diagnosis (adjusted odds ratio (aOR): 6.61, 95% CI: 1.85 — 23.9, p=0.004), and far advanced CXR changes (aOR: 4.26, 95% CI: 1.72 — 10.52, p=0.002).



**Conclusions:** Pulmonary fungal pathogens are highly prevalent among active PTB patients with persisting respiratory symptoms, and especially those with history of prior PTB treatment and those with advanced CXR changes. Aspergillus species, which cause an important co-morbidity, Chronic Pulmonary Aspergillosis, were especially prevalent. We recommend routine screening for pulmonary fungal pathogens in this subset of patients.

### SOA03-824-15 HIV infection in people screened for COVID-19 and TB at a rural community post in Chókwè District, Southern Mozambique

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**Background and challenges to implementation:** In 2021, the world registered 1.5 million new infections and 650,000 deaths from HIV-related causes. In the same period, almost 25 million people lived with HIV in sub-Saharan Africa, and Mozambique reported around 2 million cases. The COVID-19 pandemic affected HIV control programs worldwide. In Mozambique, 233,214 COVID-19 cases and 2,242 deaths related to COVID-19 were reported. Strategies have been implemented to integrate COVID-19 screening and testing with HIV and TB case finding, particularly in community settings.

**Intervention or response:** During the last year, we implemented simultaneous COVID-19 and TB screening in people presenting with respiratory symptoms in a community post in a rural district in Southern Mozambique, served by two community health workers.

Symptomatic cases received AgRDT COVID-19 testing, providing sputum samples for GeneXpert testing which were transported daily to a nearby laboratory.

The results were captured in a TrackerApp supporting the linkage to care of presumptive cases, developed through the UNITAID-funded I4C19 project. Information related to co-morbidities such as HIV and Diabetes Mellitus was also collected, and people received follow-up as per national protocols.

**Results/Impact:** From April 2022 to March 2023, the community post screened 1179 people, 94% of them for COVID-19, while 21% provided samples for TB testing. We found 65 people positive for COVID-19 and 9 for TB.

Almost 73% of people with COVID-19 and 100% with TB were confirmed to be PLHIV and had moderate respiratory symptoms.

**Conclusions:** Community-based screening and testing for COVID-19 and TB may improve access to healthcare and facilitate early detection, particularly for people with comorbidities. This approach enables a person-centered linkage to care and facilitates contact screening.

Furthermore, integrating HIV testing in community posts can increase awareness of HIV status and promote access to appropriate care. This multi-faceted approach can improve the health outcomes of individuals and communities affected by these diseases.

### SOA03-825-15 HIV-TB co-infection rate among TB patients for active TB case-finding interventions, a case study from Malawi

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**Background and challenges to implementation:** People leaving with HIV are at high risk of suffering from TB due to low immunity. This programmatic assessment is to demonstrate the effectiveness of a Mobile diagnostic unit equipped with Gene-Xpert and X-ray in diagnosing TB presumptive to narrow the gap for missing HIV clients among TB patients who come for routine TB screening

**Intervention or response:** Methods: In 2022 one of the Mobile Diagnostic units for active TB case finding was deployed in some selected three districts to assist in the diagnosis of individuals suspected of TB. Upon mobilizing communities and sensitizing them, individuals were screened for both TB and HIV. Those that screened positive for TB underwent Chest X-ray, HIV testing and TB Gene Xpert testing on site to confirm the TB diagnosis. Positive cases were referred to the nearest public health facility for treatment. initiation.

**Results/Impact:** In the year 2022 15,909 were screened for TB, out of the total screened 7% (1035) were likely to have TB disease and 132(1%) screened clients tested

positive for HIV. Upon testing all TB presumptive clients 363 TB cases were diagnosed positive. In terms of HIV among the TB patients, 56(42%) tested positive

**Conclusions:** The findings indicate that Mobile diagnostic units are a viable strategy in Active TB and HIV case finding for cases which go undetected and untreated leading to continued disease spread. People leaving with HIV still are at risk of developing TB as the sample data shows 42% co-infection rate. The numbers could be higher and some could be missed. It is recommendable for continued integration of TB and HIV services in country and across the region to intensify case detection efforts for the two diseases.

### SOA04 TB Diagnostics, including drug-resistance determination: Technical aspects and new developments

#### SOA04-827-15 Ethical challenges of TB patient participation in human genomic research in Ethiopia: A qualitative study of stakeholder perspectives

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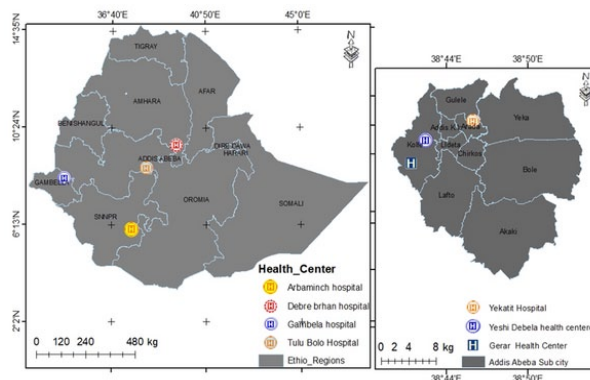
**Background:** Researchers should consider the information participants might need in order to understand the risks and potential benefits of participating in Human Genomics Research (HGR), with attention to cultural context and other special circumstances. Genomics research is conducted without ensuring that all stakeholders adequately understand the potential risks.

The study objectives are to explore the understanding of TB patients and members of National and Institutional Ethics Review Boards (IRBs) about ethical challenges related to consenting to HGR and to explore areas where TB patients need protection, avoidance of harm, and maximization of their well-being.

**Design/Methods:** 19 TB patients who participated in TB-GEN Project, which uses Whole Genomic Sequencing, and are under directly observed therapy from 4 regions and 3 health facilities of the federal state of Ethiopia and 9 Members of IRB were selected for in-depth interviews and focus group discussions, respectively, through purposive sampling.

The desired outcome is to get the emic perspectives of the participants on the ethical challenges of informed consent. The interviews and focus group discussions

were recorded and transcribed into text-based versions through Express Scribe Transcription Software. To ensure the quality of the transcription, the researchers an independent person verified the accuracy of the audio version against the transcribed text-based version. The data was analyzed thematically using MAXQDA Analysis Software.



**Results:** The main ethical concerns of the use of genomics in understanding disease among TB patients in Ethiopia are therapeutic misconception, low health literacy, lack of comprehension, language barriers, undue influence, and misinformation.

**Conclusions:** Given the sensitive nature of the genetic research and the ethical challenges, participants are neither well informed nor do they fully understand the information they are given.

These challenges can be overcome through training researchers, adequate planning, advanced involvement of IRBs, local interpretation of information sheets, and professional approaches to consenting and community engagement.

### SOA04-828-15 Development and validation of novel diagnostic assays for the diagnosis of pleural TB

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**Background:** Pleural tuberculosis (pTB) is a grave clinical challenge due to its non-specific clinical presentations and lack of accurate diagnostic tools. We assessed the diagnostic utility of 2 *M.tb*-specific-biomarkers; cell-free *Mycobacterium tuberculosis* DNA (cfM.tb-DNA) and mycobacterial antigens for pTB diagnosis. The developed assays were cfM.tb-DNA probe-based qPCR assay targeting *devR* (109-bp) gene of *M.tb* and magnetic nanoparticle antibody-conjugate-based aptamer-based assay (Mag-nano-Ab-Ap assay) targeting 4 *M.tb*-specific-antigens (GlcB, MPT51, MPT64 and CFP-10) in pleural fluid (PF).

**Design/Methods:** cfM.tb-DNA qPCR assay development included the standardization of a novel laboratory-based, cost-effective and PF-specific cfDNA extraction method followed by cfM.tb-DNA quantitation by qPCR. Mag-nano-Ab-Ap assay was developed by conjugating polyclonal antibodies raised in rabbits (anti-GlcB/anti-MPT51/anti-MPT64/anti-CFP-10 IgG) on surface of magnetic nanoparticles followed by capturing of *M.tb*-specific antigens in PF and detection by antigen-specific 5'-biotinylated aptamers.

Patient categorization was done by 'Composite Reference Standard' formulated for study. Assays were developed using the 'Development-set' (n=17; 'Definite+Probable' pTB; n=9 and 'Non-TB'; n=8) and cut-offs were determined by using this set by ROC-curve analysis (DNA-assay) and by calculating Mean±3SD of OD<sub>450</sub> of 'Non-TB' group (antigen-detection assay) and applied to the 'Validation set' (n=114 or 118; 'Definite' pTB; n=8, 'Probable' pTB; n=34, 'Possible' pTB; n=28 and 'Non-TB'; n=44/48).

**Results:** *devR*-based-qPCR assay had a sensitivity of 62.5% (95% CI:24.4,91.4) in 'Definite' pTB group and 59.5% (95% CI:43.2,74.3) in combined 'Definite+Probable' pTB group with 95.2% (95% CI:83.8,99.4) specificity.

Of the 4 antigens tested, MPT51-based Mag-nano-Ab-Ap assay performed the best with 62.5% (95% CI:24.4-91.4) sensitivity in 'Definite' pTB group and 66.6% (95% CI:50.4-80.4) in 'Definite+Probable pTB' group with 95.4% (95% CI:85.1-99.4) specificity.

Xpert MTB/RIF assay detected only six-samples in 'Validation set'. Logistic regression-analysis indicated that the developed 'new-tests' could provide an incremental advantage over existing diagnostic algorithms and can provide an aid in clinical diagnosis of pTB.

**Conclusions:** We conclude that the detection of *M.tb*-associated biomarkers could provide a direct evidence of *M.tb* etiology and can pave the way for improved pTB diagnosis.

### SOA04-829-15 Discordance between Xpert MTB/XDR assay and phenotypic drug susceptibility testing in assessing isoniazid and ethionamide resistance

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**Background:** The Xpert<sup>®</sup> MTB/XDR assay (XDR assay) (Cepheid, Sunnyvale, USA) is performed as a reflex test to *M. tuberculosis* positive samples. The assay uses a 10-colour module GeneXpert system to test for resistance to isoniazid (H), fluoroquinolones (FQ), ethionamide (ETH), and second-line injectable drugs (SLI) from sputa or clinical isolates of *M. tuberculosis*. XDR assay is classed as a low complexity automated nucleic acid amplification test (NAATs) by World Health Organization (WHO).

Since implementation at QMSRL, discordant results were observed between the XDR assay and phenotypic drug susceptibility testing (pDST). Whole genome sequencing (WGS) was performed to understand the cause of these discrepancies.

**Design/Methods:** *M. tuberculosis* isolates cultured at the QMSRL were subjected to XDR assay and pDST (MGIT 960) of respective drugs including low and high concentration for H and Moxifloxacin (Mox). All isolates with discrepant results were subjected to WGS using Illumina MiSeq. Results were analysed with TB profiler, Mykrobe and a custom pipeline.

#### Results:

- H-resistance: Two isolates (1 with mutation *katG*<sub>c</sub>-10A>C<sup>#</sup> and 1 with *katG*<sub>c</sub>-p.Phe720Ser) were XDR assay H susceptible but phenotypically resistant to H 0.1µg/ml. One<sup>#</sup> was also phenotypically resistant to H 0.4µg/ml. One isolate with mutation (*fabG*<sub>1</sub><sub>c</sub>-8T>C) was XDR assay H resistant (low) but phenotypically susceptible to H. One isolate with *aphC*<sub>c</sub>-90G>A mutation was XDR assay H resistant, however, phenotypically susceptible.

- ETH-resistance: Six isolates with inhA\_c.-154G>A (fabG1 p.Leu203Leu) mutation, were XDR assay susceptible and phenotypically resistant to ETH (5µg/ml).
- All mutations observed fell within the target regions of the XDR assay.
- No discrepancies were seen with FQ and SLI.

**Conclusions:** This study highlighted the possibility of getting discrepant results from XDR assay in comparison with pDST and WGS. This may have clinical repercussions when XDR assay results cannot be verified by additional methods. XDR assay results are to be interpreted cautiously before initiating treatment.

### SOA04-830-15 Urine Xpert Ultra testing for TB diagnosis in people living with HIV: A multicentre diagnostic accuracy study

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**Background:** Diagnostic delay for tuberculosis remains common, leading to high rates of mortality. Urine Xpert Ultra (Urine-XPU) is not yet widely available, but could improve timeliness of identification of *Mycobacterium tuberculosis* (*Mtb*) and Rifampicin resistance in patients in whom sputum cannot be collected. We investigated the diagnostic accuracy of Urine-XPU for tuberculosis diagnosis in people living with HIV, and compared this to Determine™ TB LAM Ag (AlerLAM, Abbott).

**Design/Methods:** We recruited inpatient and outpatient adults (≥18 years) living with HIV in seven countries.

The primary objective was to assess the diagnostic sensitivity, specificity and diagnostic yield of Urine-XPU against both an extended microbiological and a composite reference standard (eMRS and CRS).

We also assessed the relationship between index tests and mortality.

**Results:** We enrolled 1,692 patients between 2019-2021 (median CD4: 376cells/µl; microbiologically-confirmed TB: 15.8%; outpatients: 56%). Against the eMRS, the sensitivity of Urine-XPU and AlerLAM were 32.9% and 31.8% respectively, increased to 46.1% and 43.0% for inpatients, and 52.8% and 51.2% for CD4≤200cells/µl. Against the eMRS, the specificity of Urine-XPU and AlerLAM were 98.1% and 90.3%. Against the CRS, the sensitivities of Urine-XPU and AlerLAM were 31.0% and 21.0%, and the specificities were 99.2% and 95.2% respectively. The combination of sputum Xpert Ultra (sputum-XPU) and AlerLAM could diagnose 79.5% of eMRS-positive patients, sputum-XPU and Urine-XPU 79.2%, and all three tests 83.0% (Figure1).

Overall ten-week mortality was 7.3%, but was disproportionately higher in those with positive Urine-XPU (15.9%; adjusted odds ratio: 1.39; 95% CI: 0.77-2.19) or AlerLAM (17.1%; adjusted odds ratio: 1.83; 95% CI: 1.17-2.81).

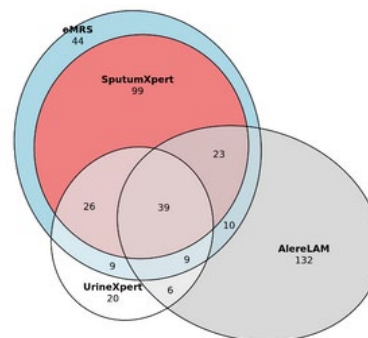


Figure 1. Euler diagram demonstrating diagnostic yield per rapid test (Sputum Xpert Ultra, AlerLAM and Urine Xpert Ultra) against the extended microbiological reference standard (eMRS).

**Conclusions:** Urine-XPU offers promising diagnostic utility in combination with AlerLAM, showing similar sensitivity but improved specificity, whilst also being able to confirm *Mtb* and rifampicin resistance. Both tests should be offered to patients at high risk of death, to improve survival through rapid diagnosis and treatment initiation.



## SOA04-831-15 Diagnostic accuracy and comparison of lipoarabinomannan in serum, plasma and urine for TB disease among adults with and without HIV

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**Background:** Accurate diagnostics ensuring timely initiation of Tuberculosis (TB) treatment are urgently needed to reduce transmission and mortality. Point-of-care assays to detect urine Lipoarabinomannan (LAM) have demonstrated inadequate sensitivity or lot variation.

We compared the diagnostic performances of two LAM-specific antibodies in three non-sputum specimens on an electrochemiluminescence immunoassay platform.

**Design/Methods:** We evaluated 130 adults with TB disease (positive sputum by Xpert Ultra or culture) and 20 TB-negative adults from South Africa.

All participants endorsed TB-related symptoms and were tested for HIV. Matched serum, plasma and urine samples were tested on the Meso Scale Diagnostics (MSD) platform for LAM by two capture antibodies (FIND 28 and S4-20), and A194-01 as the common detection antibody. We calculated the sensitivities and specificities of LAM results against the microbiological reference standard.

**Results:** The sensitivities of LAM in plasma/serum/urine by FIND 28 were 0.65 (95% confidence interval [CI] 0.56-0.73), 0.70 (0.61-0.78), and 0.67 (0.58-0.75) respectively.

Corresponding specificities were 0.90 (0.68-0.99), 0.95 (0.75-1.00), and 0.85 (0.62-0.97) in plasma/serum/urine. Sensitivity increased among HIV+ participants with CD4 counts < 200 mm<sup>3</sup> by FIND 28 in plasma (0.87, (0.76-0.94)), serum (0.90, (0.80-0.96)), and urine (0.90, (0.80-0.96)).

Sensitivities of LAM captured by S4-20 in plasma/serum/urine were 0.29 (0.22-0.38), 0.32 (0.24-0.41), and 0.61 (0.52-0.69) respectively, while specificities were all 1.00 (95% CI 0.83-1.00).

		N	Plasma	N	Serum	N	Urine
FIND28	All (N=150)	sensitivity (95%CI)	84/130 0.65 (0.56-0.73)	91/130	0.70 (0.61-0.78)	87/130	0.67 (0.58-0.75)
		specificity (95%CI)	18/20 0.90 (0.68-0.99)	19/20	0.95 (0.75-1.00)	17/20	0.85 (0.62-0.97)
	HIV+ & CD4 <200 mm <sup>3</sup> (N=65)	sensitivity (95%CI)	54/62 0.87 (0.76-0.94)	56/62	0.90 (0.80-0.96)	56/62	0.90 (0.80-0.96)
		specificity (95%CI)	2/3 0.67 (0.09-0.99)	2/3	0.67 (0.09-0.99)	2/3	0.67 (0.09-0.99)
	All (N=150)	sensitivity (95%CI)	38/130 0.29 (0.22-0.38)	42/130	0.32 (0.24-0.41)	79/130	0.61 (0.52-0.69)
		specificity (95%CI)	20/20 1.00 (0.83-1.00)	20/20	1.00 (0.83-1.00)	20/20	1.00 (0.83-1.00)
S4-20	HIV+ & CD4 <200 mm <sup>3</sup> (N=65)	sensitivity (95%CI)	26/62 0.42 (0.30-0.55)	27/62	0.44 (0.31-0.57)	54/62	0.87 (0.76-0.94)
		specificity (95%CI)	3/3 1.00 (0.29-1.00)	3/3	1.00 (0.87-1.00)	3/3	1.00 (0.29-1.00)

Table 1. Diagnostic Accuracy of LAM detected by FIND28 and S4-20 in Plasma, Serum and Urine.

**Conclusions:** LAM was detectable in serum and plasma, but at lower concentrations than observed in urine. The FIND 28 and S4-20 antibodies had comparable accuracy in urine, and the FIND 28 antibody had higher sensitivities in plasma and serum. Since the diagnostic performance of LAM detected by FIND 28 was similar across three specimen types, testing blood specimens for LAM may provide another non-sputum diagnostic option for some people.

## SOA04-832-15 Nanoplasmonic-enhanced immunoassays to detect *M. tuberculosis*-derived extracellular vesicles in the blood for TB diagnosis

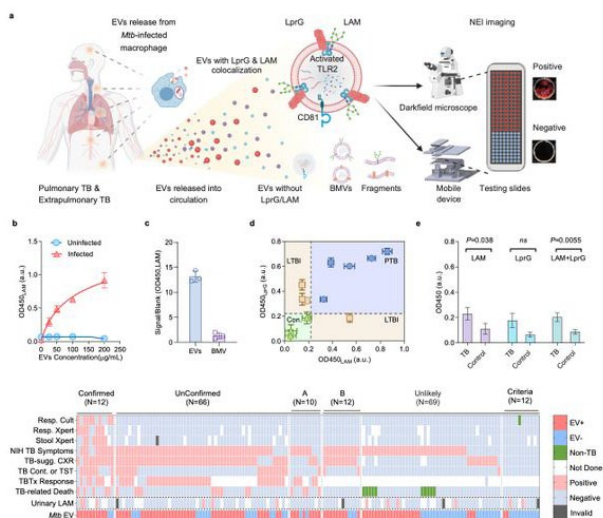
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**Background:** Current TB assays rely on the respiratory samples can miss >50% of pediatric TB, and sensitivity is lower in children living with HIV, who have higher TB mortality. Detection of *Mtb*-derived biomarkers in serum provides direct evidence of TB.

Extracellular vesicles (EVs) actively participate in infectious diseases and can thus carry information for analysis and diagnosis of active TB and TB cases that can be challenging to diagnose by current TB assays and clinical algorithms.

**Design/Methods:** We developed a nano plasmonic-enhanced immunoassay (NEI) to detect two factors we discovered, whose co-expressed on extracellular vesicles (EVs) (Fig. 1), where EVs are captured directly from serum by an EV-specific antibody, then hybridized with gold nanorods conjugated with TB-specific antigen antibodies. after which nanorod light scattering is cap-

tured using a benchtop-based or portable smartphone-based dark-field microscope (DFM) and the specific signal from target EVs expressing *Mtb*-associated factors is quantified by image processing.



**Results:** NEI shows high sensitivity toward pediatric TB cases diagnosed by microbiologic (83%) and clinical findings (73%). NEI measurement showed different negative rates to unlikely pediatric TB cases who did (46%) and did not meet any criterion for clinical TB diagnosis (83%), indicating the potential for undiagnosed TB cases in the former group, and higher specificity was detected in other non-HIV-exposed pediatric cohorts (92%-100%). NEI signal decreased in pediatric TB cases after anti-TB treatment, to reflect *Mtb* containment or clearance during anti-TB treatment or immune reconstitution.

**Conclusions:** Our results imply that the analysis of serum EVs by detecting *Mtb*-derived biomarker signatures can identify active TB and TB cases that are challenging to diagnose by current TB assays and clinical algorithms. Notably, this approach should also be adaptable to other types of diseases, including non-tuberculous mycobacteria superfamily members, which can also be difficult to diagnose.

## SOA04-833-15 Reduced critical concentration may not improve MGIT-based DST sensitivity to rifampicin

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**Background:** Discordances between Mycobacteria Growth Indicator Tube (MGIT) based phenotypic drug-susceptibility testing (pDST) and genotypic DSTs to rifampicin are largely attributable to occult resistance conferred by borderline *rpoB* mutations. In 2021, the World Health Organization (WHO) reduced the critical concentration (CC) of rifampicin in MGIT from 1.0 µg/ml to 0.5 µg/ml intending to reduce the occurrence of such discordance.

**Design/Methods:** In this analysis, we included twelve isolates that originated from the endTB and endTB Q clinical trial sites in Karachi, Pakistan, found resistant to rifampicin by GeneXpert MTB/Rif but susceptible to rifampicin at 1.0 µg/ml in MGIT. We re-tested these isolates with the current CC in MGIT using the standard MGIT-DST procedure recommended by BD and performed targeted sanger sequencing of the *rpoB* gene. **Results:** All twelve isolates carried known borderline *rpoB* mutations [His445Asn (n=2), His445Lue (n=3) Asp435Tyr (n=3), Asp435Gly (n=1), Leu452Pro (n=1), Leu430Pro (n=1), Asp435Tyr+Met434Ile (n=1)] and were still susceptible to rifampicin at 0.5 µg/ml in MGIT.

Our results suggest that lowering the CC in MGIT has not resolved the impaired sensitivity of MGIT-based pDST for rifampicin.

**Conclusions:** Torrea *et al* have shown that extending the incubation period beyond the standard maximum of 13 days increased the sensitivity for borderline mutations significantly, from 5.7% using the standard procedure at 1µg/ml with the pre-set incubation time, to 68.6% using 1µg/ml at 21 days, and to 65.7% using 0.5µg/ml at 15 days.

However, extending the incubation time of the MGIT DSTs should be further evaluated on a larger *rpoB* wild-type sample to determine the risk of generating false-resistant results.

Additionally, extended incubation requires the TBx-IST software module, which requires manual interpretation of the DST data. Therefore, our data support the recommendation that genotypic DST should overrule MGIT DST for rifampicin, and MGIT should not be used for confirmation of genotypically determined rifampicin resistance.

### SOA04-834-15 Time-to-results for first- and second-line anti-tuberculosis drugs using whole-genome sequencing and BACTEC MGIT 960: A comparison

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**Background:** Peru is considered one of the 30 countries in the world with the highest burden of multidrug resistant tuberculosis (MDR-TB). Laboratory tests are essential for the detection of MDR-TB, as well as the time these tests take to obtain the results.

The objective of the study is to analyse the time to obtain results in the evaluation of first- and second-line anti-tuberculosis drugs using Whole Genome Sequencing (WGS) and BACTEC MGIT 960 in a routine workflow.

**Design/Methods:** 100 solid cultures of drug resistant *Mycobacterium tuberculosis* strains from Lima and Callao were prospectively selected in December 2021 at the Peruvian National Institute of Health. Cultures were simultaneously processed by phenotypic BACTEC MGIT 960 and WGS methodologies according to routine laboratory workflow.

The time to obtain results for both methods were calculated considering the difference between the initial time (since the solid culture arrives at the laboratory), and the final time (when the validated results reports were generated according to each workflow).

**Results:** WGS allowed 100% (100/100) strains had valid complete results of susceptibility for 13 anti-TB drugs, whereas BACTEC MGIT 960 had different number of valid results for each drug.

The average time to obtain results of WGS for the complete set of drugs was 11.2 days; whereas this result was variable for each drug using BACTEC MGIT 960 system (41.3 for isoniazid, 31.1 for rifampicin, 32.1 for pyrazinamide, 30.8 for moxifloxacin, levofloxacin and amikacin, 31.3 for capreomycin, 55.6 for bedaquiline, 47.5 for linezolid, clofazimine and delamanid (Fig. 1).

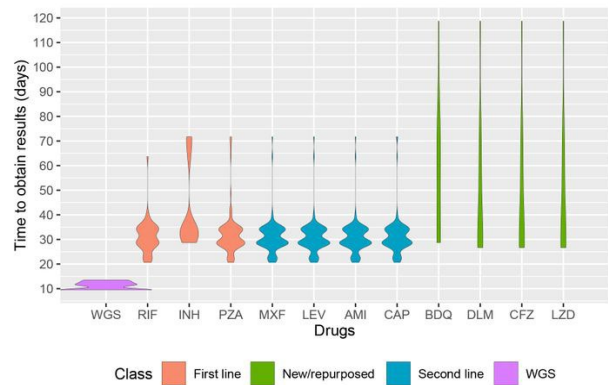


Figure 1: Comparison of time to results analysis between WGS and BACTEC MGIT.

**Conclusions:** In Peru, under routine conditions, obtaining results in the evaluation of all anti-TB drugs had an average of 11.2 days by WGS, however, for the phenotypic analysis the times vary depending on each drug evaluated, obtaining from 30.1 until 55.6 days.

### SOA05 Access to quality TB care and services

#### SOA05-835-15 Strategic initiative to find people with TB among hospital attendees: Unprecedented efforts to detect and notify additional TB cases in North Central, Nigeria

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**Background and challenges to implementation:** Globally, TB incidence increased by 3.6% between 2020 and 2021, reversing annual decreases of roughly 2% for most of the preceding two decades. (WHO, 2022). Nigeria has the highest burden of tuberculosis (TB) in Africa with over 300,000 missing TB cases annually. Active TB screening of hospital attendees is pivotal in finding missing TB cases. We evaluated the contribution of this intensified TB case finding intervention in public health facilities in North-central Nigeria (Benue, Nasarawa, Plateau and Taraba States) to their quarterly public facilities TB case notification to the Nigerian National TB Program.

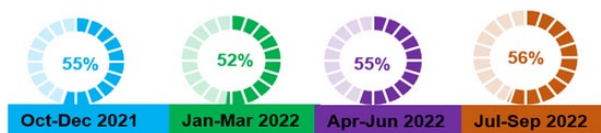
**Intervention or response:** Through USAID funded TB LON Project being implemented in these four states, active TB screening was initiated at key service delivery points in 257 public-owned health facilities (8 tertiary, 48 secondary and 201 primary health facilities) in these 4 states.

All patients visiting the facilities with their accompanying relations were screened for TB by Adhoc staff recruited for this purpose. Using a hub and spoke mechanism, patients who were presumptive from the lower facilities (primary health facilities) were actively linked to a suitable secondary or tertiary facility for further evaluation using available molecular diagnostic tools (GeneXpert, TB LAMP or Truenat). Persons identified with active TB were immediately placed on treatment and properly documented in the National registers with program data uploaded on COMMCARE app.

**Results/Impact:** Within twelve months (4 quarters) of implementation, (October 2021 to September 2022), 1180736 persons were screened across 257 ICF-Public facilities with 64498 (5%) presumptive TB identified, 64439 (99.9%) evaluated and 6498 (10%) TB cases detected. 97% were commenced on treatment.

	NTP Notified TB Cases- (Public Facilities)	ICF-Public TB Cases Contribution	%tage Contribution
Oct-Dec 2021	3004	1642	55%
Jan-Mar 2022	2990	1547	52%
Apr-Jun 2022	2946	1618	55%
Jul-Sep 2022	3012	1691	56%
<b>Total</b>	<b>11952</b>	<b>6498</b>	<b>54%</b>

Table. TB cases contribution via ICF-Public to NTP Notified TB cases



Quarterly progress chart of TB cases contribution to NTP Notified TB cases from public facilities via ICF-Public facilities intervention within Nasarawa Cluster.

**Conclusions:** Active case finding among hospital attendees continues to be the game changer in finding persons with TB who ordinarily would have been missed by the health care workers especially in facilities with very busy personnel and limited resources.

## SOA05-836-15 Contextual factors impacting the implementation of TB digital adherence technologies: A scoping review

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**Background:** Digital adherence technologies (DATs) may facilitate more person-centered treatment monitoring for tuberculosis (TB) disease and infection; however, their effectiveness may be undermined by implementation challenges. We used the RE-AIM framework to identify contextual factors that impact DAT implementation, focusing on RE-AIM dimensions: “Reach” (DAT engagement by people with TB) and “Adoption” (DAT uptake by healthcare providers).

**Design/Methods:** We conducted a systematic search spanning January 2000 to April 2022 of MEDLINE, Embase, CENTRAL, CINAHL, Web of Science, medRxiv, Europe PMC, and clinicaltrials.gov. Studies involving TB DATs relevant to RE-AIM constructs were included.

To understand contextual factors influencing “Reach” and “Adoption,” we organized qualitative and quantitative findings using the Unified Theory of Acceptance and Use of Technology (UTAUT), which posits that these constructs predict technology acceptance and use: perceived usefulness of the DAT, ease of DAT use, social influences, and facilitating conditions. Common findings were synthesized into “meta-themes” that may inform DAT acceptance and use.

**Results:** Of 12906 abstracts identified, 674 underwent full-text review, of which 147 studies met inclusion criteria. An interim analysis including 76 of these studies identified positive and negative meta-themes across UTAUT constructs that inform DAT “Reach” and “Adoption” (Table).

Findings reveal potential reasons for heterogeneity in DAT “Reach” among people with TB, with DATs performing better when they made patients feel more “cared for” by the health system, provided flexibility in use, facilitated family involvement in care, and were provided with adequate training.

“Adoption” by healthcare providers was better when DATs improved efficiency and convenience of care delivery, had an easy-to-use platform, enhanced communication among providers, and involved adequate training.

RE-AIM dimension	UTAUT construct	Positive meta-themes (i.e., factors enhancing DAT uptake)	Negative meta-themes (i.e., factors negatively affecting DAT uptake)
REACH (i.e., engagement by people with TB)	Perceived Usefulness (Whether the DAT improves care)	DAT improved relationship with health system (feeling of being "cared for"), Improved quality of care, Improved convenience of care	Technology fatigue, Negative impact on relationship with providers, Inequity in access to DAT limited benefits, Greater access to information about TB was desired
	Ease of Use (Whether the DAT is easy to use)	DAT provided flexibility in its use, DAT is easy to use, No literacy or language barriers, No challenges with network function	Suboptimal DAT function, DAT too technically complex for patient, Literacy and language barriers, Loss or destruction of DAT
	Social Influences (How family or other people affect DAT use)	Low stigma with DAT compared to DOT, Positive family involvement in care due to the DAT, Increased autonomy	High or increased stigma, Concerns about family involvement in care, Desire for greater social contact not fulfilled by DAT, Concerns about high monetary value of DAT, Socially desirable behavior to please provider limited DAT accuracy
	Facilitating Conditions (Counseling and other support by providers for DAT use)	Provision of phones enabled the intervention, Adequate training in DAT reported by the patient, Optimal DAT function, Quick resolution of a problem that emerged	Complexity of cellular accessibility challenges, Lack of adequate DAT counseling, Suboptimal DAT function, Loss or destruction of DAT
ADOPTION (i.e., uptake by healthcare providers)	Perceived Usefulness (Whether the DAT improves care delivery)	Convenience of care delivery, Efficiency of care delivery, Improved communication between provider and patient, Increased job satisfaction, Better data quality, Improved relationship with patients	DAT does not address core patient problems, Decreased efficiency of care delivery, Negative impact on patient-provider relationship, Poorer quality of care, Suboptimal accuracy of observation
	Ease of Use (Whether the DAT platform is easy to use)	DAT platform easy to use, DAT platform convenient to use	Poor network coverage, Limited functions of DAT platform, Suboptimal accuracy/dose reporting created inefficiencies for providers
	Social Influences (How other providers affect DAT use)	Improved "culture of care", Enhanced communication with provider team, Gives people with TB a "human face" for providers	Reduced culture of care, Decreased communication among providers
	Facilitating Conditions (Infrastructure and support by the health system in DAT implementation)	Pre-existing strong culture of care, Good working environment, Adequate training provided to providers, Positive provider participation in DAT implementation	Insufficient staff, Low technology skills among staff, Inadequate training in using DAT, Poor management of DAT program, Lack of electricity or poor network coverage

**Conclusions:** This scoping review identifies numerous contextual factors that can inform improvements in future DAT design and implementation to achieve higher engagement by people with TB and healthcare providers, thereby potentially improving future intervention effectiveness.

## SOA05-837-15 TB active case-finding in Malawi: The role of community volunteers and community sputum collection points

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### Background and challenges to implementation:

The annual incidence of TB in Malawi in 2021 is estimated to be 132 per 100,000. Through the USAID supported TB Local Organization Network-2 and the implementing partner Development Aid from People to People, 105 Community Sputum Collection Points (CSCPs) were linked to twenty-one health facilities (HF) in three districts (Mangochi, Machinga and Mulanje). CSCPs operate with up to ten Community Volunteers (CVs).

**Intervention or response:** CVs reside in the communities they serve and provide TB and stigma reduction messages, screen for presumptive TB, and collect and deliver sputum samples for diagnostic testing. CVs are provided with sputum collection boxes, personal protective equipment, and 'enablers', e.g. t-shirts, backpacks, gumboots, and umbrellas that identify them in the community as trusted health workers.

Each CSCP is provided with one bicycle for outreach to remote areas and for the delivery of specimens to the nearest laboratory for testing. In addition, twenty-one Community Health Workers (one per HF) conduct supportive visits to the 105 CSCPs at least once a month in support of the CVs.

**Results/Impact:** Between January and December 2022, 320,694 community members were reached with information on TB and provided stigma reduction messaging; 52.9% (169,771) were screened for TB; 7.4% (12,557) were presumptive for TB disease, and 233 (1.9%) were diagnosed with TB compared to 36 diagnosed and notified in 2021.

**Conclusions:** CVs are trusted in their communities and when enabled and provided supportive supervision are an effective and efficient means to identify presumptive TB in their communities. Through TB education, stigma reduction, and the collection of sputum for diagnostic testing CVs provide essential TB services to remote rural areas of Malawi that otherwise would not be served.

### SOA05-838-15 The potential yield of geographically targeted TB contact investigations in urban Uganda

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**Background:** To increase TB case detection, a pillar of the End TB Strategy, it is important to identify approaches to improve active case finding among populations at increased risk for TB.

We aimed to investigate the potential yield of active case finding conducted within a defined geographic radius (50 or 100m) around the households of individuals diagnosed with TB at local health facilities in Kampala, Uganda.

**Design/Methods:** Adult (>15 years) residents of a well-defined study area who were diagnosed with TB were enrolled through two mechanisms: passive case detection at four study area facilities (May 2018–November 2019) and active case finding via door-to-door Xpert Ultra testing offered to the entire community (regardless of symptoms, February–November 2019).

We classified door-to-door screening locations as being <50m, 50–100m, or >100m from the nearest self-reported household location of a patient diagnosed with TB at a health facility. We compared the prevalence of TB within potential screening radii of 50 or 100m compared to >100m.

**Results:** Eighty-five people were diagnosed with TB at health facilities, and 60 people were diagnosed with TB during door-to-door screening. Among door-to-door testing participants, there were 10 Xpert-positive individuals living within 50m of an individual with facility-diagnosed TB (number tested=1,016, prevalence=0.98%) and 15 living between 50m and 100m from an individual with facility-diagnosed TB (number tested=1,829, prevalence=0.87%).

Compared with people living >100m from any person diagnosed with TB in study facilities, the prevalence ratio (95% confidence interval) among those living within 50m was 1.4 (0.69–2.9), and among those living 50–100m away was 1.2 (0.63–2.2).

Blue dots indicate the location of residence of patients with facility-diagnosed TB and black dots indicate residence of individuals who had positive Xpert results during door-to-door screening. The circles represent areas within 50 and 100m radii from each patient diagnosed with TB at a health facility. Dots inside the screening radii indicate individuals with TB who could be detected by geographically targeted screening within that radius. The number of individuals with Xpert results in each administrative zone is indicated by the shading (darker colors indicate a larger number of individuals screened).

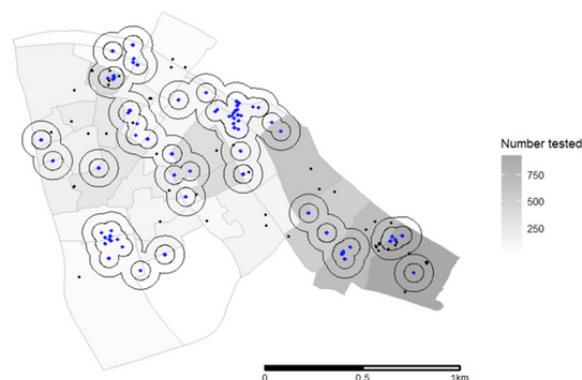


Figure 1. Potential yield of screening for TB within 50 and 100m of an index patient.

**Conclusions:** Expanding household contact investigation to include neighbors may identify additional people with undiagnosed TB, but our results suggest this strategy is at most moderately more efficient than screening the general population. Focusing on shared exposures or risk factors (e.g. venues, social networks, or demographics) may have higher yield.

### SOA05-839-15 Differing pathways to care: A qualitative study on the gendered barriers to accessing TB services in Nigeria

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**Background:** In Nigeria, despite an increase in Tuberculosis treatment coverage from 30% to 44% between 2020 and 2021, a significant proportion of people with TB miss out on care. The National prevalence survey showed men constitute two-thirds of people outside TB care and experience delays reaching TB services. This contributes to the large gender differential in the TB prevalence notification ratio (7.25 in men vs 4.63 in women). This research aimed to examine the gender-related barriers affecting access to TB services in peri-urban communities in Nigeria from the perspectives of both men and women.

**Design/Methods:** We conducted 17 in-depth interviews with men (n=10) and women (n=7) from local communities, six focus group discussions with men (n=24) and women (n=24) from local communities, and 13 key informant interviews with patent medicine vendors (PMVs), TB program officers, and community health extension workers. Content analysis was applied to derive key summaries, patterns, and commonalities in the data.

A comparison between the responses of community respondents versus respondents who provided services and/or care.

**Results:** Key barriers affecting men's access to care included poor access to information about TB, its services, and its location. To be able to provide for their families, men faced difficulties in taking time away from work to seek care.

Additionally, financial costs associated with care, stigma, and an unwittingly dismissive attitude towards cough posed significant impediments. When they did seek care, men resorted to community-embedded informal providers such as patent medicine vendors, prolonging their delay before reaching TB care in the formal care settings.

**Conclusions:** To facilitate men's access to TB care, gender-specific awareness-creation strategies need to be developed and combined with approaches that bring TB screening and testing closer to men and reduce TB stigma in the community.

### SOA05-840-15 Direct benefit transfer for nutritional support of patients with TB in India: Analysis of 5-year programme data, 2018-2022

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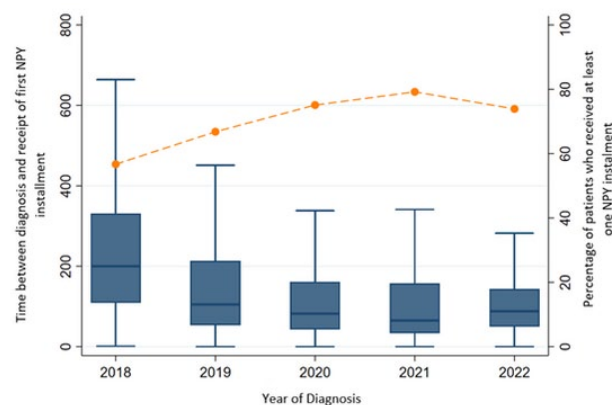
**Background:** A significant proportion of the cost incurred by patients during TB care is towards meeting their additional nutritional requirements. *Nikshay Poshan Yojana* (NPY) is one of the direct benefit transfer schemes under the National Tuberculosis Elimination Programme (NTEP), providing INR500 per month during anti-TB treatment to all notified patients.

We evaluate the performance of NPY in nine selected Indian states for the five years since its inception.

**Design/Methods:** Objective: To calculate the proportion of patients with TB receiving at least one NPY instalment and the median time for receipt of the first instalment.

**Method:** We conducted the study under USAID-funded TIFA project implemented through JSI Research & Training Institute Inc. We selected nine states by stratified random sampling, three states each from three strata based on TB score, a composite score measuring NTEP performance and TB burden. We analysed secondary data from *Nikshay*, the online portal for NTEP data from 2018 to 2022, for the nine states.

**Results:** Of 37,22,082 notified patients with TB, 10.7% were children, 34.7% were females, and 83.0% have completed the treatment. At least one instalment of NPY was credited to 26,21,578 (70.4%) patients. The median (IQR) total amount received by new and retreatment patients was INR3000 (2500-3000). The median (IQR) delay in receiving the first instalment of NPY was 96 (48-192) days. The median (IQR) delay had reduced from 200 (109-331) days in 2018 to 88 (50-143) days in 2022. The state of Odisha (91.1%) reported the highest proportion receiving at least one instalment of money and the shortest median (IQR) time to receive the first instalment of 63 (35-120) days.



**Conclusions:** NPY coverage has improved over the past five years in all states, and the delay in the credit of benefits to beneficiaries has declined. There is a need to explore the reasons for non-receipt and delay in receipt of NPY for effective implementation.

### SOA05-841-15 Tuberculous meningitis - patient pathways and delays to diagnosis in Indonesia

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**Background:** Delays in diagnosis and treatment contribute to high mortality of tuberculous meningitis (TBM). We studied TBM patient pathways including delays to diagnosis, and their alignment with available diagnostic services in Indonesia.

**Design/Methods:** We recruited patients admitted to two tertiary hospitals who started TBM treatment. Participants or their relatives were interviewed to recall healthcare visits preceding TBM treatment.

We also surveyed available diagnostic capacity for TBM at hospitals that had been visited by at least two patients preceding their study enrolment. Data were analysed descriptively.

**Results:** Of 175 participants (median age 31 years, 57.1% male), 85.1% had reduced consciousness or coma, and 46.9% had motor deficits including hemiparesis. Patients attended a first healthcare provider, most often private clinics (38.3%) or informal healthcare providers (22.3%), at a median 14 days (IQR 1-34) after symptom onset. They visited multiple providers (median 5, IQR 3-8) over a prolonged time period (median 31 days, IQR 10-79) preceding TBM diagnosis.

Of 40 surveyed hospitals, 52.5% could not or not always perform lumbar puncture, 22.5% lacked cerebral imaging facilities, and 31.6% and 84.2%, respectively, could not provide routine microscopy or GeneXpert MTB/Rif on cerebrospinal fluid.

**Conclusions:** In these urban settings in Indonesia, pathways to TBM diagnosis are complex and lengthy, and not well aligned with appropriate diagnostic services. There is an urgent need for interventions to strengthen health literacy and diagnostic and referral processes in public and private health sectors for complex patient groups like TBM.

### SOA05-842-15 Hub-and-spoke operational model for optimising the utilisation of upfront molecular testing in Haryana, India

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**Background and challenges to implementation:** Effective management of tuberculosis relies on the rapid detection and prompt initiation of treatment with an appropriate regimen. While the national TB elimination program encourages the use of upfront molecular testing, the underutilization of these diagnostics remains an operational challenge.

This cross-sectional study is an attempt to understand the operational schema of 'Hub-and-Spoke' model to increase the utilization of molecular diagnostics for TB in field conditions.

**Intervention or response:** A 'Hub-and-Spoke' model was conceptualized in Ambala district of Haryana in the year 2022 to address the challenge of underutilized molecular testing. A total of 7 Nucleic Acid Amplification Test (NAAT) sites were linked to all the peripheral labs which acted as a Hub while the sputum collection centres were established at all Government and private health facilities to function as spokes.

Effective transport mechanism was established using the courier services and human carriers. The peripheral labs in the Hub were run in shifts to cover 24 hours a day and ensure the same-day testing and reporting of results.

**Results/Impact:** After establishing this model in 2022, a total of 8115 upfront molecular tests for TB were conducted, out of which 1189 (14%) reported as tuberculosis positive. The newly placed model in the district translated into 36% yield in TB case detection for the year 2022 as compared to previous year ( $p < 0.05$ ).

**Conclusions:** Simple, scalable mechanisms that are locally developed can effectively increase the utilization of molecular diagnostics for TB in field conditions. This study provides an operational schema of the 'Hub-and-Spoke' model that can be replicated in other similar settings with contextualized adaptation.



### SOA05-843-15 Innovation to enhance case detection, treatment adherence and outcomes in drug-resistant TB among internally displaced persons in Northeast Nigeria

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**Background and challenges to implementation:** Despite the impact of the COVID-19 pandemic on the TB Program, Nigeria significantly increased TB notification for both drug sensitive and drug resistance TB in 2021 compared to 2020.

However, DR-TB case finding and poor TB treatment outcomes were recognized as a major gap in 12 States including Bauchi. The gap has disproportionately affected Internally Displaced Persons (IDP).

We launched a project with funding from TB REACH to increase DRTB detection and improve treatment outcomes in IDP host communities of Bauchi State, Nigeria.

**Intervention or response:** We purposefully selected four LGAs with high IDP populations for the intervention and four LGAs with comparable populations as controls. We mapped IDP communities, identified and trained volunteers and implemented door-to-door health education and active TB screening and linkage to TB prevention and care services.

Newly diagnosed DRTB patients were enrolled on treatment and provided nutritional support. Counselling was done before and during treatment while DR-TB support groups were established.

**Results/Impact:** From October, 2021 to March, 2023, a total of 65 DRTB patients were identified in 4 intervening LGAs; this translates to 62% of the total DRTB cases (86) reported in all 20 LGAs of Bauchi State in 2022. Their ages ranged from 18 to 78 years; 35 (55.1%) of the patients were males. So far, 34 individuals have treatment outcomes out of which 21 (62%) were cured, 6 (18%) completed treatment, 3 (9%) were lost to follow-up while 4 (11%) died.

Overall, the treatment success was 80%, which was higher than the 39% before the intervention and 52.4% in the four control LGAs over the same period.

**Conclusions:** Innovative approaches to DRTB care could improve case detection, treatment adherence, and outcomes if scaled up.

### SOA06 Meaningful Collaborations to End TB

#### SOA06-844-15 Peer group counselling by TB Champions help in improving adherence and expedite TB elimination: Lessons learnt from India

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**Background and challenges to implementation:** Unite to ACT Project intended to demonstrate Community TB Care delivery by engaging TB survivors (TBS) as TB Champions (TBC). Project envisages TB-free communities by active participation of communities through TBC and going forward to adopt the integrated approaches of TB-free communities by National TB Elimination Program (NTEP).

Also, TBC to percolate the NTEP services through various communication channels, mitigating the stigma in communities and improving the quality of life of persons with TB (PwTBs) thereby facilitating the goal of TB elimination.

**Intervention or response:** In Patiala district of Punjab, India, Unite to Act Project rolled out from February'22 to August'22. Under the mentorship program, 14 TBS were identified from TB communities and trained as TBC to establish them as an advocate who represent TB-affected communities.

Project also trained them on counselling techniques with structured tools enabling them to provide adequate counselling to people diagnosed with TB from the public sector, encouraging them towards adherence thus improving the treatment outcomes.

**Results/Impact:** During the mentorship program of 6 months, 14 trained TBC were facilitated 74 community meetings, 62 anti-stigma campaign with village level governing bodies, counselling of 1325 on treatment PwTB out of total counselled, 794 (60%) PwTB outcome was declared on Nikshay (Government Portal for TB reporting) till March'23. Out of 794, 691(87%) PwTBs successfully completed their treatment and remaining are currently being followed up by the TBC. 16 sensitized village leaders are robustly supporting the program.

**Conclusions:** The Government of India is putting aggressive efforts through NTEP to increase the awareness regarding TB among communities, also to shift the entire focus of the programme from provider driven to beneficiary driven approach.

In this endeavor the way ahead is to upscale peer group counselling and advocacy which will help in improving adherence and expedite the overall process in the core area of Program.

### SOA06-845-15 Community-led TB interventions: improving TB services in rural South Africa

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**Background and challenges to implementation:** Tuberculosis (TB) is a significant public health concern in South Africa, with high incidence and mortality rates. Despite substantial efforts to control TB, poor treatment adherence and lack of community involvement remain significant challenges. Community-led TB programs have been proposed as an effective strategy to address these challenges and improve TB treatment outcomes. In the USAID TB LON project, THINK partnered with local community-based organisations to expand TB services in communities in four districts in KwaZulu Natal over a four-month pilot.

**Intervention or response:** THINK appointed four CBOs after a due diligence process and trained them to address capacity gaps. Community caregivers utilised multiple approaches, including door-to-door services, events, and workshops with traditional practitioners to integrate TB services and dialogues.

To effectively measure the reach and impact of these community activities, we designed tools to track the number of households and people actively reached with TB services, including prevention, diagnosis, and linkage to treatment.

**Results/Impact:** This intervention resulted in 54 community care groups (CCGs) being trained on TB and TB services in this project. The CCGs screened 54,991 individuals for COVID and TB, of whom 3,339 were already receiving TB treatment. The teams visited 11,306 households, 113% more than the objective required.. 2700 people received treatment adherence counselling, and 765 tuberculosis patients who were lost to treatment were located and linked back to care.

In addition, 95% of the 3,139 identified TB cases contacts were traced and received TB services.

**Conclusions:** By leveraging the capacity and reach of local CBOs and implementing rigorous tracking mechanisms, this approach can improve TB outcomes in resource-limited settings.

This study sheds light on the effectiveness of community-based interventions in addressing TB and provides insights into how to design and measure such interventions optimally.

### SOA06-846-15 Engaging local organisations for sustainability: Role of patient survivors in community TB care in Ethiopia

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**Background and challenges to implementation:** Ethiopia introduced the health extension program (HEP) executed by health extension workers (HEWs) to support community-based TB care (CBTC). However, HEW are handling 16 health packages and are usually overstretched. TB survivors are an underutilized resource to support CBTC.

**Intervention or response:** The USAID Eliminate TB Project collaborated with local organizations in Amhara, Oromia, and SNNP to improve CBTC and ease the burden on HEWs. Local organizations have trained and engaged TB survivors and established TB survivors' clubs.

These clubs supported community mobilization, presumptive TB case referral, TB treatment supporters, contact tracing, adherence counselling, and follow-up.

**Results/Impact:** From October 2021 to September 2022, local organizations established 80 TB survivors' clubs in 73 supported districts. They referred 33,595 presumptive TB cases from the community to health facilities; 11% of these were positive TB cases. They traced 13,106 contacts of 5,107 ex-TB index cases through retrospective contact tracing where 95% of these contacts were screened, and 86 TB cases were identified, making a TB case notification rate of 693 per 100,000 screened contacts.

Survivors also provided adherence support for 794 TB patients and provided TB preventive therapy for 3,968 eligible children, a coverage of 86%. The contribution of CBTC to total TB cases increased from 17% to 38% in supported districts.

**Conclusions:** The engagement of TB survivors in local organizations in CBTC resulted in a five-fold increase as compared to the national case notification rate of 132 per 100,000 people in the general population, and more than doubled the CBTC contribution. Building the capacity of local organizations and engaging TB patients' clubs in CBTC may help sustain community TB care.

## SOA06-847-15 'INSIGHT study' - uncovering insights into the lived experiences of caregivers of children suffering from drug-resistant TB

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**Background:** With paediatric drug-resistant tuberculosis (DR-TB), caregiver and child journey together. The emotional trauma of diagnosis, adverse effects and hospitalisation may impact the caregivers' wellbeing, affecting the child's outcome.

The study aimed to understand the experiences of caregivers of children with DR-TB at a high-burden facility in Nelson Mandela Bay, Eastern Cape, South Africa.

**Design/Methods:** This was a cross-sectional study involving in-depth interviews with adult caregivers of children (<15 years) diagnosed with DR-TB attending the selected site.

Interviews focused on the challenges and emotions of bringing their child to the hospital and their experiences in the community. Interviews were recorded, transcribed and then analysed using Atlas.ti. v 23.

**Results:** Three major themes were identified.

Theme 1: Experiences with the healthcare system – long waiting times, leaving children behind for hospitalisation was stressful and social grants are insufficient.

Theme 2: Experiences of caring for a child with DR-TB – limited education about TB, positive support from family and friends, and financial challenges.

Theme 3: Diverse experiences – difficulty accepting their child's diagnosis, difficulty separating from the child, challenges of adverse effects of medication, and nutritional deficits.

**Conclusions:** Separation from the child due to hospitalisation was difficult and financial challenges can impact the number of caregiver visits and treatment adherence. Strengthening of health education is needed while taking into account the emotional state of the caregiver at the time.

Paediatric DR-TB requires a holistic approach, where additional consideration is required for the caregiver for the overall wellbeing of the child. Department of Health should re-evaluate facility infrastructure to accommodate short or long-term caregiver visits.

Collaboration between departments of social development and health is imperative for the child's wellbeing. This includes proper nutrition through food parcels or increased social grants to ensure optimal child development, as well as recovery from DR-TB.

## SOA06-848-15 Immersive art-based strategies to enhance uptake of COVID-19 testing among adolescents

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**Background and challenges to implementation:** Evidence from epidemics suggests that stigma and stereotypes attached to diseases such as COVID-19 negatively affect testing uptake. IRD established a school-based COVID-19 surveillance testing model to understand the prevalence of COVID-19 via offering antigen-based Rapid Diagnostic Testing (RDT) to adolescents.

We compared the impact of using art-based strategies versus conventional orientation (verbal information dissemination) on willingness for testing uptake.

**Intervention or response:** Out of twenty three schools engaged, we piloted art-based strategies in eight schools in Karachi Pakistan, to deliver critical messages about infection control practices and tackle misinformation and stigma around COVID-19 testing and preventive measures.

These activities focused on sensitising participants to the importance of preventive practices through immersive theatre-based performances and eliminating misinformation through myth-busting and sharing circles.

Students shared the obstacles they encountered as a result of fear and discrimination around COVID-19 and discussed implementable strategies for prevention. Post-intervention, RDT testing was offered to encourage preventive practices amongst participants.

**Results/Impact:** Between July to October-2022, we engaged 9,660 students aged 11-17 years (mean age= 14.15 years) in 23 schools and offered COVID-19 testing to all participants. The overall testing uptake across all schools was 8.5%. In the schools where the conventional strategy was adopted, 9226 students were engaged, and we saw a 4.2% testing uptake. Among the asymptomatic students, 3.7% agreed to undertake the COVID-19 RDT test.

In the eight schools where the art-based strategies were piloted, 434 students were engaged, and 100% testing uptake was observed. Of these 434 students, 91% were asymptomatic, and 100% showed a willingness to undertake the COVID-19 RDT test.

Districts	Symptomatic				Asymptomatic				Total		
	Engaged	Testing Uptake	Engaged	Testing Uptake	Engaged	Testing Uptake	Engaged	Testing Uptake	Engaged	Testing Uptake	
	N	%	N	%	N	%	N	%	N	%	
Central	2	6.7	2	100	28	93.3	28	100	30	30	100
East	-	-	-	-	83	-	83	100	83	83	100
Korangi	-	-	-	-	34	-	34	100	34	34	100
Malir	32	30.8	32	100	72	69.2	72	100	104	104	100
South	5	2.7	5	100	178	97.3	178	100	183	183	100
<b>Total</b>	<b>39</b>	<b>9.0</b>	<b>39</b>	<b>100</b>	<b>395</b>	<b>91.0</b>	<b>395</b>	<b>100</b>	<b>434</b>	<b>434</b>	<b>100</b>

Table. COVID-19 associated symptom status & testing uptake amongst participants in 8 schools engaged through art-based strategies

Districts	Symptomatic				Asymptomatic				Total		
	Engaged		Testing Uptake		Engaged		Testing Uptake		Engaged	Testing Uptake	
	N	%	N	%	N	%	N	%	N	N	%
Central	40	1.4	2	5.0	2804	98.6	33	1.2	2844	35	1.2
East	1	0.3	-	-	335	99.7	0	-	336	-	-
Korangi	-	-	-	-	21	-	0	-	21	-	-
Malir	87	1.9	42	48.3	4442	98.1	132	3.0	4529	174	3.8
South	30	2.0	5	16.7	1466	98.0	175	11.9	1496	180	12.0
<b>Total</b>	<b>158</b>	<b>1.7</b>	<b>49</b>	<b>31.0</b>	<b>9068</b>	<b>98.3</b>	<b>340</b>	<b>3.7</b>	<b>9226</b>	<b>389</b>	<b>4.2</b>

Table. COVID-19 associated symptom status & testing uptake amongst participants in 15 schools engaged through conventional strategies.

**Conclusions:** The pilot results indicate that the use of art-based strategies can possibly improve the uptake of surveillance testing amongst school-age children in Low Middle-Income Countries. In-depth research must be conducted to understand the impact of using art-based strategies when integrating health surveillance activities within schools.

### SOA06-849-15 Engaging AYUSH health institutions in accelerating TB case-finding efforts in Himachal Pradesh, India

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**Background and challenges to implementation:** AYUSH, an acronym for Ayurveda, Yoga and Naturopathy, Unani, Siddha, Sowa-Rigpa and Homeopathy represents the alternative systems of medicine recognized by Government of India and is preferred by patients as the first point of care for seeking health services. Since 2019, Himachal state TB program in collaboration with AYUSH health institutions (AHIs) have collaborated to improve case finding activities across the State through the network of AHIs.

This cross-sectional study was conducted with the objective of assessing the impact of AHIs on TB case finding efforts in the state of Himachal Pradesh.

**Intervention or response:** Department of AYUSH was formally included in state and district level TB elimination committees with nodal officers identified at both levels since 2019.

Reporting mechanisms and TB presumptive referral linkages were established. 11 TB diagnostic centres and 1 NAAT laboratory was established in AHIs where infrastructure facility from allopathic system of medicine was unreachable due to hilly terrain. Cascade trainings

on TB program guidelines was conducted at different levels of AHIs. The impact on case finding was assessed since its collaboration from 2019 for the state.

**Results/Impact:** In 2022, a total 7473 presumptive TB cases were identified at AHI TB NAAT lab which was 2.3% of the total presumptive TB examination rate of the state. There were 206 (2.7%) TB cases who have been diagnosed through patient referrals from AHIs. This contributes to 1.3% of the total TB notification rate of the state. 584 new cases have been diagnosed in TB diagnostic centres established in AHIs since its collaboration with TB program.

**Conclusions:** Engagement with AYUSH department has shown significant impact on TB case finding in the state as a new partner for the program. Strong policy inducements which promote partnership with alternate system of medicine should be given additional weightage while formulating end-TB strategies in hard-to-reach areas.

### SOA06-850-15 National TB testing week in Nigeria – lessons on innovative national TB outreaches to bridge the gap in TB notifications

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**Background and challenges to implementation:** Nigeria is among the high TB burden countries globally. TB notification increased by 50% from 138,591 in 2020 to 207,785 TB cases in 2021. TB case notification in 2021 represent a treatment coverage of 44% with about 259,000 missing TB cases. The National TB testing week was conceptualized and conducted from 1<sup>st</sup> – 7<sup>th</sup> August 2022 to address the huge gap in case finding. This study describes the impact of the testing week and lessons learnt that could be scaled up to bridge the gap in TB notification in different settings.

**Intervention or response:** Guidance for conducting the testing week was developed and disseminated, High TB burden communities were identified using the programme data and hotspot mapping (EWORS and EP-CON). The existing resources were used to intensify massive clinical and radiological screening in communities. Specimen from identified presumptive-TB were sent for GeneXpert test and diagnosed cases placed on treatment.

**Results/Impact:** 67,838 clients were screened for TB in one week from 27 states, out of which 31% (21,182) of those screened were identified as presumptive TB,

90% (18,981) of the presumptive TB had Xpert MTB/RIF and 8% (1,582) were diagnosed with TB. Children constitute 6% (99) of the diagnosed TB cases. 5 states (Kebbi, Sokoto, Zamfara, Anambra, Osun) accounted for 67% (1,053) of TB cases. Lagos state which accounted for 28% (18,702) of clients screened for TB only contributed 5% of TB cases detected. Only 12 (44%) out of the 27 states notified at least one case of childhood-TB. **Conclusions:** TB cases (1,582 TB cases) diagnosed in one week demonstrated the potential yield from a targeted nationwide outreach, the yield is high in states with high malnutrition index and where focus was on hot spot areas, lack of focus on childhood-TB during outreaches is a missed opportunity for diagnosing childhood-TB cases. This intervention can be implemented in setting with huge case notification gap.

### **SOA06-851-15 Domestic resource mobilisation for TB intervention sustainability: experience of the USAID Afya Shirikishi Project**

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**Background and challenges to implementation:** The importance of advocacy for TB financial resources is a top priority for Country 2020-2025 NSPVI and ACSM strategy. USAID/Afya Shirikishi, under Amref worked with CHMTs advocate for TB in the selected councils, specifically from Domestic Resources Mobilization.

This abstract explores the TB financing trend and, highlights the importance of involving councils in DRM for TB, and outlines the necessary steps to continue TB budgetary advocacy to achieve the goal of ending TB by 2030.

**Intervention or response:** Between 2021 and 2022, The project organized budget analysis workshops to study the allocation and expenditure of TB interventions across all selected councils. Targeted Budget advocacy workshops were conducted to councilors, Member of Parliaments and district executive directors, empower and equip them with accurate TB information to include DRM funds that were absent from the comprehensive council healthcare plan.

The workshops aimed to encourage the decision-makers to allocate budgets for TB interventions since none were initially allocated.

**Results/Impact:** The selected councils committed (in writing) to allocate between 0.1% to 2% of Council Own Resources for TB in FY 2022/23 and 2023/24. Other councils made further commitment to specific interventions, (paying stipend to Community Health

Workers/Ex-TB experts and waivers for X-RAY costs for presumptive TB individuals who can't afford). Also promised to raise awareness and fight stigma on TB. Such commitments from councilors indicate continuity of support to TB interventions beyond the project.

**Conclusions:** To effectively mobilize domestic resources for TB, it is important to involve councilors, because they have shown a willingness to allocate resources as part of domestic resource mobilization for TB.

Involving districts has broader positive effects, including raising awareness and making TB a permanent agenda in Ward Development Committee forums. By involving these stakeholders, not only is funding increased but a culture of awareness and sustainable action towards addressing TB is cultivated.

### **SOA06-852-15 Using a people-centred participatory process to explore community and stakeholders' perceptions that enable research teams to design plans that meet community needs**

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**Background and challenges to implementation:** Clinical Research Sites (CRSs) conduct research with communities and the community is an important asset to the research. The community is a holistic organism that includes its experiences and perceptions, values, attitudes, behavior, emotions, ideas aspirations and meanings that are all interlinked. Community perceptions can influence whether community members will be willing to participate in research or support the research. It is for this reason that research teams need to have a deep understanding of the communities, with who we conduct our research with.

Before we start with actual recruitment activities, at the Aurum Klerksdorp CRS we engage in a people-centred participatory process with our communities and community stakeholders.

**Intervention or response:** We were intentional about placing people first, upholding people's human rights and learning from our communities. We started where the people are at and build from there, focusing on the strengths and assets.

The process is a bottom-up learning process and not a top-down blueprint approach. We respected the diversity and complexities of people and communities and took this into consideration when designing community engagement plans and recruitment plan which are designed in collaboration with our identified key stakeholders.

During this process our key stakeholders because of the trust that had been established felt comfortable to share their inputs on what strategies would work best in reaching out to the target community. Through the pro-

cess research teams facilitate the community to develop their own responses to the research which are tailored to the needs of the community.

**Results/Impact:** The co-created plans had a high degree fit where the research fits into the needs of the people and their lifestyles resulting a better recruitment and enrollment outcomes.

**Conclusions:** Adopting a people-centered participatory contributes to enhancing the quality and the relevance of the research and increases research literacy in communities.

## SOA07 TB control: Digital technology for data Collection and Screening for TB and LTBI

### SOA07-853-15 Digital screening tool: Revolutionising the TB recording and reporting system

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**Background and challenges to implementation:** Paper-based recording and reporting systems have certain drawbacks. It is time-consuming; data inaccuracy, inadequate storage space, document transportation, environmental problems, and data security are some common hindrances.

To eliminate these obstacles of paper-based screening and to accelerate tuberculosis (TB) detection and tracking at the field level, USAID's Alliance for Combating TB in Bangladesh (ACTB) Activity uses a digital tool and android application as a data collection tool for Intensified case finding (ICF) and Active case finding (ACF) and web-based dashboard for real-time monitoring.

**Intervention or response:** An android-based application was developed for field staff which consists of a set of screening questions based on NTP's algorithm. Upon filling the screening form, the application automatically gives results on whether the participant is TB presumptive or not. Moreover, records of test results, diagnosis, and treatment initiation are also available.

Data approval mechanism is in place, where information about individuals with TB are re-checked by supervisors for validity. Considering field-level internet connectivity, the application has offline data capture capability as well.

	Tertiary level hospital		Upazila level hospital and Community		Total
	Adult	Child	Adult	Child	
<b>Total Screened</b>	3,333,916	1,760,955	1,674,186	586,529	7,355,586
<b>Total Presumptive</b>	102,236 (3.06%)	49,658 (2.81%)	38,971 (2.32%)	8,318 (1.41%)	199,183 (2.70%)
<b>TB Diagnosed</b>	14,573 (14.25%)	3,690 (7.43%)	3,064 (7.86%)	461 (5.54%)	21,788 (10.93%)

Data Period: Tertiary Level Facility Screening (01<sup>st</sup> April 2021 – 28<sup>th</sup> February 2023) and Community ACF (01<sup>st</sup> January 2022 – 28<sup>th</sup> February 2023)

Table.

**Results/Impact:** From April 2021- February 2023, 7,355,586 individuals were digitally screened for TB. Screening efficiency also increased compared to paper-based screening. They can easily track and communicate with TB presumptive individuals when needed.

**Conclusions:** The burden on screeners is reduced and their daily screening rate is increased when using digital tools compared to paper-based screening. Additionally, all data is stored in the cloud, making it easily accessible and secure.

It is also difficult to track TB presumptive data with paper-based screening, whereas using digital tools enables trackability and provides up-to-date data in a user-friendly way. NTP can take the initiative to implement paperless screening nationwide.

### SOA07-854-15 Strengthening the recording and reporting system for nucleic-acid amplification test external quality assurance in TB laboratories in India

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**Background and challenges to implementation:** GeneXpert EQA was introduced in Feb'18 with a pilot of 41 public and private TB labs. It was scaled up in a phased manner to 202 sites in Jul'18, 664 site machines in May'19 and 1187 site machines for pan-country coverage in Aug'20. GeneXpert EQA continues to be implemented once a year.

With introduction of Truenat in diagnostic algorithm, its EQA was piloted in Aug'21 and introduced in phased manner in Feb'22 to 841 site machines.

As the NAAT EQA PT program evolved, its recording, reporting, and monitoring (R-R-M) system were improvised to meet the requirements of the rapidly expanding program.

**Intervention or response:** As the GeneXpert program scaled up, R-R-M system evolved from paper-based system to a web application [www.nateqa.in](http://www.nateqa.in) to address various challenges in R-R-M system such as:

- i. Managing a large number of sites;
- ii. Streamlining site enrolment;
- iii. Training a large number of site staff on R-R-M system;
- iv. Realtime tracking of PT panels during shipment and receipt;
- v. Confirming receipt of test results to sites;
- vi. Monitoring timeliness and completeness of PT results submission;
- vii. Data compilation, collation and analysis of large datasets;
- viii. Submitting PT report to individual sites and relevant stakeholders.

Further, this application was customized as per the requirement for Truenat EQA.

**Results/Impact:** The evolution of R-R-M system from paper to Excel to google sheet to web application is shown in Figure 1.

This open-source web application helped streamline site enrolment, panel tracks, results submission, monitoring and analysis of PT results, and auto report generation. It was adapted to include Truenat EQA. In 2022, all NAAT sites were enrolled and successfully submitted the EQA results.

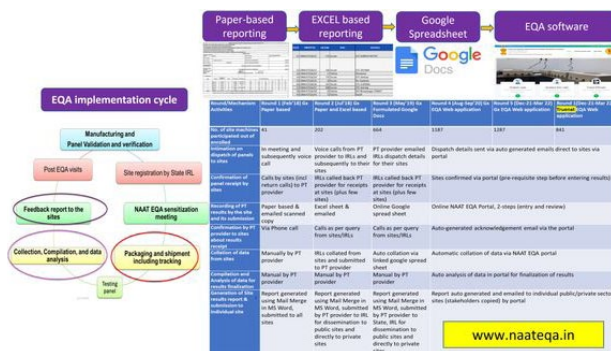


Figure 1.

**Conclusions:** NAAT EQA portal has streamlined EQA PT implementation and resolved operational challenges. It can be adapted for PT program of other countries as required.

## SOA07-855-15 Improving TB data quality with interoperability and data exchange in Nigeria

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**Background and challenges to implementation:** Stakeholders and implementing partners generate data and reports using various data platforms and algorithms, which frequently has impact on data quality and programmatic actions. This study demonstrates the relevance of data interoperability, exchange, harmonization, analysis and report performance on the TB LON project and USAID contribution to national TB case notification.

**Intervention or response:** Across the two implementing partners, complex excel data systems were used to generate high-frequency weekly performance report and monthly TB cascade data. The limitation of excel tool (collaborative working, file size, and limited use for visualization) and inability to customize for tracking data quality attributes such as timeliness and data completeness, necessitate transition from excel-based system to Automated Partners Progress Report (APPR) platform. TB DIAH in collaboration with the IPs re-designed the USAID APPR to serve as central TB database while Application Programming Interface (APIs) were established to harness data from excel-based platforms. Reviews, harmonization, and standardization of reporting templates, indicators, and data elements were conducted. Dashboard of interactive custom charts and other visualizations were also developed.

**Results/Impact:** The IPs share reports directly on APPR. Data entry updates were not necessary shared as attachments on excel and custom interactive charts were developed by IPs while previously reported excel-based data were extracted to the APPR. This availed opportunity to showcase cascade analysis of the different interventions implemented by the TB LON projects, the priority indicators contained in the USAID performance-based M&E framework, and demonstration of the contribution of the LON project to national TB notification. Between April and September 2022, reporting rate increased from 85% to 100%, completion rate moved from 90% to 100% and timeliness increased from 78% to 85%.

**Conclusions:** The unification of data platforms through health information exchange is helpful in standardizing data systems, improving data quality, facilitating data reporting, and frequent and regular interactions among stakeholders.

## SOA07-856-15 Real-time digital management of large, simultaneous, multi-lingual, community-based TB surveys in India

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**Background and challenges to implementation:** India's National TB Elimination Programme (NTEP) developed a novel methodology for district and State level (sub-national) estimation of TB incidence by external agencies. The design included, multiple district level community-based surveys.

Implementation challenges in this design were multiple languages, dialects, hundreds of districts requiring surveys, large number of surveyors, planning and training of surveyors, coordination between multiple agencies at different levels.

**Intervention or response:** To overcome these implementation challenges, WHO Country Office for India developed an online, generic platform for overall planning, execution and monitoring of these surveys. The application had android mobile version for field data collection and web version for district, state and national level users of all implementing agencies.

Application modules included mapping of state, district, survey teams and clusters with surveyors mobile, bank account details of surveyors and nodal officer for payment management and attendance and claim submission.

Multiple language management functionality, participant interview details, details of deaths, eligibility for sputum sample collection, transport and testing results were included. Special functionality was added for replacement of mobile devices or surveyors in case of eventuality.

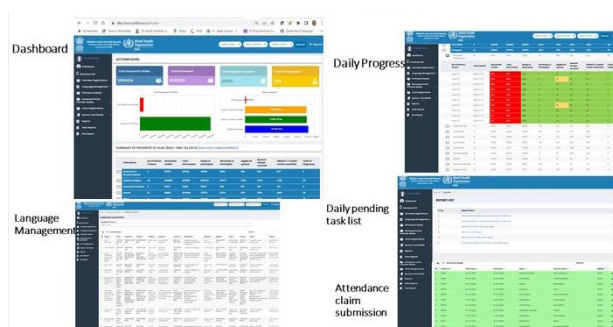


Figure. Sample of online survey platform.

**Results/Impact:** Using this digital platform 73, 214 and 337 districts were covered in three rounds respectively, covering total of 1.2 million, 4.6 million & 8.9 million participants by 11350 surveyors. Monitoring was facilitated by dashboard showing real-time summary statistics of each survey team, district-wise i households visited, registered, individuals enrolled, consented and interviewed with full interview details, eligibility for sputum examination and molecular tests results. Pending tasks list for each activity helped in follow-up of field activities and overall monitoring. Overall, total cost per record for data management was less than 0.02 US dollars.

**Conclusions:** It is feasible to develop and deploy generic, customizable, low-cost digital platform for large scale, multiple, simultaneous community based TB surveys. This can be replicated in other countries with similar settings.

## SOA07-857-15 Digitising TB referrals by private community pharmacies: a gamechanger for TB control in Myanmar

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**Background and challenges to implementation:** In Myanmar, pharmacies are often the primary access point for healthcare. Population Services International Myanmar and Sun Community Health work with a large pharmacy network for TB case screening and referral activity. In recent years, COVID-19 pandemic and political unrest caused reduced referral rates, TB diagnosis, and treatment enrolment. Community Mobilizers (CM) who support pharmacies with patient follow-up, face challenges with traditional paper-based referral approaches due to delayed referral information from pharmacies, resulting in lost referrals.

**Intervention or response:** To address this challenge, in July 2022, PSI developed a digital Pharma TB Referral and Follow-up System utilizing a social media Viber chatbot for pharmacies, linked to a DHIS2 mobile application for CM and real-time data monitoring dashboards. Once the pharmacy refers presumptive TB case via the chatbot, the respective CM is automatically notified through SMS and mobile application to support the case for confirmatory diagnosis and treatment. As of December 2022, the system was introduced to 469 pharmacies in Bago East and West regions and their 19 CMs. **Results/Impact:** From July-December 2022, the newly introduced digital solutions were used to refer 1,630 presumptive TB cases by 268 pharmacies, with 99% of



them being contacted by CM for referral facilitation. About 32% of presumptive cases have been diagnosed and enrolled as TB patients. Following the introduction of the social media chatbot, there was no significant change among active pharmacies in referrals. However, about 32% of 118 previously inactive pharmacies started referring cases, contributing about 7% of the total referrals.

**Conclusions:** This innovative digital intervention enabled more pharmacies to make referrals, leading to improved and faster facilitation by CMs. The findings highlight the digital system's potential for TB control in pharmacies and private sector providers, and adoption in other low-resource settings. Thus, PSI intends to expand it to pharmacies in other high TB burden regions of Myanmar.

### SOA07-858-15 TB screening and yield among health workers in Ethiopia: Findings from routine programme interventions

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**Background:** Health workers are at higher risk of TB because of their occupational exposure. There should be a system to ensure that health workers are regularly screened for TB for early identification and treatment. Ensuring that health workers are free from TB also protects the patients they serve.

**Design/Methods:** The USAID Eliminate TB Project supports the Ethiopia National TB Program in training and development of guidelines and standard operating procedures. The project also provides technical support to health workers to institute effective TB infection control interventions, including regular screening of health workers. We used a standard-of-care-based supervisory tool to collect TB screening data. Data were captured from an average of 972 health facilities from October 2020 to September 2022 (October–September 2021 is project year 1 of implementation and October 2021–September 2022 is year 2).

**Results:** A total of 9,869 and 21,735 health workers were screened in 844 and 1,101 health facilities during year 1 and year 2, respectively. The burden of TB per 100,000 health workers was 385 in year 1 and 267 in year 2, which showed a three-fold and two-fold increase compared to the respective national TB estimates of 132 and 119, re-

spectively. The number needed to find a TB case among health care providers were 260 and 275 in year 1 and 2, respectively.

Indicators	Year 1	Year 2
# of health facilities	844	1,101
# of health workers screened	9,869	21,735
# of staff diagnosed with drug-susceptible TB	34	54
# of staff diagnosed with drug-resistant TB	4	4
# of all TB cases diagnosed	38	58
TB case notification rate/100,000	385	267
Number needed to screen	260	375

Table: Performance of health workers TB screening and yield, October 2020 to September 2022

**Conclusions:** There is a significantly higher burden of TB among health workers in Ethiopia, which needs continuous attention. There was a decline in TB burden from year 1 to year 2, which could be attributed to interventions.

### SOA07-859-15 Universal test and treat to end TB: The screening cascade

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**Background:** Ending TB in high burden countries may require widespread treatment of latent TB infection (LTBI). We are currently conducting a cluster randomized controlled trial of community-wide active cases finding and treatment for LTBI in Viet Nam.

**Design/Methods:** A tuberculin skin test (TST) survey was conducted among all consenting persons aged 5 years and over. Those with a positive TST were invited to undertake further screening including providing spontaneously expectorated sputum for testing by Xpert Ultra and having a chest X-ray (CXR). Those who were Xpert positive or had a CXR consistent with active TB were requested to produce two further sputums for mycobacterial culture. Active TB was defined as bacteriologically confirmed TB (Xpert and/or culture positive). Those who were TST positive and did not have active TB were assessed for eligibility for treatment with isoniazid and rifampentine once weekly for twelve weeks (3HP).

**Results:** So far, we have screened 28 clusters in whom the eligible population was 34,770. Of these, 23,803 (68.5%) agreed to be screened by TST and 8077 participants (33.4% of those tested) had a positive TST. 647 participants (2.71%) reported TB symptoms.

Among 9380 people eligible for further screening, 7024 (74.9%) had a CXR and 8335 (88.9%) provided sputum for Xpert testing. We identified 92 participants with active TB (prevalence 386/100,000). 5724 participants (70.1% of those with LTBI) have been recommended for treatment with 3HP. A further 767 (9.5%) are waiting to resolve medical issues prior commencing treatment for LTBI.

**Conclusions:** These early results show that recruitment for a program of universal test and treatment for latent TB infection is feasible. However, there is room for further improvement in the uptake of initial screening.

### SOA07-860-15 Prevalence of latent TB infection in Ukrainian refugees in Germany

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**Background:** The war against Ukraine has led to large inner European migration movements. In Germany, over 1 million refugees from Ukraine were registered in 2022. One of the infectious diseases with a higher incidence in Ukraine than in Germany is tuberculosis (TB), which is important to consider for public health planning. We aimed to assess the prevalence of latent TB infection (LTBI) in this population.

**Design/Methods:** We performed a population-specific cross-sectional study of Ukrainian refugees in reception centers and other points of contact in Germany. We aimed to include Ukrainian refugees as randomly as possible, recruited from September, 1st to December, 31st 2022 in 12 centers in Germany. We performed TB-specific Interferon Gamma Release Assays (IGRAs, n=1796), and calculated and presented crude proportions with 95% confidence intervals. We performed a targeted literature and grey report review to compare our results to existing estimates of the Ukrainian population.

**Results:** 392 children and adolescents (54.6% female, median age 11.7), and 1404 adults (78% female, median age 41) were included. Overall in adults, IGRAs were positive in 13.1% (95%, 11.4-15), and in children in 1.7% (95%, 0.8-3.6). We found the lowest positivity in the age group of 0-12 years (0.48%, n=206) and the

highest in >65 (32.92%, n=82), with positivity increasing with older age. In the targeted literature and grey reports review, we did not find relevant comparison data due to a lack of investigations into latent tuberculosis in Ukraine.

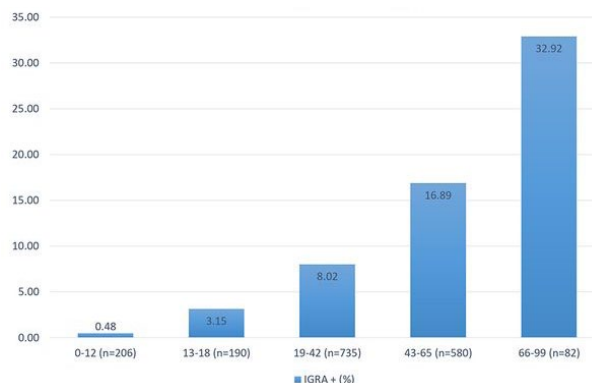


Figure. IGRA + in % different age groups of Ukrainian refugees in Germany.

**Conclusions:** Overall in the refugee population from Ukraine – in particular in the older people - presenting in Germany we found a public health relevant prevalence of LTBI. Public health guidelines should address LTBI screening, testing, and treatment algorithms for both adult and pediatric populations also in Germany. Cross-border initiatives across Europe able to treat both active and latent TB in this highly mobile population should be established.

### SOA07-861-15 Management of TB and LTBI follow-up after the 2023 earthquakes in Turkey

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**Background and challenges to implementation:** In 2012, a real-time electronic recording and reporting system was implemented in Turkey for tuberculosis (TB) patients and latent tuberculosis infection (LTBI) cases. In 2018, this national system was updated and all TB Dispensary (TBD) healthcare workers are able to monitor and evaluate any person who registered to a TBD all over the country. Turkish identification numbers (both

native and foreign citizens) or passport numbers are used for registration. Since 2017, 10 volunteer medical doctors with experience in TBD and TB control studies have been assigned by the Ministry of Health TB Department (MoHTBD) as 'field consultants' to support all TB units in 81 provinces of Turkey.

**Intervention or response:** After devastating earthquakes, the loss of both TB healthcare workers and facilities has forced us to find new solutions. MoHTBD staff and 7 field consultants organized to reach 11 affected provinces. First, MoHTBD shared the identification numbers and data of registered patients with this team. A checklist was made for the management of patient follow-up. All patients were called by phone (phone numbers of the individual/family member and family physician) registered in their files. Checklist details are listed separately. Although patients were surprised to receive calls from unknown TB personnel, volunteer team members were very happy to reach them live and direct their TB treatment. Then, MoHTBD staff organized to search and refer people for LTBI in the same way.

	907 (both native and foreign)
No. of TB cases whose situation learned after telephone calls	Alive: 903 Dead: 3
Still unable to reach, ongoing call (04.12.2023)	1
Cases who left the region- staying at another location	213
<b>Number of registered LTBI cases who were ongoing chemoprophylaxis during the earthquakes in 3 provinces (most damaged provinces where we focused first)</b>	
	694 (both native and foreign)
No. of LTBI cases whose situation learned after telephone calls	Alive: 532 Dead: 4
Still unable to reach, ongoing calls (04.12.2023)	158
Cases who left the region- staying at another location	148

*Number of registered TB cases who were ongoing treatment during the earthquakes in 11 provinces.*

**Results/Impact:** Recording with identification or passport numbers enabled us to access TB and LTBI patients' data quickly, monitor their treatment as soon as possible, to connect/ collaborate with local TBDs for procuring drug regimens.

**Conclusions:** Access to patients' data makes it convenient to manage treatment promptly, not only TB but LTBI at the same time. It can be managed at local, national, also international levels. Thanks to Dr. Elif Dağlı for mentoring.

## SOA08 TPT - how far are we?

### SOA08-862-15 TB preventive treatment: Global trends in access and completion among risk populations

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**Background and challenges to implementation:** About one quarter of the world's population has been infected with tuberculosis (TB) bacilli and 5-10% of them will develop TB disease. Tuberculosis preventive treatment (TPT) is a scalable intervention that can stop progression to disease and help reduce global TB incidence to the levels envisaged by the End TB Strategy.

The WHO End TB targets aims to cover  $\geq 90\%$  eligible contacts and people with HIV with TPT by 2025. Achieving this will require coordinated activities to identify and treat eligible populations safely.

**Intervention or response:** We present recent trends in TPT coverage using data from annual country TB reporting to the World Health Organization (WHO)

**Results/Impact:** In 2021, 2.8 million people with HIV started TPT, up from 960,000 in 2017. About 1.3 million children aged  $< 5$  years were estimated to be contacts of bacteriologically confirmed pulmonary TB patients in 2021. In 2021, 125 countries reported  $> 420,000$  contacts aged  $< 5$  years starting TPT, an increase of  $> 40\%$  from 2017, while 100 countries reported  $> 330,000$  contacts aged  $\geq 5$  years starting TPT, a threefold increase from 2017.

Median TPT completion was 87% (IQR, 64–96%) in people with HIV and 86% (IQR, 68–94%) in contacts starting TPT in 2020, with wide variation between countries.

**Conclusions:** If current access stays the same, the WHO End TB strategy targets for TPT in contacts and people living with HIV will not be reached by 2025. Efforts to provide more people at risk with TPT need to be matched with continued price reductions of rifampentine-based regimens and more resources.

Integrating active TB case finding with TPT provision can create synergies in many situations where risk groups are reached. Safer treatments and new scalable tests of TB infection can facilitate the expansion of TPT and maximize its benefit in future.

### SOA08-863-15 Effectiveness of latent TB infection treatment among residents in long-term care facilities, Taiwan

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**Background:** More than 60% of Tuberculosis(TB) patients in Taiwan were age $\geq$  65 years with highest age-specific incidence of 111.3 per 100,000 population in 2021. In long-term care facilities(LTCFs), the risk of TB transmission would be higher than the elderly in communities. Testing and treatment of LTBI had been conducted in voluntary participating LTCFs since 2018. The aim of our study is to evaluate the effectiveness of Tuberculosis preventive therapy(TPT) in LTCFs.

**Design/Methods:** We conducted a retrospective cohort study to enroll health care workers(HCWs) and residents in LTCFs from 2018 to 2021. We used IGRA testing and the TPT regimen including 9H, 4R, 3HR and 3HP were provided for free among those with positive/indefinite IGRA results. We collected the demographic characteristics and BMI, dialysis, having/ever smoking history of participants. Logistic regression model was applied for factors associated with non-completion of TPT. Furthermore, we used Cox proportional hazard model to evaluate the effectiveness of TPT.

**Results:** A total of 4742 participants with positive/indefinite IGRA results was enrolled. After excluding HCWs and those found to be active TB within 100 days after the date of IGRA testing, 3772 residents with median age of 79.5 years(IQR 69.6-86.3) were eligible for analysis. The TPT coverage was 74.3%. The majority of initial chosen regimen was 9H(60.5%), following by 3HP(27.3%), 3HR(8.2%) and 4R(4%). Factors associated with non-completion of TPT included age(aOR=1.02, 1.01-1.03), IGRA of mitogen-nil<0.5(aOR=1.85, 1.30-2.62), and regimen of 3HR(aOR=2.39, 1.63-3.51) and 9H(aOR=2.38, 1.85-3.07). We followed the eligible participants till Oct. 10, 2022 and identified 25 incident active TB cases with incidence rate of 321.4/100,000. Those without TPT were more likely to develop active TB(aHR=4.96, 2.21-11.12) than those receiving TPT after adjusting age and gender (Table 1).

	Number of active TB patients	person-year	incidence rate per 100,000	Univariate analysis HR (95% CI)	Multivariate analysis aHR (95% CI)
Men	18	4102.9	438.7	2.33 (0.97-5.57)	2.95 (1.23-7.11)
Women	7	3674.6	190.5	1	1
Age (years)				1.06 (1.02-1.11)	1.06 (1.02-1.10)
TPT, Yes	10	6143.5	162.8	1	1
TPT, No	15	1634	918	5.65 (2.54-12.58)	4.96 (2.21-11.12)

Abbreviations: HR, hazard ratio; aHR, adjusted hazard ratio; TPT, tuberculosis preventive therapy

Table 1. Risk of active TB among residents eligible for TPT in long-term Care Facilities (n=3772).

**Conclusions:** The regimen of 9H and 3HR were associated with non-completion of TPT which significantly reduced risk of TB and the subsequent transmission in LTCFs.

### SOA08-864-15 Situational analysis of TB preventive treatment coverage among under-fives in Uttar Pradesh, India

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**Background and challenges to implementation:** India has the highest estimated burden of tuberculosis infection globally. Prevention of tuberculosis (TB) disease by treating TB infection in susceptible population is one of the core pillars of India's end-TB strategy. TB preventive treatment (TPT) guidelines recommend TB screening of household contacts (HHC) and initiation of preventive treatment to eligible contacts.

This observational study aims to assess the TPT cascade interventions targeting the household contacts below 5 years age from 2019-2022 in Uttar Pradesh, India.

**Intervention or response:** TPT cascade information of under five years children who were contacts of bacteriologically confirmed drug sensitive pulmonary TB cases from year 2019 to 2022 was extracted from the country's digital TB surveillance platform (Ni-kshay).

Key informant interviews (KII) were conducted to understand the strategies to increase the TPT coverage. Quantitative data was analysed using SPSS software. Transcripts of the KII were analysed with software R version 4.2.3 with package "RQDA" using thematic content analysis.

**Results/Impact:** In Uttar Pradesh, 621,588 bacteriological confirmed cases were diagnosed from 2019-2022. The number of household contacts eligible for TB screening were 1,963,903 of which 90.9% were screened. Observed contact to case ratio was 3.15:1. Among the screened individuals, 0.44% children below 5-years of age had TB. The proportion of eligible children given TPT showed a progressive increase in coverage from 17.6% in 2019 to 65% in 2022. Qualitative assessment showed that partnership strategies, uninterrupted procurement and supply of regimens for TPT, understanding the patient's perception of threat towards getting TB, along with continuous supportive supervision from the program were the key context specific strategies which enabled this scale-up.

**Conclusions:** The study recommends effective implementation of contextualized strategies - supply of TPT regimens, testing facilities and strategic interventions to

improve uptake and outcomes of TPT -to expand TPT coverage is imperative to achieve end-TB goals in high burden settings.

### SOA08-865-15 Barriers and facilitators to TB preventive treatment initiation and completion among people living with HIV in three sub-Saharan African countries

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**Background:** TB preventive treatment (TPT) is effective in preventing tuberculosis among people living with HIV (PLHIV). Patient experiences and preferences contribute to optimizing the delivery cascade for TPT among PLHIV. We describe barriers and facilitators in initiating 3HP and INH in Ethiopia, South Africa, and Zimbabwe.

**Design/Methods:** We conducted in-depth interviews with adult PLHIV who had either initiated, completed, discontinued or refused to initiate TPT in South Africa, Zimbabwe, and Ethiopia. Participants were attending routine HIV care in six healthcare facilities and interviewed using a study-designed interview guide.

The guide explored five categories: TB and TPT knowledge, reasons for TPT initiation, experiences of taking TPT and ART, and views on the EvriMED device (an electronic pill box to monitor adherence).

Data were analysed using a coding scheme based on the informational-behavioural skills model and implementation outcomes framework to identify barriers and facilitators across participating countries.

**Results:** We conducted 141 in-depth interviews: Ethiopia n=45 South Africa n=45; and Zimbabwe n=51. Of the 141 participants, 28 were still on TPT, 66 completed, 22 discontinued and 25 refused to initiate TPT. The majority were female (61%, 86/140) with an average of 36 years.

Facilitators of initiation and completion were prior TB experiences, fear of TB, perceived benefits of TPT, TPT education, and family situation.

Barriers to initiation and completion were side effects, concerns about drug-drug interactions, high pill burden, negative experiences with healthcare workers, and prior TB treatment experiences. Participants noted the adoption of adherence strategies such as reminders as use-

ful for the treatment process. Perceived and experienced stigma linked with initiating ART and TPT hindered adherence. The EvriMED device was perceived as useful and safe.

**Conclusions:** Participants identified multiple barriers and facilitators that could be modified through clinic-level and community-level interventions. Such modification may increase the uptake and completion of TPT.

### SOA08-866-15 Barriers and facilitators to contact investigation and TB preventive treatment in Bangladesh: A mixed-methods study

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**Background and challenges to implementation:** Tuberculosis is a major public health concern in Bangladesh. Intensifying tuberculosis active screening, contact investigation, and TPT strategies are recommended to ensure early diagnosis among household contacts (HHCs) of smear-positive TB patients and reduce the burden of TB infection.

This study explored the barriers and facilitators for household contact tracing of index TB cases and PT initiatives in Bangladesh.

**Intervention or response:** A community-based, cross-sectional, mixed-methods study was conducted in selected urban and rural settings between September 2020 - December 2020.

Data was collected through a HH survey among randomly selected 602 index TB patients and 602 HHs contacts of index TB patients (one matching contact from the same HH of each TB patient).

The qualitative data was collected through 36 in-depth interviews (IDIs); 12 focus group discussions (FGDs) with 98 index TB patients, HH contacts, and service providers; and 14 key informant interviews (KIIs) with policymakers, and program implementers.

**Results/Impact:** This study found a low level of contact tracing among eligible HH contacts of index TB patients. The quantitative data highlighted, of 602 index TB cases HH contact tracing was done only 49.5%. Of these (eligible HH contacts 1,247), fifty-six (51.9%) of 108 under five children for whom HH contact investigation was conducted were enrolled for latent TB treatment with INH.

Consistent with quantitative findings the qualitative data further confirmed, there is low household contact tracing and IPT, and also explored a variety of barriers and facilitators with a wide spectrum of factors related

to the health system, health workers, index TB cases and HHCs and socio-economic and cultural factors that affected TB contact tracing of index TB cases.

**Conclusions:** This study provides important new information for understanding the dynamics of contact tracing and TPT initiatives in Bangladesh and suggests that TPT should be a key initiative for ending TB efforts in Bangladesh.

### SOA08-867-15 Assessing eligibility and initiation for TB preventive treatment among people living with HIV in Malawi, 2022

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**Background and challenges to implementation:** The World Health Organization and President's Emergency Plan for AIDS Relief (PEPFAR) recommend tuberculosis (TB) preventive treatment (TPT) for people living with HIV (PLHIV) without contraindications. Malawi began offering TPT to PLHIV in 2017, but coverage remains low. Based on routine program data alone, it is unclear whether TPT ineligibility or other factors influence low uptake. We undertook a continuous quality improvement (CQI) project to catalyze implementation and monitoring of TPT eligibility, uptake, and adherence among PLHIV.

**Intervention or response:** Nine high-volume PEPFAR-supported facilities serving  $\geq 2,500$  PLHIV each, with an average TPT initiation rate of 60%, were selected for the TPT CQI. Providers were re-oriented on TPT policy and updated M&E tools to enhance TPT eligibility screening and initiation.

Following site activation in October 2022, we conducted biweekly data review meetings to monitor progress and identify gaps in the TB prevention cascade. We report preliminary results from October–December 2022 for new antiretroviral therapy (ART) clients, including TB screening, and TPT eligibility and initiation.

**Results/Impact:** During the period assessed, 1,484 clients initiated ART (Figure 1). All were screened for TB, 209 (14%) screened positive for TB and were referred for diagnostic processes. ART clients who screened negative and those in whom TB was ruled out were assessed for TPT eligibility. 384 (26%) clients were ineligible for TPT, 192 (50%) of whom were due to pregnancy or <3

months postpartum, and 149 (39%) due to active TB disease. Among the 1,100 who were eligible, 99% initiated TPT. The overall initiation rate among new ART clients was 73%.

**Conclusions:** Preliminary findings from TPT CQI suggest TPT eligibility is an important component of the TB prevention cascade. Pregnancy and <3 months postpartum status were substantial drivers of TPT ineligibility. Despite being a contraindication in Malawi, improved TPT coverage in this TB-susceptible population would be crucial to consider.

### SOA08-868-15 Characteristics of adults with TB infections who accepted and rejected TB preventive treatment: a baseline data analysis from a prospective cohort study in Cambodia

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**Background:** Tuberculosis (TB) preventive treatment (TPT) effectively prevents the progression from TB infection to TB disease. Although the efforts from the national TB program, TPT rejection has still been reported. This study explores the characteristics of adults with TB infections who accepted and rejected TPT in Cambodia.

**Design/Methods:** We analysed data collected in 2022 in the baseline survey of a longitudinal cohort study in 10 operational districts. Participants included adults aged  $\geq 18$  years old living in the same house, neighbours, and other households within 100 metres radius of people with bacteriologically confirmed TB.

We evaluated TPT eligibility using the latent TB infection guideline from the national TB programme. We collected sociodemographic and behavioural characteristics, TB exposure and contact history, and TPT knowledge, attitude, practices, and acceptance status

using Research Electronic Data Capture (REDCap). Chi-square or Fisher's exact test was used for categorical variables and Student's *t*-test for continuous variables.

**Results:** Among 511 TPT-eligible participants, 20 (3.9%) refused it. Compared to those who accepted TPT, those who refused it were significantly more likely to live farther from health facilities (4.6 km vs. 2.9 km,  $p = 0.006$ ) and spend longer traveling to the nearest health facility (11.4 min vs. 8.1 min,  $p = 0.009$ ).

A significantly lower proportion of participants who refused TPT knew that cough (60% vs. 87.0%,  $p = 0.003$ ) and fever (0.0% vs. 39.7%,  $p < 0.001$ ) are TB symptoms.

**Conclusions:** Accessibility to health facilities and TB knowledge may affect the decision on TPT acceptance among TB close contacts in Cambodia. Alternative mechanisms for TPT implementation, such as using village health support groups to provide and monitor TPT, especially for those living far from health facilities, could be considered. In the meantime, improving TB knowledge in the community should also be prioritized.

### SOA08-869-15 Teleconsultation to mitigate challenges in medical evaluation during TB preventive therapy provision: Initiatives from India

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**Background and challenges to implementation:** Guidelines on Programmatic Management of TB preventive Treatment (PMTPT) in India documents that there is significant loss of household contacts (HHCs) along the TB infection (TBI) care cascade. Only 18.8% completed the entire cascade which included symptom screening, medical evaluation/diagnosis, TPT initiation, and follow-up. Major drop out of 57% was noticed during the stage of medical evaluation/diagnosis. Teleconsultation was introduced to mitigate this challenge.

**Intervention or response:** TB-Alert India, in partnership with FIND-India with support of National Tuberculosis Elimination Program (NTEP) under Joint Effort for Elimination of Tuberculosis (JEET) rolled out TBI intervention from September'21 onwards in five districts (Amritsar, Jalandhar, Ludhiana, Mohali and Patiala) of Punjab, India.

Project recruited TBI coordinators to visit HHCs of pulmonary TB (PTB) patients to complete the TBI cascade. Medical evaluations were facilitated by TBI coordinators through tele/video-consultation for the HHCs who

were unable to reach health facilities owing to multiple reasons. Project team identified a group of public and private providers willing to support the cause.

**Results/Impact:** From September'21 to June'22, 13,306 PTB were notified of whom 11,555(87%) were contacted, 9,043 (68%) consented for visit, and 7,591(57%) of them were visited. Coordinators identified 37,803 contacts in these households of which 30,528 (81%) underwent medical evaluation though tele/video-consultation. Of these, 18,915 (50%) were provided TPT and 14,971(40%) successfully completed treatment. Project demonstrated higher treatment completion rate (40%) as compared to global studies (18.8%).

More than 80% of HHCs preferred tele/video consultation as this helped them to receive care from the comfort of their home, without incurring catastrophic cost, thus improving compliance.

**Conclusions:** Initial outcome of tele/video-consultation strategy is promising in mitigating the apprehension of the HHCs to visit health facilities. Addition of new providers to the group will be critical while scaling up the process

### SOA08-870-15 Rifampicin and isoniazid (3HR) and isoniazid (6H) uptake: A comparative study

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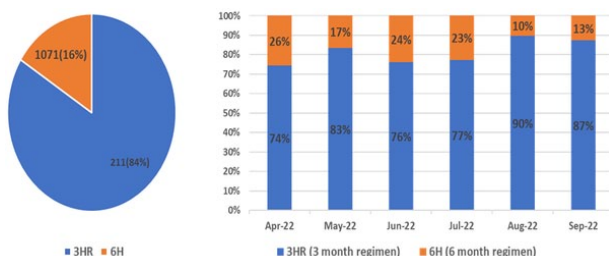
**Background:** Isoniazid (6H) (IPT) has been in use over the years, and it is taken daily for 6 months for TB prevention treatment among contacts of TB patients. However, there has been enormous challenges to the uptake of 6H due to the duration needed for completion, as against the relatively new of 3HR given for a duration of 3 months. This study compares 3HR and 6H uptake among contacts of TB patients in Lagos, Nigeria.

**Design/Methods:** A comparative study using data on TPT uptake from 10 LGAs supported by USAID TB LON 3, where 3HR prophylaxis (3 months regimen) available, was done against 6H prophylaxis in another 10 LGAs between April 2022 to September 2022.

**Results:** A total of 1,282 contacts of index TB cases received TPT from the 20 LGAs in Lagos State from April 2022 to September 2022 using project data. 1071 (87%) contacts received TPT (3HR) in 10 LGAs supported by USAID TB LON 3 project where 3HR was implemented, while 211 (13%) contacts received TPT (6H) in 10

LGAs supported by another IP. A further breakdown shows increased uptake of TPT (3HR) over time; April 74, May 139, June 171, July 211, August 277, and September 373 contact, (see graph for percentage distribution) across the 6 months more patients accepted the 3 months regimen when compared to the 6 months regimen (see graph).

Contacts of index TB patients given the option of 3HR (3 months regimen) are more likely to accept TPT prophylaxis (84%;  $P = <0.002$ ).



**Conclusions:** Comparative study above shows increased uptake of TPT in the 10 LGAs where 3HR was implemented by USAID TB LON 3 Project, when compared with the 10 LGAs 6H was implemented by other IP. To increase TPT uptake 3HR should be made available and much shorter regimen if provided will increase uptake TPT.

## SOA09 COVID-19: Is it really over?

### SOA09-871-15 Context analysis and intervention design to improve health and well-being of people after COVID-19 in South Africa

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**Background:** Most Covid-19 patients recover completely and without sequelae, but many continue to suffer Covid-19 symptoms months after the acute infection, impacting their daily activities and quality of life. This situation analysis aimed to explore post-Covid-19 rehabilitation by assessing the needs, preferences, challenges and existing rehabilitation interventions and strategies for patients post-Covid-19 in Johannesburg, South Africa.

The findings guided the design of a context-specific group intervention for patients post-Covid-19.

**Design/Methods:** We performed a mixed-methods study between December 2022-March 2023. Questionnaires and focus-group discussions (FGDs) with patients and healthcare providers affected post-Covid-19, and healthcare provider interviews on post-Covid-19 management and services were conducted. Analysis was performed by descriptive statistics and thematic analysis.

**Results:** Healthcare providers, including medical doctors, physiotherapists, occupational therapists, dieticians, and psychologists completed 13 interviews; 3 FGDs (total 20 people) and 60 questionnaires were completed. We established that most patients did not receive rehabilitation or support after SARS-CoV-2 infection, and about half of these patients reported that they would have liked to receive rehabilitation, including physiotherapy, psychological support, and education. For those who did receive rehabilitation, it occurred during the acute disease period, and most did not extend beyond one month. Almost all patients (53/60) reported that they would find a support group helpful in assisting their post-Covid-19 care. Healthcare workers who were interviewed recognized that Covid-19 care is focused on the acute disease and guidelines for the management of post-Covid-19 consequences are limited. The need to focus on mental healthcare and support was stressed both for patients and for healthcare workers. Based on this, we have developed an 8-week group program, which includes exercises, counselling, group discussions and home-assignments. It will be implemented and assessed June-December 2023.

**Background and challenges to implementation:** Most Covid-19 patients recover completely and without sequelae, but many continue to suffer Covid-19 symptoms months after the acute infection, impacting their daily activities and quality of life. This situation analysis aimed to explore post-Covid-19 rehabilitation by assessing the needs, preferences, challenges and existing rehabilitation interventions and strategies for patients post-Covid-19 in Johannesburg, South Africa. The findings guided the design of a context-specific group intervention for patients post-Covid-19.

**Intervention or response:** We performed a mixed-methods study between December 2022-March 2023. Questionnaires and focus-group discussions (FGDs) with patients and healthcare providers affected post-Covid-19, and healthcare provider interviews on post-Covid-19 management and services were conducted. Analysis was performed by descriptive statistics and thematic analysis.

**Conclusions:** This context analysis helped us to develop a targeted group intervention for patients and health care providers affected by post-Covid-19 consequences.



### SOA09-872-15 The Kongsu-COVID intervention to combat the pandemic: a concerted effort by the Padang community, Indonesia

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**Background and challenges to implementation:** The community is the vanguard that has been forgotten so far; it has more impact and builds social solidarity and cooperation in combating Covid-19.

This innovation project aims for early detection, treatment, and a concerted effort by the Padang community.

**Intervention or response:** Kongsu-Covid innovation is a local community-based preparedness and response strategy. The sub-village RT/RW is subordinate to the village as a cluster with supervision directed in the community and requires 10-14 volunteers.

The activity model is as follows:

Collaborating with cross-sectoral partners such as Youth Organizations, NGOs, Head villages, Head sub-district, and Health Offices;

Preparing the establishment of the Kongsu-Covid at the sub-village level and its organizational structure duties and responsibilities;

Making periodic reports that describe conditions in each RT/RW sub-village using the application;

Form socialization by using print media and online media;

Create an RT/RW WhatsApp group for monitoring; Monitoring and evaluating the implementation of RT/RW Kongsu-Covid through regular virtual meetings;

Creating a Covid Positive community monitoring system through an application that contains: case identification, reporting of suspected Covid-19, recording of suspected Covid-19, and monitoring of independent isolation that occurs in each sub-village.

All activities are monitored, coordinated, and supervised by the village leader, sub-district, community health centers, and city health offices.

**Results/Impact:** The Padang region had developed 1,252 Kongsu-covid, covering 100% of sub-villages. Over 3000 people with positive confirmed cases with asymptomatic or mild symptoms were self-isolation under Kongsu-Covid local monitoring. The government of Padang was awarded the Best Rating second due to its policy for preparing strategic planning, including efforts to deal with the COVID-19 pandemic through the innovations of the Kongsu-Covid.

**Conclusions:** Kongsu-Covid strengthens existing partnerships to reach and engage with broader community networks. It has an active role in combating Covid-19, battling stigma, and strengthening family resilience for villagers in Padang-Indonesia.

### SOA09-873-15 Temporal association between COVID-19 and TB notifications and deaths, Kenya 2019-2022

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**Background:** Mathematical models predicted that COVID-19 would reverse tuberculosis (TB) mortality gains to levels experienced a decade earlier. The Kenya HIV program integrated COVID-19 and TB infection prevention measures; introduced differentiated service delivery models (DSD) for TB/HIV treatment; and promoted COVID-19 vaccination among people living with HIV (PLHIV).

We analyzed routine program data to determine the correlation between COVID-19 waves with TB and TB/HIV notifications and mortality.

**Design/Methods:** We abstracted routine TB case notification and mortality data from the national electronic TB surveillance system and obtained monthly COVID-19 notification data from the national public health emergency operations center for the period January 2019-December 2022.

We computed trends and cross-correlation plots of COVID-19 and TB notifications (all-forms of TB, HIV-positive and HIV-negative TB), and mortality in respective TB categories. These variables were assessed for Granger causality and analyzed simultaneously using Vector Autoregressive (VAR) models implemented in the R library vars.

**Results:** Overall, there was a decline in TB case notification after onset on COVID-19, from 85,818 in 2019 to 72,649 in 2020 with recovery surpassing pre-COVID-19 levels to 90,896 in 2022. There were 5,392 (6%) deaths among TB patients in 2019, 5,200 (7%) in 2021 and 4,843 (6%) in 2022.

There was no correlation between COVID-19 waves and TB case notification. However, overall deaths among TB patients increased 8-fold, with a 4-month time lag after the COVID-19 waves: [t(4)=7.70,p=0.03].

Stratified by HIV status, this statistically significant increase in deaths was observed among HIV-negative TB patients [t(4)=8.73,p=0.04] but not among HIV-positive TB patients [t(4)=8.22,p=0.10].

**Conclusions:** The increase in risk of death among TB patients after COVID-19 waves likely reflects delays in diagnosis, and interruption in TB treatment.

The lack of significant correlation between COVID-19 waves and deaths among HIV-positive TB patients may be attributed to infection prevention measures, DSD, and COVID-19 vaccination by the HIV program.

## SOA09-874-15 TB-associated mortality before and during the COVID-19 pandemic in Kenya, 2019–2021

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**Background:** Studies described increases in TB and TB/HIV mortality following disruption in TB services by the COVID-19 pandemic. We assess changes in TB case-fatality among HIV-negative and HIV-positive people with TB before and during the COVID-19 pandemic to inform public health interventions in Kenya.

**Design/Methods:** In a retrospective analysis of 2019–2021 national TB treatment outcome data, we assessed TB case-fatality across age-groups among HIV-positive and HIV-negative adults and children with TB. Using the 2019 data (pre-COVID-19) as baseline, we compared changes in case-fatality with the 2020 and 2021 data (COVID-19 period).

Using Epi-info<sup>®</sup> we calculated frequencies, proportions and Chi-square test for difference in proportion. p-values <0.05 were considered significant.

Tuberculosis mortality by age group and year of notification 2019–2021										
		2019			2020			2021		
		Dead	Not dead	p-value	Dead	Not dead	p-value	Dead	Not dead	p-value
HIV positive	0–14	139	955	Ref	94	601	0.61	88	710	0.27
	15–24	188	1616	Ref	138	1201	0.92	117	1177	0.2
	25–34	650	5439	Ref	524	4150	0.38	473	4011	0.83
	35–44	806	6146	Ref	744	5240	0.14	645	5287	0.19
	45–54	472	3628	Ref	502	3063	<0.001	432	3222	0.67
	55–64	169	1340	Ref	214	1151	<0.001	190	1259	0.11
	65+	89	500	Ref	85	396	0.25	85	493	0.85
All HIV+ve	2513	19624	Ref	2301	15802	<0.001	2030	16159	0.55	
HIV negative	0–14	239	6130	Ref	195	4135	0.053	212	5636	0.71
	15–24	171	13410	Ref	212	11026	<0.001	187	11131	0.01
	25–34	391	15162	Ref	367	13249	0.33	347	13507	0.96
	35–44	448	10819	Ref	474	9800	0.02	443	10637	0.93
	45–54	379	6222	Ref	427	5781	0.008	429	6398	0.18
	55–64	398	3655	Ref	425	3395	0.058	392	3744	0.6
	65+	749	4069	Ref	716	3473	0.047	678	3899	0.32
All HIV-ve	2775	59467	Ref	2816	50859	<0.001	2688	54952	0.09	

**Results:** Among HIV-negative people with TB, case-fatality increased from 4.5% in 2019 to 5.2% in 2020 (p<0.001) but was similar to 2019 (4.7%) in 2021 (p=0.09). Among those HIV positive, case-fatality increased from 11.4% in 2019 to 12.7% in 2020 (p<0.001) but was similar to 2019 (11.2%) in 2021 (p=0.55).

From 2019 to 2021, TB case-fatality increased significantly with age for all HIV-positive and HIV-negative persons (p<0.001).

Significant increases in case-fatality in 2020 was noted among the middle-aged PLHIV aged 45–54 years (p<0.001) and 55–64 years (p<0.001).

In 2020, among HIV-negative persons, significant increases in case-fatality were seen across a wider range of age groups including those aged 15–24 years (p<0.001), 35–44 years (p=0.020), 45–54 years (p=0.008) and 65+

years (p=0.047). From 2020 to 2021, TB case-fatality significantly increased only for the 15–24 years old HIV-negative subgroup (p<0.001).

**Conclusions:** TB case-fatality increased in 2020 at the height of the COVID-19 pandemic. Increased TB case-fatality among PLHIV during COVID-19 occurred predominantly among those middle-aged. Increases in case-fatality among HIV-negative persons involved a larger number of age groups including young people. Programs may consider preparing for future pandemic to ensure continuity of TB care and avert mortality.

## SOA09-875-15 Interrupted time series analysis of the COVID-19 Delta wave's impact on and recovery of national TB notifications

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**Background:** Tuberculosis (TB) care infrastructure was often repurposed for COVID-19 control. Many high TB burden countries also resorted to stringent social distancing and lockdowns with a devastating impact on TB notifications. In Viet Nam, the Delta variant's emergence in 2021-Q3 was a pivotal moment that caused treatment coverage to drop below 50% for the first time since the National TB Program (NTP) expanded nationwide.

**Design/Methods:** We accessed quarterly all forms TB notification data from eight socio-economic regions of Viet Nam between 2018-Q1 to 2022-Q4 (20 data points per region). We conducted an interrupted time series analyses using segmented regression methods to incorporate pre-interruption trends; the interruption was set for 2021-Q3. We fit generalized linear negative binomial models with Newey-West standard errors. We reported risk ratios at the point of interruption and subsequent trend of recovery.

**Results:** Based on the fitted models, national all forms TB notifications declined by -38% (IRR=0.62; p<0.001) in 2021-Q3 and recovered at a rate of +15% per quarter thereafter. At the regional level, the decline in notifica-

tions in 2021-Q3 ranged from -15.2% (Northwest) to -46.6% (Mekong Delta); the declines in seven of eight regions were significant ( $0 < p \leq 0.032$ ), with the Northwest being the notable exception ( $p=0.164$ ). The average recovery rate of TB notifications ranged from +7.4% (Red River Delta) to +20.8% (Mekong Delta) per quarter. Recovery trends were significant across all regions ( $0 < p \leq 0.025$ ).

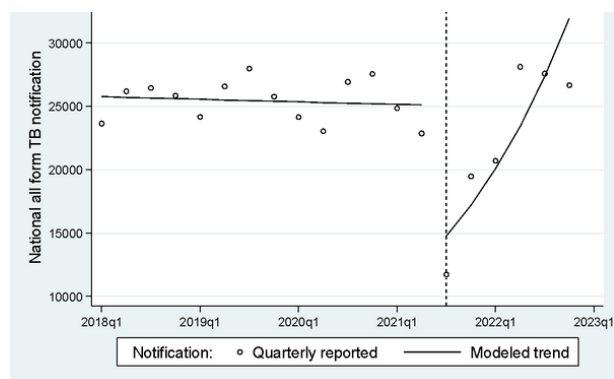


Figure. Quarterly national TB notifications, Q1/2018 - Q4/2022. All forms TB, Delta wave began: Q3-2021.

**Conclusions:** The COVID-19 pandemic had a devastating impact on TB notifications nationally and in all regions, except the mountainous Northwest. However, our analyses also showed a rapid recovery highlighting a strong commitment of the Government of Viet Nam to re-establish TB prevention and care services immediately after the Delta outbreak was contained and vaccine coverage expanded.

### SOA09-876-15 Impact of COVID-19 on the TB care cascade in Beira, Mozambique: A 4-year historical cohort study

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**Background:** Mozambique implemented non-pharmacological measures aiming to contain transmission of the SARS-CoV-2 virus, slow the peak of the epidemic curve and reduce the burden on health systems. Although these measures were extremely necessary, their impact on TB treatment cascade (TBTC) after four epidemic waves is poorly known. We estimated the impact of COVID-19 on the TBTC of bacteriologically confirmed pulmonary TB (BC-PTB) in Beira city.

**Design/Methods:** A 4-year retrospective study was conducted involving six TB treatment (TBT) centers in Beira city. Data from 24 months before COVID-19 (April

2018 to March 2020) and after (April 2020 to March 2022) were extracted from TBT registers. Differences in proportions of linkage to TBT, follow-up sputum smear examination results (FUSSER) at 2/3-months from the TBT initiation, and TBT outcome were compared between the two periods using the chi-squared test at 5% significance level.

**Results:** About 4,975 patients with BC-PTB were linked to TBT, of which 44% in the post-COVID-19 period, representing a reduction by 21% from the pre-COVID-19. After 2/3-months from TBT initiation 83% (4,122) had a documented FUSSER, of which, 41.4% in the post-COVID-19 period, representing a decrease by 17.2%. The positivity rate of the FUSSER in the post-COVID-19 was almost 3 times higher (14.4%) than the pre-COVID-19.

While there were no statistically significant differences in mortality rate (19.7% v 15.1%), treatment success rate declined by 14.6%, and lost to follow-up rate increased by 10.6%, when compared with the pre-COVID-19 period.

**Conclusions:** The non-pharmacological measures against the COVID-19 have negatively impacted on the linkage, follow-up, and TBT outcomes, however, there was not observed any statistically significant difference in TB mortality rate.

These results, suggest the importance of strengthening the quality of TB services throughout the TBTC, with a special attention to linkage to care, follow-up, and provision of psychosocial support for TBT during public health emergencies.

### SOA09-878-15 Recovery of the Kenya National Tuberculosis Programme after the COVID-19 pandemic

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**Background:** Kenya is a high-burden TB country with a wide case detection gap and high mortality, exacerbated by the COVID-19 pandemic. We assessed TB program recovery from the impact of COVID-19 on TB case notification and mortality.

**Design/Methods:** We retrospectively analyzed routine TB case notification and mortality data from the national electronic TB surveillance system and COVID-19 notification data from the national public health emergency operations center from January 2019 to December 2022. TB-related mortality was assessed up to December 2021. 2019 was the pre-COVID-19 period. To account for heterogeneity in disease burden, we analyzed county data, stratified by the relative burden of COVID-19.

We used Epi-info® to calculate changes in frequencies, proportions, and odds-ratios (OR) with 95% confidence intervals (CI).

**Results:** Nationally, there was a 15% decline in TB case notification from 85,818 in 2019 to 72,649 in 2020, followed by a 6% and 18% increase to 77,357 and 90,896 in 2021 and 2022, respectively, surpassing pre-COVID-19 level (Table 1). In Nairobi, there was a 24% decline in TB case notification from 12,398 in 2019 to 9,437 in 2020, followed by a 12% and 15% increase in 2021 and 2022, respectively, but falling short of pre-COVID-19 level. Compared to 2019, there was an increase in TB-related mortality nationally in 2020 [OR 1.150; 95% CI:(1.105, 1.196)] but no difference in 2021 [OR 0.996; 95% CI:(0.957, 1.037)]. This recovery was observed in the regions with medium and low burden of COVID-19. In Nairobi, the increase in mortality persisted in 2020 [OR 1.453; 95% CI:(1.291, 1.635)] and in 2021 [OR 1.308, 95% CI:(1.163, 1.471)].

Region	COVID-19 Burden	Year	TB cases notified	TB-related Deaths	% Deaths among TB patients	Odds Ratio	95% Confidence Interval
National	343,855	2019	85,818	5,392	6.3%	1.149938	[1.105, 1.196]
		2020	72,649	5,200	7.2%		
		2021	77,357	4,843	6.3%		
		2022	90,896	-	-		
Nairobi	160,349 (High, 47% national)	2019	12,398	560	4.5%	1.453176	[1.291, 1.635]
		2020	9,437	607	6.4%		
		2021	10,572	616	5.8%		
		2022	12,153	-	-		
12 Counties (Medium, 33% national)	114,850	2019	29,357	2,076	7.1%	1.112178	[1.043, 1.186]
		2020	25,170	1,964	7.8%		
		2021	26,513	1,829	6.9%		
		2022	31,549	-	-		
34 counties (Low, 20% national)	68,656	2019	44,063	2,756	6.3%	1.112685	[1.053, 1.176]
		2020	38,042	2,629	6.9%		
		2021	40,272	2,398	6.0%		
		2022	47,194	-	-		

**Background and challenges to implementation:** Kenya is a high-burden TB country with a wide case detection gap and high mortality, exacerbated by the COVID-19 pandemic. We assessed TB program recovery from the impact of COVID-19 on TB case notification and mortality.

**Conclusions:** The COVID-19 pandemic negatively impacted TB services in Kenya. The significant decline and incomplete program recovery in Nairobi calls for intensified efforts in high-burden settings and long-term strategies to prevent and mitigate the impact of future pandemics.

## SOA09-879-15 Effects of the COVID-19 pandemic on TB notifications in Ukraine

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**Background:** We aimed to examine the impact of the COVID-19 pandemic on TB notifications in Ukraine, stratified by age, refugee/migrant status, and drug resistance profiles.

**Design/Methods:** We analyzed all TB cases diagnosed between January 2015-December 2020 and reported to the Ukrainian National TB Program. We considered March 2020 to be a transition period (a national emergency was declared on 20<sup>th</sup> March 2020) and used an interrupted time series negative binomial model with population offset to compare notification rates from pre-COVID-19 (January 2015-February 2020) to during the pandemic (April-December 2020). We compared the observed number of cases in April 2020 to the counterfactual estimated number of cases in April 2020 had the pandemic not occurred, and stratified this by age, refugee/migrant status, and drug resistance profiles. We estimated trends through the rest of 2020.

**Results:** In April 2020, there were 39% (95% CI: 36-42%) fewer TB notifications than the estimated counterfactual (3060 notifications, [95% CI: 2918-3202] versus 1872 observed; Figure). We observed a greater decrease in notifications among refugees and migrants compared to non-refugees/migrants (64% [95% CI: 60-67%] versus 39% [95% CI: 36-42%]), and individuals aged <15 years compared to those aged 15 years and older (60% [95% CI: 57-64%] versus 38% [95% CI: 36-41%]). We also observed a larger decrease in all drug-resistant TB notifications (43% [95% CI 40-46%]) compared to drug susceptible TB (36% [95% CI 33-39%]). Overall, notifications rose slightly during 2020 but in December 2020 were still 34% lower than the expected notifications in the absence of the pandemic.

**Conclusions:** The COVID-19 pandemic led to substantial decreases in TB notification rates across all demographic groups in Ukraine. These findings remain important as Ukraine continues to experience serious disruption due to the Russo-Ukrainian war, especially given the substantial increase in the number of refugees within and leaving Ukraine.

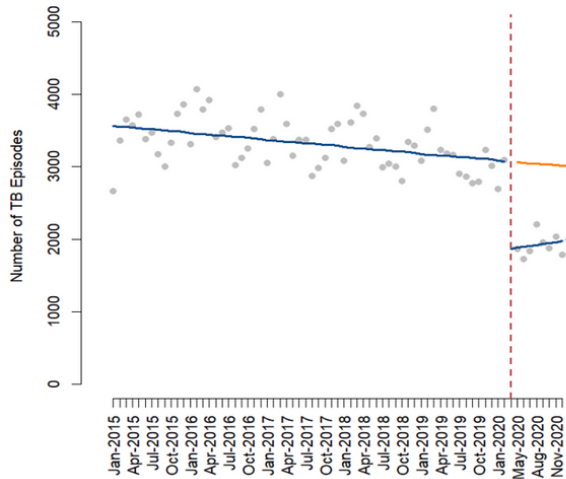


Figure. Number of monthly TB notifications in Ukraine January 2015 - December 2020 (grey dots) and fitted linear trend lines through these notifications (blue line) separated into pre-COVID-19 pandemic and during the COVID-19 pandemic. The vertical red dotted line falls on April 2020 to indicate the start of the pandemic in Ukraine and the separation of these two fitted trend-lines. The orange line indicates the predicted monthly notifications if the pandemic had not occurred and notifications had continued the trend observed January 2015 - February 2020.

## E-POSTER SESSION (EP)

### EP01 TB Diagnostics - Operational and clinical studies

#### EP01-1000-15 Experiences and lessons learnt in piloting stool Xpert testing in children in Kinshasa, DR Congo

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**Background:** Bacteriological confirmation of TB in children remains a challenge because of the requirements for sputum samples. Children may not produce sputum spontaneously and present with paucibacillary disease. DRC conducted an implementation pilot to investigate the acceptability, feasibility and potential impact of stool testing to gain practical information to inform nationwide scale up and integration within routine care.

**Design/Methods:** The pilot was conducted over 5 months period from July through November 2022 in Kinshasa in 25 sites, of which 7 with a GeneXpert. All children aged 0-14 years with signs and symptoms of TB presenting at any entry point were included and asked for a stool sample in addition to any routine samples. Stool was processed with the Simple One Step (SOS) stool method and samples were tested with Xpert MTB/RIF Ultra cartridges. Training was conducted for health care providers on management of TB in children and for laboratory technicians on stool processing.

**Results:** Among 703 children (48% 0-4 years, 32% 5-9 years and 20% 10-14 years), 684 stool samples and 107 respiratory samples were received. Of these 684 stools 542 were MTB Not detected, 125 (18%) MTB detected (52 Trace, 25 Very Low, 34 Low and 14 Medium) and 17 had a non-determinate result. Two children with Rif-resistant TB were identified. Both stool and sputum were collected for 84 children and 76 (91%) had concordant results.

**Conclusions:** It is feasible to diagnose TB in children using stool in DRC. Stool was easier to collect and reduced the need for gastric aspiration, an invasive procedure

that is not widely available. More children obtained bacteriological confirmation for TB when offered stool as an alternative sample.

Based on pilot results, the NTP has incorporated stool into the routine algorithm for bacteriological testing of children and is in the process of scale up throughout the country.

#### EP01-1001-15 Evaluation of Deeplex Myc-TB for detecting *M. tuberculosis* and drug resistance in clinical samples

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**Background:** Tuberculosis (TB) is a major global health threat. Emergence of drug-resistant TB (DR-TB) jeopardizes the efforts to eliminate TB in many countries. Rapid and reliable drug susceptible testing (DST) is necessary for DR-TB eradication programs. Next-generation sequencing (NGS) may be a solution for existing DST methods and a means of improving the understanding for drug resistance.

This study aimed to evaluate targeted NGS using clinical samples in Korea.

**Design/Methods:** A total of 112 Mtb-positive samples were collected at Seoul Clinical Laboratories. Of 112 samples, 90 samples were tested for real-time PCR (Advansure MTB/NTM kit, LG Chem, Korea). Xpert MTB/RIF (Cepheid, USA) were positive for 22 samples. In addition, six samples were positive for AFB smear microscopy without molecular test. All the samples were confirmed by culture. Conventional drug susceptibility testing (DST) was done by using 7H10 agar proportion method. Targeted NGS assay was conducted by using Deeplex Myc-TB assay (Genoscreen, France) according to the manufacturer's instruction.

**Results:** Deeplex detected Mtb in 94 out of 112 samples. For Xpert positive samples (n = 22), Deeplex missed two medium and one high positive samples. Smear positive samples were all positive for Deeplex. Ct values were well correlated with Sequencing result acceptability of Deeplex. Deeplex correctly identified 6 of 7 isoniazid-resistant and 7 of 9 streptomycin-resistant samples.

One rifampin-resistant sample and ethambutol-resistant sample was detected by Deeplex. 17 samples showed false resistant results. All samples except one were susceptible to all drugs tested by DST. Proportion of variants were usually very low and the most common type of false result was fabG1 mutation (c-15t).

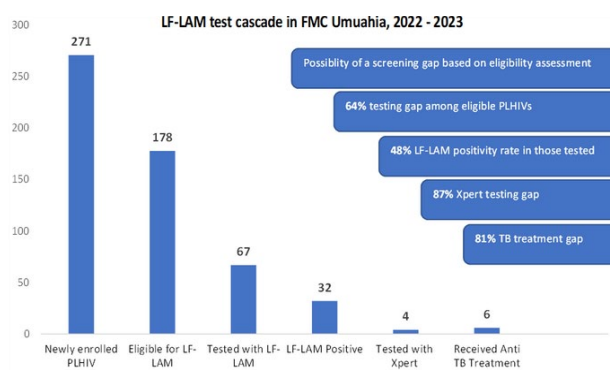
**Conclusions:** Deeplex detected Mtb for 83.9% samples and provided reliable susceptibility results for 65.2% samples. Therefore, Deeplex could be useful for Mtb-positive clinical samples. However, further study is needed to elucidate a high rate of false positive results in clinical samples.

## EP01-1003-15 Using lateral-flow lipoarabinomannan for TB diagnosis in advanced HIV disease: an implementation cascade analysis in a Nigerian hospital

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**Background:** In 2020, The Federal Ministry of Health adopted the use of LF-LAM as a Point-of-care test for the diagnosis of TB in patients with advanced HIV disease (AHD). Operationally, AHD was defined as a CD4 count of  $\leq 200$  cells-per- $\mu$ l or clients deemed to be *seriously ill* – unable to walk unaided, fever of  $\geq 39^{\circ}\text{C}$ , respiratory rate of  $\geq 30$  cycles-per-minute, and heart rate of  $\geq 120$  beats-per-minute. The aim of this research was to examine the implementation of LF-LAM using a cascade-of-care approach.

**Design/Methods:** Data for this retrospective analysis covered the period between January 2022 and February 2023. The number of PLHIVs meeting eligibility criteria for the test was collected as well as the number and proportion that had the test, received results, and had clinical decisions made based on the result. We triangulated client records with data from service registers at the ART clinic, laboratory, and TB clinic.



**Results:** As shown in the figure above, over the 14-month period, 271 PLHIVs were newly enrolled into care at the facility out of which 178 (65.6%) were deemed eligible for LF-LAM. 35.9% (67/178) of those eligible received the test with a 48% (32/67) positivity rate amongst those tested. 12.5% (4/32) and 18.8% (6/32) of those who test-

ed positive for LF-LAM received a bacteriological test and anti-TB medicines respectively leaving an 81.3% treatment gap. Ten (31.3%) people who tested LF-LAM positive were started on TPT, whilst 29 (90.6%) were started on ART.

**Conclusions:** Significant gaps exist along the LF-LAM implementation cascade resulting in many missed opportunities for TB diagnosis and treatment amongst PLHIVs. There is a need for more capacity building amongst healthcare workers to improve adherence to national guidelines and clinical decision-making using LF-LAM test results.

## EP01-1004-15 Multi-centric validation of Truenat MTB Rif Dx for the diagnosis of extrapulmonary TB

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**Background:** Despite the availability of potent anti-TB drugs, Tuberculosis (TB) accounts for highest number of deaths around the world among infectious diseases categorized among curable infections. Reduction in TB-related morbidity and mortality is impeded by the lack of rapid, cost-effective diagnostic tests that are implementable in resource-limited settings. Extrapulmonary TB (EPTB) is more difficult to detect as the symptoms and ease of sampling vary by the site involved. The study was designed to evaluate the diagnostic accuracy of Truenat MTB-Rif Dx (MolBio Diagnostics, India) in EPTB. **Design/Methods:** Truenat MTB-RIF is a chip-based nucleic acid amplification test for detection of *Mycobacterium tuberculosis* (MTB) and resistance to rifampicin, in clinical specimens. We have collected samples (biopsy, lymph node, pleural/peritoneal fluid, CSF & pus) from 2103 treatment naive adult patients with presumptive EPTB. The samples were analyzed by WHO recommended diagnostics, smear microscopy, liquid culture (MGIT-960) and GeneXpert MTB/RIF (Xpert) (taken together as Microbiological Reference Standards). The results were compared to MRS and Composite reference standards including, histopathology and radiology findings, response to treatment and follow-up.

**Results:** As per the standard definitions, among 2103 patients, 697 had confirmed, 1113 had unconfirmed, while 293 patients were unlikely (non-TB) TB cases. The Truenat/MTB test was found to have sensitivity & specificity of 73.7% and 90.4% against Xpert, 62.3% & 84.9% against liquid culture and 89.2% & 79.6% against smear. The sensitivity and specificity against the gold standard MGIT culture varied with sample types. Pus samples demonstrated highest sensitivity while highest specificity was seen in CSF samples.

	MGIT				Sensitivity	GeneXpert	MGIT				Sensitivity
	Truenat	Pos	Neg	Total			Pos	Neg	Total	Total	
AFB smear (+) (n=83)	Pos	55	19	74	93.2 (83.5, 98.1)	Pos	57	18	75	56.2 (50.4, 61.9)	85.8 (84.1, 87.4)
	Neg	4	5	9	(7.13, 42.2)	Neg	2	6	8	(84.1, 87.4)	40.8 (36, 45.7)
Total		59	24	83	PPV 74.3 (62.8, 83.8)		59	24	83	NPV 55.6 (21.2, 86.3)	91.9 (90.4, 93.1)
	MGIT				Sensitivity	GeneXpert	MGIT				Sensitivity
	Truenat	Pos	Neg	Total			Pos	Neg	Total	Total	
AFB smear (-) (n=2020)	Pos	168	244	412	56.2 (50.4, 61.9)	Pos	185	169	354	61.9 (56.1, 67.4)	90.2 (88.7, 91.5)
	Neg	131	1477	1608	(84.1, 87.4)	Neg	114	1552	1666	(84.1, 87.4)	52.3 (46.9, 57.6)
Total		299	1721	2020	PPV 40.8 (36, 45.7)		49	1721	2020	NPV 91.9 (90.4, 93.1)	93.2 (91.8, 94.3)

*Table 1. Diagnostic performance of Truenat & GeneXpert in smear positive and negative specimens with MGIT-culture*

**Conclusions:** The study establishes the Truenat MTB-Rif test as a minimally labor-intensive, rapid detection method for the diagnosis of TB and Rifampicin resistance. This test can be utilized in near-care settings for quick and accurate diagnosis of EPTB.

## EP01-1005-15 TB treatment monitoring tools in routine practice: Study design guidance for evidence generation

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**Background:** Tuberculosis (TB) treatment monitoring is a key element of TB care. Currently deployed methods, sputum smear and culture, cannot accurately predict poor treatment outcomes. Research into new TB treatment monitoring tools (TMT) is growing, but data are unreliable. A previous systematic review of biomarkers used for TB treatment monitoring showed that publications were generally at high risk of bias. We determined that guidelines for study design and result reporting would help generate evidence that can be meaningfully compared. We aim to provide guidance for studies investigating and evaluating TB TMT for use during routine clinical care.

**Design/Methods:** This project was initiated by the Biomarkers Task Force of the New Diagnostics Working Group. An initial draft, informed by observations from the systematic review, was circulated to a small content expert group. After revision, feedback from substantive experts in product development partnerships, research institutes, universities, and non-governmental agencies was sought.

**Results:** The proposed considerations and recommendations for studies evaluating TB TMTs fall into nine domains. We provide specific recommendations regarding study design and recruitment, outcome definitions, reference standards, participant follow-up, clinical setting, study population, treatment regimen reporting, index tests, and data presentation. Overall, TB TMTs should be evaluated in a manner similar to diagnostic tests, but TB TMT accuracy will be assessed at multiple timepoints throughout the treatment course. Study design and outcome definitions must be aligned with the



developmental phase of the TB TMT under evaluation. Relatedly, we propose a hierarchy of reference standards to estimate TB TMT accuracy, as no gold standard for TB treatment monitoring exists.

**Conclusions:** Implementing these recommendations will lead to higher quality TB TMT studies, which will facilitate the development of tools to guide individual therapy. Newer, improved TB treatment monitoring tools will lead to better patient outcomes and higher rates of treatment success.

### EP01-1006-15 Evaluation of loop-mediated isothermal amplification for TB diagnosis in children in Cameroon

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**Background:** In Cameroon, only about half of pediatric tuberculosis (TB) cases are reported each year. The loop-mediated isothermal amplification (TB-LAMP) is a point of care WHO Recommended Rapid Diagnosis test for pulmonary TB diagnosis in adults with signs and symptoms of TB. Since 2017, Cameroon implemented TB-LAMP and about 50 TB-LAMP equipments are available today. But their use in children are unknown. The aim of this work was to assess the performance of TB-LAMP in non-sputum specimens for the detection of pediatric TB in Cameroon.

**Design/Methods:** A retrospective study was conducted using 450 samples consisting of Gastric aspiration (GA), Nasopharyngeal aspirations (NA) and Stool from 150 children. Statistical analysis were performed using R and Rstudio software to compare diagnostic performances of TB-LAMP with that of Xpert MTB/RIF using each sample type and by considering culture as gold standard.

**Results:** The sensitivity (Se) and specificity (Sp) of TB-LAMP were 66.67 and 93.33 % respectively when GA was used. TB-LAMP presented a Se of 61.54% and a Sp of 94.16 with NA. Using stools, TB LAMP showed a Se of 64.71% and the Sp of 93.98.

However, Xpert MTB/RIF showed higher sensitivity and specificity compared to TB-LAMP when using GA ( Se:73.33%, CI: 44.90-92.21; Sp: 99.26%, CI: 95.94-99.98), NA(Se: 92.31%, 95% CI: 63.97-99.81; Sp: 98.54%, 95% CI: 94.83-99.82) and stool (Se: 70.59%, CI: 44.04-89.69; Sp: 98.50%, CI:94.67-99.82). Nevertheless, there was no statistical difference between TB-LAMP and Xpert MTB/RIF.

**Conclusions:** This is the first study which evaluate the diagnostic performance of TB-LAMP in pediatric TB. TB-LAMP and Xpert MTB/RIF displayed similar performances in the three specimen's types. Further studies are needed to assess the applicability of this test in non-sputum samples. This result imply a potential use of TB-LAMP for the diagnosis of pulmonary TB in children.

### EP01-1007-15 Determining the best diagnostic approach in yield and performance using digital chest X-ray, Truenat and microscopy during outreaches

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**Background:** The introduction of new TB screening and diagnostic tools, such as Truenat has provided a rich array of diagnostic choices in comparison to the old tools employed in the country. However more operational research needs to be done to inform policy on the best diagnostic approaches to employ during patient management.

**Design/Methods:** This was a cross-sectional study where all participants underwent a TB symptom screen using a standardized tool followed by subjecting sputum samples to smear microscopy, Digital Chest Xray and TrueNat. This was carried out during outreaches to determine the best diagnostic approach to employ.

**Results:** Of the 828 presumptive TB participants enrolled during outreaches, 11% (91/828) were confirmed positive bacteriologically by TrueNat. Of all the sputum samples submitted for microscopy (502/828) only 8% (40/500) were AFB positive.

Compared to chest xray, 20-30% more cases could have been picked if combined with TrueNat, microscopy and symptom screening. Radiologists' readings graded 182 (22.1%) CXR images as 'Highly suggestive of TB', 198 (23.9%) as 'Possibly TB', 83(10%) as 'Other finding', 323(39%) as 'Normal' and 41(4.9%) as 'Image not clear'. About fifty percent of participants whose CXRs were graded as 'Highly Suggestive of TB' were TrueNat positive n = 91 (50%). The proportion decreased to 22% (n = 44) among participants whose CXRs were graded as 'Possibly TB'.

The results were similar for smear with 48.9% of smears among those with 'Highly suggestive of TB' images were positive on smear while 11% of those with 'possibly TB' CXR readings had smear-positive results. Almost all TrueNat positive results (n = 91, 11% )of total Bac+ cases) came from people with CXR graded as either 'Highly suggestive' or 'Possibly TB'.

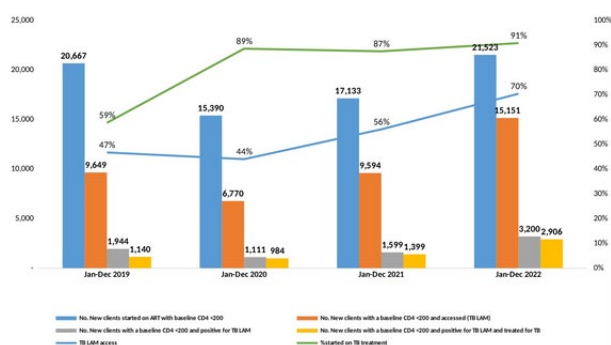
**Conclusions:** TrueNat and Chest Xray detected a large proportion of bacteriological confirmed cases missed by microscopy.

## EP01-1008-15 Impact of integrating lateral-flow lipoarabinomannan into advanced HIV disease management in high TB-HIV burden settings

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**Background and challenges to implementation:** In 2016, Uganda piloted the use of LF-LAM testing at 14 Regional Referral Hospitals. An early program evaluation on Implementation of LF-LAM was conducted in October 2018 to guide countrywide scale up. This evaluation revealed suboptimal utilization of LF-LAM test at 25%. The major implementation challenges identified were; lack of supportive structures such as CD4 cell testing, LF-LAM diagnostic algorithm, recording and reporting procedures and stock management procedures.

**Intervention or response:** In June 2019, a Technical Working Committee (TWC) was formed for Advanced HIV Disease (AHD) which included members from the National TB and Leprosy Program and AIDS Control Program. The TWC created a tool kit and implementation plan for AHD management, addressing issues such as a lack of testing capacity. They identified high-volume health facilities capable of performing CD4, LF-LAM, and CRAG testing, procured and distributed reagents for CD4 testing, and provided diagnostic algorithms, reporting and stock management procedures to AHD sites. By the end of 2019, orientation meetings and training for health workers on AHD care were held across Uganda's 12 health regions. Bi-weekly surge meetings with the regional implementing partners and district officials were also initiated in early 2022 to further improve on LF-LAM uptake and TB treatment initiation among LF-LAM diagnosed individuals.



**Results/Impact:** Results shows that LF-LAM utilization improved from 47% (9,649/20,667) in 2019 to 70% (15,151/21,523) by end of December 2022 whereas TB

treatment initiation of LF-LAM positive individuals increased from 59% (1,140/1,944) in 2019 to 91% (2,906/3,200) in 2022.

**Conclusions:** The integration of LF-LAM into AHD management package led to an improvement in its utilization and linkage to TB care for LF-LAM diagnosed individuals. We recommend collaborative efforts in the implementation of LF-LAM as integral part of AHD package by the joint TB and HIV/AIDS National Programs so as to ensure its optimal performance.

## EP02 Cost and cost effectiveness?

### EP02-1009-15 Personnel costs of TB contact tracing in urban and rural South Africa

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**Background:** Perceived cost is a major barrier to implementing household contact investigation for tuberculosis. Although a recommendation of the World Health Organization, it is not routinely done in high burden settings.

**Design/Methods:** We conducted a time and motion (TAM) survey using REDCap, coupled with data on personnel salaries and budgetary review, between October 2022 and February 2023 in the context of Kharituwe, a four-arm parallel individually randomized trial assessing household contact investigation strategies in rural and urban South Africa. TAM data were collected via self-report and direct observation to estimate activity-based implementation costs. Costs are reported in 2022 US dollars from the health system perspective.

Variable	Soshanguve (Urban)	Limpopo (Rural)
<i>Process measures</i>		
Mean (SD) number of households visited per day	3 (2)	2 (1)
Median (IQR) duration per household visit, minutes	42 (27-61)	66 (43-88.25)
Median (IQR) travel time per household visit, minutes	55 (37.75-123.5)	126.5 (69.25-192.75)
Median (IQR) travel time per day, minutes	201.5 (170.75-242.5)	207 (163.5-280.75)
<i>Costs</i>		
Mean (SD) cost per day (2022 USD)	\$8.64 (2.87)	\$3.26 (1.07)
Mean (SD) cost per household visit (2022 USD)	\$3.12 (2.12)	\$2.11 (0.90)

**Results:** A total of 17,938 minutes of staff time were observed through TAM. Staff in the urban site spent a median 201.5 minutes of travel per day to complete three household visits (median 55 minutes per household). In the rural site, staff spent a median 207 minutes of travel per day to complete two household visits (median 126.5 minutes per household). Activities within the household took a median of 42 minutes per household in the urban site and 66 minutes per household in the rural site. Despite shorter transportation times and less time spent at households, the mean cost of a household visit was \$3.12 in the urban site versus \$2.11 in the rural site owing to higher staff salaries in the urban site.

**Conclusions:** Household contact investigation can be performed at reasonable cost to the health system in both urban and rural areas. Human resource requirements for transportation are higher in rural settings but may be offset by lower hourly costs if staff with less formal training can be employed.

## EP02-1010-15 Is convenience really king? Comparing catastrophic TB costs among public and private sector patients in Viet Nam

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**Background:** Tuberculosis (TB) represents a devastating life-event with an exorbitant price tag. In Viet Nam, indirect costs from lost income was the biggest driver of catastrophic costs ( $\geq 20\%$  of household income lost due to TB). Thus, many TB patients seek private TB care for its superior flexibility and convenience. It is unclear, however, whether these advantages translate to a difference in catastrophic cost incurrence.

**Design/Methods:** As part of a TB REACH-funded private sector engagement project in three Vietnamese urban provinces, we conducted 110 longitudinal patient cost surveys among 50 people privately treated for TB and 60

treated by the National TB Program (NTP). Using a locally adapted version of the WHO patient costing tool, participants were surveyed during the intensive phase, continuation phase and post-treatment. We compared income levels, direct and indirect treatment costs, and catastrophic cost incurrence between the two cohorts.

**Results:** The median household income was significantly higher in the private treatment cohort at treatment initiation (USD 868 vs. USD 578;  $p=0.010$ ), during the intensive phase (USD 763 vs. USD 419;  $p=0.003$ ) and after treatment concluded (USD 710 vs. USD 464;  $p=0.007$ ). However, intra-treatment costs were also significantly higher among privately treated participants, driven by direct medical expenditures that were 39x higher than for NTP patients (USD 625 vs USD 16). This resulted in no significant difference in catastrophic cost incurrence between the two cohorts (private treatment: 42% vs NTP treatment: 33%;  $p=0.347$ ).

Median (IQR), USD	Private (n = 50)	Public (n = 60)	All (n = 110)	p-value
Pre-treatment total costs	196 (123-296)	169 (78-358)	178 (91-322)	0.365
Direct medical costs	160 (87-213)	102 (43-247)	143 (55-225)	0.069
Direct non-medical costs	6 (8-22)	9 (5-30)	9 (0-25)	0.053
Indirect costs	8 (0-42)	22 (6-57)	15 (1-56)	0.116
During treatment total costs	1,836 (1,184-2,947)	1,036 (508-1,961)	1,571 (699-2,432)	<b>0.001</b>
Direct medical costs	625 (409-954)	16 (1-98)	210 (15-631)	<b>0.000</b>
Direct non-medical costs	389 (114-748)	323 (189-399)	344 (151-489)	0.358
Indirect costs	605 (0-1,899)	500 (15-1,588)	548 (0-1,720)	0.987
Catastrophic cost incurrence (%), n	42% (21/50)	33% (20/60)	37% (41/110)	0.347

**Conclusions:** The substantially higher treatment costs in the private sector negated any income gains from the greater flexibility offered by seeking private TB treatment. Thus, the convenience of private-sector care remains a privilege of those with higher socioeconomic status who are less susceptible to catastrophic cost incurrence.

## EP02-1011-15 Catastrophic expenditure of multidrug-resistant TB treatment on households in Pakistan: A cross-sectional study

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**Background and challenges to implementation:** Tuberculosis (TB) is a highly epidemic disease inflicting high mortality and costs. Economic deprivation and staggering costs are often considered its important determinants, but the drivers of these costs have rarely been investigated. This study aims to identify leading factors contributing to catastrophic costs of MDR-TB diagnosis in Pakistan.

**Intervention or response:** This study is based on primary data collected from MDR-TB patients using WHO's generic tool measuring health expenditure. To estimate the costs owing to MDR-TB and to determine the proportion of MDR TB-affected households experiencing

catastrophic expenditure, a total of 212 patients undergoing MDR-TB treatment within the National TB Program (NTP) network in Islamabad and Rawalpindi divisions of Pakistan, were surveyed. The underlying costs were estimated using the human capital approach.

**Results/Impact:** The study finds that the overall mean total cost for every single MDR-TB episode, including pre-and post-diagnostic costs, is about US\$ 1800 (0.36 million PKR). The mean total cost is five times higher compared to DS-TB patients than DR-TB patients. Direct non-medical costs and income loss accounted for PKR 340,793 and PKR 11,895 respectively. These accounted for 95% and 3.30% of the total cost borne by MDR-TB patients. Nearly all (95.28%) of TB-affected households experienced TB-related costs above 20% of their annual household expenditure, with the main cost drivers being non-medical expenditures including travel, nutritional supplements, and food. Up to 74 % of households borrowed, used savings, or sold assets to defray these costs.

Finally, around 92% of the patients who had been on the edge of the poverty line before treatment, had fallen below the poverty line during treatment.

**Conclusions:** The financial deprivation of patients of low socioeconomic status increases as TB treatment proceeds. This negatively impacts treatment adherence, resulting in poor treatment outcomes.

## EP02-1012-15 Cost-effectiveness of low-complexity screening tests in community-based TB case-finding

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**Background:** In high-burden settings, low-complexity screening tests for tuberculosis (TB) could expand the reach of community-based case-finding efforts. The

potential costs and cost-effectiveness of approaches that use these tests are not well understood.

**Design/Methods:** We developed a microsimulation model to assess four approaches to community-based case-finding in hypothetical populations with TB prevalence four times that of national estimates:

1. No case-finding,
  2. Screening with a point-of-care C-reactive protein (CRP) test followed by a sputum molecular test (Xpert MTB/RIF Ultra, “Xpert Ultra”) if positive,
  3. Screening with a more sensitive “Hypothetical Screening test” (95% sensitivity for Xpert Ultra-positive TB, 70% specificity) followed by sputum Xpert Ultra if positive, and;
  4. Testing all individuals with sputum Xpert Ultra.
- Costs are expressed in 2021 US dollars (USD) and include treatment costs.

**Results:** Universal Xpert Ultra was estimated to cost a mean \$3.7 million (95% uncertainty range [UR]: \$3.1 to \$4.3 million) and avert 3,200 (95% UR: 2,600 to 3,900) TB-related disability-adjusted life years (DALYs) per 100,000 people screened (\$590-\$1700 per DALY averted). CRP improved cost-effectiveness to \$500-\$1400 per DALY averted, but with 36% fewer DALYs averted. The Hypothetical Screening test (assuming equipment/labor costs similar to Xpert Ultra, but using a \$2 cartridge) had minimal impact on costs (4% reduction) and cost-effectiveness. Improving the Hypothetical Screening test’s specificity to 95% and per-test cost to \$4.5 (all-inclusive) improved cost-effectiveness to \$360-\$890 per DALY averted.

Figure 1 depicts the total costs (y-axis) of each case-finding strategy plotted against the number of DALYs averted (x-axis). The slope of the solid/dashed lines represents the cost per DALY averted when shifting from one strategy to the next most effective strategy (values noted for non-dominated strategies).

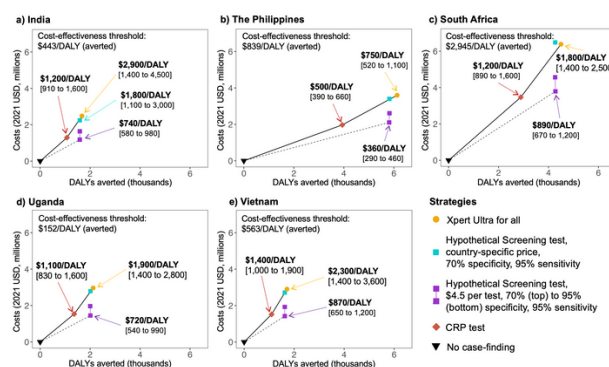


Figure 1.

**Conclusions:** Screening tests can meaningfully improve the cost-effectiveness of community-based case-finding for TB, but only if they are sensitive, specific, and inexpensive.

## EP02-1013-15 Cost-effectiveness of TB diagnostic technologies in Ethiopia: A modelling study

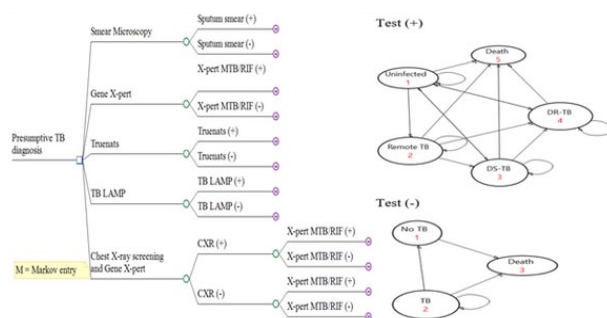
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**Background:** Tuberculosis (TB) represents the main public health threat globally. Effective and efficient rapid diagnostic technologies play a paramount role in the early detection and treatment of TB in a high burden country, like Ethiopia. The national TB diagnostic algorithms recommend rapid TB diagnostics as a primary test for TB, whenever possible, notwithstanding the lack of data on the resource impact of deploying various type of diagnostic tools.

This study aims to evaluate the cost-effectiveness of currently recommended WHO-approved rapid TB/MDR-TB diagnostic strategies in Ethiopia.

**Design/Methods:** A hybrid Markov model for hypothetical adult cohort of presumptive TB cases was constructed to estimate the cost-effectiveness of rapid TB/MDR-TB diagnostics in Ethiopia. Four TB diagnostic strategies were evaluated: X-pert MTB/RIF, Truenat, chest X-ray screening followed by X-pert MTB/RIF, TB-LAMP, and smear microscopy.

Incremental costs per Disability-adjusted life years (DALY) averted of less than three times GDP per capita are used to establish the cost-effectiveness. Data on the estimate of transition probabilities, costs, and utilities of health states were obtained from secondary sources.



**Results:** The incremental cost-effectiveness ratios for X-pert MTB/RIF compared to the next best alternative is \$276 per DALY averted, respectively. The cost-effectiveness of X-pert MTB/RIF was less than half of Ethiopia's GDP per capita, deeming it highly cost-effective.

Moreover, chest X-ray screening followed by an X-pert MTB/RIF test is cost-effective (ICER \$1,666 per DALY averted). In comparison to smear microscopy, using X-pert MTB/RIF would avert 9,600 DALYs for a cohort of 10,000 TB patients at a cost of \$3,816,000.

**Conclusions:** The Gene X-pert test is the most cost-effective diagnostic tool compared to others. The use of this diagnostic tool improves the early detection of cases and prompt treatment of TB in high-load facilities. Improved funding for this diagnostic tool will increase access, close the TB detection gap, and ensure effective treatment of patients.

## EP02-1014-15 The cost and impact of scaling up South African National Tuberculosis Programme interventions: A cost-effectiveness analysis

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**Background:** South Africa's National Tuberculosis (TB) Programme is informed by the World Health Organization's End TB Strategy, which aims to reduce TB incidence by 80% and mortality by 90% by 2030, in comparison to 2015. We assessed the cost and health impact of expanding TB programme intervention services under the National Strategic Plan for HIV, TB and STIs (NSP) for 2023-2027 coverage targets, and an aggressive "Maximum" scenario, compared to the baseline TB programme.

**Design/Methods:** The NSP scenario included expanded TB preventative therapy (TPT), Xpert Ultra testing, symptom screening at primary health clinics (PHC), screening household contacts of people with TB, and community-based screening (door-to-door and digital chest X-ray), as well as targeted universal testing for TB (TUTT) in people living with HIV, household contacts of people with TB and individuals with a history of TB, and reduced initial loss-to-follow-up (ILTFU), to levels deemed feasible by NSP stakeholders. In the Maximum scenario, we assumed maximised screening, TPT and treatment initiation in efforts to substantially reduce TB incidence and mortality. We used the Thembeisa TB model to estimate the incremental cost-effectiveness per life year saved (LYS) for individual interventions, or interventions combined (NSP and Maximum scenarios), over 2023-2042.

**Results:** The most cost-effective interventions were expanding Xpert Ultra testing (US\$23/LYS), symptom screening at PHC (US\$25/LYS), reducing ILTFU (US\$29/LYS), TUTT for household contacts (US\$106/LYS) and symptom screening for household contacts (US\$110/LYS) (Table 1). The NSP scenario cost US\$467/LYS and reduced TB incidence and mortality rates by 35% and 40%, respectively, by 2030. The Maximum scenario increased costs by 1.7-fold and further reduced TB incidence (40%) and mortality (50%) by 2030.

**Table 1: Interventions, incremental cost and life years saved over 20 years (2023-2042)**

Description of interventions	Assumed average annual intervention coverage	Incremental cost (USD 2021/2022) to TB programme over baseline, millions	% incremental cost increase over baseline	Life years saved over baseline, millions	% life years saved over baseline	Incremental cost-effectiveness per life year saved (USD 2021/2022)
<b>Individual interventions per NSP coverage targets</b>						
Xpert Ultra testing per diagnostic algorithm	3.3 million Xpert Ultra tests	42	+1.1%	1.8	+5.2%	23
TB symptom screening in general PHC	34 million symptom screens	51	+1.3%	2.02	+5.8%	25
Improve linkage to treatment	Reduce ILTFU by up to 50%	30	-0.9%	0.09	-2.0%	37
TUTT for all contacts of persons with TB	0.4 million Xpert Ultra tests	107	+4.2%	1.36	+4.5%	106
TB symptom screening for HH contacts of persons with TB	0.4 million symptom screens	216	+5.4%	1.96	+5.6%	110
TB symptom screening for PLWH on ART	11 million symptom screens	94	+2.4%	0.55	+1.6%	171
TPT (3HP) indications for HH contacts of persons with TB	0.26 million indications (10% IPT; 90% 3HP)	396	+10.0%	1.99	+5.7%	199
TUTT for individuals with history of TB	0.3 million Xpert Ultra tests	149	+3.8%	0.49	+2.0%	217
Annual DDT symptoms screening	3 million symptom screens	285	+7.2%	0.82	+2.4%	148
Culture in liquid medium testing per diagnostic algorithm	0.7 million Xpert Ultra tests	29	+0.7%	0.33	+0.1%	870
TUTT for PLWH	3 million Xpert Ultra tests	1452	+36.6%	1.11	+3.2%	1307
ACOR screening in asymptomatic persons	0.42 million ACOR screens	187	+4.8%	141 643	+0.4%	4 145
TUTT (2HP) indications for PLWH	0.3 million indications (10% IPT; 90% 3HP)	8	-0.2%	-0.003	-0.0001%	
<b>NSP scenario - combined interventions</b>	<b>Combined interventions at per NSP coverage targets above</b>	<b>2 938</b>	<b>+74.0%</b>	<b>6.29</b>	<b>+18.1%</b>	<b>467</b>
<b>Maximum scenario</b>						
Double DDT screening	95 million screens	6 676	+168.2%	9.92	+28.6%	673
Double TPT indications for PLWH	0.8 million indications (10% IPT; 90% 3HP)					
TPT for HH contacts of persons with TB	0.2 million indications (10% IPT; 90% 3HP)					
TUTT for all contacts of persons with TB	0.2 million Xpert Ultra tests					
Improve linkage to treatment	Reduce ILTFU by 100%					

Abbreviations: Digital chest X-ray-DCXR; Door-to-door-DDT; 3 months of isoniazid-rifampin-3HP; Household-HH; Initial loss to follow-up-ILTFU; National strategic plan-NSP; Primary health care clinic-PHC; People living with HIV-PLWH; Tuberculosis-TB; Tuberculosis prevention therapy-TPT; Targeted universal testing for tuberculosis-TUTT. Notes: Baseline represents continuation the current TB programme interventions with no further improvements. \*Coverage level targets of NSP (2023-2027) interventions are sustained to 2042. % life years saved calculated as: 1.0-[life years lost in the intervention scenario]/life years lost in the baseline scenario). Costs are converted to US\$, using average exchange rates between 2021-2022 (<https://www.reuters.com/markets/currencies/forex-statistics-key-statistics/forex-toolkit.html>).

**Conclusions:** Scaling up TB interventions to NSP coverage targets will save lives and reduce TB incidence. However, the End TB targets will not be met, even with an aggressive prevention, screening, and treatment initiation strategy.

**EP02-1015-15 TB catastrophic cost survey in Cameroon, 2020**

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**Background and challenges to implementation:** The overall management of tuberculosis (TB) in Cameroon still faces many direct (consultations, paraclinical examinations) and indirect (transport, food, and hospitalization) catastrophic costs. These catastrophic costs may be partly responsible for the under-reporting of TB cases ; and may also constitute an obstacle to the “End TB 2035” strategy by lack of TB chain transmission in our communities. Hence the purpose of this survey is to assess the total costs borne by the households of patients undergoing treatment for TB.

**Intervention or response:** This is a cross-sectional study following the CAPI method that took place in November-December 2020 in 6 regions of Cameroon for a sam-

ple size of 750 patients (i.e. 25 clusters of 30 patients each). Was included in the survey, any TB patient (with informed consent), under treatment for at least 14 days ≥ 21 years old or accompanied minor. Data collected from smartphones were analyzed using statistical methods based on exploratory analysis and logistic regression.

**Results/Impact:** The results of this survey revealed that in 2020, a household with a tuberculosis patient in its midst incurred total costs related to the diagnosis and treatment of tuberculosis equal to 140,071 FCFA (213 euros).

Analysis of the incidence of total catastrophic costs shows that 64.33% and 33.99% of households with at least one member with TB suffer from catastrophic costs at the 10% and 25% thresholds, respectively. Households of TB patients in the Northern (94%), Western (89%) and Central (74.9%) regions are more likely to incur catastrophic costs .

**Conclusions:** This survey has made it possible to evaluate the costs borne by households for the management of tuberculosis in the Cameroonian health system. This will facilitate the implementation of universal health coverage, which will enter its pilot phase in Cameroon in 2023 and which already eliminates certain direct costs (free sputum examination).

**EP02-1016-15 High levels of TB treatment-associated catastrophic costs in Namibia, an upper middle-income setting**

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**Background:** Tuberculosis (TB) is a top public health priority in Namibia which is ranked among the top 30 countries with the highest high TB burden. The country is considered an Upper Middle-Income country by the World Bank, yet it has the second highest Gini coefficient, a measure of income inequality. We present the results of the first-ever TB patient cost survey in Namibia.

**Design/Methods:** In a cross-sectional survey of a sample of TB patients in nine regions across the country, survey questionnaires were administered electronically in Kobotoolbox by trained healthcare workers. Patients were interviewed on cost, time loss, coping measures and asset ownership.

**Results:** Of the 559 participants interviewed (313 male, 246 female), 123 (24.3%) had drug-resistant (DR) TB and 436 (75.7%) had drug-susceptible (DS) TB. DS-TB patients spent on average US\$789 on TB-related care per episode while MDR-TB patients spent an average of US\$3,061. Major pre-diagnosis cost drivers were medical then food costs for DR-TB compared to food costs followed by nutritional supplement costs for DS-TB.

Post-diagnosis cost drivers for DR-TB were wage hours lost, and food and nutritional supplements, yet for DS-TB patients the main cost drivers were food costs, wage hours lost and nutritional supplements costs.

A third (29.1%) of the TB patients in the survey reported having taken a loan/borrowed as a coping mechanism to defray TB costs and 14.6% sold their assets/properties. Other reported social consequences included social exclusion in 166 (29.7%), food insecurity in 147 (26.3%), lost formal employment in 75 (13.4%), children dropping out of school in 13 (2.3%) and divorce/separation in 12 (2.1%). Catastrophic costs (>20% of income) were experienced by up to 82.2% of households.

**Conclusions:** Despite the country having a generally high income, TB patients in Namibia experience disproportionately high costs and income. This necessitates the prioritization of social protection mechanisms for TB patients.

### EP02-1017-15 Impact of a conditional cash transfer programme on TB incidence, mortality and case-fatality rate in a cohort of low-income individuals in Brazil

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**Background:** Tuberculosis (TB) is considered a disease related to poverty, in fact, a higher burden of TB is often observed in populations with low socioeconomic status. During the COVID-19 pandemic, a substantial increase in the global TB burden caused by disruption of TB health services and increased poverty was predicted. Therefore, social interventions such as conditional cash transfers (CCT) can be effective in mitigating the effect of the pandemic on TB.

We estimated the effect of PBF on TB incidence, mortality, and fatality rate using a national cohort of 53 million individuals.

**Design/Methods:** We analyzed individuals who entered the Cohort of 100 Million Brazilians between 2004-2015 and compared BFP beneficiaries and non-beneficiaries. We used multivariate Poisson regressions, adjusted for all relevant demographic and socioeconomic variables, and weighted with inverse probability of treatment weight (IPTW). We also perform a wide range of stratifications and sensitivity analyses.

**Results:** Exposure to PBF was associated with lower rates of TB incidence (RR:0.59, 95% CI:0.58-0.60) and mortality rates (RR:0.69, 95% CI:0.65-0.73), was positively associated with a decrease in TB case fatality rates – although not statistically significant.

Individuals from historically neglected ethnic groups, indigenous peoples and blacks had a greater impact of the PBF on the incidence compared to whites, (RR:0.37 indigenous; RR:0.58 black and RR:0.67 white) on mor-

tality, the discrepancy between the ethnicity was even higher, RR:0.35 indigenous versus RR:0.83 white. Individuals living in extreme poverty had a greater impact of the PBF compared to less poor, (RR:0.49 versus RR:0.95 for incidence; RR:0.60 versus RR:1.00 for mortality and RR:0.80 versus RR:0.92 for fatality rate).

**Conclusions:** CCT can significantly reduce tuberculosis incidence and mortality, especially in extremely poor populations, by decreasing the unequal distribution of the TB burden in the most vulnerable populations, essential at this time with the dramatic increase in global poverty due to the COVID-19 pandemic.

### EP02-1018-15 Catastrophic cost from symptom onset to treatment initiation of drug-susceptible and drug-resistant TB in India: Implications for policy

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**Background:** Indian government provides free diagnosis and treatment for TB, but studies have shown that a significant proportion of people with TB face catastrophic cost during TB treatment. Most studies have not disaggregated costs in different phases of treatment; however, for planning social protection measures, it is important to understand in which phase of treatment people with TB are experiencing catastrophic cost. In this study, we filled this knowledge gap.

**Design/Methods:** 1482 people with drug-susceptible TB and 149 people with drug-resistant TB from four Indian states were interviewed at the beginning and end of their treatment to understand costs incurred in pre-treatment (i.e., from TB symptom onset to treatment initiation), intensive and continuation phases of treatment.

Costs were calculated using WHO's guidelines on TB patient cost surveys. Catastrophic cost in each phase was defined as treatment cost in that phase  $\geq 20\%$  of pre-TB annual household income.

**Results:** Average delay from symptom onset to drug-susceptible TB diagnosis was 9 weeks while the same for drug-resistant TB was 14 weeks. During this period, people with symptoms of TB visited several providers before they were diagnosed (Figure 1) and spent money on consultations, medicines, diagnostics, travel expenses. 19%-21% people with drug-susceptible TB faced catastrophic cost in pre-treatment period while another 11% faced catastrophic cost during treatment period. 32% people with drug-resistant TB faced catastrophic cost in pre-treatment phase. Indian government provides INR 500 per month as direct benefit transfer to all registered people with TB for nutritional support, however,

our study shows 6%-8% participants received this benefit in intensive phase and 45% in continuation phase of treatment.

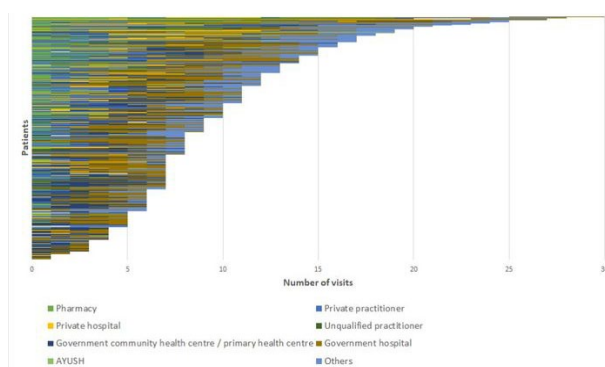


Figure 1. Treatment pathway in the pre-treatment phase for people with TB in urban slum areas (N=521).

**Conclusions:** As majority of catastrophic cost was incurred in pre-treatment phase and government benefits were not received on time, we strongly advocate for measures to reduce costs incurred in the pre-treatment phase and better management of direct benefit transfer.

## EP03 DR-TB New Developments

### EP03-1019-15 Anti-tuberculosis drug susceptibility of multidrug-resistant *Mycobacterium tuberculosis* in Japan: 2019–2022

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**Background:** Recently, the foreign born TB patients with relatively high potential of multidrug-resistant tuberculosis (MDR-TB) are increasing in Japan. MDR-TB collected over Japan in 2019–2022 were investigated for the drugs susceptibilities including linezolid (LZD), bedaquiline (BDQ) and delamanid (DLM), and genetic inter-relations.

**Design/Methods:** Eighty-five strains diagnosed as MDR-TB were collected from 21 hospitals in Japan. Drug susceptibility testing was performed by minimal inhibitory concentration (MIC) using broth microdilution method US CLSI M24 3<sup>rd</sup> ed. In parallel, whole-genome sequence analysis was performed for each isolate using NextSeq (Illumina), and genome-wide SNP-based linkage was analyzed using MTBseq.

**Results:** The MIC<sub>90</sub> (µg/mL) are as follows; isoniazid (INH): 32, rifampicin (RIF): >64, rifabutin (RBT): 16, ethambutol: 16, amikacin: >64, kanamycin (KM): >64, capreomycin: 32, levofloxacin (LVFX): 8, moxifloxacin (MFLX): 2, ofloxacin (OFLX): 8, LZD: 1, BDQ: 0.125, DLM: 0.06, respectively. Drug resistance rates estimated by MIC breakpoints are as follows; RBT: 83.5%, KM: 17.6%, LVFX: 37.6%, LZD: 2.4%, BDQ: 16.3%. Also 2 strains showed MIC 4 µg/ml for DLM. 16.5% of RIF-resistant strains showed the MIC for RBT less than 0.5 µg/ml. Comparing the MICs of three fluoroquinolones, MFLX, LVFX and OFLX were lower in that order. A total of three extensively drug-resistant *M. tuberculosis* was identified. One strain had resistance both to BDQ and DLM. The genomic linkage analysis did not identify any suspected direct transmission of MDR-TB in this population.

**Conclusions:** As LZD, BDQ and DLM showed high MICs in several isolates, MIC measurement was considered necessary before use for MDR-TB treatment.

### EP03-1020-15 Performance evaluation of ExiStation AccuPower TB & MDR Real-Time PCR Kit: the experience of Kazakhstan

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**Background:** Diagnosing of drug-resistant TB is essential for the establishment of a therapeutic strategy. Several assays based on PCR are available for diagnosing tuberculosis, including drug-resistant forms.

We report of our experiences in evaluating the performance of the AccuPower® TB&MDR and AccuPower® XDR-TB kit that were implemented at NRL, Kazakhstan.

**Design/Methods:** In total 358 clinical Mycobacterium tuberculosis isolates from national TB center were analyzed with the AccuPower® TB&MDR and AccuPower® XDR-TB Real-Time PCR Kit and MGIT 960. Discrepant results of tests were confirmed by sequencing.

**Results:** Sensitivity and specificity of AccuPower® TB&MDR and AccuPower® XDR-TB for cultured isolates were 94.9% and 95.72% for Rifampicin resistance, 79.8% and 96.3% for Isoniazid resistance, 82.4% and 97.6% for fluoroquinolone resistance, and 69.2% and 98.7% for second-line injectable drug resistance. The sensitivities of each drug were equivalent to other molecular DST methods. The efficiency of detecting drug-resistant tuberculosis among patients with a negative smear microscopy was 69.6% versus 43.2% at MGIT. In this study we also founded that AccuPower® TB&MDR and AccuPower® XDR-TB test can de-



tect MDR-TB in isolates with the low level resistance-associated mutations which were missed by phenotypic method.

**Conclusions:** Based on these results, AccuPower® TB&MDR and AccuPower® XDR-TB Real-Time PCR Kit-A can be used in routine practice to detect MDR-TB and pre-XDR-TB.

### EP03-1021-15 Descriptive analysis of mutations associated with TB drug resistance in Peru

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**Background:** Peru is considered among the 30 countries with the highest burden of multidrug-resistant tuberculosis (MDR-TB) worldwide. The study aims to describe the prevalence of mutations associated with antituberculosis resistance in Peru.

**Design/Methods:** 585 representative strains of phenotypically drug-resistant *Mycobacterium tuberculosis* stored at the National Institute of Health of Peru between 2015-2018 were selected. Strains were whole genome sequenced on Illumina HiSeq 2500 instruments at the University of Oxford. Genotypic drug susceptibility test was performed for rifampicin, isoniazid, ethambutol, streptomycin, pyrazinamide, levofloxacin, moxifloxacin, amikacin, kanamycin, capreomycin, ethionamide, delamanid and linezolid. Resistance-associated variants were identified with TBProfiler v4.1.1 using the catalogue of mutations published by the World Health Organization (WHO). Most frequent mutations were established as those found in at least 10 strains.

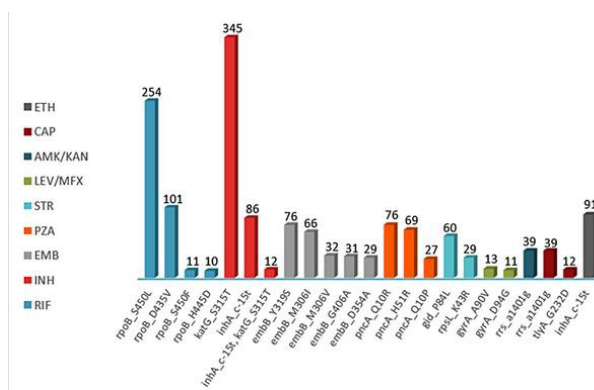


Figure 1. Most frequent mutations determined on Peruvian *Mycobacterium tuberculosis* strains for 11 antituberculosis drugs, 2015-2018. Numerical values represent the number of strains where each mutation has been found.

Likewise, mutations not included in the WHO catalogue were defined as “no data” being 14% (23/170). 20 mutations were set as most frequent (Figure 1). 53 isoniazid-mono-resistant TB (HR-TB), 32 rifampicin-mono-resistant TB (RR-TB), 348 MDR-TB and 50 pre extensively drug-resistant TB (Pre-XDR-TB) strains were obtained. Mutations showed a constant prevalence pattern throughout the analyzed years. Common and rare mutations were more prevalent in the political center of Peru (Lima and Callao).

**Conclusions:** In Peru, there is a high variability of mutations associated with resistance to first- and second-line drugs. However, there is a limited number of highly prevalent mutations driving resistance to the main anti-tuberculosis drugs, except for delamanid and linezolid. In addition, mutations are centralized in the capital of Peru.

### EP03-1022-15 Precision diagnosis to detect drug-resistant TB in a high TB burden setting

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**Background:** Drug resistant Tuberculosis (DR-TB) threatens to erase the global progress made towards eliminating TB. Existing phenotypic and genotypic drug susceptibility tests (DST) procedures have many limitations including high turnaround time, low accessibility, and none of these tests are exhaustive. AarogyaAI® has developed a genomics based, Artificial intelligence-powered diagnosis tool for DR-TB.

The input required is the sequencing data from the patient specimen, and the output is the drug report with the drug sensitivity status of the antibiotics used for treating TB.

**Design/Methods:** *Mycobacterium tuberculosis* (*M. tb*) H37Rv (NC\_000962.3) genome was used as the standard genome for aligning high quality sequence reads using the proprietary AarogyaAI® algorithm (trained on 7000 WGS *M. tb* data).

In case of sputum samples, a list of all microbial agents present were prepared and reads aligning to *M. tb* were taken for further drug resistance analysis. A variant calling protocol, part of the algorithm, was applied to these filtered reads.

Low quality variants were marked separately, remaining variants detected in the aligned reads are parsed by the AarogyaAI® machine learning algorithm. The algorithm considers the reference mutations standardised by the World Health Organisation (June 2021), NIAID, CARD, CRYP TIC as well as its own learning from training.

As an output, the algorithm generated the DR status against 19 anti-TB drugs and the microbial diversity detected in the samples.

**Results:** The gDST results obtained for each dataset was compared with corresponding pDST results to check for concordance. A summary of the features offered by AAICARE™-TB has been tabulated above.

Serial No.	Noticeable feature	Output/application
I.	Patient specific DST report	Pipeline generates a patient-specific DST report for 19 anti-TB drugs.
II.	Culture-free approach	Slow growth rate of <i>M. tb</i> takes higher time for pDST and removing a culture step can reduce the total time taken for the analysis. Pipeline offers an entire genome analysis that includes detection of resistance-causing mutations lying outside the genomic regions targeted by the probe-based methods.
III.	Whole genome coverage	Pipeline separately analyses the reads that do not align to <i>M.tb</i> , which allows the detection of NTM.
IV.	Nontuberculous mycobacteria (NTM) detection	The output provides co-infections and hetero-resistance reports which can guide a patient specific treatment regimen.
V.	Hetero-resistance detection	Pipeline separately analyses the reads that do not align to <i>M.tb</i> , which allows identification of the microbial diversity in the sample.
VI.	Microbial Diversity	The pipeline comprises a quality control report
VII.	Quality control	

**Conclusions:** Overall, our gDST test results have shown significantly high levels of concordance with pDST results, thus reinforcing the credibility of our tool. Based on the unique features listed above and the credibility analysis performed, AAICARE™-TB seems to be a promising asset for surveillance and elimination of DR-TB, globally.

### EP03-1023-15 Isoniazid resistance pattern among pulmonary TB patients in Bangladesh: An exploratory study

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**Background:** In many high tuberculosis (TB) burden countries including Bangladesh, most of the research and policy efforts are predominantly focused on multidrug-resistant TB (MDR-TB) and rifampicin (RIF) resistance. For this reason, many TB patients with RIF sensitive but isoniazid (INH) resistant (Hr-TB) remain undiagnosed and do not receive appropriate treatment.

In this study, we aimed to explore the INH resistance pattern and its impact on the treatment outcome in Bangladesh.

**Design/Methods:** We conducted this study in nine public-private TB Screening and Treatment Centers located in Dhaka, Chittagong, and Sylhet divisions. Sputum samples from 1084 Xpert positive pulmonary TB patients were collected between April, 2021 to December, 2022, and subjected to culture in Lowenstein-Jensen medium. Drug susceptibility testing (DST) was performed on culture positive isolates against INH, RIF, ethambutol, kanamycin, levofloxacin, and moxifloxacin. The patients were followed-up to assess the outcome without interfering the current treatment modality.

**Results:** Among the available DST results of 845 isolates, overall resistance rate of any INH was 6% (51/845) (95% CI, 4.4-7.9) in all cases. The rate was significantly higher in retreated cases (21.7%, 15/69; 95% CI, 12.2-35.9) compared to new cases (4.6%, 36/776; 95% CI, 3.2-6.4) ( $p < 0.001$ ). The rate of Hr-TB was 3.9% (33/845) (95% CI, 2.7-5.5), which was almost double compared to the MDR-TB rate (2.1%; 95% CI, 1.3-3.4) found in the current study.

Although there were no significant differences on the treatment outcome but the death rate was higher among Hr-TB cases (6.1%; 95% CI, 0.7-21.8) compared to drug sensitive TB cases (1.8%; 95% CI, 0.9-3.0) ( $p = 0.083$ ).

**Conclusions:** This study shows that there is a high prevalence of Hr-TB in Bangladesh but the patient remains undetected with the current policy in practice, which emphasizes the importance of adopting molecular tools at national level for rapid detection of INH resistance and to ensure appropriate therapy.

### EP03-1024-15 Impact of using GeneXpert testing as a WHO rapid diagnostic test for TB case notification: Experience from Karonga District Hospital, Malawi

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**Background and challenges to implementation:** Malawi is among the 30 WHO-identified high TB/HIV burden countries. One of the End TB Strategy targets is to ensure that all patients notified with TB are tested with a WHO-recommended rapid test (WRD) as the initial test by 2025.

Despite 2020 marking a decade since the first WRD was recommended, only 33% of people diagnosed with TB received a WRD. In 2017, Karonga district hospital no-

tified 118 TB patients but only 31% had WRD due to poor referral system and coordination among providers.

**Intervention or response:** Malawi released its national guideline in 2018 which indicated that all notified TB cases should have a WRD result. Karonga district hospital was one of the facilities that were trained on the new updates and started implementing in the 4<sup>th</sup> quarter of 2018 to date. Monitoring and evaluation initiatives were intensified to improve on recording and reporting as well as sensitizing all providers during ongoing morning meetings and CPD presentations to make sure that all TB patients are referred for WRD test. Onsite quarterly supportive supervision and mentorship by the national and zone supervisors were conducted to TB officers, clinicians and nurses.

**Results/Impact:** The results in Table 1 show an increase in the notified TB cases done by Gene expert, for those with HIV negative it has moved from 16% in 2017 to 91% in 2022, while for HIV positive it has tremendously increased from 50% in 2017 to 97% in 2022. Most HIV positive cases were tested on expert than those with HIV negative.

Year	Total notified cases	Total TB/HIV- cases	Total TB/HIV- with Xpert	Total TB/HIV+ cases.	Total TB/HIV+ cases with Xpert
2017	118	62	10(16%)	54	27(50%)
2018	145	74	18(24%)	71	29(41%)
2019	168	81	56(69%)	87	65(75%)
2020	138	69	60(87%)	69	65(94%)
2021	105	42	36(86%)	63	60(95%)
2022	145	70	64(91%)	75	73(97%)

Table 1. Case notification with WRD.

**Conclusions:** Karonga district hospital has shown that it is feasible to achieve the set targets using WRD test for all TB cases by 2025. This was done through capacity building, improvement of M&E initiatives, good coordination and continuous onsite mentorship and supportive supervision. Other facilities can learn from what Karonga hospital has achieved for a period of 3 years.

### EP03-1025-15 Fluorescent quantitative urine lipoarabinomannan strip for rapid TB diagnosis in adults without HIV: An antigen diagnostics study

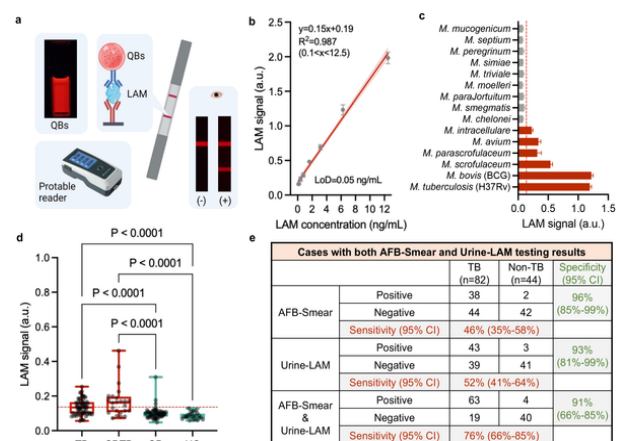
Z. Huang,<sup>1</sup> H. Huang,<sup>1,2</sup> L. Xia,<sup>1</sup> X. Liu,<sup>1</sup> J. Hu,<sup>3</sup> W. Kang,<sup>4</sup> Y. Fang,<sup>4</sup> W. Sha,<sup>4</sup> Y. Xiong,<sup>3</sup> S. Lu,<sup>1</sup> X. Fan,<sup>2</sup> <sup>1</sup>The Third People's Hospital of Shenzhen, National Clinical Research Center for Infectious Disease, Shenzhen, China, <sup>2</sup>Fudan University, Shanghai Public Health Clinical Center, Shanghai, China, <sup>3</sup>Nanchang University, Jiangxi-OAI Joint Research Institute, Nanchang, China, <sup>4</sup>Tongji University, Shanghai Pulmonary Hospital, Shanghai, China. e-mail: Huang.zhen@outlook.com

**Background:** Tuberculosis (TB) remains a major underdiagnosed public health threat worldwide. Although analyzing lipoarabinomannan (LAM) in urine can aid in TB diagnosis, its performance is unsatisfactory, particu-

larly for those without HIV. Our study aim was to evaluate whether novel test strips, enhanced with ultrabright fluorescent probes, can improve TB diagnosis.

**Design/Methods:** We developed a novel fluorescent lateral flow strip by employing the quantum dots nanobeads (QBs) probe and a portable reader for point-of-care quantifying LAM in urine samples. The newly developed assay was evaluated by testing archived urine collected from two hospitals and one university from TB and non-TB patients and healthy. Wilcoxon rank-sum tests were used to compare Urine-LAM signals between TB classifications.

**Results:** The proposed assay (Fig. 1a) can detect as low as 0.05 ng/ $\mu$ L LAM in urine (Fig. 1b) and accurately identify *Mycobacterium tuberculosis* and BCG and several slowly growing mycobacteria that cause disease (Fig. 1c) during 15 min. The novel strip detected 50% (32/64) of microbiologically confirmed TB cases and 58% (14/24) of clinically diagnosed TB (CDTB) cases (Fig. 1d), which showed a pool-sensitivity of 52% (95% CI, 41% - 63%). All (25/25) healthy control (HC) and 53 of 56 other diseases (OD) patients show negative urine LAM test (Fig. 1d), indicating the 96% (95% CI, 90% - 99%) specificity of the novel assay. By combining the AFB-Smear test with the urine LAM test, the TB diagnosis rate in this study population could be increased to 77% (95% CI, 66% - 85%), with specificity slightly decreased to 91% (95% CI, 78% - 97%) (Fig. 1e).



**Conclusions:** The ultrabright fluorescent probes enhanced urine LAM strip shows promise to increase the identification of adult TB patients without HIV. By using both AFB-Smear and urine-LAM assay in clinical practice, it is possible to improve non-HIV TB diagnosis efficiency in low-resource settings.

### EP03-1026-15 TrueNat, an effective diagnostic tool for detecting drug-resistant TB: A case study from the TB LON 1 and 2 Projects

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**Background and challenges to implementation:** Drug-resistant Tuberculosis in Nigeria is a growing concern, and it poses a significant challenge to TB control efforts. According to the 2022 global TB report, there is a high prevalence of DR-TB with an estimated 33,000 cases but only 15,000 cases were reported.

The actual number of DR-TB cases in the country is likely higher as many cases go undiagnosed or unreported. Nigeria adopted Xpert MTB/RIF assay in 2016 as the first-line test for TB diagnosis & the detection of DR-TB.

However, some challenges including limited coverage & irregular power supply made it difficult for the country to derive maximum benefit from the utilization of Xpert MTB/RIF assay for DR-TB diagnosis. In 2020, The World Health Organization recommended Truenat MTB-RIF Dx as a rapid molecular assay for TB diagnosis and detection of Rifampicin resistance. Nigeria adopted its use in 2021.

This paper aims to project TrueNat as an effective diagnostic tool for DR-TB detection.

**Intervention or response:** In November 2021, The USAID funded TB LON 1&2 Project through KNCV Nigeria introduced 28 Truenat machines across 11 high burdened sites in the 14 supported states of the project. Laboratory health workers were trained on the operational guidelines & procedures of Truenat and provided the National Recording & Reporting tools for data collection and collation.

**Results/Impact:** The chart below captures data from January-December 2022 across all 14 states in the project. At 100% optimal functionality, the Truenat contributed 4% of the total DR-TB yield while Gene Xpert contributed 3%.

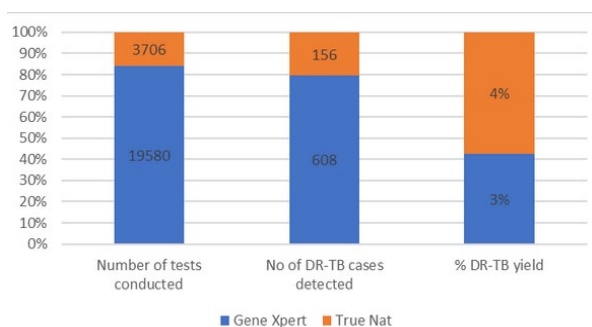


Figure.

**Conclusions:** Truenat contributed 4% of the DR-TB case detection owing to its easy-to-use nature & accessibility to hard-to-reach areas. There is a need for increased investment in diagnostic tools like the TrueNat machine across TB high burdened countries to bridge the gap in access to DR-TB diagnosis and treatment.

### EP03-1027-15 A pilot study of detecting latent TB infection with a breath test using mass spectrometer

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**Background:** One-fourth of the world's population may develop active tuberculosis (ATB) due to Mycobacterium tuberculosis (M.tb) infection. However, there is currently no widely accepted method for diagnosing latent tuberculosis infection (LTBI).

Immunodiagnostic tests can detect LTBI, but cannot differentiate between LTBI and ATB. Meanwhile, the breath test can diagnose ATB, but has not been evaluated for LTBI diagnosis.

This study explores the potential of high-pressure photon ionization time-of-flight mass spectrometry (HP-PI-TOFMS) in detecting volatile organic compounds (VOCs) in exhaled breath for LTBI diagnosis.

**Design/Methods:** The study enrolled 185 LTBI subjects and 129 healthy controls (HC). Participants were randomly split into three groups for model construction, internal validation, and model-blinded testing. Data produced by HPPI-TOFMS underwent noise reduction, baseline correction, and feature extraction. A total of 1,500 ion features in the mass-to-charge (m/z) range of 20 to 320 were extracted, and features without significant differences were excluded. The top ten VOC ions were selected for LTBI detection.

**Results:** The LTBI detection model based on breath test via HPPI-TOFMS had a sensitivity of 91.1% (83.2%-98.9%) and a specificity of 87.2% (76.7%-97.7%), with an area under the curve (AUC) of 0.967 (0.930-1.0007). The top eight VOC ion combinations were selected based on the model feature importance coefficient.

**Conclusions:** The study suggests that a breath test via HPPI-TOFMS could be a noninvasive, simple, and fast method for LTBI diagnosis, especially in screening large populations for LTBI. However, further studies with a larger sample size are necessary before clinical application.

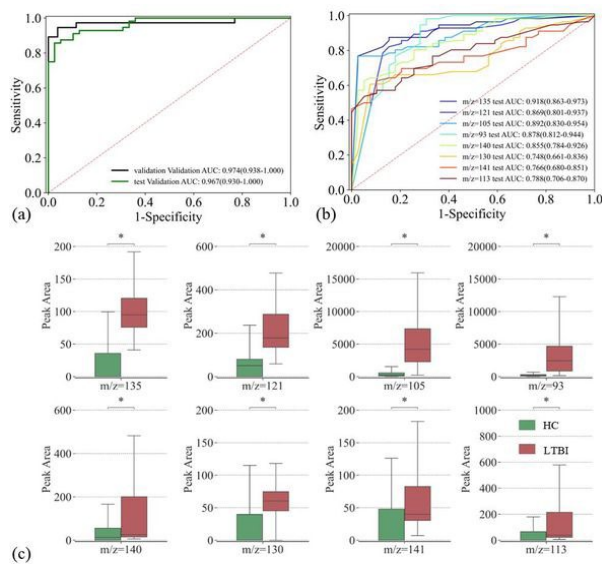


Figure 1. The performance of the LTBI model, and the detection power and intensity analysis of the top eight VOC ions ROC in validation and test sets (a). The LTBI detection power of top eight selected VOC ions in test set (b). The intensity distribution of the top eight VOC ions in all participants' breath samples (c).

## EP04 TB Comorbidities

### EP04-1028-15 Glycated haemoglobin levels in a cohort of patients with drug-susceptible TB, during and after treatment

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**Background:** TB and diabetes mellitus (DM) are leading causes of death in South Africa (SA). HbA1c is diagnostic for DM but there is concern about its accuracy in TB patients. Our objective was to compare in newly diagnosed TB patients HbA1c results with random, fasting and 2hour glucose(2hPG) following an oral glucose load.

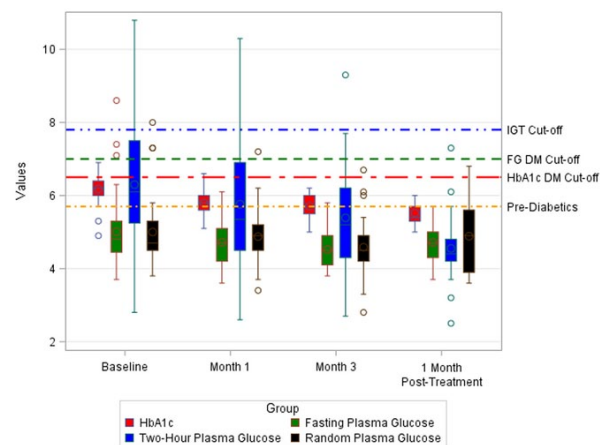
**Design/Methods:** This prospective cohort recruited adults aged 25-65 years old with DSTB (diagnosed on Xpert MTB/RIF Ultra and mycobacterial culture) between February 2019-March 2022 who had taken  $\leq 4$

doses of anti-TB treatment(ATT). Blood was tested for NGSP-certified HbA1c, RPG, and the following day, FPG and 2hPG in those who were not known diabetics. This testing schema was repeated at months 1(M1) and 3(M3) of ATT, and a month after ATT.

**Results:** Of 59 patients whose median age was 36 years (IQR:31-45); median BMI 20.0kg/m<sup>2</sup> (IQR:17.6-23.1); 66.1% were men; and 45.8% were living with HIV. Eight self-reported DM; their median HbA1c was 10.95% (IQR:10.23-12.92) and RPG:14.45 mmol/l (IQR:8.85-20.00).

Eight had no prior history of DM, yet their baseline HbA1c was  $\geq 6.5\%$  but all their RPGs were normal, 3/8 had FPG  $\geq 7.0$ mmol/l, and an additional 2/8 had 2hPGs  $\geq 7.8$ mmol/l. Thirty-two had pre-DM(HbA1c 5.7-6.4mmol/l), but their RPGs were  $\leq 11.1$ mmol/l, FPGs were  $\geq 7.0$ mmol/l in only 1/32 and 2hPG was  $\geq 7.8$ mmol/l in 7/32.

Finally, 11/59 had normal HbA1c, RPG and FPG results at baseline; 1/11 had 2hPG $\geq 7.8$ mmol/l which normalised by M1 (Table). Of 40 with an elevated baseline HbA1c and no prior history of DM, nine had impaired glucose tolerance which resolved in all by the end of TB treatment.



**Conclusions:** Definitive diagnosis of DM in newly diagnosed patients with TB is difficult. HbA1c appears to over-diagnose diabetes and pre-diabetes. FPG and/or 2h-PG may be better screening tests for DM at TB diagnosis and definitive DM should be confirmed once TB is cured.

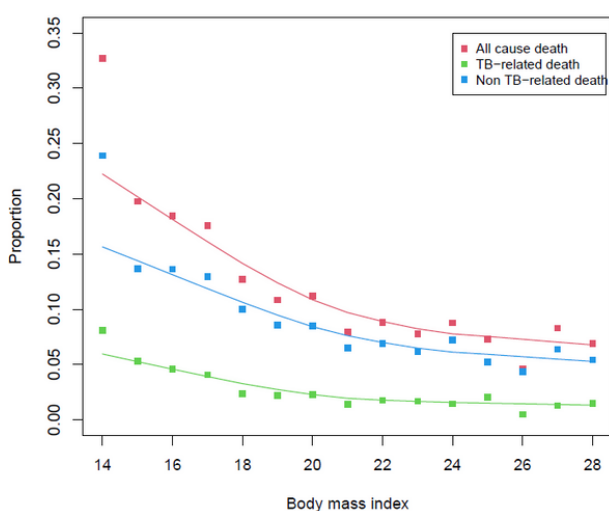
### EP04-1029-15 The effect of underweight and overweight on mortality and disease severity among patients with pulmonary TB

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**Background:** Poor nutrition increases disease severity and mortality in patients with tuberculosis (TB). There are gaps in our understanding of the effects of underweight and overweight on TB in relation to sex.

**Design/Methods:** We generated a nationwide TB registry database and assessed the effects of body mass index (BMI) on the initial severity and mortality in pulmonary TB patients. Six outcomes of interest were TB-related symptoms, positive acid-fast bacilli smear test results, chest radiographic findings of cavitation and bilateral infiltration, and TB-related and non-TB-related deaths. Logistic regression was performed to assess the association between BMI (a continuous variable) and each outcome. Subgroup analyses of the multivariable logistic regression model were performed in male and female patients separately.

Further sensitivity analysis was conducted to assess the impacts of underweight (<18.5 kg/m<sup>2</sup>) and overweight (≥23.0 kg/m<sup>2</sup>) on each outcome with reference to normal weight (18.5-22.9 kg/m<sup>2</sup>).



**Results:** Among 9,721 patients with pulmonary TB, the mean age was 61.8 years, and 3,544 (36.5%) were female. The mean value of BMI was  $21.3 \pm 3.4$ ; 1,927 (19.8%) were underweight, and 3,987 (41.0%) were overweight.

On the multivariable logistic regression analysis, we observed statistically significant negative associations between BMI, baseline severity indices, and mortality. On sensitivity analyses, underweight patients had significantly higher odds of mortality, especially TB-related death (adjusted odds ratio [aOR] = 2.057, 95% confidence interval [CI] = 1.546-2.735).

Overweight patients had a significant protective effect on TB-related death in only females (aOR = 0.500, 95% CI = 0.268-0.934), whereas its effect on non-TB-related death was observed in only males (aOR = 0.739, 95% CI = 0.587-0.930).

**Conclusions:** Underweight was linked to severe presentations and high mortality, whereas overweight had beneficial effects in patients with pulmonary TB. It is necessary to incorporate nutritional assessment at the time of TB diagnosis into standard TB care.

### EP04-1030-15 Nutritional status of adult TB patients in Puducherry, India - a community-based, mixed-methods study

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**Background:** Undernutrition is a widely prevalent comorbidity for tuberculosis disease and mortality in high burden countries like India. As per NFHS-4 the overall burden of under-nutrition in Puducherry was 21.4%. The objective of the study was to assess the nutritional status of TB patients diagnosed in Puducherry between December 2019 to December 2020 through 1) Dietary assessment (72-hour recall), anthropometric measurements (Body mass index (BMI) & Mid-upper arm circumference (MUAC) and laboratory investigation (Haemoglobin (Hb) measurement). It also attempts to explore the perceptions of various stake holders regarding the nutritional care and support for TB patients.

**Design/Methods:** This sequential mixed-method study was conducted in two phases. Phase I was quantitative wherein eligible individuals were selected by multi-stage sampling technique. A semi-structured, validated questionnaire was administered for dietary recall. Anthropometrics and lab investigations were simultaneously conducted. Phase II was qualitative wherein twelve IDIs (In-depth interviews) were conducted among patients and providers selected by purposive sampling. Appropriate statistical tests were applied to the quantitative data and manual content analysis was done for the qualitative transcript.

**Results:** Based on BMI and MUAC, 50.1% and 63.7% were undernourished respectively. 54.8% of the study participants had anemia. The mean of average intake of calorie and proteins, was  $1651 \pm 184.58$  and  $51.42 \pm 6.29$  respectively.

Two themes emerged from manual content analysis:

1. Nutritional counselling by health staff,
2. NI-KSHAY Poshan Yojana (NPY- NTEP initiative of cash benefits to patients as nutrition support).

The knowledge, practices and attitude of the interviewees on these themes were further categorized from the transcripts and analyzed.

**Conclusions:** One in every two TB patient in Puducherry was under-nourished and anemic. TB patients were consuming lesser calories and proteins than the recommended daily allowance. Though there are schemes like Nikshay Poshan Yojana additional interventions are needed to improve the nutritional status of TB patients.

#### EP04-1031-15 The impact of vitamin D on TB treatment outcomes: A systematic review

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**Background:** Persons with tuberculosis (PWTB) frequently have nutritional deficiencies. There has been great interest in the role of vitamin D to improve tuberculosis (TB) treatment outcomes, but data are conflicting. We conducted a systematic review to explore the effects of vitamin D supplementation on TB treatment outcomes.

**Design/Methods:** Following PRISMA guidelines, publications were identified via PubMed, BIOSIS, CINAHL, Cochrane, Embase, LILACS, SciELO, and Web of Science (to September, 2022). Only articles published in English, Spanish, and French were considered for inclusion. Eligible manuscripts were screened independently by two review authors according to inclusion criteria. Primary exposure was vitamin D supplementation. The primary outcome was TB treatment success and the secondary outcome was sputum smear conversion at two months. We conducted meta-analyses using a random effects model.

**Results:** We found 2 controlled trials (constituting 762 participants) studying the impact of vitamin D on TB treatment outcomes and a total of 10 studies (constituting 1,408 participants) evaluating the impact of vitamin D supplementation on sputum smear conversion. Compared with placebo, vitamin D supplementation

was found to have no significant effect on tuberculosis treatment success (odds ratio [OR] = 0.77; 95% confidence interval [CI] = 0.00 to 876.63;  $p = 0.632$ ). Vitamin D supplementation did significantly influence sputum smear conversion (OR = 1.56; 95% CI = 1.09 to 2.25;  $p = 0.005$ ).

**Conclusions:** This review shows that vitamin D supplementation does not have a meaningful benefit on tuberculosis treatment success but does influence sputum conversion. PWTB have numerous nutritional deficits which blunt the immune response to TB. We hypothesize that the failure of vitamin D supplementation to improve treatment outcomes is because repletion of just one nutrient is insufficient to resuscitate the TB immune response. Future studies should consider providing multiple micronutrients and macronutrients to meet the nutritional needs of PWTB.

#### EP04-1032-15 Alcohol's effect on TB treatment response: A cohort study in the Western Cape, South Africa

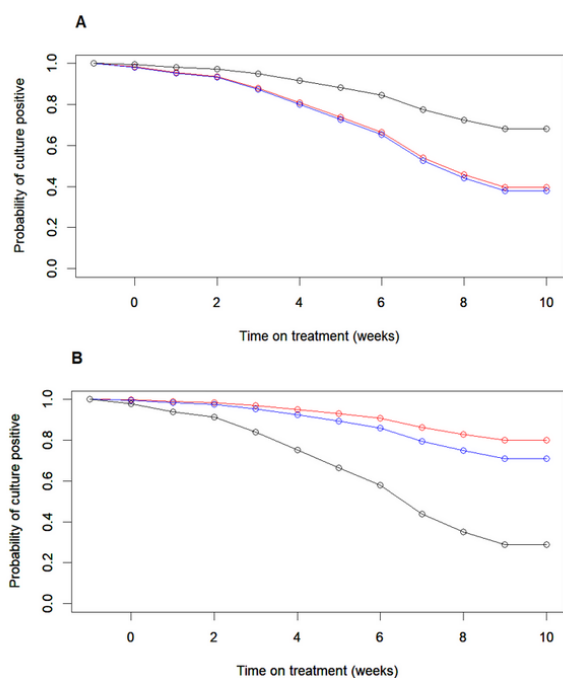
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**Background:** People who use alcohol (PWUA) may experience delayed tuberculosis (TB) sterilization during treatment. Potential reasons include behavioral factors like poor medication adherence or biological mechanisms via alcohol's impact on alveolar macrophages. Documenting sputum conversion for PWUA after adjusting for TB medication adherence is a first step to disentangling alcohol's behavioral and biological effects.

**Design/Methods:** 305 participants initiated rifampicin-susceptible TB treatment. Participants provided weekly sputum specimens for 12 weeks and had 5-weekdays of directly observed therapy. Our outcome was time-to-culture conversion (TCC), defined as two consecutive weeks with no *Mycobacterium tuberculosis* growth. We categorized alcohol exposure into low, moderate, high

using the Alcohol use disorders identification test, two-week Timeline follow-back, and Phosphatidylethanol biomarker. We defined 12-week treatment adherence as  $\geq 80\%$  versus  $< 80\%$ . We fit a cox proportional hazards model with adherence as an effect modifier for the association between alcohol exposure and TCC, adjusting for age, sex, HIV, isoniazid resistance, smoked drug use, tobacco use, and baseline culture time to positivity.

**Results:** Median TCC was 7



**Figure 1.** Survival curves from cox proportional hazards model stratified by adherence. Panel A,  $< 80\%$  adherence; panel B,  $\ge 80\%$  adherence. Line colors represent alcohol exposure (black, low; red, moderate; blue, high)

(IQR: 6,8) weeks. 72.2% (95% CI: 71.3%, 73.2%) converted by week 10. Participants with  $< 80\%$  adherence and moderate (HR: 2.19, 95% CI: 1.06, 4.52) or high alcohol exposure (HR: 3.20, 95% CI: 1.35, 7.67) culture converted faster than those with low. This association did not hold for participants with  $\ge 80\%$  adherence.

Older age (HR: 0.9, 95% CI: 0.9, 1.0), and a longer baseline TTP (HR: 1.7, 95% CI: 1.6, 2.0) were associated with faster conversion. Participants with high alcohol exposure trended to less with HIV, more employed, more with normal BMI, less smoking drugs, and lower bacterial burden.

**Conclusions:** For participants with  $\ge 80\%$  adherence, alcohol did not impact sterilization, indicating that PWUA can respond to TB therapy. Those with lower adherence had better sterilization with higher alcohol intake, potentially reflecting unmeasured confounding related to better underlying health.

## EP04-1033-15 Epidemiology of TB multimorbidity in India

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**Background:** Multimorbidity is a recognized public health problem globally. Especially low-and middle-income countries such as India, with burgeoning urbanization, not only the prevalence of non-communicable disease increasing, it is occurring with chronic infectious disease.

One such condition is Tuberculosis (TB) multimorbidity, defined as occurrence of TB with other chronic conditions. A critical knowledge gap exists as to the magnitude of TB multimorbidity in India.

**Design/Methods:** We undertook a longitudinal study to identify the prevalence and patterns of multimorbidity among primary care TB patients and its impact on the outcomes in Odisha and Telangana states of India. A total of 320 patients attending primary care facilities in each state were interviewed using a structured multimorbidity assessment questionnaire (MAC-PC).

Multimorbidity patterns (dyad and triad) were identified for 21 chronic conditions. The study employed cross-tabulation and Pearson's chi-square for analysis.

**Results:** The prevalence of multimorbidity among TB patients was found to be 65%. Most common dyad were depression (42.3%) followed by diabetes Mellitus (14.1%), hypertension (11.2%), arthritis (9.6%), etc. The most common triad (combination of two diseases with TB) was diabetes mellitus and depression (7.7%) followed by hypertension and depression (7.2%) and hypertension and diabetes mellitus (6.9%).

A high healthcare expenditure and out-of-pocket expenditure was observed among TB multimorbid patients compared to those without multimorbidity.

Around 26.8% TB multimorbid rated their overall health as fair to poor whereas among TB patients without multimorbidity, 8% rated their health as fair to poor. This was also statistically significant ( $p < 0.05$ ).

**Conclusions:** We highlight the co-existence of multiple chronic conditions with TB. This presents both challenges (increasing complexity and the impact on health services, providers and patients), and opportunities for screening in a population already linked to care.



It also necessitates re-thinking of models of healthcare delivery and requires policy interventions to integrate management of other co-morbidities.

#### EP04-1034-15 Psychosocial support for people with TB in healthcare and community settings in Sumenep Regency, Indonesia

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**Background and challenges to implementation:** People with TB experience mental health challenges from stigma, side effects, coping with comorbidities and medical complications, and diminishing or losing income. Indonesian TB program stakeholders are ill-equipped to provide the quality TB care needed when mental health issues are looming on successful program delivery.

Therefore, Stop TB Partnership Indonesia (STPI) aims to accelerate TB elimination amidst the pandemic by leveraging psychosocial interventions to support people with TB in overcoming negative emotional states and cognition during TB care.

**Intervention or response:** In 2022, In-house training was facilitated for the healthcare workers (TB nurses, mental health nurses, and doctors) from the 3 Primary Health Care (PHC) intervention sites. The healthcare workers were trained to integrate TB and mental health services. In-service training was conducted to ensure that the HCWs implemented their learned skills. Besides, community volunteers (cadres) were recruited and trained to be supporters and motivators. Following the training, the HCWs provided psychosocial support once the people with TB or their families visit the PHC, while the cadres conducted a home visit once a week to provide psychosocial support. Once a month, the people with TB and their families were also facilitated with a support group.

**Results/Impact:** The intervention provided support to 56 people with TB and their families. Based on the measurement of baseline and endline assessment using Depression, Anxiety, and Stress Scale 42, there was a significant difference in the depression level ( $p: 0,004$ ), anxiety level ( $0,001$ ), and stress level ( $0,000$ ). The support shortened the delay in starting the treatment and increased the awareness of the patient to complete their treatment.

**Conclusions:** Providing psychosocial support for people with TB and their families in healthcare settings and community settings may lead to positive mental health outcomes for patients and their families. Well-being may increase treatment adherence and affect the immune system of people with TB.

#### EP04-1035-15 Screening hazardous alcohol use among people with TB or HIV in Pune, India

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**Background:** Globally, prevalence of alcohol use (AU) among people with tuberculosis (PWTB) and people with HIV (PWH) is very high. In India, AU is one of the known risk factors associated with poor Tuberculosis (TB) and HIV treatment outcomes.

However, data on Hazardous Alcohol Use (HAU) is unavailable in the health system. In this study, we assess the prevalence of HAU among PWTB and PWH in programmatic settings in Pune, Maharashtra, India.

**Design/Methods:** Cross-sectional assessment of HAU was done among adult ( $\geq 18$  years) PWTB or PWH using WHO recommended Alcohol Use Disorder Identification Test -C (AUDIT-C) to assess the intensity of AU. We classified the AU as HAU if the AUDIT-C score was  $\geq 4$ . The study was conducted between September 2022 and March 2023 in TB and HIV clinics of tertiary care public health facilities in Pune.

**Results:** Overall, 570 PWTB (327 males, 243 females) and 3375 PWH (1743 males, 1625 females, 7 transgender) attending TB and HIV treatment clinics were screened for AU. None of the females were reported AU. The prevalence of AU among males was 45.6% (CI: 40.1-51.1) and 18.3% (CI: 17-20.1) in PWTB and PWH respectively. The median age of AU among PWTB is 40 years (IQR: 34-45) and PWH is 43 years (IQR: 36-51). The overall prevalence of HAU was 72.9% (CI: 67.9-77.2), 90.6% (CI: 84.2-95.1) among PWTB and 63.5% (CI: 57.1-69.4) among PWH. Age group of 46-60 reported the highest prevalence of HAU (76%, CI: 67.5-83.2).

**Conclusions:** Given the very high prevalence of AU among males, mandatory screening for HAU among PWTB and PWH in India is needed for initiation of early counselling and better TB and HIV treatment-outcomes.

### EP04-1036-15 Screening for HIV among persons with TB: Lessons from engaging non-orthodox platforms in Akwa-Ibom State, Nigeria

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**Background and challenges to implementation:** Nigeria is one of the high-burden countries for TB and TB/HIV that accounts for 89% of all new HIV infections. Only about 11% of persons with TB, know their HIV status in Nigeria. The engagement of non-orthodox platforms in the active search for TB proposes a great chance to increase knowledge of HIV status among Persons with TB in the community, extending means of access to TB and HIV treatment.

**Intervention or response:** The Global-Fund Public-Private Partnership TB (PPM TB) project was implemented in Akwa Ibom state Nigeria for a period of 24 months (January 2019 to December 2020). A hub-spoke model was used to identify non-orthodox platforms such as the Patent Medicine Vendors (PMV).

About 7-10 PMVs were mapped and clustered around health facilities (hub), which provide technical supervision, logistics, and laboratory support for TB diagnostics (using GeneXpert technology) and treatment as well as monitoring and reporting. All partner PMVs were trained on TB screening, HIV education, referral systems, and reporting. 197 PMVs were mapped to 21 Health facilities.

**Results/Impact:** 572 new persons with TB were started on TB treatment across the 21 health facilities. 355 were from non-orthodox platforms. The PMVs contributed 62% of the new TB cases recorded in the health facilities (hubs) during this period. 100% of the 355 people diagnosed with TB from the non-orthodox platforms, were tested for HIV and knew their HIV status for the first time. 104 tested HIV positive and 251 tested HIV negative.

**Conclusions:** These results add to reported evidence that decentralized health services and devolution of care increase access to care and increase client involvement in their own clinical management. Non-orthodox platforms helped in TB screening and HIV testing increasing access to HIV testing services by 100% for the new persons receiving TB treatment through the hub-spoke referral system of the PMVs.

### EP05 One breath at a time: Pediatric lung health

#### EP05-1037-15 Development of a novel scoring tool to detect aspiration risk in children with pneumonia using healthy breastfed infants in Malawi

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**Background:** Pneumonia is the leading infectious cause of death in children under 5-years-old in low- and middle-income countries (LMICs). Feeding-related aspiration has been implicated in some child pneumonia deaths; however, validated techniques for detecting aspiration-risk in LMICs are lacking. To begin development of a feasible tool to accurately assess aspiration-risk among Malawian infants with pneumonia, we initially sought to establish normative feeding values.

**Design/Methods:** We prospectively enrolled healthy infants (0-12 months) at a government vaccination clinic in Lilongwe, Malawi, excluding those with respiratory symptoms, craniofacial abnormalities, neurologic disorders, or altered mental status. Prior to enrollment, candidate scoring system variables were selected from the literature and expert opinion.

We collected sociodemographic and clinical information and evaluated infants while feeding/swallowing during five minutes of breastfeeding. Descriptive statistics were performed on variables collected during breastfeeding. Distributions and frequencies of candidate variables were examined and assigned a point value per expert consensus to create the score framework.

**Results:** 87 participants were enrolled; 5 were excluded from analysis due to current and/or prior illness. Of 82 analyzed participants, 65% (n=53) were female, median age was 3-months (interquartile range 1,6), 5% (n=4) were born  $\leq$ 37 weeks, and 32% (n=26) were HIV-exposed. Seventy participants (85.4%) were classified as "normal feeding/swallowing" with cumulative scores ranging 0-2. The scoring system classified six participants (7.3%) as "atypical feeding/swallowing" and six (7.3%) as "dysfunctional feeding/swallowing."

Feeding/Swallowing Evaluation Variables	N*	Mean $\pm$ SD	5%	10%	Median	90%	95%	1 Point	2 Points
Post-feed respiratory rate	81	46.18 $\pm$ 11.48	30	33	45	62	68	>90-95% tile	>95%
Change in respiratory rate after feeding	80	2.85 $\pm$ 10.56	-16.5	-10	2.5	14.5	31	>1SD-2SD	>2SD
Post-feed oxygen saturation	67	98.25 $\pm$ 1.53	95	96	99	100	100	<10-5% tile	<5%tile
Change in oxygen saturation after feeding	66	0.42 $\pm$ 2.69	-3	-3	0	4	5	<(-1SD) - (-2SD)	<-2SD
Cough episode count during feeding	81	0.22 $\pm$ 0.47	0	0	0	1	1	90-95% tile	>95%
Wet breath sounds & vocal change counts during feeding	81	1.69 $\pm$ 2.37	0	0	0	4	6	>1SD-2SD	>2SD
Change in work of breathing during feeding	81	0.07 $\pm$ 0.26	0	0	0	0	1	-	>2SD
Emesis count during feeding	81	0.02 $\pm$ 0.15	0	0	0	0	0	-	>2SD

\*Number of participants with data on specific variables

*Table. Feeding/Swallowing Evaluation Variables: Distributions and Point Allocations in Aspiration Risk Scoring System*

**Conclusions:** We developed a novel, pragmatic data-driven scoring system using the distribution of key variables evaluated during healthy infant breastfeeding in Malawi. "Normal feeding/swallowing" was classified for 85% of infants; remaining scores demonstrated expected clinical variability.

Next, we will attempt validation by applying the score framework to an at-risk pediatric pneumonia population in Malawi.

## EP05-1038-15 Computerised lung sound analysis for child pneumonia in low-resource settings: Agreement with expert listening panel and bedside auscultation in Malawian children

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**Background:** Pneumonia is a leading cause of paediatric mortality. The World Health Organization (WHO) case management algorithm is the diagnostic standard for child pneumonia in resource-limited settings, but lacks accuracy. Although lung auscultation could improve algorithm performance, implementation is challenging in settings with limited training.

Thus, we developed a prototype digital stethoscope capable of automated denoising and lung sound classification. We evaluated agreement between the automated algorithm, paediatrician listening panel, and bedside physician in a noisy paediatric ward in Malawi.

**Design/Methods:** We enrolled children aged 2-59 months at Kamuzu Central Hospital in Lilongwe, Malawi with WHO-defined severe pneumonia. A paediatrician performed auscultation with a conventional stethoscope at six positions bilaterally (back, axilla, chest). Interpretable positions were classified as normal or abnormal. Lung sounds were immediately recorded using a prototype digital stethoscope (Sonavi Labs) from identical positions. A paediatrician listening panel calibrated to a standard interpretation schema and our automated computerized algorithm classified recordings using the same approach.

We determined pair-wise agreement between each modality using percentages, Cohen's kappa, and Prevalence Adjusted Bias Adjusted Kappa (PABAK). In exploratory analyses, agreement was reassessed after applying a novel automated classification confidence probability to interpretations.

**Results:** 100 children were enrolled, 54% (n=54) of which were female, with a median age of 12.6 months (IQR 5.7-18.9). 497 interpretable chest position recordings were classified by all three modalities. The algorithm and panel achieved 83.1% agreement (Kappa

0.66, PABAK 0.66), algorithm and paediatrician 63.0% agreement (Kappa 0.25, PABAK 0.26), panel and paediatrician 67.0% agreement (Kappa 0.31, PABAK 0.34) (Table 1).

Restricting analyses to  $\geq 70\%$  confidence levels improved agreement between the algorithm and panel, but reduced interpretability by 46.9% (233/497).

Item	n (%)	Percent Agreement	Cohen's Kappa	PABAK*	p Value
All interpretable Positions	497/600 (82.8%)				
Algorithm & Panel		83.10%	0.66	0.66	p<0.0001
Algorithm & Paediatrician		62.98%	0.25	0.26	p<0.0001
Panel & Paediatrician		67.00%	0.31	0.34	p<0.0001
$\geq 70\%$ Algorithm Classification Confidence	284/600 (44%)				
Algorithm & Panel		89%	0.73	0.78	p<0.0001
Algorithm & Paediatrician		60.61%	0.24	0.21	p<0.0001
Panel & Paediatrician		65.53%	0.33	0.31	p<0.0001

\*Pass Scale for Cohen's Kappa and PABAK: <0, Poor; 0.01-0.20, Slight; 0.21-0.40, Fair; 0.41-0.60, Moderate; 0.61-0.80, Substantial; and 0.81-1.0, Perfect

Table 1. Summary of lung sound classification agreement.

**Conclusions:** Abnormal versus normal classification agreement between an automated algorithm and paediatrician listening panel was high on children with severe pneumonia in a challenging Malawian clinical setting with ambient noise contamination.

### EP05-1039-15 Lung impairment and associated risk factors in patients with cough in a primary health centre

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**Background:** Tuberculosis is an important cause of chronic lung morbidity. Cough is a common symptom of active tuberculosis and other respiratory infections (ORI). Identifying risk factors for Lung Impairment (LI) and screening methods in specific populations can help define clinical strategies.

**Design/Methods:** The AcuScreen study enrolled adult patients with an infectious cough presenting to a Primary Health Center in order to develop a cough analysis algorithm. Data collected at enrollment included acoustic cough recordings, spirometry, Xpert MTB/RIF test, chest radiography (CXR), symptoms, vital signs, medical history, and socio-demographics. Spirometry was performed according to ERS/ATS guidelines, and the Global Lung Initiative Race Neutral equations for interpretation.

**Results:** 406 adults were recruited, of whom 270 (66.50%) had valid spirometries at presentation. TB was diagnosed in 87/270 (32.22%), 61/87 (70.11%) were confirmed microbiologically, and 183/270 (67.78%) had ORI.

The patients were male 136/270 (50.4%), mean BMI (SD) 22.24 ( $\pm 5.25$ ), past smokers 55/270 (20.37%), 78/270 (28.89%) living with HIV, cough  $> 2$  weeks 149/270 (55.19%), and chest pain 163/270 (60.37%). Mean Z scores for FVC, FEV1 and Ratio were -2.55, -2.46 and 0.01 for TB patients respectively vs -1.43, -1.40 and 0.02 in ORI.

The proportion of LI was 73/87 (83.91%) for TB versus 88/183 (48.09%) for ORI. The main type of ventilatory disorder was restriction 58/87 (66.67%) for TB versus 67/183 (36.61%) for ORI. The main risk factors for LI in patients with cough include CXR abnormalities, left (OR 6.60, 1.85-45.57) and right (OR 5.20, 1.95-18.45) cavities, vocational degree (OR 4.22, 1.56-15.13) and previous TB (OR 2.91, 1.42-6.50).

**Conclusions:** Acute respiratory infections presenting with cough are associated with clinically relevant LI predominantly in TB patients. 4 in 5 TB patients at presentation had LI, primarily restriction. Abnormal CXR, vocational degree and TB history are the main risk factors.

### EP05-1040-15 Latent class analysis to define cases of childhood TB with sensitivity higher than 90%

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**Background:** Brazil is ranked as 25<sup>th</sup> among 30 countries with highest prevalence of Tuberculosis (TB). On childhood TB, gold standard is absent, and symptoms are similar than other illness. Conventional diagnosis presents low accuracy in this age and anti-TB treatment is initiated with no bacteriological confirmation.

Clinical scores should confirm childhood TB and is recommended by World Health Organization (WHO), however, most of it are not correctly validate and they work as "screening" tool than diagnostic method.

Gathering a tool that contains molecular tests and clinical scores into a single diagnostic criterion can be possible on latent class analysis (LCA), which estimates sensitivities and specificities when gold standard is not possible. And it probably will find higher accuracy than clinical scores.

**Design/Methods:** Carried out in Recife-Pernambuco, Northeast of Brazil using database of children with and without TB (0-15 years of age). To define cases, clinical,

epidemiological and laboratory criteria and response to specific treatment were used, as recommended by WHO. The study evaluated a clinical score, recommended by Brazilian Ministry of Health for Pulmonary TB, and another proposed by Keith-Edwards (Pulmonary and extrapulmonary TB).

In addition, a molecular test (Nested-polymerase chain reaction - NPCR) was used to also confirm *Mycobacterium tuberculosis* in blood samples. LCA was applied to increase estimation of accuracy on childhood TB.

**Results:** A total of 208 children were included. In pulmonary and extrapulmonary forms, sensitivity ranged between 92.9%-98.2% and specificities from 85.5-86% on LCA. Isolated accuracy of clinical scores, NPCR and LCA are on Table 1.

TB	Gold Standard				Sensitivity CI(95%)	Specificity CI(95%)	Positivity Predictive Value	Negative Predictive value
	TB		Not TB					
	N	%	N	%				
<b>LCA*</b>								
TB	78	92.9	12	14	92.9% (85.3-96.7)	86% (77.2-91.8)	86.7%	92.5%
Not TB	6	7.1	74	86.1				
<b>LCA**</b>								
TB	55	98.2	11	14.5	98.2% (90.5-99.7)	85.5% (75.9-91.7)	83.3%	98.5%
Not TB	1	1.8	65	85.5				
<b>BMH score*</b>								
TB	53	94.6	5	6.6	94.6% (85.4-98.2)	93.4% (85.5-97.2)	91.4%	96%
Not TB	3	5.4	71	93.4				
<b>NPCR</b>								
TB**	24	28.6	6	7	28.6% (20-39)	93% (85.6-96.8)	80%	57.1%
Not TB	60	71.4	80	93				
<b>Keith Edwards**</b>								
TB	68	81	7	8.1	81% (71.3-87.9)	91% (84.1-96)	90.7%	83.2%
Not TB	16	19.1	79	91.9				

\* Only pulmonary TB

\*\* Pulmonary and extrapulmonary TB

Abbreviations:

BMH - Brazilian Ministry of Health score

CI - confidence interval

LCA - Latent Class Analysis

N - Absolute number of sample

NPCR - Nested polymerase chain reaction

TB - Tuberculosis

Table 1. Latent class analysis of three methods to childhood TB diagnosis.

**Conclusions:** On childhood TB, LCA was the best method to define case or exclude it. The clinical scores and NPCR evaluated by LCA, had higher accuracy than each one evaluated in separated. To associate clinical scores with a molecular test (PCR) could increase sensitivity of childhood TB diagnosis, independent of clinical form: active (pulmonary or extrapulmonary) or latent.

### EP05-1041-15 Prognosis of primary immunodeficiency diseases notified after BCG vaccination: A 10-year longitudinal cohort study in China

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**Background:** There is no report of the long-term clinical management and prognosis for primary immunodeficiency diseases (PIDs) in China. We followed up ten years to investigate the status of PIDs patients accompanying with Bacillus Calmette Guerin (BCG)-induced diseases.

**Design/Methods:** This is a cohort study from January 2012 to January 2022 in Shanghai Public Health Clinical Center.

Four hundred and twenty-two patients with BCG-induced diseases were diagnosed during this period, from these patients, 113 patients with PIDs diagnosed by genetic and functional experiments were enrolled in the study. The clinical and genetic characteristics, treatments and outcomes of these PIDs patients were summarized, the last follow-up time was recorded till August 15, 2022.

**Results:** In all the 113 patients, males accounted for 83 (73.5%), the median age at onset and at diagnosis was 3 (2-3) months, 12 (6.5-12) months, respectively. The mean STRONG<sub>kids</sub> score was 2.1±1.6. The most common presentation was fever.

All patients had BCG-induced complications, 99 (87.6%) had disseminated BCG infection (BCGosis), and 14 (12.4%) had local/regional BCG-lymphadenitis (BCGitis), other complications were pneumonia, eczema, skin abscesses, anemia, hepatosplenomegaly, and chronic fungal and viral infections.

The most three PIDs are: Mendelian susceptibility to Mycobacterial disease (MSMD) in 49 (43.7%) patients, chronic granulomatous disease (CGD) in 28 (25%) patients, severe combined immunodeficiency (SCID) in 17 (13.4%) patients. 33 (29.2%) patients received hematopoietic stem cell transplantation (HSCT), 29 (87.9%) of them were survived, the survival rate was higher than 70% (56/80), that of patients didn't receive HSCT. Total mortality was reported in 24 patients (21.2%).

**Conclusions:** BCGosis was the most common and serious complication of PID patients after BCG vaccination. interferon-gamma (IFN-γ) was helpful to treat MSMD patients. HSCT was the most effective treatment for patients with SCID.

### EP05-1042-15 Performance evaluation of the Uganda National TB Programme algorithm for childhood TB

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**Background:** Because of the challenges in diagnosing childhood TB, the Uganda national tuberculosis control program (NTLP) has developed a clinical treatment decision algorithm for children. However, there is limited data on its accuracy and how it compares to new World Health Organization (WHO) treatment decision algorithms for children.

**Design/Methods:** We conducted a secondary data analysis of children 0-14 years from Kampala, Uganda who underwent an evaluation for possible pulmonary TB (including physical examination, chest x-ray, tuberculin skin testing, HIV testing, and respiratory specimen collection for Gene-X-pert MTB/RIF testing and culture) between September 2018 and November 2022.

We calculated the TB treatment decision based on the NTLT and WHO algorithms, with and without CXR, and determined and compared the sensitivity, specificity, positive and negative predictive values in reference to the National Institute of Health (NIH) consensus definitions.

**Results:** Overall, 875 children were included in this analysis with 64% being children under 5 years, 54% male, 7% with severe acute malnutrition, 11% HIV positive, 55% had a history of TB contact, 53% had abnormal chest X-ray and 10% had positive Gene-X-pert. Using the NIH consensus definitions as a Pure reference, we had 131 confirmed TB and 361 unlikely TB compared to 371 TB cases and 361 non-TB when we considered the NIH definitions as a Composite reference. The Uganda NTLT algorithm (without addition of Chest X-ray) had a sensitivity of 80% (CI: 77-83) and specificity comparable to the WHO algorithm B (settings without Chest X-ray) (Table 1).

Algorithm	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Uganda NTLT (with X-ray)	82.81% (80.03, 85.59)	5.34% (3.69, 7.00)	79.37% (76.38, 82.35)	6.60% (4.77, 8.43)
Uganda NTLT (without X-ray)	80.03% (77.09, 82.98)	6.11% (4.34, 7.87)	78.94% (95.93, 81.94)	6.50% (4.69, 8.32)
WHO Algorithm A	82.29% (79.36, 85.22)	10.81% (8.43, 13.19)	81.83% (78.88, 84.79)	11.11% (8.70, 13.52)
WHO Algorithm B	90.93% (88.73, 93.12)	4.59% (2.99, 6.18)	82.8% (79.93, 85.69)	9.09% (6.90, 11.28)

*Table 1. Diagnostic accuracy of the 2017 Uganda national childhood TB diagnosis algorithm and the 2022 WHO childhood TB diagnostic algorithms in predicting TB (using 2015 NIH consensus definitions [Confirmed TB vs Unlikely TB] as the reference standard) among children at Mulago national referral hospital.*

**Conclusions:** The NTLT algorithm seems to perform similarly with or without chest X-ray with a very low specificity; which would result in over treatment if implemented with high fidelity.

## EP05-1043-15 Integrated management of childhood illness can be a potential platform for identifying the missing under-5 children with TB in Bangladesh

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**Background and challenges to implementation:** Major proportion of estimated children with tuberculosis (TB) are still missed in Bangladesh (3% vs. 8%), especially under-five. Integrated Management of Childhood Illness (IMCI) deals with certain diseases among under-five children.

Here, we assessed if integration of TB screening into IMCI is helpful for detecting child TB in selected districts of Bangladesh.

**Intervention or response:** USAID's Alliance for Combating TB in Bangladesh (ACTB) Activity, with support from National TB Control Programme, initiated intensified-case-finding approach in four divisions of Bangladesh. Under-five children visiting IMCI corners of 19 healthcare facilities are screened for TB using a standardized symptom-based checklist. TB presumptive children are referred to local physicians for further evaluation and necessary TB testing (Xpert on respiratory samples, chest X-ray, Mantoux test, Xpert Ultra on stool, FNAC from lymph-node etc.). Diagnosis are made bacteriologically, and clinically by physicians, and children with TB are treated according to national guideline.

**Results/Impact:** Between March 2022 and February 2023, total 393,419 under-five children [median (IQR) age 1.8 (0.8, 3.0) years] were screened for TB. Of them, 6,558 (1.7%) were identified as TB presumptive and 6,100 (93.1%) underwent TB testing.

Among tested, 5,386 (82.1%) had cough  $\geq 2$  weeks.

Among children with no-cough, 744 (63.5%) had fever  $\geq 2$  weeks, 743 (63.4%) had weight loss, 148 (12.6%) had breathing difficulty, 136 (11.6%) had TB contact in family and 476 (40.6%) had lymph-node in body. Total 305 (4.7%) children were diagnosed with TB [pulmonary-241; extra-pulmonary- 64].

Majority (53; 82.8%) of extra-pulmonary TB was TB lymphadenitis. Proportion of TB among under-five children was 30% in ACTB working sites versus nationally 10%.

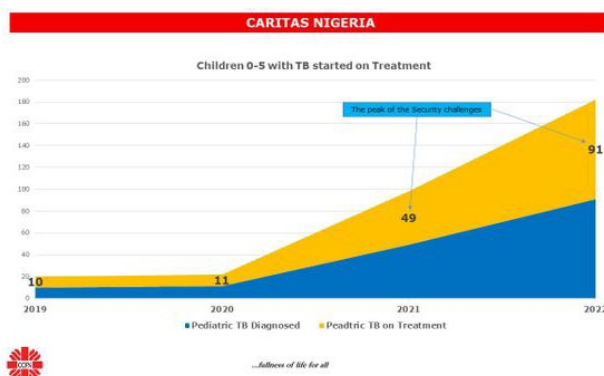
**Conclusions:** TB integration with IMCI was helpful for identifying under-five childhood TB and may add a new dimension in policy guideline. Training and sensitization of healthcare providers on TB screening can help sustain this activity and thereby improve detection of under-five childhood TB.

### EP05-1044-15 Bridging the gaps for paediatric TB notifications in a security-challenged setting: The case of Imo State, Nigeria

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**Background and challenges to implementation:** 452,000 people develop TB annually in Nigeria, and about 77,000 of them are estimated to be children. Out of the 316,680 missing TB cases in Nigeria, 68,651 of these are children. Despite significant improvements being made by the country in TB case notifications, children are being left behind as the childhood proportion remained at 7% nationally. The current security situations in some parts of the country including in the Imo state worsen this challenge.

**Intervention or response:** Community hot spots were identified. Each community hot spot had Patent Medicine Vendors (PMVs) mapped to a health facility using the hotspot mapping and identification model. These PMV centers were trained and activated to refer children to TB diagnosis and treatment services, over a 24-month period, (January 2021 to December 2022). The hot spots inclusion criteria included proximity to living areas, schools (targeting preschool and early school-aged children), Orphanages, and traditional children's clinics. PMVs served as a bridge to the health facilities which became inaccessible due to the high-security challenges in those areas. The PMVs drove targeted demand-creation around their clusters which served as sensitization for TB especially TB in children.



...Address of life for all

**Results/Impact:** On the whole, 1,104 centers were engaged, and 162 demand-creation activities were conducted leading to the referral of 579 children for TB Screening. 140 new Pediatric TB cases were placed on TB treatment during the peak of these security challenges (2021-2022), compared to a total of 21 pediatric TB cases during a more stable period (2019-2020).

**Conclusions:** The cluster coordination of the PMVs drove targeted community demand creation and successful sensitization for childhood TB. This approach is effective in ensuring pediatric TB cases are notified amidst the worsening security challenges in many parts of Nigeria.

### EP05-1045-15 Treatment outcomes among children and adolescents with multidrug-resistant TB in Haiti

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**Background:** Children and adolescents are challenging populations in which to diagnose and treat MDR-TB. We evaluated the management and treatment outcomes among a cohort of children and adolescents treated for MDR-TB.

**Design/Methods:** This is a retrospective study describing outcomes among children (ages <10) and adolescents (ages 11 – 19) diagnosed with MDR-TB and treated at GHEKIO in Port-au-Prince, Haiti. GHEKIO is the largest TB treatment center in Haiti. Patients ≤5 underwent gastric aspirate while patients >5 gave sputum. Diagnosis was based upon molecular assay positive for Mtb with evidence of rifampin resistance and/or positive Mtb culture with culture-based drug susceptibility testing positive for rifampin resistance.

In the absence of positive tests, diagnosis was based on clinical symptoms and known MDR-TB contact. Treatment regimens adhered to national and international guidelines. Data was abstracted from the GHEKIO medical record and National TB register. Laboratory results were abstracted from the GHEKIO laboratory database. Treatment outcomes were defined according to the WHO. This study was approved by both Weill Cornell and GHEKIO IRBs.

**Results:** Between 2010 – 2020, 16 children and 34 adolescents were diagnosed and treated for MDR-TB (Table 1). Forty-four patients were diagnosed based on molecular tests and/or culture. Six patients, all <5 years, had negative molecular tests and negative cultures and index cases were parent or aunt. Retention in care was achieved through monthly visits with close follow-up. Caregivers were called the week of a scheduled visit. If

the visit was missed, a health worker visited the patient at home. Nutritional support was given to patients. Educational seminars were held for patients and caregivers during initial months of treatments. Of patients who completed treatment, 93% of children and 87% of adolescents achieved a successful outcome.

	Pediatric (ages birth – 10) n=16		Adolescents (ages 11 – 19) n=34	
<b>Sex</b>				
Female	5 (31)		16 (47)	
Male	11 (69)		18 (53)	
<b>Age in years, median [IQR]*</b>	2 [0.5, 4]		17 [14, 18]	
<b>Weight at diagnosis in kg<sup>Δ</sup>, median [IQR]</b>	6.7 [5.7, 11]		45 [40.6, 47.8]	
<b>HIV status at diagnosis</b>				
Positive	0 (0)		4 (12)	
Negative	16 (100)		27 (79)	
Indeterminate	0 (0)		3 (9)	
<b>Culture result by sample type</b>	<b>Positive</b>	<b>Negative</b>	<b>Positive</b>	<b>Negative</b>
Sputum	3 (38)	0 (0)	33 (100)	0 (0)
Gastric aspirate	5 (63)	8 (100)	0 (0)	0 (0)
Other	0 (0)	0 (0)	0 (0)	1 (100)
<b>Xpert level</b>				
High	0 (0)		8 (24)	
Medium	2 (13)		20 (59)	
Low	2 (13)		3 (9)	
Very low/trace	5 (31)		0 (0)	
Not detected	5 (31)		0 (0)	
Missing/not performed	2 (13)		3 (9)	
<b>Treatment Outcome</b>				
Cure and/or Treatment complete	14 (88)		27 (79)	
On treatment	1 (6)		3 (9)	
Death	1 (6)		0 (0)	
Abandoned	0 (0)		3 (9)	
Transferred	0 (0)		1 (3)	

\* 7 patients were less than 1yo at time of diagnosis: 2, 3, 5, 5, 7, 9, 10 months  
<sup>Δ</sup> missing = 5 pediatric weights and 18 adolescent weights

Table 1. Demographic and clinical description of pediatric and adolescent MDR-TB cohort. n = 50 (%)

**Conclusions:** Successful treatment outcomes are achievable among pediatric and adolescent populations through intense follow-up and social support.

### EP05-1046-15 High bacteriologically confirmed TB among female children and adolescents - it's time to address the gender disparity in Ethiopia

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**Background and challenges to implementation:** TB can affect all population groups irrespective of age or sex. However, little has been described about the implications of sex and gender for the surveillance and response to TB program in Ethiopia.

**Intervention or response:** The Ministry of Health's District Health Information System (DHIS2) based reporting system was used to analyze bacteriologically confirmed TB cases (BCTB), based on age and gender, from July 2022 to February 2023. The disaggregation was <5 years, 5–14 years, 10–19 years, and >15 years. The male to female ratio was described among these age categories and among agrarians, pastoralists, and city dwellers of the country.

**Results/Impact:** Of the 37,413 BCTB cases, 42% were females. This proportion of TB cases among females was 41.2% and 44% in adults and under-5 children, respectively. However, the proportion of females was 54% and 51% among 5–14 years of age and under-15 children, respectively. Except in the urban cities, the ratio of males to females was <1 among children under 15 years and adolescents 10–19 years. However, the ratio is >1 in under-5 and adults in all regional categories.

**Conclusions:** BCTB cases are high among female children and adolescents in Ethiopia. Yet, males under 5 and adult males have a higher proportion of BCTB. This might be due to the economically advantageous and male dominated culture in Ethiopia.

The gender differences related to health-seeking behavior and access to health care need to be explored further in Ethiopia.

### EP06 COVID-19: Are we done yet?

#### EP06-1047-15 COVID-19 clinical management protocols in India: Evolution of national and sub-national guidelines and innovations

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**Background:** The evolving nature of the COVID-19 pandemic compelled periodic changing of treatment guidelines/protocols and evidence generation. We documented the evolution in treatment protocols officially released by Government of India (GoI) (national), and Government of Maharashtra (GoM) (sub-national/state).

We chose Maharashtra as it was the most severely affected state in India and was a leader in a variety of state-level innovations.

**Design/Methods:** Using qualitative documentary research approaches, we developed a framework to analyze the treatment protocols for GOI and GoM and mapped clinical guidance from each protocol onto the framework. Thirty-eight of the 51 documents we reviewed passed inclusion criteria.

To understand the evolution of protocols, we analyzed the documents on two levels:

- Comparison of each protocol with the immediate previous one; and
- Understanding state-level innovations.

We also reviewed WHO Living Guidelines on COVID-19 clinical management to construct a comparative timeline of key guidance on the various drug regimens.



**Results:** Evolution of guidance in protocols was documented under three key themes – patient categories, therapeutics, and supportive therapy, and were analyzed separately for GoI and GoM. Evidence-based periodic changes in discharge policies and investigational therapies revealed to what extent the local and global evidence was considered – for instance, the recommendation to use systemic corticosteroids and that against Hydroxychloroquine.

While global evidence was used sporadically, local evidence informed state-level innovations that were taken up by GoI to be scaled across the country. There were differences between GoI and GoM guidelines on antibacterial and antiviral drugs and dissemination strategies.

**Background and challenges to implementation:** The evolving nature of the COVID-19 pandemic compelled periodic changing of treatment guidelines/protocols and evidence generation. We documented the evolution in treatment protocols officially released by Government of India (GoI) (national), and Government of Maharashtra (GoM) (sub-national/state). We chose Maharashtra being the most severely affected state in India and as Maharashtra was a leader in a variety of state-level innovations.

**Conclusions:** We concluded that the evidence was generated, synthesized, and used, albeit in a non-systematic way. While protocol documents and preparation mechanisms were robust, implementation levels differed owing to administrative and communication-related factors. Key learnings emphasized the importance of systematic evidence reviews for policymaking, uniformity in drug policies, and pre-defined protocol dissemination strategies.

### EP06-1048-15 Gauging and improving COVID-19 safety in schools: Results from a surveillance programme in Dhaka City, Bangladesh

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**Background:** IRD Bangladesh and IRD Global through a WellCheck initiative established a surveillance system to assess the prevalence of COVID-19 school-aged children and collect important data to address the lack of understanding of COVID-19 infection and vaccine efficacy among children that led to prolonged school closures during the pandemic.

**Design/Methods:** From March 2022 to January 2023, we conducted COVID-19 surveillance at 416 Dhaka City schools during the government's ongoing school vaccination drive. Antigen Rapid diagnostic test was used to test all students, teachers, and staff during the initial visit, with monthly follow-up visits for symptomatic students. Community-based testing services were also provided at special needs child institutes, slums, orphanages, and upon request. Health literacy intervention, medical support, and mental health screening and counseling were offered to COVID-19-positive patients and family members. Contact tracing was also conducted in the homes of those found to be positive.

**Results:** We screened & tested 148,786 students and 4,647 school staff and contacts and identified 188 (<1%) COVID-19 positive; including 139 students, 28 school staff, and 21 contacts. Of the students screened, 95% were fully vaccinated, and only 238 (<1%) were non-vaccinated. There were no moderate or severe cases, with 40% being asymptomatic. Only 2% of the positives were identified with mild depression, while 2% reported moderate depression. None of the patients required hospitalization or any medication. The school positivity trend mirrored the national trend and we observed similar positivity rates in both children and adults during the peak periods.

**Conclusions:** The project identified a low prevalence (<1%) of COVID-19 among school children, possibly due to high vaccine coverage, and project interventions. This strategy could keep students safe during epidemics, highlighting the effectiveness of vaccination efforts and an effective surveillance system in mitigating the spread of COVID-19 among children and reducing the need for school lockdowns.

### EP06-1049-15 Identification of active TB among people seeking to rule out COVID-19 at the primary care level in a high TB burden setting

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**Background:** WHO recommends concomitant search for COVID-19 and tuberculosis (TB). People seek health care more for acute respiratory problems than for the possibility of ruling out TB. We describe the factors associated with the TB diagnosis among people seeking to rule out COVID-19 cared for by COVID-19 team of Socios En Salud (SES) in Lima, Peru.

**Design/Methods:** SES COVID-19 teams recruited people with cough during their COVID-19 activities at the primary care level in the north of Lima, jurisdiction of Dirección de Redes Integradas de Salud Lima Norte - dependency of the Ministry of Health. All people with cough seeking to rule out COVID-19 were tested for TB using the GeneXpert Ultra MTB/Rif which was processed at the SES BSL3 TB Laboratory. Epidemiological information, health history and symptoms were collected for each person tested.

**Results:** We identified 851 people with cough who were tested for TB using Xpert Ultra MTB/Rif, of whom 23 (2.7%) had a positive result.

In univariate analysis, the people living with HIV or had a history of previous TB or had a disabling neurological disease or had more than 7 days of cough were more likely to be Xpert positive.

In multivariate analysis, the risk was 6.3 (95% CI: 2.3 – 17.9) if the patient reported a history of previous TB, 4.5 (95% CI: 1.7 - 12.1) if the patient reported a disabling neurological disease, and 2.6 (95% CI: 1.1 – 6.3) if the patient reported coughing for more than 7 days.

**Conclusions:** In places with a high TB burden, it is mandatory to screen for TB among persons with cough to rule out COVID-19, focusing this search among people with a history of previous TB, disabling neurologic disease, and cough for more than 7 days. This approach does not cause us to miss opportunities for TB diagnosis.

### EP06-1050-15 Analysis of systemic equity and gender issues affecting product introduction and access to COVID-19 vaccine in Kenya

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**Background and challenges to implementation:** Equity and gender issues are major barriers affecting access to COVID-19 tools such as diagnostics, therapeutics and vaccines. Women and girls are negatively impacted by gaps both in supply and demand leading to inequitable vaccine distribution.

**Intervention or response:** We utilized a mixed methods design involving desk review and key informant interviews (52 healthcare providers, 12 Civil Society Organizations and 2 Ministry of Health officials from 19 counties). We assessed inclusion of women, People with disabilities (PWDs) and other marginalized groups at all levels of decision making, use of differentiated vaccine delivery strategies, channels for awareness and demand generation activities. Quantitative data was analyzed descriptively using MS excel and qualitative data using content analysis.

**Results/Impact:** Representation of women in the National COVID-19 response committee remained low at 19.6%. At the initiation of COVID-19 vaccination

there were more males accessing vaccines compared to females. 52% reported that gender norms significantly affected access to vaccination.

However, the trend changed towards the end with more females being vaccinated. Utilization of youth friendly interventions was reported in 45% of facilities. Vulnerable and marginalized groups were unwillingly excluded from COVID-19 response interventions. Differentiated vaccine delivery approaches were effective in enhancing vaccine uptake. Common barriers to access included beliefs and myths, inadequate information, inadequately facilitated vaccine service provision centers, gender aspects like limited decision-making power, limited time due to household care giving roles and dependency on men who control resources.

**Conclusions:** Creating demand, addressing misinformation and a mix in vaccine delivery mechanisms targeted at different priority populations improves vaccine uptake and improves equity in coverage.

Inclusion of gender/vulnerable and marginalized groups experts in the drafting of national COVID-19 response plans is crucial for ensuring gender mainstreaming and equity. Awareness creation at the grassroots is essential for vaccine uptake to address the myths and misconceptions.

### EP06-1051-15 Symptom experiences and perceived health status among individuals with long COVID within a limited follow-up system, Thailand

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**Background:** This retrospective study aimed to explore the symptom experiences of individuals with Long COVID and examine the relationship between those experiences and perceived health status.

**Design/Methods:** This study invited 385 individuals who tested positive for SARS-CoV-2 between July 2021 and October 2021, exhibited moderate to severe illness, received care at an outpatient facility in Bangkok, and did not receive follow-up. Of those invited, 86 agreed to take part and completed a telephone interview between July 2022 and November 2022, resulting in a response rate of 22.3%.

Participants recalled their experience of Long COVID, the presence of symptoms lasting for at least 2 months after acute infection with SARS-CoV-2. The COVID-19

Yorkshire Rehabilitation Screening (C19-YRS) was used to measure symptom occurrence, duration, and severity on a 0 to 10 verbal descriptor scale.

Pearson's and Spearman's correlation were performed to analyze the relationships between Long COVID symptoms and perceived health status.

**Results:** Of the 86 participants, 75.6% were found to have Long COVID, which was more prevalent among females (84.2%), those with low income (90%), those with co-morbidities (80.7%), and those who were unvaccinated (90%). The median number of symptoms was 3, with a median duration of 5.6 months.

Difficulties in doing usual activities was the most common symptom experienced (50.8%), with pain being the longest lasting symptom (mean duration of 5.9 months), and post-traumatic stress disorder screen being the most severe symptom (mean severity of 7.2). A higher number of symptoms and longer duration of cardiac-respiratory symptoms were significantly related to the poorer perceived health status ( $p < .01$ ).

**Conclusions:** The study highlights that different dimensions of Long COVID symptoms have a significant impact on the individual's health status. Effective symptom assessment and management during follow-up are necessary for future health emergency preparedness plans.

## EP06-1052-15 TB control programme recovery following the COVID-19 lockdown in KwaZulu- Natal, South Africa: An interrupted time series analysis, 2020-2022

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**Background:** The COVID-19 pandemic led to massive interruptions and reversal of gains in the TB programme. South Africa implemented a national TB recovery plan to address the negative effects of the pandemic on the national TB programme.

Through the USAID TB-LON supported programme, our study aimed to track the recovery of the TB programme in KZN province between April 2020 to March 2022.

**Design/Methods:** Descriptive statistics and Poisson regression models were used to estimate the impact of lockdown and post-lockdown trends on the TB care cascade using routinely collected programmatic data from public health facilities. Two phases of post-lockdown (April 2020 - March 2021 and April 2020 - March 2022) were respectively compared to an equal duration of pre-lockdown.

**Results:** Lockdown was associated with a 21% decrease in head count (Incidence rate ratio [IRR] 0.79, 95% CI: 0.72-0.88). After 12 months post-lockdown, the numbers had not significantly increased towards pre-lockdown levels (IRR 0.99, 95% CI: 0.98-1.02). However, after 24 months post-lockdown a decrease of 22% (IRR 0.78, 95% CI: 0.73-0.84) was observed, this was associated with an increase towards pre-lockdown levels by a trend of 0.7% (IRR 1.007, 95% CI: 1.00-1.01). TB confirmed cases decreased by 36% (IRR 0.640, 95% CI 0.480-0.850) due to lockdown, after 12 months post-lockdown the numbers had increased towards pre-lockdown levels by a trend of 5% (IRR 1.05, 95% CI: 0.99-1.12) however this was not statistically significant ( $p=0.118$ ). After 24 months post-lockdown, the decline was at 34% (IRR 0.66, 95% CI: 0.55-0.79) and the recovery towards pre-lockdown levels was at 4% (IRR 1.04, 95% CI: 1.02-1.06). None of the other three data elements evaluated showed a significant increase post-lockdown both after 12 and 24 months.

Data elements	12 months post-lockdown		24 months post-lockdown	
	IRR (95%CI)	p-value	IRR (95%CI)	p-value
<b>Head count</b>				
post-lockdown	0.79 (0.72 - 0.88)	< 0.01	0.78 (0.73 - 0.84)	< 0.01
quarter-quarter time effect	0.99 (0.98 - 1.02)	0.996	1.00 (1.00 - 1.01)	0.044
<b>TB screening</b>				
post-lockdown	0.78 (0.69 - 0.88)	< 0.01	0.84 (0.71 - 0.98)	0.025
quarter-quarter time effect	1.00 (0.98 - 1.03)	0.552	0.99 (0.98 - 1.01)	0.503
<b>TB Investigations</b>				
post-lockdown	1.37 (1.36 - 1.38)	< 0.01	1.29 (0.49 - 3.38)	0.612
quarter-quarter time effect	1.00 (0.99 - 1.00)	0.071	1.03 (0.93 - 1.14)	0.591
<b>TB confirmed</b>				
post-lockdown	0.64 (0.48 - 0.85)	0.002	0.66 (0.55 - 0.79)	< 0.01
quarter-quarter time effect	1.05 (0.99 - 1.12)	0.118	1.04 (1.02 - 1.06)	< 0.01
<b>Started on treatment</b>				
post-lockdown	0.63 (0.48 - 0.81)	< 0.01	0.68 (0.53 - 0.86)	0.001
quarter-quarter time effect	1.04 (0.98 - 1.10)	0.175	1.02 (0.99 - 1.04)	0.176

\*IRR = Incidence rate ratios

95%CI = 95% confidence interval

Table 1. Interrupted time series analysis of TB care cascade 12 and 24 months post-lockdown in KwaZulu-Natal, South Africa; 2020-2022.

**Conclusions:** This study indicates that there is still a long way to go in order to fully recover the levels of the TB programme eroded by COVID-19.

## EP06-1053-15 Towards an acceptable face mask for children to wear in public: A systematic review and narrative synthesis

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**Background:** Masks have been widely used as a preventative tool during the COVID-19 pandemic. However, the use of masks by children has been controversial, with international guidelines recommending a risk-based approach to policymakers. We aimed to conduct a systematic review exploring children's experiences of mask-

wearing, drawing on an evidence base that describes mask-wearing in different contexts including air pollution, and to prevent the spread of infectious disease.

**Design/Methods:** We searched MEDLINE, Embase and PsycINFO in June 2021, with a repeat search in August 2022, for primary research studies that explores children's experiences of masks. Included studies reported on participants between 4 and 14 years, with no restrictions on language. Two reviewers independently screened titles and abstracts and reviewed full texts of potentially eligible papers. We used the Mixed Methods Appraisal Tool for quality appraisal and thematic synthesis to identify key findings. We also conducted stakeholder consultation (PPI) with nine children, where they submitted annotated drawings of their preferred mask to complement our review findings.

**Results:** We screened 806 titles and abstracts and reviewed 73 full texts. 30 studies were included in the synthesis. Children's experiences of mask-wearing were influenced by their perceived necessity, social norms around their use and parental attitudes. Challenges related to mask-wearing were described, including difficulty reading facial expressions and physical discomfort. Children found it easier to wear masks when sitting and in cooler environments, and they benefited from unmasking during outdoor break time at school. As part of the PPI consultation, children highlighted the importance of mask design and the environmental impact of masks.

**Conclusions:** Children's experiences of mask-wearing were varied and context-dependent, with several mask-design challenges raised. Future policy on mask-wearing needs to consider the context in which mask wearing would be most beneficial, and how local adaptations to policy can respond to children's needs.

### EP06-1054-15 SARS-CoV-2 infection does not increase risk of TB disease in South African adults with HIV

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**Background:** Acute SARS-CoV-2 infection is associated with immune dysregulation and lymphopenia. The interaction between COVID-19-associated inflammatory responses (particularly in the lung) and underlying infec-

tions including TB is unknown. We investigated whether South African adults were at increased risk for TB after SARS-CoV-2 infection.

**Design/Methods:** We determined the prevalence of prior COVID-19 in unvaccinated South African adults tested for TB (May 2020–December 2021). Microbiologically confirmed TB was defined as  $\geq 1$  of a positive Xpert Ultra or TB culture. Plasma collected concurrently with TB testing was evaluated for 3 anti-SARS-CoV-2 antibodies using the MSD immunoassay platform: anti-Spike and anti-nucleocapsid IgGs to ancestral SARS-CoV-2, and anti-Spike IgG to the Beta variant. Prior COVID-19 was defined as  $\geq 1$  detectable antibody. A stricter alternate definition of prior COVID-19 required presence of all 3 antibodies.

**Results:** Of 333 adults (92% hospitalized, 178 [53%] male, median age 42y [IQR 34-52]), 81 (24%) had confirmed TB. Median CD4 count was 202 (IQR 57-441) among 314 (94%) persons living with HIV (PLWH). Prevalence of each antibody was similar in people with and without TB. There was no difference in the proportion of prior COVID-19 in people with (44%) vs. without TB (44%,  $p=1.00$ ).

Restricting the cohort to PLWH, the proportion of PLWH with prior COVID-19 did not differ among people with (40%) and without TB (44%;  $p=0.57$ ). No association was seen using the stricter definition of prior COVID-19 ( $p=0.40$ ). The odds ratio for TB in PLWH with vs. without prior COVID-19 was 0.84 (95% CI 0.48–1.48).

After adjusting for age, gender, and CD4 count, relative odds of TB in PLWH remained unchanged in persons with and without prior COVID-19 (aOR 1.09 (95% CI 0.58–2.04)).

TB disease status	TB-positive (N=81)	TB-negative (N=252)	p-value (X <sup>2</sup> )
COVID Nucleocapsid Ab+	23 (28%)	88 (35%)	
COVID Spike Ab+	29 (36%)	84 (33%)	
Covid Spike-Beta Ab+	29 (36%)	82 (33%)	
Any Ab+	36 (44%)	112 (44%)	$p=1.00$
All Ab+	18 (22%)	60 (24%)	$p=0.77$
<b>Odds Ratios for TB disease in PLWH (N=314)</b>	<b>OR (95% CI)</b>	<b>p-value</b>	<b>aOR (95% CI)*</b> <small>*adjusted for age, gender, and CD4 count</small>
Prior COVID-19: Any Ab+	0.844 (0.48 – 1.48)	0.558	1.09 (0.58 – 2.04) 0.788
Prior COVID-19: All Ab+	0.690 (0.34-1.40)	0.308	0.79 (0.34-1.83) 0.575

Table 1. Prevalence of prior COVID-19 in South African adults at the time of TB diagnostic testing, and odds ratios for TB in PLWH.

**Conclusions:** There was no association between prior SARS-CoV-2 infection and newly diagnosed TB in South African PLWH. SARS-CoV-2 infection did not increase the risk of reactivation TB.

## EP07 Lessons learnt from health systems strengthening for TB control

### EP07-1055-15 Enhancing counselling skills for frontline TB staff to achieve End TB goals: a first in the Indian National TB Programme

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**Background and challenges to implementation:** Saksham (which means capable) is a project of the Tata Institute of Social Sciences, a publicly funded national academic institution which had demonstrated experience of strengthening the national HIV and TB programme on counselling aspects. Owing to the counselling acumen and demonstrated impact of counselling services for TB treatment outcomes, the national programme entrusted Saksham to develop a national strategy for building capacities of front-line TB staff on Counselling Soft Skills. **Intervention or response:** Saksham drew on other university partners and academic rigour to develop a national strategy for skill building on counselling soft skills. A National Curriculum and resource pool of Regional Master Trainers was developed for this purpose. The training programmes are experiential and participatory in nature and focus on “un-learning” as much as on learning. The training programmes are power points presentation free and are designed for reflection, introspection and developing a person centric, empathetic approach and practicing skills – unprecedented until now!

Between April 2022-March 2023, 409 Master Trainers, 83 DR TB Counsellors, 759 STS, 383 TB HV, 22 SDPS, 17 PPM coordinators have been trained on counselling soft skills.

**Results/Impact:** To assess the immediate impact of training Saksham developed a pre and post training evaluation form which is filled by all participants.

	Pre-Training Score	Post-Training Scores
Minimum Score	2	3
Maximum Score	15	20
Average Score	7.75	12.4
	<b>Paired Sample t-test</b>	
Variance	9.483	12.981
<b>Sig. (2-tailed)</b>	<b>0.000</b>	

Table 1: Pre and Post Training Scores Comparison

90% of respondents said the training has equipped them with the skills required for counselling people with TB and their families, 88% said the training has helped them develop a new perspective towards people with TB. Principles of Empathy, non-Judgemental Attitude, Acceptance was identified as three most useful learnings from the Saksham training.

**Conclusions:** Skill building of Front-Line TB staff to go beyond the medical aspects of TB and focus on person centric care while upholding principles of counselling is an important and innovative strategy in India's fight against TB.

### EP07-1056-15 Point-of-care programme in HIV, TB and associated conditions: A strategic global virtual initiative

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**Background and challenges to implementation:** According to the World Health Organization, there will be a 10 million healthcare workers shortage by 2030, primarily in low and lower-middle-income nations. The quality of care for HIV and TB care is hugely impacted by this. Some plausible explanations include an aging healthcare workforce, greater burnout, subpar educators, and disproportionate workforce distribution. This demands the need of novel approaches to ensure delivery of standard care.

**Intervention or response:** A competency-based model, Point-of-care continuing medical education (POC-CME) was established engaging the clinicians in self-reliant, independent learning pertinent to their clinical practice while earning CME points.

The program was designed to receive queries through a dedicated email/ web-based form along with laboratory and imaging data.

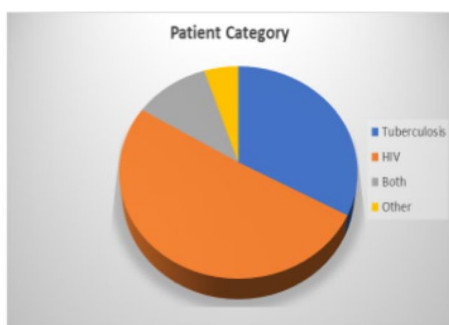
A consultant assigned on a weekly basis provides expert opinion on the queries supported by evidence-based resources. The program is complemented by educational opportunities like in-person lectures, conferences and webinars.

**Results/Impact:** Over 16 different countries sent 197 requests, resulting in over 2000 emails. Ninety-four queries involved females and 94 involved males; gender was not provided for nine patients. Hundred enquiries dealt with HIV infection, 65 with TB, 22 with both, and 10 with related disorders. Most common HIV-related categories were management of co-infections, ART in treatment-experienced, and management of co-morbidities. Most

common TB categories were TB disease diagnosis, disease treatment, and others. 1750 clinicians attended webinars and virtual conferences; 968 individuals attended live courses and lectures.

Feedback ranged between excellent to satisfactory for overall experience and the quality of consultation provided. For promptness of responses, one responder was unsatisfied with timing, but others provided excellent to satisfactory feedback.

TB Diagnosis (n)	HIV Diagnosis (n)	Both (n)	Other (n)	Total (n)
65	100	22	10	197



**Conclusions:** The POC-CME program has contributed to enhancing clinicians' proficiency. The transition from a traditional passive model into a competency-based self-directed CME model can be utilized to optimize patient outcomes and mitigate the workforce shortfall.

### EP07-1057-15 Four years of pharmacovigilance strengthening for drug-resistant TB in Eswatini, Ethiopia, Nigeria and Tanzania: Results from the PhArmacoVigilance in Africa (PAVIA) project

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**Background and challenges to implementation:** In the past decade, new drugs and regimens for the treatment of drug-resistant tuberculosis (DR-TB) have been introduced globally, often based on limited drug safety data and before being approved by national medicines and regulatory authorities (NMRAs) for distribution and selling in a country. This made active drug safety monitoring and management (aDSM) crucial. Responsibility for aDSM was primarily assigned to national TB programmes (NTPs), whereas NMRAs are usually responsible for drug safety monitoring and any regulatory actions in case of a safety issue.

Moreover, for a complete global picture of the safety of new DR-TB drugs and regimens, all adverse event reports should be submitted to the global pharmacovigilance (PV) database at the Uppsala Monitoring Centre. Therefore, stronger relationships between national medicines regulatory authorities (NMRAs) and NTPs needed to be built.

**Intervention or response:** The PhArmacoVigilance in Africa (PAVIA) project hypothesized that national PV programmes could be strengthened by improving the relationships between public health programmes (PHPs), starting with the NTPs, and the NMRAs. Strengthened relationships were thought to improve awareness about PV, reporting and analysis of adverse events.

**Results/Impact:** The relationships between NTPs and NMRAs were strengthened in all four PAVIA countries. This led to a more prominent role of PV in the TB guidelines in all countries, improved adverse event reporting in Eswatini, Ethiopia and Tanzania, drug safety results sharing in Eswatini and Ethiopia, and more staff on PV within the NTPs in Nigeria. In some countries, the ex-

perience gained in the PAVIA project has led to engagement with other PHPs, such as the HIV/AIDS, malaria and expanded immunization programmes.

**Conclusions:** Stronger relationships between NMRA and NTPs can be built, and this can lead to improvements in adverse event reporting and analysis, and, ultimately, better patient safety.

### **EP07-1058-15 Capacity-building of *gram panchayat* Task Force members through distance learning: experience from Karnataka State, India**

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**Background and challenges to implementation:** Gram Panchayats (GP) are centres of village administration with immense potential for delivering decentralized services that can improve health and well-being of villagers. Gram Panchayat Task Force (GPTF), is supporting in strengthening community ownership of different health programs at panchayat level.

As many of GPTF members were new to COVID, TB and other disease responses, adequate training and knowledge sharing with >45000 GPTF members was challenging considering urgency and resources needed.

**Intervention or response:** Training was imparted to GPTF members in collaboration with Department of Rural Development and Panchayath Raj (RDPR) and Abdul Nazir Sab State Institute of Rural Development (ANSSIRD), Mysore, which has employed a technology called, Satellite Based Interactive Communication System (SBICS).

At each block level there were already established SBICS receiving stations. GPTF members were mobilized at block level to attend sessions at receiving stations and were instructed through circulars about satellite transmissions, methodology, their functions prior, during and after sessions. Identified master trainers conducted sessions.

**Results/Impact:** In November 2021, satellite training sessions were delivered to 27,212 GPTF members from 2339 GPs across 114 blocks in 14 Karnataka districts. Sessions covered topics like reaching vulnerable population with health services using Health Management kits, COVID-19 vulnerabilities, diabetes, TB, women vulnerabilities, and GPTF members roles and responsibilities. Questions were answered by eminent panelists. Recorded case studies were broadcasted to educate par-

ticipants. In this training within short time 20954 male, 6258 female GPTF members trained with limited resources to implement health programs locally.

**Conclusions:** Providing information and training via Satcom route has enabled grass root functionaries like Panchayat Raj Institution's ability to implement health programs effectively. This approach can also be employed to conduct reviews, monitoring and evaluation, preparation of perspectives plans.

There is less scope of different interpretations and ambiguity as there is single communications reaching wider audience along with interactive systems.

### **EP07-1059-15 Applying the Plan-Do-Study-Act approach for the optimisation of district-level TB programme managers' capacity in India**

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**Background and challenges to implementation:** In India, under the National TB Elimination Program (NTEP), district-level program managers called District TB Officers (DTO) is accountable for TB program implementation in respective districts with constant exposure to operational and management challenges. As the efficient and effective functioning of NTEP relies on the management capacity of DTOs, their capacity for addressing these challenges needed to be built.

Under the USAID-supported iDEFEAT TB project led by The Union, a program managers' executive course was designed with the aim to build the capacity of DTOs to identify areas for operational improvements in NTEP.

**Intervention or response:** The executive training course was delivered over six months consisting of one on-line session (two hours) per week. The content covered themes of Quality Improvement (QI), Leadership, Team building, and Data Analysis, culminating in a Plan-DO-Study-Act (PDSA) cycle exercise. Individual-level hand-holding support was provided to conduct the PDSA.

As part of the training, DTOs learn to improve work situations by answering three questions, viz, What aims to be accomplished, What changes are to be made for improvement, and, How to assess the change.

**Results/Impact:** Overall 220 DTOs have participated in the five batches of the course from 26 major states and UTs of India. All the 220 DTOs have completed at least one PDSA cycle. The majority of the PDSAs were planned to improve TB case notification, TB Aarogya

SAATHI app download, Direct Benefit Transfer (DBT), increased adoption of TB patients for nutrition supplements, etc. The PDSA was found to be a good tool to identify management challenges and make incremental improvements in program implementation.

**Conclusions:** PDSA can be utilized as one of the approaches by TB program managers to identify and address management challenges faced during program implementation.

### EP07-1060-15 Exploring potential barriers and facilitators to integrate TB, diabetes mellitus and tobacco-cessation programmes in India

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**Background:** The integration of Tuberculosis (TB), Diabetes Mellitus (DM), and Tobacco-Cessation (TC) programs in India is maybe a promising strategy to tackle the triple burden of these diseases. However, there is limited information on the feasibility of this integration and the factors that may influence its success.

This study aimed to investigate the potential barriers and facilitators to integrate TB, DM, and TC programs in Maharashtra and Haryana state in India.

**Design/Methods:** We designed a qualitative in-depth interview study in the Khed Block of Pune District in Maharashtra and the Ballabgarh Block of Faridabad District in Haryana in India.

We conducted 32 in-depth interviews among health workers, programme managers, and other stakeholders implementing the TB, DM and TC programs in these two states. The respondents were chosen using purposive and snowball sampling strategies.

The interviews were coded and analyzed using thematic analysis, following the WHO Health System Building Blocks framework.

**Results:** The study identified barriers and facilitators for the integration of TB-DM-TC programs in India. The maximum challenges for integration are at the level of service delivery which is largely attributed to inadequate implementation of all three programs and negligible involvement of private practitioners in program implementation.

See Table 1 for detailed results.

THEMES	FACILITATORS	BARRIERS
<b>Service Delivery</b>	<ul style="list-style-type: none"> <li>• Smooth and sufficient supply of medicines</li> <li>• Relatively robust program guidelines for TB when compared to DM</li> </ul>	<ul style="list-style-type: none"> <li>• Inadequate implementation of protocols for transport of sputum samples and patient referral</li> <li>• Lack of counselling of follow-up or referral with presumed cases of TB and DM</li> <li>• Limited availability of rehab centre for tobacco and alcohol cessation</li> </ul>
<b>Health Workforce</b>	<ul style="list-style-type: none"> <li>• Well-defined staff responsibilities for TB program implementation</li> <li>• Availability of training facilities</li> </ul>	<ul style="list-style-type: none"> <li>• Responsibilities for DM program implementation are not defined</li> <li>• Overburdened human resources with multiple disease programs</li> <li>• Lack of regular training to the Healthcare Personnel.</li> </ul>
<b>Medical Products &amp; Technology</b>	<ul style="list-style-type: none"> <li>• Ni-kshay portal and NPY (Ni-kshay Poshan Yojana)</li> <li>• Infrastructure available</li> </ul>	<ul style="list-style-type: none"> <li>• Frequent non-availability of DM supplies and medicines</li> </ul>
<b>Information</b>	<ul style="list-style-type: none"> <li>• Information material is developed and available</li> <li>• Resources for IEC activities available</li> </ul>	<ul style="list-style-type: none"> <li>• Less awareness of Ni-kshay portal, NPY in community and private practitioners</li> <li>• Less awareness within the community</li> </ul>
<b>Finance</b>	<ul style="list-style-type: none"> <li>• Financial resources are available</li> <li>• Integration will ensure no duplication of expenditures</li> </ul>	<ul style="list-style-type: none"> <li>• Different financial mechanisms for each program</li> <li>• Programs can be merged depending on activities but not on financial schemes</li> </ul>
<b>Leadership &amp; Governance</b>	<ul style="list-style-type: none"> <li>• Well-designed programs</li> <li>• History of tobacco use documented in both TB and DM programs</li> </ul>	<ul style="list-style-type: none"> <li>• Under defined systems for involvement of PP (Private Practitioner)</li> </ul>

Table 1.

**Conclusions:** This study identifies strategies to integration of TB, DM and TC programmes in India. To catalyse the integration process, the study suggests cross-talk of the three programmes in order to:

1. Sensitise the peripheral health system staff for integration to enhance effective single window programme implementation and service provision;
2. Rigorous implementation of feedback and referral system; and
3. Development of common cross-programme digital data entry and reporting platforms. Policymakers and healthcare system manager should adapt a multidimensional approach to mitigate the barriers and facilitate the integration.



### EP07-1061-15 Improving case-finding for extrapulmonary TB in Meru County Teaching and Referral Hospital, Kenya

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**Background and challenges to implementation:** Extrapulmonary tuberculosis (EPTB) case finding remains suboptimal due to low level of awareness of its presentation, diagnosis, and challenges with collecting, processing and analysis of samples other than sputum by laboratory personnel.

The majority of Extrapulmonary Tuberculosis cases in Kenya are notified at tertiary facilities such as County referral hospitals. This may point to delayed diagnosis and may lead to unfavorable sequelae. In Meru County, only 9% (376) of TB cases notified in 2022 were extrapulmonary TB (EPTB) cases.

Meru county Teaching and Referral Hospital sought to improve the case finding for Extra pulmonary TB through active case finding and EPTB specimen testing.

**Intervention or response:** Facility-level situation analysis was conducted to identify EPTB case finding challenges. Low index of suspicion for EPTB, inadequate involvement of hospital pathologists and low capacity among laboratory staff for testing extra-pulmonary specimens using Genexpert. Sensitization was done at the facility level on diagnosis and management of EPTB as part of continuous medical education sessions.

All patients with signs and symptoms of EPTB had the pathology specimens subjected to Genexpert MTB/RIF<sup>(R)</sup> testing in addition to other tests so as to rule out TB.

**Results/Impact:** There was an improvement in the proportional contribution of EPTB cases to overall TB case finding by 4 percent in the two years of the intervention. (19% in 2019 to 23% in 2021). The overall diagnostic yield from EPTB specimens increased from 21% in 2019 to 56% in 2022.

**Conclusions:** Enhanced index of suspicion and testing of EPTB specimens has a positive contribution to overall case finding for EPTB. Through the involvement of the hospital Pathologist, the laboratory officers can be trained and gain skills for EPTB specimen processing and diagnosis. A robust intra-facility linkage and referral for presumptive EPTB cases and involving all service delivery points is important. This approach is scalable and sustainable.

### EP07-1062-15 Optimising private sector TB prevention and care through the strategic engagement of private laboratories: The TB LON experience in Akwa-Ibom and Kano States, Nigeria

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**Background and challenges to implementation:** The role of laboratories in TB prevention and care has largely been limited to TB testing. Nigeria has however been identified as one of the big seven (7) countries in Public Private Mix (PPM) for TB prevention and care[1], with a very large private sector presence, and a high contributor to the missing TB cases globally, and there is a need to strategically optimize the engagement of all private healthcare providers in the fight against TB.

With over 6,000 private medical laboratories in Nigeria, many individuals use laboratories as their entry point into the healthcare system, and there was a need to expand the scope of work of these laboratories to include active TB case finding.

The TB LON 1&2 Project implemented by KNCV Nigeria, identified this opportunity and engaged private medical laboratories in Akwa-Ibom and Kano states for client screening and presumptive TB identification.

[1] Engaging private health care providers in TB care and prevention: a landscape analysis, second edition. Geneva: World Health Organization; 2021.

**Intervention or response:** Following an assessment of the private laboratories in Akwa-Ibom and Kano States, 40 laboratories were engaged in May 2022, with staff trained and equipped with a screening checklist which was used to screen to all walk-in clients. Identified presumptive TB clients were counseled, and samples collected and sent to molecular testing sites, and diagnosed TB cases were linked to treatment.

**Results/Impact:** A total of 382 TB cases were diagnosed within 6 months of this intervention, and this success was attributed to the continuous mentoring provided to these laboratory staff, as well as the performance-based incentives provided in the intervention.

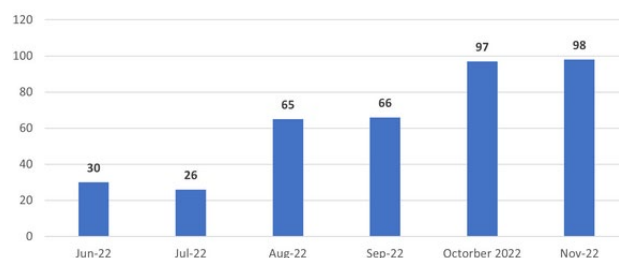


Figure. Total cases diagnosed.

**Conclusions:** The role of laboratories in TB prevention and care goes beyond testing for TB. With adequate support, these laboratories can be engaged to actively identify TB cases from their walk-in clients.

### EP07-1063-15 Delay in TB diagnosis and associated factors in Meru County, Kenya

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**Background:** Over 140,000 people get TB in Kenya every year but only 60% get diagnosed. Delay in TB diagnosis has far reaching implications including; community transmission and poor treatment outcomes. Lack of knowledge and poor access to diagnostics have been cited as some of the factors leading to delay. This study was conducted between January to December 2021 to determine delay in TB diagnosis and related factors.

**Design/Methods:** A cross sectional study in 7 health facilities in Meru county involving people newly diagnosed with TB was conducted. A representative sample of 369 was determined using Cochran (1977) formula. Semi structured questionnaire was used to collect data to estimate the time lapse between onset of TB symptoms and seeking medical care (patient delay), and time between seeking care and diagnosis (Health system delay). Data was analyzed using R statistics.

**Results:** 390 participants were interviewed; 91 (23%) females and 299 (77%) males. The median patient delay was 20 (CI 10, 30) days and the median health system delay was 20 (CI 3, 40) days. The average number of hospital visits before diagnosis was 4. The factors associated with delay were; Age ( $P=0.002$ ) with patients aged between 35 to 44 and above 55 years delaying more. Level of education ( $P=0.017$ ) with those with primary level education and no education at all delaying more. Level of facility ( $P<0.001$ ) with those who sought care in lower level facilities (level 2 and 3) delaying more and type of TB ( $P<0.001$ ) where those with clinically diagnosed TB and extra-pulmonary TB delayed more than those with bacteriologically diagnosed pulmonary TB.

**Conclusions:** There is need to build the capacity of health care workers to diagnose TB in lower level facilities and empower them to diagnose in non-classical presentations. Health education need to be enhanced to promote early TB diagnosis.

### EP07-1064-15 TB-related deaths in Norway – a quality study comparing national registries and clinical records, 1996-2019

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**Background and challenges to implementation:** Globally, tuberculosis is the top single infectious cause of death. However, even in high-income/low-prevalence countries data quality is suboptimal. We investigated the reporting of tuberculosis-related deaths to the Norwegian Cause of Death Registry (NCoDR) and the Norwegian Surveillance System for Communicable Diseases (MSIS).

**Intervention or response:** Persons reported as dead with active tuberculosis (ICD10 A15-19) in NCoDR and/or with treatment outcome died in MSIS 1996-2019 were identified. Data in the two registers were compared and corrected. Based on information in the patient records and systematic discussion in the study group, the information in the registries was further corrected and expanded regarding diagnosis, treatment outcome, and cause of death.

**Results/Impact:** Ten out of 25 hospital trusts from all 4 regions of the country participated, accounting for 37% of reported TB patients. We revised the files of 212 patients. In NCoDR, tuberculosis was mentioned among causes of death in 135 before the revision, corrected to 148 after comparing the two registers and 137 after the revision with clinical records. Tuberculosis as underlying cause increased from 74 to 86 and 90 and as contributory cause changed from 61 to 62 and 47. In MSIS, all death as treatment outcome declined from 161 to 163 and 148: death from TB increased from 37 to 86 and 89, deaths with TB as contributory cause changed from 57 to 56 and 46, while deaths from other/unknown causes reduced from 67 to 21 and 13.

Norwegian cause of death registry (Figures in parenthesis: results after final revision)						
	TB Underlying cause	TB Contributory cause	TB not mentioned	Not registered	Sum	
Norwegian surveillance system for communicable diseases	Deaths due to TB	24 (89)	4 (0)	5 (0)	4 (0)	37 (89)
	Death TB comorbidity	20 (0)	13 (46)	21 (0)	3 (0)	57 (46)
	Death cause other than TB/unknown	10 (0)	16 (0)	39 (13)	2 (0)	67 (13)
	TB but other outcome than death	4 (1)	9 (1)	3 (34)	0 (0)	16 (36)
	Not registered	16 (0)	19 (0)	0 (28)	0 (0)	35 (28)
	Sum	74 (90)	61 (47)	68 (75)	9 (9)	212 (212)

**Conclusions:** We found discrepancies between the two registries where the two should be congruent. Both TB as underlying cause of death and death from TB in MSIS were underreported. Comparing the two registries improved the quality of data on TB deaths and is now national routine. The findings indicate that clinicians need more training on coding rules and guidelines for national registries.

## EP08 Private sector engagement and TB system information

### EP08-1065-15 Active engagement of the private sector to improve TB case-finding in Nigeria

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**Background and challenges to implementation:** Nigeria has the highest burden of TB in Africa and is one of the 8 countries that account for the highest contribution to the missing cases of TB globally. About 60% of Nigerians seek health care in the private sector and as such engagement of the private sector is necessary in bridging the country's gap in finding missing TB cases.

**Intervention or response:** The National Tuberculosis, Programme in a public-private Mix model embarked on a massive engagement of private facilities which includes private-owned health facilities (clinics/hospitals),

community -pharmacies and Patent Medicine Vendors (PMVs)x, utilizing a hub and spoke model of referral (of presumptive TB). The PMVs and Community-pharmacies serve mostly as spokes referring to the private clinics and hospitals serving as hubs (for diagnosis and treatment).

Following the engagement of the facilities, the Programme integrated the supervision of private facilities into the quarterly supervision conducted by Local Government, States and National Programmes to follow up for improved case holding and reporting.

**Results/Impact:** Between 2018 and 2022 the number of private facilities reporting TB cases to the National Programme increased by 213% from 1768 in 2018 to 5529 in 2022. As a result of this, the number of TB cases reported from the private sector increased from 12,625 in 2018 (baseline) to 69,504 in 2022, which is a 451% increase in TB notifications from the private sector.

Overall, the strategic engagement of the private sector led to an exponential increase in PPM contribution to National case notification, from 12% in 2018 (12,625) to 14% in 2019 (17,250), to 26% in 2020 (35,865), to 28% in 2021 (58,219) and 24% in 2022 (69,504).

**Conclusions:** The private sector's engagement will yield huge results if the providers are properly engaged and routinely monitored.

### EP08-1066-15 Improving access to chest X-ray for TB screening among household contacts of TB patients by engaging private facilities across urban and rural areas in India

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**Background and challenges to implementation:** Tuberculosis prevalence surveys have demonstrated benefit of chest radiography for TB screening but availability, accessibility and capacity constraints at peripheral public health institutions (PHI) limit its uptake.

Implementation of TB Preventive Treatment (TPT) necessitates ruling out active disease in household contacts (HHCs) of pulmonary TB patients compounding the demand-supply gap.

**Intervention or response:** Global Fund supported Joint Effort for Elimination of TB (JEET) undertook systematic mapping and engagement of private chest X-ray (CXR) facilities across urban and rural areas. Testing facilities having quality assured, analog or digital machine, were contracted across Tuberculosis Units (TU covers population of 0.15-0.2 million).

Geographical spread, ease of access, free test (cost borne by project), reduced waiting and reporting times were key considerations. Medical officers at PHIs/NTP officers interpreted radiographs wherever radiologist's

report was unavailable. CXR was done for <5year TB symptomatic HHCs and all  $\geq$ 5year HHCs of PTB patients.

**Results/Impact:** JEET caters to 677 TUs across 65 districts 11 provinces; 418 TUs had functional public CXR facility. 1085 private CXR facilities were mapped. 114 TUs did not have any public/private CXR facility. 574 private facilities were contracted across 488 TUs. Between Jan 2022- Dec 2022, with contact screening of 1,49,261 DSPTB patients; 5,76,509 HHCs were enumerated. 289,169 HHCs were initiated on TPT of whom 2,38,032 (93% of eligible) got a CXR. Additionally, there were 49,378 HHCs who underwent CXR but refused TPT. 22% of total CXR were done in public and 78% in private. 6475 contacts had TB suggestive CXR; 1431 eventually diagnosed as active TB (70% were asymptomatic).

Availability of functional CXR facilities		Contribution to CXR from public & private facilities	
Total intervention TUs	677	Total CXR done	287410
TUs with at least one functional CXR facility (Public)	418	CXR done in Public	63230 (22%)
TUs with at least one functional CXR facility (Private)	563	CXR done in Private	224180 (78%)

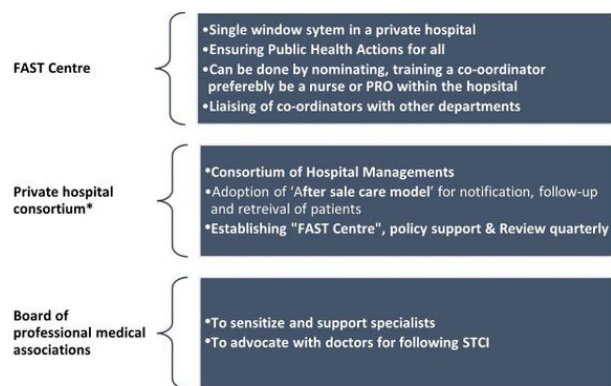
Table 1: Summary of Availability and Contribution of public & private CXR facilities.

**Conclusions:** Widespread engagement with private CXR facilities improved access, capacity and increased testing prior to TPT initiation for HHCs by reducing travel (time & cost) and waiting time. This facilitated early diagnosis. We recommend engagement with private CXR facilities under NTP to augment screening and early diagnosis of TB.

## EP08-1067-15 Sustainable health system strengthening in the private sector – the FAST model for ensuring standards of TB care in Tamil Nadu, India

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**Background and challenges to implementation:** More than half the TB patients in India seek care from the private sector. The national TB program has recognized that engagement with the private sector in an efficient manner is crucial for TB elimination, so several models have been tried across the nation. These projects could not be scaled up as they were heavily dependent on intermediate agencies and external funding. To overcome these challenges a zero-cost sustainable solution was envisioned.



**Results/Impact:** In the intervention period from April 2022 to March 2023, the notification from the 22 FAST centres has increased by 47% compared to 2019 while the gain in non-FAST centres was only 19%. Comorbidity testing for HIV and Diabetes has increased in these centres (HIV – 46% in 2019 and 93% in 2022; DM- 18% in 2019 and 94% in 2022). Contact tracing has increased about 6 times and 82% of the patients received nutritional support via DBT NPY in these facilities which was higher than in the pre-FAST period (67.4% in 2019).

**Conclusions:** The notification and public health action among notified TB cases showed remarkable improvement in FAST centers. This is a zero-cost scalable sustainable solution for furthering private-sector engagement.

### EP08-1068-15 Transition from donor-funded pilots for private sector engagement to domestic funding: Key learnings from India

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**Background and challenges to implementation:** National Strategic Plan (NSP) for TB elimination in India lays specific emphasis on engaging all forms of private sector to achieve ambitious goal to eliminate tuberculosis in India by 2025. Considering its importance, donor funded pilots of interface agency for private sector engagement were implemented in three cities.

These pilots showed dramatic improvement in private TB case notifications & quality of care. Based on the evidence from these pilots, interface agency models have been scaled up across the country using domestic resources.

We present over here the learning from this transition & scale-up.

**Intervention or response:** In 2013, National TB Elimination Program, India (NTEP) implemented donor funded pilots in three cities wherein interface agencies were contracted to catalyze private sector engagement. Based on its success, key interventions and learnings were scaled up to 30 cities using TGF grants. Subsequently, NTEP domestically funded these strategies for nationwide need-based scale-up in an output-based financing model. This transition resulted in several interventions to strengthen private sector engagement under NTEP:

1. Capacity enhancement for contacting agencies and contract management.
2. Putting in place IT tools for streamlining monitoring, verification and financial processes.
3. Engagement of TSUs to enhance technical capacity of program for effective partnership.
4. Offering package of free services, incentives, and adherence support to Private sector.

**Results/Impact:** In 2022 under NTEP, Intermediary agencies have been contracted in > 250 districts across India. As a result, NTEP achieved highest private sector TB case notification so far of 736,000 cases & saw active private providers engagement under the programme increasing from 38613 (2019) to 45718 (2022). Further, incentive of INR 21,326 million to private patients & INR 738 million of private providers were released.

**Conclusions:** Scale up of Interface agency has been a crucial instrument in strengthening private sector engagement in India, with numerous learnings which are worth disseminating for cross learning.

### EP08-1069-15 Interface agencies as catalyst of private sector engagement – lessons from India's National TB Elimination Programme

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**Background and challenges to implementation:** The National TB Elimination Programme (NTEP) is focusing on ending TB epidemic in India by 2025, five years ahead of global targets of 2030. Private sector engagement has been prioritized as one of the foremost strategic interventions under the National Strategic Plan<sup>1</sup> (NSP) 2020-25 to realize country's ambitious target.

In line with this, national programme has adopted and scaled up Interface Agency model across the country to detect and ensure quality TB care in private sector, under output based contracting mechanism, using domestic resources.

**Intervention or response:** An impact of Interface Agencies, before and after their engagement for one year, is analyzed by studying the private sector notifications trends. Bihar and Uttar Pradesh are the two high TB burden states of India contributing to 1/3<sup>rd</sup> of total private sector notification. Hence, Interface Agency scenario from 19 districts of Bihar and 20 districts of Uttar Pradesh is studied, wherein Interface Agency operations were rolled out using domestic funding in June 2020 and May 2022 respectively.

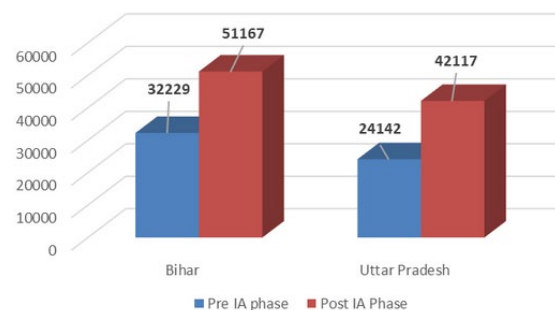


Figure. Private sector notification trend before and after interface agency (IA) operations.

**Results/Impact:** In 19 districts of Bihar<sup>2</sup>, prior to introduction of interface agency, total private TB notification was 32,229 & post engagement it rose to 51167 over a continuous 12-month period (59% net notification increase). Similarly in 20 districts of Uttar Pradesh<sup>2</sup>, private notification in a year, prior to introduction of

interface agency was 24142, which increased to 42117 (with net increase of 75%) within 12-month of engagement of the agencies. There was no net of any decrease in public notifications observed.

**Conclusions:** Engagement of private sector through Interface Agency model using output-based contracting is an effective strategy in reaching out to the missing patients and linking them for quality TB care.

### EP08-1070-15 Institutionalising corporate sector engagement to accelerate progress in ending TB in India

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**Background and challenges to implementation:** Engaging the Corporate sector is one of the activities envisioned in India's Multi-Sectoral Action plan for TB Elimination. The Corporate TB Pledge (CTP), a joint initiative by the Government of India and USAID, was launched in 2019 to complement the national TB elimination efforts. The corporate entities take the pledge that commits them to utilize their resources – both financial and human, to raise awareness and improve TB health outcomes.

**Intervention or response:** Hosted under the USAID-supported iDEFEAT TB project led by The Union, the secretariat of CTP focuses on mobilizing the corporates with a tiered approach and provides them with technical support to initiate TB care interventions in their workplace and community. Different strategies are adopted including engaging with the business associations, Public Sector Undertakings (PSU), and states with a high concentration of corporates and sensitizing the state and district program managers to ensure ownership and long-term sustainability. The secretariat conducts regular training and sensitization activities, consultation/meetings/workshops, and campaigns for the corporates to enhance engagement. The CTP provides various platforms such as the DR-TB consortium, partner Hall of Fame, and an online platform, ensuring visibility to their work.

**Results/Impact:** More than 300 corporates across various sectors were mobilized to pledge for TB Elimination efforts. Nearly USD 2.4 million were unlocked from the corporates for TB/DR-TB care interventions; Technical support was provided to 114 community-level and workplace interventions, resulting in the screening of around 2.4 million persons, and testing of more than 100,000 persons with TB symptoms.

**Conclusions:** The CTP has amplified corporate engagement, mobilized investments, and ensured efficient TB/DR-TB care by the corporate sector. It has demonstrated

at-scale govt buy-in and support to engage corporates for public health programs; continued commitment and leadership of the private sector to eliminate TB among their workforce and catchment areas. This model could be replicated in other countries.

### EP08-1071-15 Ensuring TB care services among tea garden workers by an employer-led holistic TB care model in India

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**Background and challenges to implementation:** The Tea industry in India is one of the oldest corporate enterprises offering employment to unskilled Tea Garden workers. The workers are marginalized for health care services and are at higher risk for various health conditions. Taking the Corporate TB Pledge (CTP) in 2020, a commitment to end death and suffering due to TB, Goodricke Tea initiated an employer-led model to extend TB care and prevention services to its 30,000 employees across 29 tea estates of Assam and West Bengal.

**Intervention or response:** The model involved a multi-pronged strategy to address issues of inaccessibility, diagnostic delays, treatment non-completion, and stigma. It leveraged upon the existing health infrastructure and health facilities of the Government and Goodricke Tea. Their approach includes the development of workplace TB policy, management and community engagement, awareness generation, screening, and early detection, free treatment at company-owned medical facilities, and nutrition support to facilitate a TB-free environment in all their tea estates, as well as nurturing TB champions from the community. Non-workers residing in the gardens are also included in their TB elimination intervention.

**Results/Impact:** Over 180,000 populations are being screened periodically. In the last two years, 44,020 people with symptoms were screened out of which 11,914 were tested for TB. As on December 2022, more than 422 patients were initiated on TB treatment. Linkages with District TB Cells and district diagnostic facilities in 8 districts in Assam and 3 districts in West Bengal have improved access and delivery of TB diagnostic and treatment services. The demand for early diagnosis and treatment had increased progressively whereas stigma and discrimination reportedly declined with the empowerment of people affected by TB.

**Conclusions:** This employer-led holistic approach is exemplary in converging and utilizing existing resources in addressing the access issues faced by marginalized workers for TB care.

## EP08-1072-15 Post-pandemic engagement of formal and informal private health facilities to find the missing people with TB in Kenya

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**Background and challenges to implementation:** The COVID-19 pandemic has caused a need to optimize TB control interventions in the private sector, including strengthening public-private partnerships, enhancing provider engagement, improving patient-centered care, and leveraging digital technologies.

**Intervention or response:** To strengthen public-private partnerships, Kenya has been fostering collaboration between public and private entities in the development, implementation, and monitoring of TB control interventions.

This has been achieved through the existing PPM Action Plan, regulatory and policy frameworks, financing mechanisms, and capacity-building initiatives.

Engagements have been enhanced through targeted training programs that improve private providers' diagnostic and treatment skills, as well as incentivizing private providers to report cases and follow treatment guidelines.

Patient-centered care was achieved through interventions that prioritize patient needs, preferences, and perspectives, such as the provision of personalized care, health education, and social support.

Finally, leveraging digital technologies, TIBU and t-bu lite mobile solution, improved access to TB care in the private sector, increased symptomatic screening, patient engagement and adherence, and enhanced data collection and monitoring.

**Results/Impact:** There was a notable increase (15%) in case notification in the private sector in 2022 compared to 2020. A total of 17,064 cases were notified in 2022, 15,384 in 2021, and 14,881 in 2020. A total of 1,311 private facilities have consistently reported for the past 2 years, an increase from 935. Through the t-bu lite app, 1169 facilities were screened, of which 469 were private facilities, with 151 of them managing patients through the app.

**Conclusions:** Optimizing the implementation of TB control interventions in the private sector post-COVID era requires a comprehensive approach that addresses regulatory, financial, and capacity-building challenges.

Meaningful engagement and support of private providers is key to finding the missing people with TB. These strategies are essential for achieving the goal of ending TB by 2030, as outlined in the Sustainable Development Goals.

## EP08-1073-15 Exploring the *M. tuberculosis* burden in the population using the median Xpert MTB/RIF Ultra cycle threshold in South Africa

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**Background:** South Africa's national *Mycobacterium tuberculosis* complex (MTBC) positive Xpert MTB/RIF Ultra (Ultra) test results generate *rpoB* cycle threshold (Ct)-values, which approximate organism load in tested specimens. The median Ct was explored in context of tested volumes and detection-rates before-,during-and post-COVID19.

**Design/Methods:** The National Health Laboratory Service performed 10,419,021 Ultra tests between 2017-2022, with *rpoB1* Ct extracted from 905,192 results reporting MTBC-detected. *rpoB1* Ct values were transformed into mycobacterial load (colony forming unit, CFU/ml) using previously reported equation ( $y = -2,092x + 29,563$ ).

Total tested numbers, MTBC-detection rates and median CFU/ml were aggregated within testing periods: pre-COVID19 (October 2017–March 2020), COVID19 (April 2020–April 2022) and post-COVID19 (April 2022–December 2022).

COVID19-period was further split into 'testing-decline' (April–August 2020), 'testing-recovery' (September 2020–November 2021) and 'testing-above-forecast' (TAF) (December 2021–April 2022). Exploratory trends between MTBC-detection and CFU/ml were assessed by coefficient of determination, R<sup>2</sup>.

**Results:** Annual tested volumes remained characteristically cyclical across all periods (Figure), reducing by ~50% during 'testing-decline' and exceeded any previous test volumes in the post-COVID19 period. 'Testing-decline' corresponded to highest detection rates.

There was progressive annual decrease in MTBC-detection from 2017 (11.5%) to 2022 (7.3%), most marked from TAF. However, during 'testing recovery', specimens with MTBC-detected had highest mycobacterial load recorded since Ultra uptake ('testing decline' IQR, 4.5–

4.58CFU/ml and ‘testing-recovery’ IQR, 4.7– 4.8CFU/ml), including compared to pre- and post-COVID19 (both 4.4CFU/ml [IQR 4.3-4.5]). MTBC-detection and mycobacterial load varied considerably:  $R^2=0.67$  (pre-COVID19), 0.31(testing-decline), 0.26 (testing-recovery), 0.72 (TAF) and 0.80 (post-COVID19). Mycobacterial load remained elevated post-COVID19 compared to pre-COVID19.

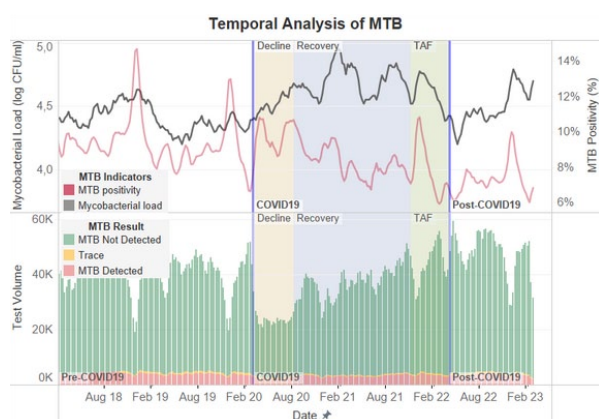


Figure. South Africa's national Xpert MTB/RIF Ultra test volumes pre-during-and post-COVID19. The COVID19 period is reflected between the vertical blue bars.

**Conclusions:** High MTBC-detection with higher mycobacterial load may reflect delayed testing and diagnosis, especially during the pandemic when access to, and services were limited. Diagnostic delays potentially give more opportunity for community transmission and worse disease burden in individuals. The aggregated quantitative Ct-variable may be an accessible measure for community surveillance to improve testing algorithms and monitor interventions.

### EP08-1074-15 TB case-finding outcomes following automation of TB screening questions in the electronic medical records: A case study of Matata Hospital, Homa Bay County, Kenya

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**Background and challenges to implementation:** Homa Bay County ranks high in tuberculosis (TB) and HIV burden in Kenya. Early detection and treatment are key in reducing transmission and mortality. TB screening rate is 77% among outpatient clients seeking care. Non-standardized screening has been used before inclusion

of Active Case Finding (ACF) questions in the electronic medical record (EMR). We sought to evaluate the impact of automating TB-screening questions within hospitals outpatients' EMR system.

**Intervention or response:** We conducted a comparative analysis of TB screening outcomes among all clients and all age groups in the outpatient for pre and post automation of the TB screening questions. We compared the workload, screening rates and ACF yield in Jan-August 2020 vs Jan-August 2021. We hypothesized that automation of the screening process would improve these outcomes. We used a statistical test (independent samples t-test) to compare the means of the two time periods.

**Results/Impact:** Screening rate increased from 90% (n=24,234 out of 26,954 patients) in 2020 to 100% (n=25,429 out of 25,429) in 2021 which is the national target goal. Active Case Finding average yield also improved from 9% (n=23 out of 255 presumptive cases) in 2020 to 19% (n=53 out of 273 presumptive cases) in 2021. A two-tail t-test of independence gave a mean difference of -149.375 with an observed value of -0.838 and a p-value of 0.416 (14 d.f,  $\alpha =0.05$ )mj. We therefore rejected the null hypothesis that there would be no significant difference between in means.

**Conclusions:** Our analysis demonstrate that the automation of TB screening led to improvement in screening rates, achieving the National target goal of 100% screening. ACF increment suggest that the automation process effectively identified more cases of TB.

Our findings provide valuable insights for healthcare facilities seeking to improve their TB screening and emphasize the importance of automation in achieving high screening rates and improving ACF yield.



## ABSTRACT PRESENTATIONS THURSDAY 16 NOVEMBER 2023

### ORAL ABSTRACT SESSION (OA)

#### OA12 Pharmacokinetics studies for better treatment of TB

##### OA12-289-16 Bedaquiline exposure in the breast milk of women treated for rifampicin-resistant TB

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**Background:** There are limited data describing the exposure of bedaquiline and its metabolite M2, in the breast milk of women treated for rifampicin-resistant tuberculosis (RR-TB). Quantifying bedaquiline and M2 exposure in breast milk is critical to understand drug exposure in breastfeeding infants. We validated an assay for bedaquiline and M2 in breast milk, and explored the relationship between maternal plasma and breast milk concentrations in a clinical trial setting.

**Design/Methods:** BEAT-tuberculosis, funded by US-AID, is a randomised clinical trial comparing a novel RR-TB treatment regimen, including bedaquiline with the standard of care. We performed plasma and breast milk sampling approximately six weeks post-delivery: pre-dose and 2, 4, and 6 hours post-dose. We validated the breast milk assays using protein precipitation and solid-phase extraction, and analysed samples using liquid chromatography-tandem mass spectrometry to measure the analyte concentrations. We used STATA to compare bedaquiline and M2 peak concentrations ( $C_{max}$ ) and area under the concentration time curve to six hours ( $AUC_{0-6}$ ) in plasma and breast milk.

**Results:** We assessed the overall accuracy and precision of the breast milk assays in three consecutive independent validation batches. The methods were reproducible and robust, and both bedaquiline and M2 proven to be stable in breast milk when subjected to various stability tests. The analytes were differentiated from endogenous components present in six different lots of breast milk.

Correlation data, from three participants, indicated higher concentrations of bedaquiline and M2 in breast milk than in plasma: the mean  $C_{max}$  and  $AUC_{0-6}$  (breast milk/plasma) ratios of bedaquiline and M2 were 9.76 and 12.79, and 1.52 and 3.42, respectively.

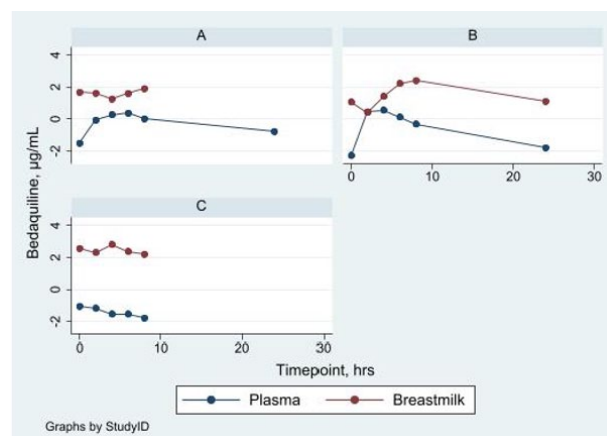


Figure. Concentration-time profiles (Log) of bedaquiline, comparing plasma and breast milk in three participants treated for multidrug-resistant tuberculosis.

**Conclusions:** We successfully developed, validated and applied an assay for bedaquiline and M2 in breast milk to correlate breast milk and plasma concentrations. The impact that high concentrations of bedaquiline measured in breast milk may have on infant safety, requires further evaluation.

##### OA12-290-16 Pharmacokinetic-toxicity analysis of long-term linezolid use in children with multidrug-resistant TB

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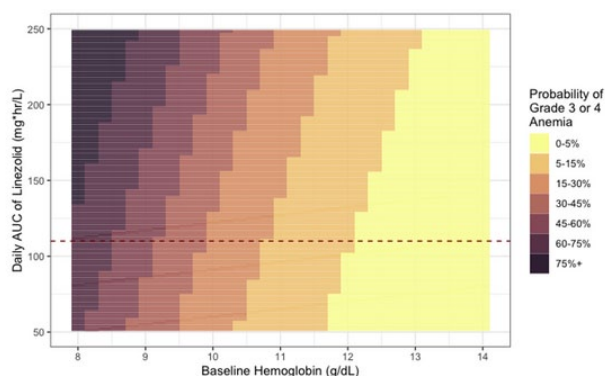
**Background:** Linezolid is associated with treatment-limiting dose- and duration-dependent toxicities, including anaemia.

However, patient-level and linezolid pharmacokinetic risk factors for anaemia have not been well described in children treated for multidrug-resistant tuberculosis (MDR-TB).

**Design/Methods:** We evaluated linezolid pharmacokinetic and longitudinal hemoglobin data to validate a previously developed population pharmacokinetic model with a prospective cohort of children routinely treated for MDR-TB, and to evaluate the impact of linezolid pharmacokinetics on anemia risk using Division of AIDS Adverse Event Grading Tables.

Validation of a previously published population pharmacokinetic model was done via nonlinear mixed effects modeling using NONMEM. A multivariable ordinal logistic regression model was built for prediction of anemia.

**Results:** 112 children were included from South Africa and India, median age 7.2 yo (IQR: 2.2-13); 24 of these contributed new linezolid pharmacokinetic data. The previously published 1-compartment population pharmacokinetic model that informs the currently recommended dosing was validated with the prospective pharmacokinetic data with the typical clearance value estimate refined to 4.78 L/h. A multivariable ordinal logistic regression model with significant covariates including baseline hemoglobin and daily AUC of linezolid predicts the probability of any grade anemia event. As visualized in Figure 1, decreasing baseline hemoglobin and increasing average daily AUC of linezolid each increase the probability of a child experiencing anemia. The adjusted odds ratios from the multivariable model are 2.64 (1.98 – 3.62, 95% CI) for every decrease in 1 g/dL of hemoglobin and 1.012 (1.007 – 1.017, 95% CI) for every increase in 1 mg\*hr/L of daily linezolid AUC, respectively.



*Figure 1. Probability of experiencing a grade 3 or 4 anemia event given baseline hemoglobin and when starting long-term linezolid treatment for TB and average daily exposure of linezolid. The dashed red line corresponds to the target AUC of 110mg\*hr/L.*

**Conclusions:** New linezolid pharmacokinetic data confirm currently recommended pediatric doses. With currently recommended linezolid doses, if baseline hemoglobin is normal, treatment with linezolid minimally increases the probability of a grade 3/4 anemia event. However, children even with moderately low baseline hemoglobin (10 g/dL) are still at risk (15-45%) of experiencing grade 3/4 anemia.

## OA12-291-16 Cerebrospinal fluid penetration of delamanid, clofazimine and terizidone in pulmonary TB patients

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**Background:** Whether or not drugs used for pulmonary TB can be used for TB meningitis is unclear, in part owing to lack of information on site-of-disease PK. If only the unbound drug diffuses freely into cerebrospinal fluid (CSF), such low concentrations are difficult to measure(1,2). Delamanid and clofazimine are highly protein bound (>99.9%) with a minimum inhibitory concentration (MIC) in MGIT of 60 and 500 ng/mL, respectively(3,4). Cycloserine penetrates CSF well, though CSF PK of cycloserine administered as the prodrug terizidone has not been explored, and the MIC is unknown(2,5). We investigated the CSF PK of these critical second-line drugs in two studies (NCT02583048, TASK-CSF-01).

**Design/Methods:** In Cape Town, South Africa, 35 participants with pulmonary DR TB (without meningitis) established on regimens including delamanid, clofazimine and/or terizidone multiple blood and one CSF sample collected into low-binding tubes on the same day (figure 1). Concentrations were quantified with validated LC-MS/MS assays and analysed in WinNonlin v8.3.

**Results:** Median areas under the concentration-time curve (AUC<sub>last</sub>) in plasma were 4630ng\*h/mL, 9447ng\*h/mL and 839573ng\*h/mL for delamanid, clofazimine and cycloserine, respectively, with median maximum concentration (C<sub>max</sub>) of 247ng/mL, 497ng/mL and 50791ng/mL occurring at 4, 6 and 4 hours, in keeping with prior reports (6,7). C<sub>max</sub> (range) in CSF was 1.53ng/mL (0.491-1.77ng/mL), 0.636ng/mL (0.127-2.21ng/mL), and 29147ng/mL (3466-45754ng/mL) with a median CSF to plasma ratio for paired samples of 0.00512, 0.00128 and 0.463 for delamanid, clofazimine and cycloserine respectively. Clofazimine CSF concentrations were similar to estimated unbound plasma concentrations, while delamanid concentrations were approximately 5 fold higher. Terizidone achieved higher C<sub>max</sub> in CSF than prior reports of cycloserine administration.

**Conclusions:** All drugs were measurable in CSF of TB patients without meningitis. CSF concentrations were at least similar to active, unbound plasma concentrations, suggesting that these drugs could be effective for TB meningitis and should be evaluated in trials.

### OA12-292-16 Development of a new drug adherence measure for multidrug-resistant TB

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**Background:** Measuring adherence to multidrug-resistant tuberculosis (MDR-TB) treatment, which has historically been poor, is important. Dried blood spots (DBS) is an objective adherence measure, which is minimally invasive and has simple storage requirements, therefore advantageous for use in resource-limited settings. We validated a multiplex DBS assay to quantify bedaquiline, N-desmethyl bedaquiline metabolite (M2), linezolid, levofloxacin and clofazimine in clinical trial samples.

**Design/Methods:** BEAT-tuberculosis, funded by USAID, is a randomised clinical trial comparing a novel MDR-TB treatment regimen with the standard of care. We performed plasma and DBS sampling simultaneously at seven timepoints over 24 hours, after four weeks of treatment. We prepared DBS by spotting 50 µL of blood onto a Whatman 903 filter card; a ten-millimetre punch of DBS disk was then sonicated, followed by solid phase extraction. We used liquid chromatography-tandem mass spectrometry for assay quantification, and Deming regression and Bland and Altman's plot to evaluate the agreement between the DBS measurements and analyte-specific plasma concentrations. We compared area under the concentration-time curves from 0-24 hours (AUC<sub>0-24</sub>) between plasma and DBS.

ated plasma AUC<sub>0-24</sub> were 22.2 vs 20.5 for bedaquiline, 5.88 vs 5.92 for M2, 189 vs 187 for linezolid, 158 versus 152 for levofloxacin, and 6.51 versus 5.30 µg·hr/mL for clofazimine.

**Conclusions:** We report the simultaneous validation and quantification of bedaquiline, M2, linezolid, levofloxacin, and clofazimine in DBS with accuracy and precision, meeting FDA acceptance criteria. Our DBS assay demonstrates high correlation between plasma and estimated plasma concentrations. The agreement between plasma and estimated plasma AUC<sub>0-24</sub> demonstrates comparability, and therefore validates DBS as an adherence measurement tool in MDR-TB treatment settings.

### OA12-293-16 TBAJ-876 CL001: pharmacokinetics and safety data from a phase I trial of TBAJ-876, a novel second-generation diarylquinoline, in healthy participants

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**Background:** TBAJ-876 is a diarylquinoline with greater antimycobacterial potency and a potentially better safety profile than bedaquiline.

**Design/Methods:** 3-part study: Single ascending dose (SAD) of 68 participants [13 on placebo, 55 on TBAJ-876 10-800 mg in the fasted state or 100 mg in the fed state to evaluate food effect; multiple ascending dose (MAD) of 39 participants (12 on placebo, 25 on TBAJ-876 25, 75, and 200 mg daily for 14 days in the fed state); bioavailability part of 30 participants (3 groups receiving a single tablet of 100 mg in either the fasted or fed state, or 4 tablets of 25 mg in the fasted state) to compare PK/exposures of the suspension and tablet formulations.

**Results:** The concentrations of TBAJ-876 increased proportionally with dose. Administration with food increased the AUC of TBAJ-876 by 60% and 90% for the single 100 mg doses of suspension and tablet formulations, respectively. The bioavailability of the oral suspension and tablet formulations was similar. Mean half-lives were 4.4 – 11 weeks across cohorts. There were no serious AEs; most of the AEs were mild, and all resolved. There were very few clinically significant changes in safety laboratory tests, and all resolved. In both the SAD and MAD portions, the AE profile was generally similar in the TBAJ-876 and placebo groups. There was no evidence of treatment related myocardial, musculoskeletal, hepatic, or pancreatic toxicity. There were also no clinically significant QT prolongations based on ECG review. In the third part of the trial, the tablet formulation was also generally safe and well tolerated.

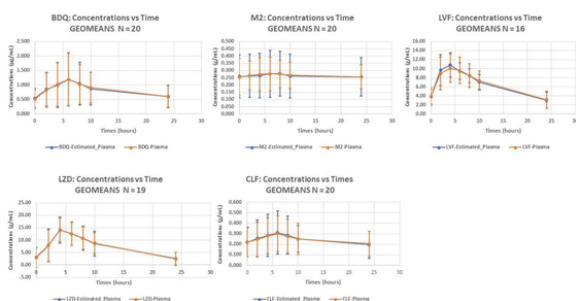


Figure: Concentration versus time profile (0 – 24 hours) presented as a geometric mean with standard deviations. Estimated\_Plasma: estimated plasma concentrations calculated by applying the Deming regression equation to the concentration derived from the dried blood spot assay measurement.

BDQ:bedaquiline, M2:N-desmethyl bedaquiline metabolite, LZD:linezolid, LVF:levofloxacin, CLF:clofazimine.

GEOMEANS: Mean drug concentration

**Results:** The assay method was validated over the following concentration ranges: 0.0181 to 4.94, 0.00905 to 2.47, 0.113 to 30.9, 0.0741 to 20.2 and 0.00814 to 2.22 µg/mL for bedaquiline, M2, linezolid, levofloxacin and clofazimine, respectively. Median plasma versus esti-

**Conclusions:** TBAJ-876 was dose proportional, with similar bioavailability of oral suspension and tablet formulations. Food increased exposure by 60% - 90%. Mean half-lives of 4.4 – 11 weeks support once daily dosing. TBAJ-876 was generally safe and well tolerated in healthy participants, and no safety signals were identified.

### OA12-294-16 Population pharmacokinetics of pyrazinamide in plasma and cerebrospinal fluid in South African adults with tuberculosis meningitis

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**Background:** Pyrazinamide achieves excellent brain concentrations in animal models and may be an important drug in the treatment of tuberculosis meningitis (TBM). We aimed to describe the plasma and cerebrospinal fluid (CSF) pharmacokinetics of pyrazinamide in patients with HIV-associated TBM.

**Design/Methods:** This study was nested in a randomised controlled trial to evaluate the safety of intensified antituberculosis therapy among adults with HIV-associated TBM in South Africa. All participants received pyrazinamide 25 mg/kg daily as part of standard TBM therapy and those randomised to the intervention arms were provided additional rifampicin (35mg/kg daily) plus linezolid with or without high-dose aspirin, for the first 56 days of treatment.

Plasma sampling was performed on day 3 and day 28 after study enrolment and a lumbar CSF sample was collected at each visit. The samples were analysed with validated liquid chromatography tandem mass spectrometry assays. Data were analysed with nonlinear mixed-effects modelling.

**Results:** A total of 414 plasma and 44 CSF concentrations were available from 49 participants, with median (interquartile range) age 38 (34–45) years, weight 60 (54–74) kg, and fat-free mass (FFM) 46 (39–51) kg. Plasma pharmacokinetics of pyrazinamide was best described by a one-compartment model with first-order elimination and transit compartments absorption. The typical values of clearance and volume of distribution,

allometrically scaled by FFM, were 4.19 L/h and 44.2 L, respectively. CSF concentrations were modelled using a hypothetical effect compartment linked to the plasma concentrations.

The plasma-to-CSF equilibrium half-life, which describes the delay in CSF equilibration with plasma, was 0.58 h, and the CSF-to-plasma partition coefficient, describing extent of pyrazinamide penetration into the CSF was 99%.

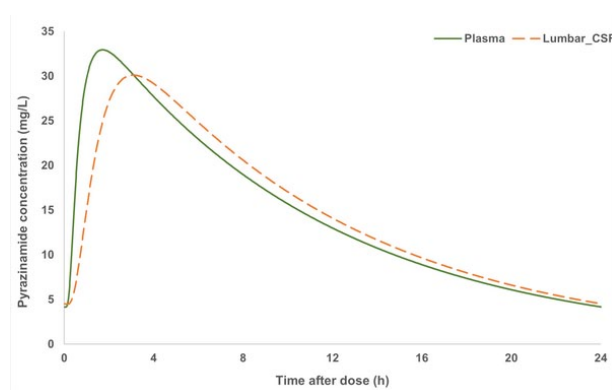


Figure. Simulated concentration-time profiles at steady-state for a typical individual (FFM = 46 kg).

**Conclusions:** Our model confirms that pyrazinamide quickly reaches the CSF and achieves concentrations similar to plasma, supporting further efficacy evaluations in TBM.

### OA12-295-16 Pharmacokinetics of standard vs. high-dose rifampicin for TB preventive treatment: a sub-study of the 2R<sup>2</sup> randomised controlled trial

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**Background:** No data are available on the pharmacokinetics (PK) of high-dose rifampicin for tuberculosis preventive treatment (TPT). We aimed to describe rifampicin PK at higher and standard doses for TPT and assess predictors of exposure to rifampicin.

**Design/Methods:** An intensive PK sub-study was performed in Bandung, Indonesia, among participants in the 2R<sup>2</sup> randomized trial, which compared TPT regimens of 2 months of high-dose rifampicin at 20 mg/kg/day (2R<sub>20</sub>) and 30 mg/kg/day (2R<sub>30</sub>), with 4 months of standard-dose rifampicin at 10 mg/kg/day (4R<sub>10</sub>) in adolescents (aged 10-17 years) and adults (aged 18-65 years).

PK sampling was performed after drug intake at 2-8 weeks of treatment. PK measures were assessed non-compartmentally and log-transformed before analyses. Total exposures (AUC<sub>0-24</sub>) and peak concentrations (C<sub>max</sub>) for each high-dose arm was compared with standard-dose arm using unpaired t-test. Multiple linear regression analyses were used to assess the effects of dose, sex, age, body weight and sampling day since the start of treatment on PK measures.

**Results:** Fifty-one participants (24 adolescents and 27 adults) were included. In the 4R<sub>10</sub>, 2R<sub>20</sub> and 2R<sub>30</sub> arms, the geometric mean AUC<sub>0-24</sub> was 70.7, 200.9 and 325.7 h×mg/L, and C<sub>max</sub> was 19.1, 39.1 and 58.4 mg/L, respectively; high inter-individual variabilities were observed. Compared with the 4R<sub>10</sub> arm, AUC<sub>0-24</sub> and C<sub>max</sub> were significantly higher in the 2R<sub>20</sub> and 2R<sub>30</sub> arms (all p<0.001).

Higher doses were strongly associated with AUC<sub>0-24</sub> and C<sub>max</sub> (p<0.001), while higher weight and female sex were moderately associated with C<sub>max</sub> (p<0.05) and non-significantly associated with AUC<sub>0-24</sub> (p<0.1). Rifampicin concentrations were found to be much higher than seen in Indonesian tuberculosis patients given equivalent doses.

**Conclusions:** Doubling and tripling the rifampicin dose for TPT resulted in, respectively, three- and five-fold greater exposure than seen with the standard dose. The associations of body weight and sex with rifampicin exposures require confirmation in population-PK modeling studies.

## OA12-296-16 Pyrazinamide pharmacokinetics and urine colorimetry for the evaluation of TB in adults and children

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**Background:** Pyrazinamide (PZA) is a potent sterilizing anti-tuberculosis (TB) drug, and low PZA serum concentrations are associated with poor outcomes. Adults and pediatric patients can have varying exposures and dose adjustments can be personalized by serum concentrations; however, serum measurements involve sophisticated procedures that may be unavailable in many high-burden TB settings. Urine colorimetry provides a low-cost alternative with simple sampling and quantification methods.

**Design/Methods:** We conducted a prospective, observational study of adult and pediatric patients on first-line anti-TB treatment in the United States and Tanzania, respectively. Serum was collected pre-dose, 1, 2, 4, 6, and 8 hours post-dose for measurements of pyrazinamide (PZA) concentrations using validated LC-MS/MS methods. Urine was collected between 0-4, 4-8, and 8-24 hour intervals post-dose, and pooling was done to determine concentrations at 0-8 and 0-24 hours. Urine concentrations of PZA were measured using colorimetric methods. Pharmacokinetic parameters were calculated using non-compartmental analysis.

**Results:** We enrolled 50 adults and 89 children with average ages 44 and 9 years, respectively. The average peak concentration and total area under the time curve (AUC<sub>0-24hours</sub>) were 45 mg/l and 442 mg\*<sup>h</sup>/l for adults, and 42 mg/l and 174 mg\*<sup>h</sup>/l for children. Correlation between serum parameters and amount of drug eliminated in urine was overall poor, but highest during the 0-4 hour interval for adults (correlation coefficient, r = 0.2) and during the 0-24 hour pooled interval for children (r = 0.2) due to a greater proportion of PZA dose excreted in the urine at later times among children.

**Conclusions:** There were considerable differences in total PZA exposure between adults and children, despite adequate weight-based dosing in all patients. While personalized dosing strategies based on an individual's pharmacokinetics appear necessary for populations to reach target exposures, the urine colorimetric assay as currently configured for PZA does not provide adequate correlation with serum exposures.

### OA12-297-16 Palatability preferences in children: The swish-and-spit taste panel approach for formulation development

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**Background:** Young children experience a disproportionate TB burden. Many TB medicines are poorly palatable, adding to the treatment burden and negatively impacting administration accuracy, adherence, and clinical outcomes. We report lessons learnt from a 'swish-and-spit' taste-panel approach implemented among children in South Africa.

**Design/Methods:** We worked with two pharmaceutical manufacturers to each supply three formulation flavour blends of moxifloxacin and linezolid. Blends were independently developed through the manufacturers' standard in-house practices to optimize palatability. We recruited healthy child volunteers (target n=96) aged 5-17-years-old (stratified by gender, into three age bands, and four ethnicities, from 2 diverse sites) to complete two assessments (one assessment per 6 blends per drug). Participants swished a small volume of each formulation blend in ~5ml water in their mouth for a few seconds. Tasting order was randomised with palate cleansing between. Assessments included an iterative relative ranking of palatability preferences, five Likert scales of absolute palatability, and a brief qualitative interview.

**Results:** Overall, the study was implemented rapidly, requiring ~12 weeks total for all recruitment and assessments for both assessments at both sites. Although some parents/guardians of potential participants were initially sceptical, once the project rationale and procedures were explained, many were enthusiastic to consent. Enrolling healthy volunteers meant a large pool of potential participants. All participants were able to successfully swish-and-spit without swallowing the blends. Participants' comprehension of the assessment procedures was intuitive, with preferences indicated clearly and without hesitation even among the youngest (5-7-years-old). Assessments were sufficiently brief (~30-40mins) that participants' concentration did not wander. Participants reported that they valued the opportunity to have their preferences 'heard'. Findings from the assessments were meaningful and informed further formulation development choices.

**Conclusions:** The swish-and-spit taste panel approach is feasible to implement, generates essential data, and should be a standard component of TB drug formulation development for children.

### OA13 Advances in drug and vaccine development

#### OA13-298-16 Antimycobacterial activity of a novel diarylquinoline (TBAJ-876) against diverse drug-susceptible and drug-resistant clinical isolates of *M. tuberculosis*

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**Background:** Standardized in vitro MIC assays are used to compare relative potency of antimycobacterial drugs. For some classes of drugs, potency differences can be observed amongst different clades of Mtb. For second-generation drugs, the potential for cross-resistance or reduced potency may limit the effectiveness of new agents.

Testing large panels of clinical isolates and strains having known resistance profiles is needed before advancing a novel Mtb drug into clinical development. Validating the in vitro activity in mouse infection models provides added confidence.

**Design/Methods:** The MICs of TBAJ-876 and BDQ were evaluated by an agar proportion method against a panel of 96 DS and DR clinical isolates representing broad phylogenetic and geographic diversity. MICs were also determined by MABA method for TBAJ-876, BDQ, and their mono-N-desmethyl metabolites (M3 and M2, respectively) against a panel of 5 DS clinical isolates representing 5 phylogenetic clades and against a panel of clinical and laboratory isolates with diverse Rv0678 mutations.

The activity of TBAJ-876 and BDQ in combination with pretomanid and linezolid (PaL) was also assessed in BALB/c mice infected with an isogenic BDQ-R Rv0678 mutant selected in an H37Rv strain.

**Results:** Against 96 DS and DR clinical isolates, TBAJ-876 had an MIC<sub>90</sub> of 0.016 mg/L vs. 0.16 mg/L for BDQ. TBAJ-876 and 876-M3 were at least 10x more potent

than BDQ and BDQ-M2 against DS and Rv0678 mutant strains. TBAJ-876 also provided improved activity vs BDQ in mice infected with an Rv0678 mutant strain.

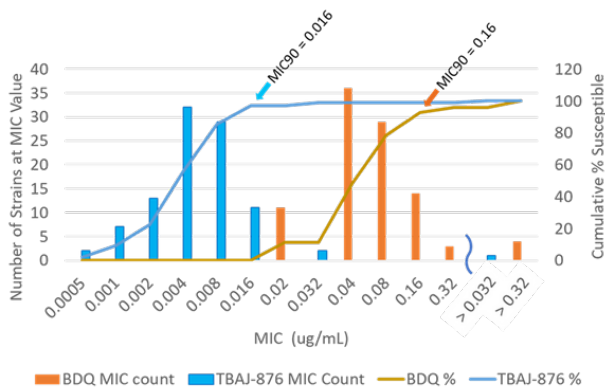


Figure. MIC frequency and distribution for 96 globally diverse drug-resistant and drug-sensitive clinical isolates of MTB.

**Conclusions:** TBAJ-876 has consistent activity and ~10-fold better potency than BDQ against DS and DR Mtb including activity against some BDQ-R strains.

**OA13-299-16 Enhanced sterilising potential of regimens containing a novel diarylquinoline (TBAJ-876) in a preclinical mouse model of TB**

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**Background:** The relapsing mouse model (RMM) effectively predicted the clinical mycobactericidal and sterilizing potential of the BPaL and BPaMZ regimens. The new diarylquinoline clinical candidate, TBAJ-876 combined with PaL, has been evaluated in RMMs to assess the exposure/response relationship and sterilizing potential relative to HRZE, BPaL, and BPaMZ. The model data will be used to evaluate the potential clinical activity of TBAJ-876 vs. Bedaquiline in PaL-containing regimens and will guide clinical dose selection and impact of using lower doses of L (linezolid).

**Design/Methods:** The BALB/c RMM with Mtb strain H37Rv was used. Dosing began 2 weeks post-infection ( $\geq 10^7$  lung CFUs). Groups of mice (~5-10/arm/time-point) were treated for various periods (0.5-6 months); 3 months after the end of each dosing period, lungs were harvested and assessed for bacterial burdens by plating. All marketed drugs were dosed orally 5 days per week to provide approximate human-equivalent dose (HED) ex-

posures at approved doses. TBAJ-876 was dosed at 1.56, 3.125, 6.25, and 12.5 mg/Kg in the dose ranging study (~25, 50, 100, and 200 mg HED). Drug PK was assessed for some studies.

**Results:** Dose-dependent efficacy of TBAJ-876 was observed at doses up to 12.5 mg/Kg. The 3.125 mg/Kg dose of TBAJ-876 provided faster time to sterilization than 25 mg/Kg doses of bedaquiline when combined with PaL. The 6.25 mg/Kg of TBAJ-876 provided an approximately one month decrease in time-to-sterilization vs. bedaquiline when combined with PaL (with L dose lowered to achieve a 600 mg human equivalent dose) and provided a similar time-to-sterilization as the BPaMZ treated group.

Comparison of TBAJ-876 dose ranging vs. BDQ in combination with PaL: BALB/c Relapsing Mouse Model (Standard BPaL regimen human equivalent exposures: 200 mg for BDQ and Pa; 1200 mg for linezolid)

Regimen	Months of treatment prior to 3 months off treatment to assess relapse (# of culture-positive mice / total # of mice in the treatment group)							
	M1	M1.5	M2	M2.5	M3	M3.5	M4	M4.5
BDQ (25 mpk) + PaL	1/9na10*	na	1/3	0/5	0/6	0/6	0/6	0/5
876 (1.56 mpk) + PaL	4/9na10*	na	3/3	5/5	3/6	0/6	0/6	0/5
876 (3.125 mpk) + PaL	1/8na10*	na	3/3	0/5	1/6	0/6	0/6	0/5
876 (6.25 mpk) + PaL	1/8na10*	2/6	0/6	0/6	1/4	0/3	na	na
876 (12.5 mpk) + PaL	1/4na10*	0/6	0/6	0/5	0/4	na	na	na

\* CFUs measured after one month of dosing in separate groups of mice (n=4 mice/group)

TBAJ-876 (6.25 mpk dose) vs. BDQ (25 mpk dose) in combination with PaL\* in BALB/c Relapsing Mouse Model \*(Linezolid Dose = 600 mg hu dose equivalent used for first two months only)

Regimen	M1.5	M2	M2.5	M3	M3.5	M4	M4.5	M5	M5.5
BDQ (25mpk)Pa + L for 2 Mo; BDQPa (BPaL600)	na	na	na	na	4/4	5/5	4/5	2/4	0/2
BDQ (25mpk)Pa + L for 2 Mo; 876Pa (876Pa600)	5/5	5/5	3/5	0/5	0/4	0/3	na	na	na
876 (6.25 mpk)Pa + L for 2 Mo; 876Pa (876Pa600)	1/5	0/5	0/5	0/5	0/4	0/2	na	na	na
BDQ (25mpk) + Pa/MZ (BPaMZ)	1/5	0/6	0/5	0/4	na	na	na	na	na

R= Rifampicin; H= Isoniazid; Z= Pyrazinamide; E= Ethambutol; M= Moxifloxacin; BDQ= Bedaquiline; 876= TBAJ-876; SOC= Standard or Care  
 ■ = Mouse lungs did not have MTB growth when cultured at 3 months after the end of the treatment period noted

**Conclusions:** These RMM studies show the potential for significant improvement in the sterilizing activity of regimens containing TBAJ-876 vs. bedaquiline at the likely achievable human exposures.

**OA13-300-16 Toxicological assessment of TBAJ-876, a second-generation diarylquinoline anti-tubercular drug, in rats and dogs**

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**Background:** TBAJ-876 is a second generation diarylquinoline under development for treatment of pulmonary tuberculosis (TB) and was selected for its reduced QT prolongation risk compared with the first generation diarylquinoline, bedaquiline (BDQ), based on in vitro (hERG assay) results and absence of adverse effects on electrocardiograms in safety pharmacology and toxicology studies.

**Design/Methods:** The toxicological profile of TBAJ-876 was characterized in GLP repeat-dose oral toxicity studies of 13-weeks duration in rats and dogs.

**Results:** Both studies identified no-observed-adverse effect levels (NOAELs) in terms of dose level and systemic exposure to TBAJ--876 and its major metabolite. All findings were either reversible or showed evidence of reversing after a 13-week treatment-free period and are clinically monitorable. Dose limiting toxicities included diarrhea, histopathologic findings of degeneration/necrosis and/or hyperplasia in the stomach mucosa, elevated serum transaminase activities in both species, and skeletal muscle myopathy in rats.

At higher doses and exposures in the toxicology studies, findings also included hepatocellular necrosis in rats and elevated serum amylase activity without histopathologic findings in the pancreas, decreased bone marrow cellularity, and myocardial muscle fiber necrosis/infiltrate accompanied by an increase in serum troponin I concentrations in dogs.

At the NOAELs, daily plasma exposure for TBAJ-876 and its major metabolite, as assessed by area under the concentration-time curve ( $AUC_{0-24h}$ ), were higher or approximately comparable to the NOAEL exposure for similar duration studies with BDQ in rats and dogs, respectively.

However, TBAJ-876 has an approximately 10-fold greater anti-mycobacterial activity in vitro and faster time to sterilization in relapsing mouse models.

**Conclusions:** Taken together, these nonclinical data suggest that TBAJ-876 has a larger therapeutic index than BDQ and has the potential to enable safer and shorter TB treatment regimens that could be used for all forms of pulmonary TB.

### OA13-301-16 A novel anti-*M. tuberculosis* drug, Contezolid (MRX-I): drug activity and resistance in vitro

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**Background:** Linezolid is one of the key drug in treatment regimen of *M. abscessus* pulmonary disease. It develops adverse effects, including peripheral neuropathy, bone marrow suppression etc. Contezolid (MRX-I) is also one of oxazolidinones. It showed antibiotics effects against MRSA, MRCNPs, similar with Linezolid, while it showed lower adverse effects than Linezolid. The present study evaluated Contezolid anti-mycobacterium tuberculosis effects in vitro.

**Design/Methods:** The *M. tuberculosis* (MTB) clinical strains were isolated from sputum specimens of patients enrolled in the National Twelve Five-year Science and Technology Major Project of China. The isolates were conducted drug susceptibility tests and detected the MIC (minimum inhibitory concentration). The spontaneous mutation frequencies induced by Linezolid or Contezolid in the clinical isolates were tested. The Li-

nezolid or Contezolid resistance MTB colonies were selected and sequenced. The cytotoxicity was evaluated by the lactate dehydrogenase leakage assay.

**Results:** Five isolates, nine isolates and seventeen isolates were culture-confirmed as sensitive, MDR-TB and pre-XDR-TB, respectively. The Contezolid MIC<sub>50</sub> and MIC<sub>90</sub> of nine MDR-TB isolates were 2mg/L and 4mg/L, and they were in seventeen pre-XDR-TB isolates were 1mg/L and >16mg/L. The spontaneous mutations induced by Contezolid were tested in six isolates, showed higher than Linezolid. The inhibitory rate of intracellular MTB replication by Contezolid presented similar with Linezolid. mce3R mutation were detected in colonies induced by Contezolid. The cytotoxicity of CZD was evaluated in mouse peritoneal macrophages, compared with LZD. The results showed that CZD at a range of concentration from 100µg/mL to 0.4µg/mL had no significant cytotoxicity.

**Conclusions:** Contezolid demonstrated anti-MTB effects, similar with Linezolid and no significant cytotoxicity. No cross-resistance were observed for Contezolid. It deserved more clinical research to evaluate its values in anti-MTB.

### OA13-302-16 Safety of the investigational TB vaccine M72/AS01<sub>E-4</sub> in people living with HIV

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**Background:** The investigational tuberculosis vaccine M72/AS01<sub>E-4</sub>, a recombinant fusion protein derived from *Mycobacterium tuberculosis* antigens and the AS01<sub>E-4</sub> adjuvant, was previously found to be well-tolerated and immunogenic in people living with HIV (PLHIV) and effective for preventing pulmonary TB in a Phase 2b trial in HIV-negative adults. The current trial assessed safety and immunogenicity of M72/AS01<sub>E-4</sub> in people living with well-controlled HIV in a tuberculosis-endemic region.



**Design/Methods:** This observer-blind, Phase 2 trial was conducted in 6 sites in South Africa. Approximately 400 participants, ages 16-35 years, were randomized 1:1 to M72/AS01<sub>E-4</sub> or saline placebo, with 2 intramuscular doses one month apart. Eligibility criteria included antiretroviral therapy for ≥3 months, with HIV viral load <200 copies/mL and CD4+ cell counts ≥200 cells/μL. Solicited adverse events (AEs) were recorded during the first 7 days after each dose. Criteria for severe AEs were redness/swelling ≥100 mm, fever ≥39.3 to <40.0°C, and AEs preventing normal daily activities. Serious AEs were recorded throughout the trial. Blood chemistries/hematology were collected before each dose. Viral loads and CD4+ cell counts were collected at baseline and Days 57, 210, and 390. Immunogenicity data will be disclosed when available.

**Results:** 401 participants were included in safety analyses. Solicited AEs (all grades and severe) were more frequent after M72/AS01<sub>E-4</sub> versus Placebo (Table). For M72/AS01<sub>E-4</sub> recipients, the median number of days with solicited symptoms ranged from 1 to 3. Among 9 serious AEs (4 in M72/AS01<sub>E-4</sub>), none were related to vaccine. Blood chemistries/hematology results yielded no notable abnormalities. The proportion of participants with viral loads >200 copies/mL increased over time with no differences between groups at any timepoint.

	M72/AS01 <sub>E-4</sub> ; N=201 (*N=200 for swelling at injection site)				Placebo; N=197			
	All AEs		Severe AEs		All AEs		Severe AEs	
Solicited AE	n (%)	[95% CI]	n (%)	[95% CI]	n (%)	[95% CI]	n (%)	[95% CI]
Pain at injection site	167 (83.1)	[77.4, 87.8]	32 (15.9)	[11.3, 21.5]	50 (25.4)	[19.7, 31.8]	2 (1.0)	[0.2, 3.3]
Redness at injection site	67 (33.3)	[27.1, 40.1]	0 (0)	-	19 (9.6)	[6.1, 14.4]	0 (0)	-
Swelling at injection site	83 (41.5)*	[34.8, 48.4]	0 (0)*	-	17 (8.6)	[5.3, 13.2]	0 (0)	-
Fever	87 (43.3)	[36.6, 50.2]	3 (1.5)	[0.4, 4.0]	44 (22.3)	[16.9, 28.5]	2 (1.0)	[0.2, 3.3]
Headache	132 (65.7)	[58.9, 72.0]	21 (10.4)	[6.8, 15.3]	78 (39.6)	[32.9, 46.6]	7 (3.6)	[1.6, 6.9]
Fatigue	119 (59.2)	[52.3, 65.8]	13 (6.5)	[3.6, 10.5]	74 (37.6)	[31.0, 44.5]	4 (2.0)	[0.6, 4.8]
Myalgia	96 (47.8)	[40.9, 54.7]	18 (9.0)	[5.6, 13.5]	45 (22.8)	[17.4, 29.1]	2 (1.0)	[0.2, 3.3]

**Conclusions:** The M72/AS01<sub>E-4</sub> tuberculosis vaccine was well-tolerated with no safety signals in participants aged 16-35 years with well-controlled HIV. These data support the inclusion of PLHIV in a planned Phase 3 registration trial.

### OA13-303-16 Evaluation of a dry powder, inhaled BCG vaccine for protection against TB in a natural transmission, low-dose exposure guinea-pig model

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**Background:** Earlier studies suggested that BCG delivered directly to the lung or gut mucosa might hold immunological and physiological advantages over intradermal administration in preventing tuberculosis disease in the vaccinated.

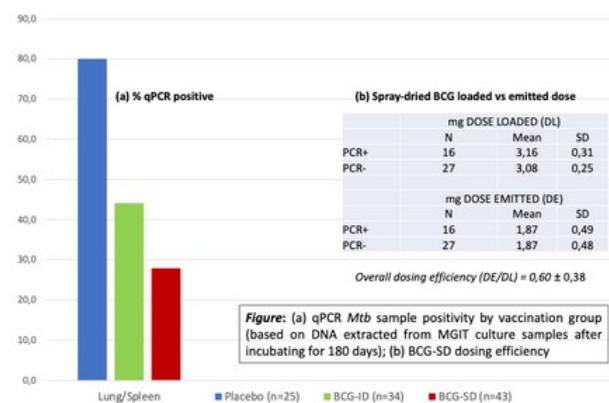
In this study, guinea-pigs received a stable spray-dried formulation of viable BCG (Pasteur strain) (BCG-SD) by insufflation, followed by exposure to natural sources of infection (confirmed TB patients) in a unique airborne infection transmission facility, a novel feature of the experimental model.

**Design/Methods:** Duncan-Hartley guinea pigs (n=102) were randomly assigned to either BCG-SD insufflated, approximately 3-4 mg pre-loaded into an endotracheal delivery device (concentration 2x10<sup>6</sup>cfu/mg) or solution for intradermal injection (BCG-ID); controls received placebo preparations.

*Week 0:* Vaccination;

*Weeks 4-9:* Animals exposed to infectious MDR-TB patient ward air;

*Week 10:* Animals euthanized, lung and spleen tissue removed for MGIT culture (180 days incubation) followed by real-time qPCR (IS6110 and IS1081) of cultured samples to confirm the presence/absence of *Mycobacterium tuberculosis* (*Mtb*) in the target organs.



**Figure:** *Mtb* positive qPCR results from lung/spleen samples in 80% (20/25), 44.1% (15/34) and 27.9% (12/43) of the Placebo, BCG-ID and BCG-SD groups, respectively.

**Results:** Dosing efficiency (emitted/loaded) of BCG-SD was only about 60%, and similar in the PCR+ and PCR- groups. Less than the intended dose of at least 2 mg per administration was achieved. No negative effects were observed in any of the animals.

**Conclusions:** BCG-SD vaccine delivered by insufflation offered a high degree of protection in the TB natural-infection guinea pig model over placebo controls. By comparison, intradermal BCG group were statistically not different from the BCG-SD group in protection demonstrated. Results are encouraging, despite suboptimal dosing in the BCG-SD study arm. Larger, adequately powered studies with optimal and consistent dose delivery (higher than 2 mg per administration) are required to assess whether inhaled BCG vaccination enhances protection over injected, or not. Needle-free vaccination is attractive.

### OA13-304-16 A modified BCG vaccine with depletion of enzymes associated with peptidoglycan amidation induces enhanced protection against TB in mice

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**Background:** *Mycobacterium tuberculosis* (Mtb) causes Tuberculosis (TB), which remains a leading cause of death from an infectious disease worldwide. Mechanisms by which Mtb evades pathogen recognition receptor activation during infection may offer insights towards the development of improved TB vaccines. Whilst Mtb elicits NOD-2 activation through host recognition of its muramyl dipeptide (MDP), it masks its endogenous NOD-1 peptidoglycan ligand through amidation. As the BCG vaccine is derived from pathogenic mycobacteria, a similar situation prevails. We targeted this NOD-1 evasion capability to potentially improve efficacy of the BCG vaccine.

**Design/Methods:** We used CRISPRi to inhibit expression of the essential enzyme pair, MurT-GatD, implicated in amidation of peptidoglycan side chains to enhance the immunogenicity of BCG. A monocyte training assay, followed by testing in a murine model of TB infection were used to assess the efficacy of the recombinant BCG strain compared to the parental strain.

**Results:** We demonstrate that depletion of MurT-GatD in BCG results in reduced growth, cell wall defects, increased susceptibility to antibiotics and altered spatial localization of new peptidoglycan. In cell culture experiments, training of monocytes with the recombinant BCG strain yielded improved control of Mtb growth. In the murine model of TB infection, we demonstrate

that depletion of MurT-GatD in BCG, which expresses the normally hidden D-glutamate diaminopimelate (iE-DAP) NOD-1 ligand, is superior to standard BCG vaccine in prevention of Mtb disease.

**Conclusions:** These results demonstrate the feasibility of gene regulation platforms such as CRISPRi to inhibit essential pathways *in vivo* in mycobacteria and unmask pathogen-associated molecular patterns (PAMPs) which may stimulate immunity against Mtb infection. Collectively, our work demonstrates that MurT-GatD can be targeted to develop a new TB vaccine candidate.

### OA13-305-16 *In vitro* activity of tedizolid and linezolid against multidrug-resistant *M. tuberculosis*

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**Background:** linezolid (LZD) has been classified as a group A drug by the WHO in the recent MDR-TB treatment guideline. Although LZD is effective against *Mycobacterium tuberculosis*, it causes many serious adverse events including bone marrow suppression, and requires careful monitoring during treatment. tedizolid (TZD), a same oxazolidinone class drug, may show less adverse events compared to LZD. To test whether TZD is a potential replacement of LZD, we compared the TZD and LZD by measuring their MICs in MDR-TB isolates from Japan.

**Design/Methods:** A total of 54 MDR-TB isolates and 5 LZD resistant strains generated from H37Rv were tested against TZD and LZD. A two-fold diluted MIC plate ranging from 0.015 to 16 µg/mL was prepared in-house. In parallel, whole-genome sequence analysis was performed for each isolate using MiSeq (Illumina), and known LZD-related drug resistant genes were analyzed using TBProfiler version 2.8.6.. Statistical analysis was performed using JMP ver. 12.1 (SAS Institute Inc.) for Student's T test to compare the MIC differences. A p value of <0.05 was considered significant.

**Results:** The MIC<sub>50/90</sub> for TZD and LZD were 0.25/0.5 µg/mL and 0.5/1.0 µg/mL, respectively. The MIC ranges for TZD and LZD were 1.0–8.0 µg/mL and 8.0–32 µg/mL, respectively, in the induced LZD resistant mutants (*n*=5). TZD showed a significantly lower MIC than LZD against in total of isolates *in vitro* (*p*<0.01). As the detected variants did not show a high MIC compared to other wild-type isolates, the genetic variants were considered not significant (*p*=0.18). We found LZD resistance related to *rrl* and *rplC* mutations among the induced LZD resistant strains.

**Conclusions:** This is the first report to evaluate the MIC of TZD against Japanese MDR-TB isolates. Although a limited number of MDR-TB isolates collected in Japan was used for this study, TZD may be a potential candidate to replace LZD.

## OA14 Diagnosis of TB in Children

### OA14-306-16 The use of novel assays for point-of-care samples to diagnose childhood TB disease – a multi-centre prospective study in low- and middle-income countries

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**Background:** Missed diagnosis of childhood TB causes significant morbidity and mortality and could be improved using novel diagnostics and easy-to-collect samples. We evaluated the diagnostic accuracy of a urinary lateral-flow assay (FujiLAM) and a stool-processing kit coupled with Xpert®MTB/RIF-Ultra (SPK/Ultra) for childhood TB.

**Design/Methods:** RaPaed-TB was a multi-centre prospective diagnostic validation study in five lower-middle income countries. Children (<15years) with presumptive TB provided at least two sputum samples and one nasopharyngeal aspirate if <5 years for TB testing (culture and Ultra). Standardised microbiological, radiologic, and clinical data were used to define TB status, following published consensus criteria for diagnostic evaluation studies, informing applied reference standards.

**Results:** Of 974 children enrolled, 632 (10.1% malnourished; 42.7% <5years; 16.6% living with HIV) had a valid TB status and a FujiLAM and SPK/Ultra result available. 28.3% (179/632) had confirmed TB, 32.9% (208/632) unconfirmed TB, and 38.7% (245/632) unlikely TB. FujiLAM had a sensitivity of 31.3% (95%CI 24.6-38.6) and specificity of 91.0% (95%CI 86.3-94.5),

and SPK/Ultra a sensitivity of 33.0% (95%CI 26.1-40.4) and specificity of 87.2% (95%CI 81.9-91.4), comparing children with confirmed to those with unlikely TB. Application of both FujiLAM and SPK/Ultra yielded an increased sensitivity of 44.7% (95%CI 37.3-52.3) but with reduced specificity of 78.7% (95%CI 72.5-84.0). Sensitivity was higher in key subgroups, including infants (73.9%, 95%CI 51.6-89.8) and children with severe acute malnutrition (58.3%; 95%CI 36.6-77.9). For FujiLAM, tendencies of test readout associated with manufacturing lot were observed, not reaching statistical significance.

**Conclusions:** Our results suggest a benefit of applying both FujiLAM and SPK/Ultra in children investigated for TB. While WHO's high-priority target product profiles for new TB diagnostics were not met, the assays operational simplicity and diagnostic yield might contribute to improve TB diagnosis for children, especially those who are at risk of most severe disease.

### OA14-307-16 Introduction of the Simple One-Step stool processing method to diagnose TB in children, lessons learnt from the pilot implementation in Malawi

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**Background and challenges to implementation:** Bacteriological confirmation of Tuberculosis (TB) in children is challenging due to difficulties collecting sputum and low bacillary load. Since 2020, WHO recommended stool as an initial test to diagnose TB in children using the Xpert platform with the Ultra cartridge. The Malawi National TB and Leprosy Elimination Program (NTLEP) is assessing the feasibility of stool based Xpert testing using the simple one-step stool method (SOS) to increase access to bacteriological confirmation of TB in children.

**Intervention or response:** Since December 2022, the NTLEP and its partners have introduced stool based Xpert testing in 8 pilot sites. Staff working at the sites were trained in managing childhood TB and stool testing. For each child, ages 0-14, with signs and symptoms of TB, a stool sample is requested in addition to the routine standard of care. The stool is processed using the SOS stool method on Xpert MTB Ultra. Monitoring of the results is conducted weekly, while facility-level supervision is done monthly.

**Results/Impact:** As of March 2023, 298 children (144 males and 154 females) were enrolled, of which 55 (18%) were HIV positive. Of the 298, 150 were 0-4 years, and 148 were 5-14 years. Among 23/298 (7.7%) were MTB detected on stool.

From the 23 MTB detected from stool analyses, 2 cases were rifampicin-resistant (RR). *The pilot runs through May 2023, and the results will fully be analyzed during the time of the conference.*

**Conclusions:** Initial results are promising, suggesting that the introduction of stool-based testing as an alternative sample can improve TB diagnosis in Malawi children.

### OA14-308-16 Laboratory diagnosis of TB in infants living with HIV and hospitalised with severe pneumonia

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**Background:** Tuberculosis (TB) is a leading cause of mortality in children living with HIV. Autopsy studies show that TB is often undiagnosed in children dying from HIV-associated pneumonia. Laboratory TB diagnosis is challenging in high-risk infants due to the paucibacillary nature of disease, and difficulty obtaining respiratory samples.

We assessed laboratory TB diagnosis in infants enrolled in the EMPIRICAL clinical trial.

**Design/Methods:** EMPIRICAL is a randomized controlled trial (#NCT03915366) recruiting infants living with HIV hospitalized with severe pneumonia in six African countries. We excluded infants with current/previous TB diagnosis and TB contact.

Xpert MTB/RIF Ultra (Xpert) on nasopharyngeal aspirate (NPA) and stool samples, and urine lipoarabomannan (LAM) are attempted for all participants when feasible.

**Results:** Among 410 participants enrolled from March 2020 – February 2023, 88/410 (21.5%) had laboratory-confirmed TB with at least one positive test. Mean age was 5.6 [SD:2.9] months, and 52/88 (59.1%) were male. HIV had been newly diagnosed in 59/88 (67.0%). Severe acute malnutrition was present in 33/88 (34.1%). Median baseline CD4 and viral load were 582 cells/mL [IQR:295-1101] and 3,279,585 copies/mL [IQR:534,553-10,000,000], respectively. Urine LAM results were available for 86/88 (97.7%), with 90.7% (78/86) positivity: 36/78 (46.2%) +1, 29/78 (37.2%) +2, 8/78 (10.3%) +3, and 5/78 (6.4%) +4. Stool Xpert results were available for 86/88 (97.7%), with 15.1% (13/86) positivity, and RIF resistance in 1/10 (10.0%). NPA Xpert results were available for 76/88 (86.4%) with 6.6% (5/76) positivity, and RIF resistance in 0/3 (0%). [BWC1] Correlation of positive test results is presented in Figure 1.

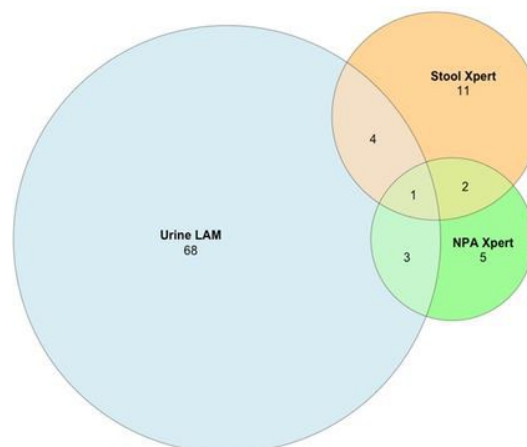


Figure 1. Test results correlation for 76 HIV-positive infants with laboratory-confirmed TB and all three tests performed.

**Conclusions:** TB was confirmed in over one-fifth of HIV-positive infants hospitalized with severe pneumonia, despite excluding infants with current/previous TB diagnosis and TB contacts. Urine LAM and stool Xpert are non-invasive tests that were more frequently feasible to perform, and had higher test positivity than NPA Xpert in this critically ill population.

### OA14-309-16 Xpert Ultra in stools and urine to diagnose TB in children: A Médecins Sans Frontières cross-sectional multicentric study in Guinea-Bissau and South Sudan

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**Background:** Over half of childhood tuberculosis (TB) remains undiagnosed yearly. TB culture is often unavailable. WHO recommends Xpert-Ultra as first test for diagnosis of paediatric TB, but microbiological confirmation remains low (<30%) and often requires invasive procedures. We aimed to determine the sensitivity/specificity of Xpert-Ultra in stools and urine samples in presumptive paediatric TB cases in two high TB burden settings.

**Design/Methods:** This cross-sectional multicentric study took place at Simão Mendes hospital, Guinea-Bissau, from July 2019 to April 2020, and in Malakal hospitals, South Sudan, from April 2021 to November 2022. Children between 6 months and 15 years with presumptive tuberculosis underwent clinical and laboratory assessment, with one respiratory or extrapulmonary sample (gold standard (GS)), one stool and one urine samples analysed with Xpert-Ultra.

**Results:** A total of 441 children were enrolled from Bissau (n=133) and Malakal (n=308), with 214 (49%) females and median (IQR) age of 4.5 (1.5-9) years. HIV infection and severe acute malnutrition (SAM) were found in 89 (20%) and 251 (57%), respectively. Confirmation of TB was achieved in 76 (17%); 198 (44%) had unconfirmed TB, and 167 (39%) had unlikely TB. Of the 441 with GS diagnosis, the overall yield of positive TB results was 13% (59/441): 10% (42/408) in pulmonary samples and 37% (19/51) in extrapulmonary samples. A total of 410 and 435 and 160 samples were used to evaluate Xpert-Ultra on stool and Xpert-Ultra on urine, respectively. Compared to GS, sensitivity and specificity of Xpert-Ultra on stools were 69.4% (95% CI: 55.5-80.5) and 98.3% (95% CI: 96.4-99.2), whereas on urine were 12.1% (95% CI: 6.0-22.9) and 99.2% (95% CI: 97.7-99.7), respectively. Eight patients were positive with stools or urine Xpert result but negative with GS.

**Conclusions:** Xpert-Ultra in stools showed similar sensitivity and specificity than described in the literature and an added diagnostic yield when gold standard was negative. Sensitivity of urine was low but more research is needed to determine its clinical indication.

### OA14-310-16 Lateral-flow urine lipoarabinomannan assay for TB diagnosis in children: A Médecins Sans Frontières cross-sectional study in South Sudan

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**Background:** Over half of childhood tuberculosis remains undiagnosed yearly. Tuberculosis (TB) microbiological confirmation is low and often requires invasive procedures. Urine lipoarabinomannan (TB-LAM, Alere Determine) has been recommended for TB-diagnosis in HIV-infected patients, but some evidence suggests its use with malnourished children.

We aimed to determine the TB-LAM positivity rate per TB group and by age, HIV and nutritional status in two high TB burden settings.

**Design/Methods:** This cross-sectional study took place in two hospitals in Malakal, South Sudan, from July 2022 to February 2023. Paediatric presumptive TB cases 6 months to 15 years of age underwent clinical and laboratory assessments with at least one sample analysed by Xpert-Ultra (pulmonary and/or extrapulmonary sample) and TB LAM in urine.

**Results:** A total of 160 children were enrolled with 87 (54%) females and a total of 87 (54%) children under 5. HIV infection and severe acute malnutrition (SAM) were found in 17 (10.6%) and 88 (55%), respectively. Microbiological confirmation of TB was achieved in 28 (18%); 71 (44%) had unconfirmed TB, and 61 (38%) had unlikely TB. Overall, LAM positivity was 19% (30/160): 57% (16/26) in confirmed TB, 10% (7/71) in unconfirmed TB, and 12% (7/61) in unlikely TB patients. The positive predictive value among TB cases (confirmed or unconfirmed) was 76.7% (23/30) (95% CI: 59-88) and the negative predictive value among unlikely TB cases was 41.5% (54/130) (95% CI: 33-50). The relative risk of positive LAM result among children who were under 5, HIV positive and SAM was 3.3 (95% CI: 1.5-7.8, p=0.002), 4.9 (95% CI: 2.8-8.4, p<0.001) and 3.3 (95% CI: 1.4-7.6, p=0.002), respectively.

**Conclusions:** Our findings suggest an additional potential diagnostic utility of urine TB LAM in presumptive TB patients under 5 or with severe acute malnutrition, in addition to the well-known role in people living with HIV.

### OA14-311-16 A multi-country assessment of the feasibility of tongue swab vs. sputum collection for TB testing in children

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**Background:** Although the sensitivity of swab-based molecular testing for TB is expected to be lower than that of sputum-based testing, diagnostic yield could be higher for children if sample collection is easier. We conducted a multi-country evaluation of the feasibility of collecting tongue swabs versus sputum samples in children with presumptive TB.

**Design/Methods:** We prospectively enrolled children less than 10 years being evaluated for pulmonary TB in The Gambia, South Africa, and Uganda. We aimed to collect at least one respiratory specimen as expectorated or induced sputum (ES and IS, respectively), and if not feasible as gastric or nasopharyngeal aspirates. Following at least 30 minutes of fasting, two tongue swabs (Copan FloqSwabs) were collected (prior to sputum collection).

We calculated the proportion of children who could provide an ES or IS sample and compared these to the proportion of tongue swabs successfully collected, overall and by age group.

**Results:** We included 789 children: 566 (71.7%) under 5 years, 46.1% female, and 11.4% living with HIV. A tongue swab was successfully collected in 98.6% (778/789) of children. In comparison, 38/519 (7.3%) could provide an ES sample ( $p < 0.001$ ). Among 743 children who did not provide an ES sample, 262 (35.3%) could provide an IS sample (compared to the 733 [92.9%] who could provide a swab [ $p < 0.001$ ]).

When stratified by age group, it was less feasible to collect sputa than a tongue swab in children under 5 compared to children 5-9 (Table).

Sample type n/N (%)	All (N=789)	0-4 years old (n=566)	5-9 years old (n=223)
Expectorated sputum	38/519 (7.3%)	9/384 (2.3%)	29/135 (21.5%)
Induced sputum	262/743 (35.3%)	178/553 (32.2%)	84/190 (44.2%)
Induced or expectorated sputum	308/789 (39.0%)	191/566 (33.7%)	117/223 (52.5%)
Tongue swab	778/789 (98.6%)	559/566 (98.8%)	219/223 (98.2%)

Table.

**Conclusions:** In a multi-country assessment, tongue swabs were far more feasible to collect from children than expectorated sputum. Swab-based molecular testing has the potential to increase the number of children with microbiologically confirmed TB, particularly in children under 5.

### OA14-312-16 Rapid and accurate diagnosis of paediatric TB by combining a novel GeneXpert host gene transcription assay and Xpert MTB/RIF Ultra

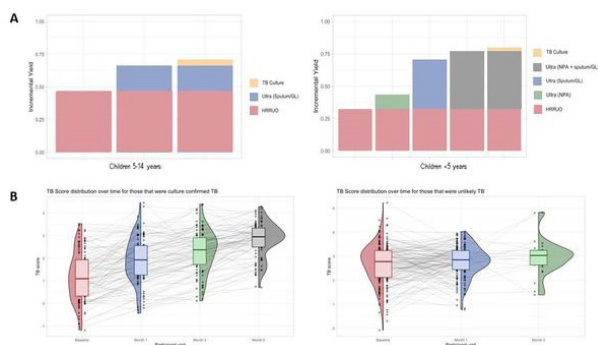
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**Background:** Childhood tuberculosis (TB) remains a major cause of morbidity and mortality due to missed diagnosis. Better diagnostics with enhanced sensitivity using easy-to-obtain specimens are needed. The Cepheid MTB-Host Response Prototype Cartridge (MTB-HR) is a candidate test that measures a three-gene transcriptional signature from fingerstick-blood showing promising performance in adults.

**Design/Methods:** RaPaed-TB was a multicentre prospective diagnostic accuracy study conducted in five countries and the first one to assess the use of MTB-HR in children. Minors <15 years of age with signs or symptoms suggestive of pulmonary and/or extrapulmonary TB were enrolled. Standardised microbiological,

radiologic, and clinical data were used to define TB status, following published consensus criteria for diagnostic evaluation studies. MTB-HR was taken at baseline, month 1, 3, and 6.

**Results:** Of the 976 children recruited, 633 had a defined TB status and at least one valid MTB-HR result. MTB-HR differentiated children with culture-confirmed TB from those with unlikely TB with area under the curve (AUC) 0.85 (95% CI: 0.80-0.89), sensitivity 59.8% (50.8-68.4), and specificity 90% (95% CI 85.5-94.0). AUC was similar in key subgroups. Repeated sampling showed a normalisation of MTB-HR readout in children treated for TB (Figure 1 A). Combining baseline MTB-HR with one Xpert® MTB/RIF-Ultra (Ultra) on sputum/gastric lavage identified 71% of children with microbiologically confirmed pulmonary TB, but with less added sensitivity from a nasopharyngeal specimen (Figure 1 B).



**Conclusions:** This first assessment of MTB-HR in children showed good diagnostic accuracy for culture-confirmed TB, including key subgroups, in a large, geographically diverse cohort. Combining MTB-HR with a respiratory specimen tested by Ultra could rapidly identify most culture-confirmed children.

Given the widespread availability of the GeneXpert platform, the short time to result, ease of use of capillary blood, and the diagnostic yield, MTB-HR is a promising tool to substantially improve TB diagnosis for children, which is currently the main obstacle towards reducing child TB mortality.

### OA14-313-16 Reaching the unreached: Access to TrueNat technology as a near point-of-care test within communities in Bangladesh

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**Background:** According to the 2022 World Health Organization Global TB Report, the percentage of presumptive tuberculosis (TB) patients tested with rapid molecular diagnostics was only 24% in Bangladesh. To address this gap, in late 2022 the USAID-funded Infectious Disease Detection and Surveillance (IDDS) project supported the National TB Control Program (NTP) to install and operationalize 38 Truenat instruments. Truenat can be used at the peripheral level to diagnose TB and RR-TB. The objective of the study was to assess the initial impact of Truenat within communities.

**Design/Methods:** Truenat was implemented at 38 sites that were previously only performing TB microscopy. Truenat test data were collected for the period October to December 2022 from all 38 Truenat sites and microscopy data were collected for October to December 2021 (before Truenat became available). Data were analyzed and compared to assess the initial impact of the Truenat intervention.

Indicators	2021 ( October- December) Before Truenat Availability	2022 (October-December) After Truenat Availability
Total new/relapse TB patients (clinically diagnosed / bacteriologically confirmed	1,336	1,688
TB patients diagnosed with rapid molecular test	56	1,407
Truenat as the initial diagnostic test resulted in an increased percentage in TB detection	4.2% (56/1,336)	83.4% (1,407/1,688)
Bacteriologically confirmed TB cases	1,025	1,546
Rifampicin Resistant TB cases	0	25

Table 1. Comparison of data of 38 Truenat sites to smear microscopy

**Results:** The number of TB patients who received a rapid molecular test increased from 56 (4.2%) before Truenat was available to 1,407 (83.4%) after Truenat became available (Table 1). The proportion of new/re-lapse TB cases that were bacteriologically confirmed increased from 1,025 (76.7%) to 1,546 (91.6%). Also, the detection of RR-TB cases increased from 0 to 25 cases. While many factors may have contributed to these increases, one key change was the local availability of Truenat compared to previous years.

**Conclusions:** The Truenat technology now offers access to a rapid molecular TB diagnostic test to the people evaluated for TB at the community level and remote settings. Rapid diagnosis of TB and drug resistance allows for prompt start of appropriate treatment and care. In this initial implementation, Truenat was shown to be operationally feasible to increase access to rapid and reliable TB diagnostics near point of care.

## OA15 Key Populations

### OA15-314-16 Women-led integrated screening camps to address gender-based disparities in TB eradication

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**Background and challenges to implementation:** WHO Global TB Update 2022 reports TB disease prevalence with a male-to-female ratio of 2:1. However, studies from Pakistan reported higher TB disease prevalence among women and their barriers to access healthcare—financial, logistical, stigma, cultural - and longer delays from presentation to diagnosis compared to men. This is consistent with observations of TB screening activities by IRD. Therefore, we implemented women-led integrated screening camps to improve women's access to TB services.

**Intervention or response:** We implemented a holistic healthcare model for women, where they were invited to participate in women-centric camps, offering TB, breast and cervical cancer screenings, mental well-being support, and medical consultations by female clinicians and health workers. Participation was further bolstered by engaging female volunteers from within the community to support camp activities.

We also raised awareness about TB-associated stigma through interactive activities (such as theater performances).

**Results/Impact:** We convened 27 conventional TB screening camps between January and March 2023. In these camps, we screened 7381 people, of whom 1855 (25%) were women, and found 236 women presumptive of TB. We also conducted five women-centric camps in March and April 2023, where 677 women were screened, yielding 72 women presumptive of TB. On average, women-centric camps screened 135 women per camp, almost double the conventional camps (69 per camp). In addition, we observed a higher yield in women presumptive of TB among women-centric camps compared to conventional camps (14 versus 9 per camp). Female participants in women-centric camps were younger than those who participated in conventional camps (median age, 33 versus 25 years).

	Conventional TB screening camps 2023				Women-centric camps 2023		
	Jan	Feb	Mar	Total	Mar	Apr	Total
Total screened	681	2512	4188	7381	574	103	677
Females	152	641	1062	1855	574	103	677
% Female	22%	26%	25%	25%	NA	NA	NA
Total Presumptive of TB	76	161	302	539	62	10	72
Female	29	74	133	236	62	10	72
% Female	38%	46%	44%	44%	NA	NA	NA

Table 1: Comparison of TB case finding and yields among women through Conventional versus Women-centric camps.

**Conclusions:** Our findings highlight the value of context-specific, women-centric strategies combined with integrated health service delivery models in increasing TB health services uptake by women. This strategy can help TB case finding programs reach younger women in high-burden settings.



### OA15-315-16 Anaemia as a risk factor among people with TB in a tribal setting – experience from Odisha, India

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**Background and challenges to implementation:** TB treatment outcomes are affected by many comorbidities, some of which like HIV and Diabetes are recorded by the National Tuberculosis Elimination Programme (NTEP) as standard diagnosis protocol.

However, people with TB (PwTB) are not screened for anaemia by the NTEP which potentially can affect the treatment outcome. National Family Health Survey 5 (2019-2021), indicates that 29% of male (15-49 years) and 64% of female (15-49 years) are anaemic.

This abstract focuses on the anaemic status of the people with TB in tribal district, Mayurbhanj, Odisha.

**Intervention or response:** The Accountability Leadership by Local communities for Inclusive, Enabling Services (ALLIES) project by REACH and supported by USAID implements a Differentiated Care Model (DCM) to assess the vulnerabilities among PwTB and linking them to supportive services. As part of this model, a pilot intervention was carried out in three Treatment Units of tribal areas in Mayurbhanj district in Odisha, where four trained TB Champions from the local communities screened PwTBs for anaemia. Newly diagnosed PwTB were counselled and referred by the TB Champions to NTEP laboratories for the recording of haemoglobin percentage in their blood. Females with  $\leq 9$  gram and Males with  $\leq 10$  gram were marked as PwTB with anaemia. Anaemic PwTBs were provided with Iron and Vitamin tablets by NTEP.

**Results/Impact:** TB Champions screened 172 PwTB (113 Males and 59 Females) for vulnerabilities including anaemia. Of the screened PwTB, 53% (91) reported anaemia. Table given below details the gender-wise distribution of the PwTB who reported anaemia as a vulnerability.

Indicators	Male	Female	Total
Number of Persons with TB screened for anaemia	113	59	172
Number of screened People with TB reporting anaemia	69	22	91
Percentage of screened People with TB reporting anaemia	61%	37%	53%

**Conclusions:** Given the high prevalence of anaemia reported among the screened PwTBs, there is a need for considering mandatory screening under the NTEP standard diagnosis protocol. Supportive services may also be provided to PwTB with anaemia for improvement in the treatment outcomes, critical for TB elimination by 2025 in India.

### OA15-316-16 Experiences of household food insecurity among individuals with TB in Kampala, Uganda

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**Background:** Food insecurity is the economic or social condition of having limited or uncertain access to adequate food at the household level. In Uganda, one of the 30 countries in the world with the highest burden of tuberculosis (TB), a large part of the population lives with food insecurity.

**Design/Methods:** This nested mixed-methods study was conducted within an observational cohort study of 285 individuals with TB in Kampala, Uganda. A consecutive sub-sample of participants were administered the Household Food Insecurity (Access) Scale (HFIAS) and the General Self-Efficacy (GSE) Scale. Household Food Insecurity (Access) Prevalence of food insecurity by severity and GSE scores were calculated in accordance with the respective scales. Participants with TB who completed both scales were selected for qualitative semi-structured interviews conducted by a Ugandan physician and TB clinic nurse for the parent study. A secondary analysis of these transcripts was conducted to identify experiences with food insecurity. Thematic analysis was used to contextualize and triangulate the quantitative data.

**Results:** 88 participants completed the survey. Of the 88 participants in the cohort, 57% (50) experienced food insecurity, including 5% (4) with mild food insecurity, 7% (6) with moderate food insecurity, and 45% (40) with severe food insecurity. 23% (3) of the 13 interviewees were rated severely food insecure on the HFIAS scale. Nearly a quarter of the interviewed participants described experiences with food insecurity and adjacent

conditions which were not captured by the scale. In interviews, participants described how prolonged gaps between illness onset and diagnosis led to declining finances and consequently limited access to food.

**Conclusions:** More than half of individuals receiving treatment for TB experienced food insecurity. There is a need to increase food security to improve TB care as well as develop more sensitive instruments to measure food insecurity among TB patients.

### OA15-317-16 Lower household income increases the risk of TB recurrence in South Korea: a retrospective nationwide cohort study

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**Background:** It is unclear whether socio-economic factors are risks for recurrent tuberculosis (rTB). We assessed the impact of household income on rTB and the long-term impact of TB on income.

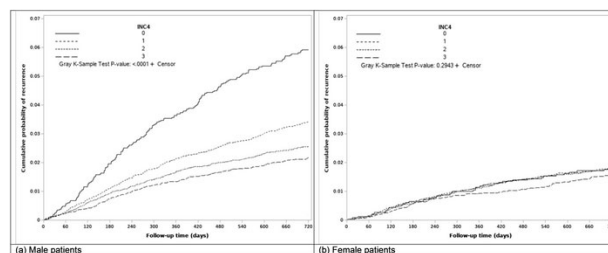
**Design/Methods:** Using a multi-year (2013-2018) South Korean national TB cohort database that integrated the national TB notification and the National Health Insurance (NHI) claims data, we identified a sub-set cohort of newly diagnosed drug-susceptible (DS) TB and rTB patients and tracked their longitudinal income data between 2007-2018. Income categories were defined as Medical aid and decile categories, which determines the household contribution for the NHI benefits.

To assess risk factors associated with the rTB, we performed sub-distribution hazard model, adjusting for the competing risks for death.

**Results:** Of 66,690 new DS-TB patients identified, 2,095 (3.1%) experienced rTB during a span of median 39 months (Inter-Quartile Range 26-52) between the two TB episodes. The incidence of rTB was 982.1 per 100,000 person-years. 50.3% of the rTB occurred within 1 year of treatment completion.

The risk of rTB increased with decreasing income levels, with the high risk observed in the lowest income group (adjusted hazard ratio [aHR] 1.77 [95% confidence interval (CI) 1.51-2.09], relative to the highest income group. The effect of income on rTB was the prominent in males (aHR 2.11, 95% CI 1.74-2.56), but this effect was not seen for females.

Overall, TB patients experienced linear decline in income levels (-0.042 per year, 95% CI -0.035- -0.05) a trend that starts several years prior to the initial episode continuing well beyond treatment completion.



**Conclusions:** TB patient's income levels at the time of their initial episode is an important risk factor for rTB, which worsens over time due to their TB illness. Long-term social protection policies these higher risk groups may be necessary to improve TB care and economic benefits.

### OA15-318-16 Engaging local youths to address access barriers and improve case notification in tribal pockets of Maharashtra, India

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**Background and challenges to implementation:** In India, the National TB Elimination Program (NETP) provides free TB diagnosis and treatment to all people seeking care. Often, these services are harder to access for rural populations and 66% of the population in India is rural.

Tribal groups in particular face access barriers because of lack of transportation, strong stigma, remote geography, lack of awareness, and fixed facility operating hours leading to low notifications and poor health outcomes.

**Intervention or response:** A TB REACH-supported project by Ashakalp Healthcare Association adopted a four-step strategy to increase TB notifications in tribal areas of Nagpur, Bhandara, Gondia and Chandrapur.

As a first step the project trained and recruited 86 local youth with motorbikes as community health workers (CHWs) and trained them in partnership with NTEP to conduct symptom screening, sputum collection, transportation of specimens to NTEP laboratories, and treatment linkage.

Secondly, the project engaged 6 private health facilities with X-ray machines to offer free chest x-rays for presumptive individuals.

Thirdly, a CBNAAT machine in the rural health facility with a transportation mechanism from all the districts was installed. Lastly, laboratory technicians were recruited in 16 labs, that reported to the NTEP.

**Results/Impact:** Official data were extracted from Nikshay (India's national TB reporting system) to indicate the impact of the project. The table demonstrates the intervention led to an increase of 55% in the sputum examination, an increase of 75% in bacteriologically confirmed notifications, and a 76% increase in all form notifications.

Indicator	Historical Baseline (4 quarters before intervention)	Change in baseline (4 quarters of project intervention)
Sputum Examination	22151	34448
Number of B+ in intervention area	1054	1854
Number of all forms of patients	1866	3291
Notification rate of B+ patients	50/1,00,000	87/1,00,000
Notification rate of all forms of patients	87/1,00,000	155/1,00,000

**Conclusions:** CHWs when trained and engaged, can effectively provide last mile services increasing access to those who are often missed by the health systems. The NTEP may formalise the role of the CHWs in taking the services to the last mile to end TB by 2025.

### OA15-319-16 Quantifying the true population-wide TB burden attributable to incarceration in Brazil

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**Background:** In South America, tuberculosis (TB) incidence is 27 times higher in prisons than in the general population. In Brazil, where incarceration rates have increased by over 500% since 1990, standard methods for calculating the population attributable fraction (PAF) of incarceration yield estimates of 8.9-11.5%. However, these likely underestimate the true effects of incarceration on population TB incidence due to not accounting for prison-acquired infections that progress to disease and generate secondary infections outside prisons. Furthermore, policy guidance for addressing TB in prisons focuses on biomedical interventions, overlooking potentially impactful interventions to reduce exposure to incarceration.

**Design/Methods:** Using a dynamic compartmental transmission model, we quantified the true population-wide excess TB burden in Brazil attributable to the historical rise in incarceration and estimated the effect of interventions to reduce incarceration exposure on population-wide TB incidence.

We used newly available, unpublished data on incarceration and TB over time in Brazil to parameterize and calibrate the model.

**Results:** We estimate that the observed national TB incidence today is 47.8% (95% CrI, 35.2-62.3) higher than that expected without the historical rise in incarceration. Looking forward in time, compared to a base case scenario of continual growth in incarceration rates, we predict that national TB incidence in Brazil could be reduced by 25.7% (95% CrI, 19.6-33.0) in ten years with policies that reverse the historical growth in incarceration rates to the levels in 1990. These findings were largely consistent across a range of assumptions and parameter distributions.

**Conclusions:** The excess TB burden attributable to incarceration has been substantially under-recognized by crude PAF estimates that do not account for the dynamic nature of incarceration and the interconnectedness between prisons and the community.

Ultimately, these results highlight the urgent need for multifactorial interventions for TB control, including those that reduce incarceration exposure.

### OA15-320-16 Building perspectives of community leaders on concepts of vulnerability and gender for an increased demand for TB services: Experiences from vulnerable populations in India

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**Background and challenges to implementation:** National Strategic Plan for Tuberculosis (2017-25), emphasizes active participation of the community to contribute to end TB. Community leaders need deeper understanding of social systems to make them informed about TB vulnerabilities and ways to deal with it. USAID-supported Breaking the Barriers project, is being implemented among mining, migrants, industrial, tribal, and urban vulnerable communities across Indian states - Assam, Bihar, Telangana and Karnataka to ensure community leaders' effective role in accelerating TB elimination efforts.

**Intervention or response:** We conducted perspective-building training to the community leaders, to understand on the complexities within individuals and social-

ly vulnerable groups. In effect, enabling them to engage with and involve communities more effectively for TB response. We adopted a blended participatory learning approach for 4-5 days, through role-play, group activities, and demonstrations to encourage introspection and discussions. Together with sessions on the basics of TB, these workshops covered concepts like deprivation, discrimination, vulnerability, gender, inequities, health rights, and disempowerment. The participants included the project staff and community leaders of project geographies.

**Results/Impact:** Between January 2021 and December 2022, 326 perspective-building workshops were conducted, and 8,217 community structure leaders were trained. As a result, by end of 2022, 80% of the identified community structures were active across project geographies and contributed effectively in screening, referrals, testing, and case detection. In the given period 80,80,348 were screened, 83,226 referred for testing, of which 70,872 were tested and 6,758 were diagnosed as TB positive.

**Conclusions:** Perspective-building workshops enable community leaders to better understand the vulnerabilities and social determinants of TB. This further supported the community leaders in contributing to enhanced demand generation for TB services.

### OA15-321-16 Last-mile tracking of missing people with TB in hard-to-reach areas in Kenya: experiences and lessons learnt from Amref Health Africa

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**Background and challenges to implementation:** About 40% of people with Tuberculosis (TB) are missed annually in Kenya. Hard-to-Reach areas are characterised by vastness, inadequate infrastructure and limited access to basic healthcare services. They are under-resourced because of low TB notification since more resources are allocated to areas with high TB notifications. Targeted outreaches are crucial to finding missing people with TB in these communities.

**Intervention or response:** Amref in collaboration with National TB program (NTP) and county health management teams through Global Fund support, implemented targeted TB screening outreaches in hard-to-reach areas. Hotspots were mapped and targeted for screening. Community Health Volunteers and Public Health officers mobilized the communities.

Between October 2021 and December 2022, 18 outreaches were conducted in 9 hard-to-reach counties. Targeted populations included pastoralists, people who use

drugs, in market places and public transport termini. Outreaches entailed symptomatic TB screening, chest X ray to TB presumptive, and sputum sample referral for GeneXpert or Tru Nat testing for people with suggestive X-rays. Data collection was through NTP tools, collated and analysed using excel.

**Results/Impact:** A total of 8,355 people were screened, 4,156 (50%) were presumptive, 4121 underwent chest X ray. Of these 1,618 (40%) had sputum tested. A total of 266 people were diagnosed with TB, 264 (99%) initiated on treatment. Total Number Needed to Screen to find one person with TB was 32, much lower than the national prevalence survey NNS of 207.

Challenges faced included; occasional failure of X ray machines due to high temperatures which were allowed sufficient time to cool.

Long turnaround time for lab tests, where more laboratory technologists were supported to run samples day and night.

**Conclusions:** Targeted outreaches are able to find missing people with TB in hard-to-reach areas presumed to have low burden. More resources will help find and treat TB patients in these neglected settings.

### OA16 CAD for Tuberculosis

#### OA16-322-16 Improving TB detection through decentralised diagnostics and computer-aided detection system in rural Lesotho

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**Background and challenges to implementation:** As 68% of tuberculosis (TB) cases in Lesotho are neither diagnosed nor treated. There is an urgent need for the decentralization of TB diagnostics and innovative diagnostic technologies in the primary health facilities in Lesotho.

The objective of this study is to assess the outcome of the establishment of TB diagnostics and computer-aided detection (CAD) systems at remote rural hard-to-reach health centers.

**Intervention or response:** In Lesotho, laboratory diagnostic and imaging services are mostly available at district hospitals. The majority of health centers have to send samples to the district hospital laboratory for processing of samples. The lack of availability of TB diagnostics at health centers creates a significant delay in diagnosis and treatment initiation.

**Results/Impact:** In August 2022, Partners In Health (PIH) supported the Ministry of Health to introduce digital x-ray, genexpert machine, sputum induction, and computer-aided detection system in the four rural hard-to-reach health centers.

Additionally, we hired and trained radiographers, laboratory technicians, and TB screeners in each health center. The outcome of the intervention was assessed in these clinics using the descriptive analysis, by comparing the performance of the health centers from August 2019 to February 2020 pre-intervention with August 2022 to February 2023 during the intervention.

TB case finding in the four health centers increased by three times (73 pre vs 201 during implementation) during the intervention period. This is 127% of the six-month performance target based on the estimated national TB incidence of 614/100000 population and a combined 51,600 population in the catchment area of the four health centers.

**Conclusions:** Decentralization of TB diagnostics at remote peripheral health centers was highly effective in closing the gaps in TB detection. Introducing digital X-ray, sputum induction, genexpert, and CAD systems helped to significantly improve TB detection. Innovative interventions are needed to address gaps in TB detection in high TB settings.

## OA16-323-16 A prospective multi-country comparison of automated chest X-ray algorithms for the triage of pulmonary TB

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**Background:** Computer-aided detection (CAD) algorithms for chest X-ray (CXR) reading have been endorsed as a TB triage test by the World Health Organization (WHO), but independent, head-to-head comparisons are needed, including among key risk groups.

**Design/Methods:** We enrolled adults with cough  $\geq$  2 weeks presenting to clinics in Uganda, South Africa, Vietnam, the Philippines, and India. We obtained a CXR and collected sputum for TB testing (Xpert MTB/RIF Ultra [Xpert]; and two liquid cultures if Xpert-negative). We applied three CAD algorithms (Lunit INSIGHT CXR v3 (Lunit), qXR v3, and CAD4TB v7) to CXRs, and selected the optimal cut-point (overall and by country) to maximize specificity at 90% sensitivity in reference to sputum Xpert and culture results.

**Results:** Among 2219 participants, median age was 41 years (IQR 29-53), 972 (44%) were female, 307 (14%) were living with HIV, 298 (13%) were living with diabetes, and 518 (23%) had confirmed TB. Overall, at 90% sensitivity, Lunit had significantly higher specificity (72.5%, 95% CI 70.2-74.7) than qXR (65.7%, 95% CI

63.3-68.0,  $p < 0.001$ ) and CAD4TB (68.3%, 95% CI 65.9-70.6,  $p = 0.001$ ). Specificity varied by country for each algorithm (Lunit: range 59.5-82.1%; qXR: 55.4-73.2%; CAD4TB: 57.2-84.9%) when using the overall optimal cut-point.

However, specificity was  $>70\%$  in South Africa, Vietnam and the Philippines when using country-specific cut-points (Table 1). Lunit had similar or higher specificity than CAD4TB and qXR among people living with HIV and people living with diabetes when using the overall optimal cut-point and when risk group-specific cut-points (Table 1).

	Lunit INSIGHT CXR Specificity n/N, % (95% CI)	qXR v3 Specificity n/N, % (95% CI)	CAD4TB v6 Specificity n/N, % (95% CI)
<b>Overall<sup>1</sup></b>	428/1556 72.5% (70.2-74.7%)	534/1556 65.7% (63.3-68.0%)	493/1556 68.3% (65.9-70.6%)
<b>Country</b>			
Uganda <sup>2</sup>	184/418 56.0% (51.1-60.8%)	188/418 55.0% (50.1-59.9%)	193/418 53.8% (48.9-58.7%)
Philippines <sup>3</sup>	84/411 79.6% (75.3-83.4%)	123/411 70.1% (65.4-74.5%)	150/411 63.5% (58.6-68.2%)
Vietnam <sup>4</sup>	26/231 88.7% (83.9-92.5%)	43/231 81.4% (75.8-86.2%)	51/231 77.9% (72.0-83.1%)
India <sup>5</sup>	84/284 70.4% (64.7-75.7%)	150/284 47.2% (41.3-53.2%)	105/284 63.0% (57.1-68.7%)
South Africa <sup>6</sup>	58/212 72.6% (66.1-78.5%)	42/212 80.2% (74.2-85.3%)	40/212 81.1% (75.2-86.2%)
<b>Risk group</b>			
People living with HIV <sup>7</sup>	107/207 48.3% (41.3-55.3%)	112/207 45.9% (39.0-52.9%)	116/207 44.0% (37.1-51.0%)
People living with diabetes <sup>8</sup>	44/182 75.8% (68.9-81.9%)	74/182 59.3% (51.8-66.5%)	51/182 72.0% (64.9-78.4%)

<sup>1</sup>cut-off 5.48 for INSIGHT, 0.139 for qXR and 30.48 for CAD4TB, <sup>2</sup>cut-off 2.49 for INSIGHT, 0.078 for qXR and 27.12 for CAD4TB, <sup>3</sup>cut-off 6.58 for INSIGHT, 0.098 for qXR and 7.169 for CAD4TB, <sup>4</sup>cut-off 31.84 for INSIGHT, 0.735 for qXR and 54.92 for CAD4TB, <sup>5</sup>cut-off 24.91 for INSIGHT, 0.048 for qXR and 20.48 for CAD4TB, <sup>6</sup>cut-off 13.8 for INSIGHT, 0.565 for qXR and 50.65 for CAD4TB, <sup>7</sup>cut-off 2.03 for INSIGHT, 0.057 for qXR and 13.03 for CAD4TB, <sup>8</sup>cut-off 8.85 for INSIGHT, 0.15 for qXR and 38.23 for CAD4TB

Table 1. Specificity of CAD Algorithms at 90% Sensitivity, overall and by country and key sub-groups.

**Conclusions:** CAD algorithms achieved or approached the TB triage test target product profile accuracy thresholds overall and in key high-risk groups. INSIGHT performed best, but there was substantial heterogeneity by country and subgroup, highlighting the need for country-led evaluations in different target populations prior to implementation.

## OA16-324-16 An analysis of the impact of portable digital X-ray on TB screening in hard-to-reach communities in Nigeria

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**Background and challenges to implementation:** Under-diagnosis of Tuberculosis (TB) due to poor geographical access to hard-to-reach communities contribute greatly to the gap between notifications and estimated incidence of TB. A key objective amongst USAID funded TB-LON 1 and 2 project is to improve access to high-quality, person-centred TB services using Portable Digital X-Ray (PDX). This paper aims to analyze the impact of Portable Digital X-Ray on TB screening in hard-to-reach areas in Nigeria.

**Intervention or response:** KNCV Nigeria with funding from USAID in January 2022 deployed seven Portable Digital X-Ray with Computer Aided Diagnosis (CAD) as TB screening/diagnostic tool for hard-to-reach communities across six states of Benue, Cross River, Delta, Kano, Katsina and Nasarawa. Enrollees with a CAD4TB (computer-aided detection for TB score)  $>60$  had Xpert (sputum) and/or clinical (radiograph) assessment for TB diagnosis. A TB screening algorithm guided the step-by-step process of identifying a presumptive TB client up to diagnosis and linkage for appropriate care and treatment. Data was collected, collated, and reported using the national TB tools.

**Results/Impact:** In the same period, PDX had the lowest Number Needed to Screen (NNS) 45 and Number Needed to Test (NNT) 4. Similarly, PDX with a presumptive TB yield of 10% had the highest TB yield of 23%.

TB Case finding strategy in 2022	Persons screened	Presumptive TB identified	Presumptive TB evaluated for TB	TB cases diagnosed	TB patients put on treatment	NNS	NNT
PDX	85,910	8,416	8,401	1,915	1,869	45	4
ICF- Public facility	3,404,939	209,975	196,406	16,559	16,124	205.6	11.9
ICF- Private facility	462,120	31,305	31,086	2,581	2,501	179.0	12.0
PPMV / CP	1,481,066	169,498	160,758	11,589	11,443	127.8	13.9
Contact Investigation	160,828	48,469	45,890	3,282	3,146	49.0	14.0
Community ACF	1,298,202	93,460	84,974	3,342	3,273	388.5	25.4

Table 1: TB screening cascade and performance of Active Case finding strategies across 6 states.

**Conclusions:** Using PDX with CAD contributed the highest TB yield during Active TB case finding in hard-to-communities of Nigeria. With a very low NNS and NNT, its national scale up and use across remote locations will greatly improve the TB case finding in Nigeria.

**OA16-325-16 Digital chest X-ray with computer-aided diagnosis: a useful diagnostic tool for TB contacts, Kenya, 2022-2023**

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**Background:** Contacts of TB patients are at risk of TB infection and disease as compared to the general population. Use of digital x-rays (d-CXR) with Computer Aided Diagnosis (CAD) is a useful tool for screening of TB in addition to symptom screening. The objective of this study was to compare the positivity of TB between household contacts and non-contacts using d-CXR as a screening tool.

**Design/Methods:** Kenya received 8 digital chest Xray with CAD software from the introducing new tools project (INTP). Screening algorithms were developed to include the use of d-CXR as a screening tool. Patients presenting to the outpatient department and contacts of TB patients received an Xray, those with a score of >60 were subjected to a laboratory investigation for TB and those confirmed with TB were initiated on treatment.

**Results:** 1,519 contacts and 9738 non contacts were symptomatically screened for TB and offered an Xray, 75% (1152) of the contacts and 62% (6043) of the non-contacts were symptomatic. On Xray, 14% (161) of the symptomatic contacts had a score of >60. Of these, 90 (56%) were offered TB lab investigations and 40 (44%) turned positive. 163/991 symptomatic contacts with CAD score of <60 were offered a lab test and 8% (13) tested positive. For the non-contacts with a score of >60 who were tested for TB in the lab, 38% turned positive while 5% of those with a score of <60 were confirmed to have TB

**Conclusions:** The availability of d-CXR with CAD helped to identify who to be sent to the lab, the positivity for TB among household contacts was high as compared to the non-contacts. There is need to invest more on this technology to identify more TB cases among person in contact with TB patients, early initiation to treatment in order to minimize further transmission.

**OA16-326-16 Use of artificial intelligence to analyse chest X-rays for TB: Results from pilot studies of two independent softwares**

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**Background:** The use of CXRs for screening and clinical diagnosis of TB as recommended by WHO has helped increase case notification. Computer-aided detection (CAD) products use artificial intelligence (AI) to analyze CXR for the presence of abnormalities suggestive of pulmonary TB and can improve the feasibility and performance of CXR for TB screening and triage. We present head-to-head comparison of 2 artificial intelligence softwares in analyzing chest radiographs from clients enrolled during active case finding intervention in Nigeria.

**Design/Methods:** KNCV Nigeria using the Wellness on Wheels truck deployed digital x-ray services with CAD4TB AI technology in hard-to-reach communities for screening and diagnosis of TB. In other to maximize these benefits a second AI technology, qXR was concurrently deployed for a trial on the northern WOW truck to assess suitability and efficiency in detecting TB cases. Presumptives identified by both softwares had their samples tested on the Xpert machine for MTB/Rif detection. Comparison was made between presumptives identified by the qXR software and those identified by CAD4TB correlating these with the GeneXpert results.

**Results:** 2291 X-rays were processed by both softwares, 123(5.4%) were identified as presumptives by CAD4TB (score≥60) while qXR identified 77(3.4%) as TB presumptives. The NNT for qXR and CAD4TB were 4.5 and 7 respectively. The positive predictive value for qXR was 26% while that for CAD4TB was 15%.

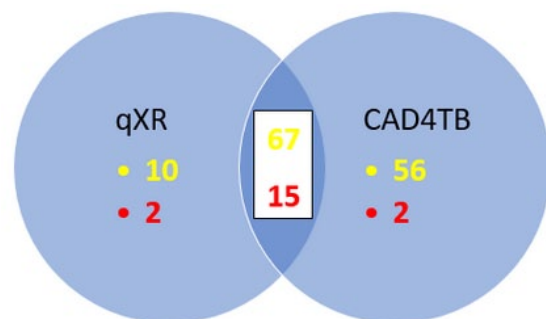


Figure 1. Venn diagram showing number of presumptives in (yellow) and number of TB cases diagnosed (in red) by each of the two softwares and the areas of overlap between the two.

**Conclusions:** Both softwares identified 17TB cases each, but qXR is more efficient based on a lower NNT and a higher PPV and reduces the number of confirmatory

tests to be carried out and has the added advantage of describing other lung pathologies. The use of CXR with CAD technology as a screening tool for TB offers the advantage of detecting early disease while saving cost and time, this should be adopted by the national TB program to improve efficiency of ACF activities.

### OA16-327-16 High-yield active case-finding with computer-aided detection does not always translate into high linkage to care

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**Background:** Active screening for tuberculosis (TB) using computer-aided detection (CAD) can increase TB detection, however linkage to care post-screening is infrequently reported. We report results of active screening using CAD in Manila, Philippines including linkage to care.

**Design/Methods:** A prospective study, October 2022 to February 2023, screening general population  $\geq 15$  years for TB with digital chest x-ray (CXR) and CAD (Delft, CAD4TB, version 7). Sputum collected from people with CAD score over threshold, or with symptoms were transported for GeneXpert MTB/RIF (Xpert) for bacteriologic confirmation. People with CXR suggestive of TB were assessed by a physician. Positive Xpert result was considered bacteriologically confirmed TB (BCTB). TB diagnosed without bacteriological confirmation was classified as clinically diagnosed TB (CDTB). People with Xpert “trace” results were advised to undergo repeat sputum collection. Patients with CDTB and non-trace Xpert results were referred for TB treatment at the local health center.

**Results:** The screening and linkage to care results of 3116 participants are shown in Table 1. Most eligible participants provided sputum for testing (1096/1110, 99%), and 14% (156/1100) had BCTB. Majority of BCTB patients were symptom screen negative (99/156, 63.5%). Among 156 Xpert results, 51 (32.7%) were trace results. Half (109/203, 54%) of all cases (BCTB and CDTB) initiated TB treatment. Higher rates of treatment initiation were observed among people with BCTB with non-trace Xpert results (81/105, 77%) compared to people with CDTB (28/47, 59%).

Reasons for non-initiation of TB treatment include uncontactable (30/94, 32%), pending health center initiation (35/94, 37%), repeat test needed (25/94, 27%), refusal to accept the diagnosis (4/94, 4%).

	Symptom screening positive	Symptom screening negative	Total
Participants with CAD score above threshold	247	863	1110
Sputum collected	246	850	1096
Positive Xpert result	57	99	156
TB diagnosed	92	111	203
Bacteriologically confirmed TB	57	99	156
Clinically diagnosed TB	35	12	47
TB treatment initiation	59	50	109
Bacteriologically confirmed TB (non-trace Xpert)	37	44	81
Clinically diagnosed TB	22	6	28

**Conclusions:** Active screening with CAD identified high rates of TB. Most people with BCTB reported no symptoms. In this setting, trace Xpert results were common, adding a challenge to TB evaluation and treatment. Barriers to treatment initiation require further exploration and action.

### OA16-328-16 Evaluating computer-aided detection software for external quality assessment during community-based TB screening in Viet Nam

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**Background:** We used qXR v3 software (Qure.ai, India) as an external quality assessment (EQA) check on radiologist chest X-ray (CXR) interpretation during community-based screening for TB.

**Design/Methods:** High-risk individuals, including contacts and people living with HIV, were mobilized from the community for CXR screening using an ultraportable Fujifilm CALNEO X-air radiography system. CXR images were interpreted by an on-site radiologist and in parallel by the computer-aided detection (CAD) software. Participants with an abnormal CXR, either by the radiologist and/or the CAD software (score  $\geq 0.50$ ), were asked to give sputum for testing with the Xpert MTB/RIF Ultra (Ultra) assay.



**Results:** The CAD software was prospectively deployed at 47 (100%) screening events in Ho Chi Minh City between April 2022 and January 2023. A total of 2,301 high-risk participants were screened by CXR, resulting in the detection of 64 people with TB (yield of 2.8%). As markers for implementation fidelity, CAD software outputs were generated for 2,253 (97.9%) participants and sputum was tested for 46 (75.4%) participants from the CAD ‘TB Presumptive’ / radiologist normal screening cohort. If only the radiologist had interpreted the CXR images, 63 people would have been diagnosed with TB (sensitivity = 98.4%), whereas if only the CAD software had interpreted the CXR images, 56 people would have been diagnosed with TB (sensitivity = 87.5%). The CAD software missed 5 Ultra-positive results; the qXR abnormality scores for these participants ranged from 0.02 to 0.48 and three had Trace Call positive Ultra results.

		CAD Software Interpretation		No CAD Software Interpretation
		TB Presumptive	TB Negative	
Radiologist Interpretation	<b>Any Abnormal</b>	288 (12.5%)	494 (21.5%)	18 (0.8%)
	Sputum tested	287 (99.7%)	484 (98.0%)	17 (94.4%)
	Ultra-positive	55 (19.2%)	5 (1.0%)	3 (17.6%)
	Trace Call	6 (10.9%)	3 (60.0%)	1 (33.3%)
	<b>Normal</b>	61 (2.7%)	1,410 (61.3%)	30 (1.3%)
	Sputum tested	46 (75.4%)	N/A	N/A
	Ultra-positive	1 (2.2%)	N/A	N/A
	Trace Call	0 (0%)	N/A	N/A

*Table. Crosstab of radiologist and CAD software CXR interpretations and follow-on sputum collection and Ultra testing yields.*

**Conclusions:** The CAD software added only +7.8% to the initiative’s testing burden, but yielded just one incremental diagnosis of TB. A lower qXR abnormality score threshold would have improved the software’s sensitivity, and possibly added additional incremental diagnoses. Additional research should focus on positioning this CAD software as a tool to reduce ‘false abnormal’ radiologist results.

**OA16-329-16 Computer-aided detection of TB from chest radiographs in a TB prevalence survey: external validation and modelled impacts of commercially available artificial intelligence software**

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**Background:** Computer-aided detection (CAD) can help identify the millions of people with active tuberculosis (TB) currently left undetected. Few studies have compared the performance of all commercially available CAD products for screening in high TB-HIV burden settings, and there is limited understanding of threshold selection across products in different populations.

**Design/Methods:** We evaluated 11 CAD products on a case-control sample of 774 participants from a TB prevalence survey in South Africa. Only those with microbiological test results were eligible, with 516 bacteriologically negative and 258 bacteriologically positive. We compared the area under the receiver operating characteristic curve (AUC) against microbiological evidence. Threshold analyses were performed based on pre-defined selection criteria and across all thresholds. We conducted subgroup analysis stratified by age, gender, prior TB history, presence of symptoms, and HIV and smoking status.

**Results:** Many products performed well, although only one met the WHO target product profile of 90% sensitivity and 70% specificity for a TB triage test. The AUCs of all products are shown in Figure 1.

Thresholds varied dramatically between products to meet the same programmatic targets in terms of target sensitivity, target specificity, and target test referral rate. Performance also varied in some subpopulations, with all CAD products performed worse in older people and those with a prior history of TB. However, HIV status and presence of symptoms did not significantly affect CAD performance in terms of AUC, although it did affect threshold selection to meet targets.

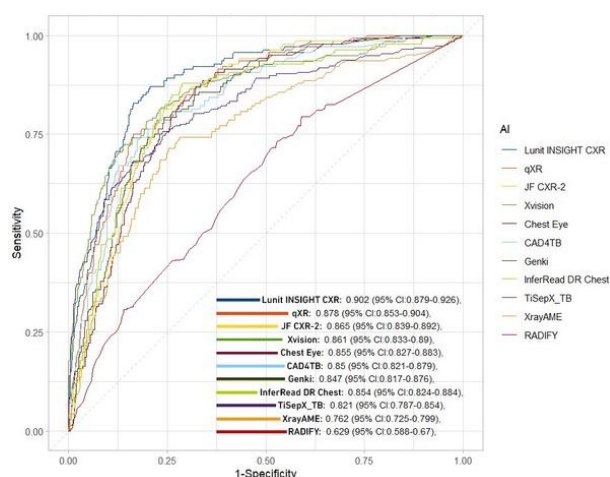


Figure 1: The ROC curves of all commercially available CAD software for TB (n=775).

**Conclusions:** Several previously unevaluated CAD products performed similarly to those evaluated by the WHO. Thresholds should not be the same between different products and subgroups. The rapid emergence of products and versions necessitate a global strategy to efficiently validate new versions and software to support vendor and threshold selections.

## OA17 Strategies to improve active case finding

### OA17-330-16 Better together: leveraging two community-based strategies for integrated active case-finding of TB disease and infection

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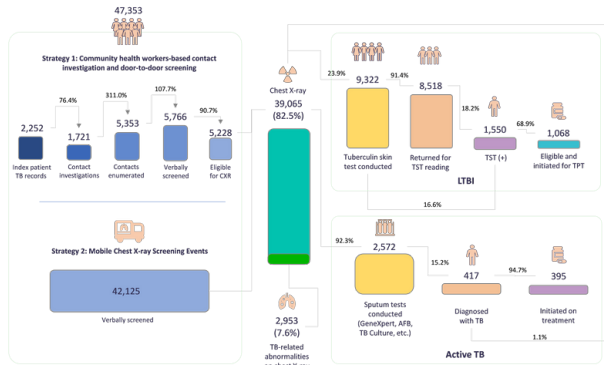
**Background and challenges to implementation:** Vietnam is among 30 countries with the highest tuberculosis (TB) burden and is aiming for a 90% reduction in TB prevalence by 2030. This goal is unlikely to be met unless comprehensive screening activities using novel technologies and community engagement approaches are undertaken for both TB and TB infection (TBI).

**Intervention or response:** We implemented two integrated TB and TBI case finding strategies in three urban provinces of Viet Nam from April-2020 to March-2023. We established community health worker networks for contact investigation and door-to-door screening in and around households of index patients. Eligible people were referred for chest X-ray (CXR) screening and tuberculin skin testing (TST) at health facilities. We also hosted community-based CXR screening and TST events for missed contacts and community members at higher risk of TB (e.g. diabetics, persons  $\geq 40$  years, urban poor, etc).

Participants with abnormal CXRs were tested with GeneXpert or Molbio molecular assays per national guidelines. People with TB or TBI were linked to appropriate care.

**Results/Impact:** In total, we enumerated 47,353 people eligible for CXR of whom 82.5% (39,065/47,353) were screened and 7.6% (2,953/39,065) presented TB-related abnormalities. Our intervention yielded 417 people with active TB, for a detection yield of 1,067 per 100,000 (417/39,065) – 6.2x the estimated national incidence rate (173/100,000).

Of these, 94.7% (395/417) were linked to care. In addition, 16.6% (1,550/9,322) of persons tested had a positive TST and 68.9% (1,068/1,550) initiated TB prophylaxis. Thus, 3.7% (1,463/39,065) of eligible participants received some form of TB intervention.



**Conclusions:** The integrated model for TB and TBI screening deployed through two community-based strategies in the project demonstrated clear synergies for deployment and health benefits for the community. These results illustrate the feasibility and emphasize the urgent need for expansion of integrated, community-based approaches in the fight to end TB.

**OA17-331-16 Household and incentive-based contact investigation in rural South Africa: Fidelity and implementation cascade**

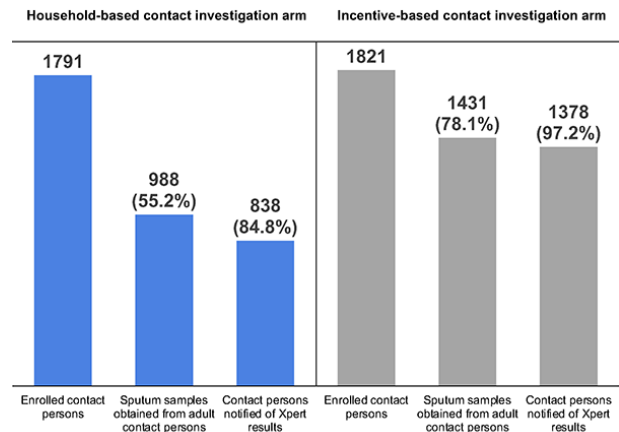
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**Background and challenges to implementation:** The World Health Organization recommends contact investigation for tuberculosis (TB) in low- and middle-income country settings. However, contextually-specific barriers to implementation exist and intervention effectiveness is variable. To understand implementation barriers, we explored the fidelity of two contact investigation strategies.

**Intervention or response:** Kharitode TB, a cluster-randomized crossover trial, implemented household- and incentive-based contact investigation in 28 public health clinics in South Africa (July 2016-January 2020). Clinics were randomised to one strategy for 18 months, switching after a 6-month washout period. Adults recently diagnosed with TB were enrolled. In the household-based arm, contact persons were screened at home. In the incentive-based arm, people with TB received coupons for

referral; participants received a cash incentive (4USD) upon presenting for screening. Study staff attempted to collect sputum from all contact persons for Xpert testing (at home in the household-based versus facilities in the incentive-based arm). The incentive-based strategy was as effective as household visits. We defined fidelity as to what extent each strategy was implemented as per protocol and used descriptive statistics to assess the implementation cascade.

**Results/Impact:** Overall, 2564 people with TB were identified, of whom 1376 (53.7%) enrolled within two months of diagnosis. In the household-based arm, 732/778 households were visited within two weeks of enrollment. Across both arms, 3612 contact persons were enrolled, of whom 2419 (67.0%) provided sputum [sputum collection fidelity: 988/1791, 55.2% household-based; 1431/1821, 78.6% incentive-based]. In the incentive-based arm, 1391/1431 sputum samples were collected within 2 months of giving out coupons. Xpert results were communicated to 2216/2419 participants (91.6% of tested) [notification fidelity: 838/988, 84.8% household-based, 1378/1431, 97.2% incentive-based]. Overall, the intervention was implemented as intended for 46.8% (838/1791) contact persons in the household-based and 75.7% (1378/1821) in the incentive-based arm.



**Conclusions:** Incentive-based contact investigation demonstrated higher implementation fidelity than the household-based arm. However, sputum collection remained challenging in both arms.

### OA17-332-16 Improving TB detection through targeted active TB screening using a peer-network hub strategy in Nigeria

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**Background and challenges to implementation:** Nigeria has the highest tuberculosis (TB) burden in Africa. Despite the recent improvements in TB case-finding, undiagnosed TB cases remain a major challenge to TB control in Nigeria. Expanding innovative approaches to case-finding has been identified as a key strategy in recent strategic planning. However, questions remain about how quickly interventions could bridge the gap in TB diagnosis.

**Intervention or response:** The USAID-funded TB LON 1 & 2 project led by KNCV Nigeria implemented a Peer-Network Hub (PHB) strategy for community TB case-finding. The gender-driven innovative approach was implemented in three high-burden states in Nigeria. Key interventions include identifying and training volunteers within men's social, cultural and age groups for TB screening and referrals. Routine symptomatic TB screening, gender-driven social and behavioural change communication awareness creation and group sensitization to address TB myths and misconceptions, logistics for sample movement for diagnostics procedures for presumptive clients, and digitally supported real-time data reporting were conducted. Confirmed TB cases were placed on appropriate treatment. The intervention efficiency was assessed using TB yield and contribution to case notification.

**Results/Impact:** Between January to December 2022, 83,585 persons were screened among men groups. Of these, 6,486 (7.8%) presumptive TB was identified, and 6,243 (96.3%) completed evaluations for TB using GeneXpert or Truenat, resulting in the diagnosis and enrollment of 582 (9.3%) TB patients to treatment. Through these efforts, the average quarterly TB notification in the local government areas increased by 36.8% and steadily across the following quarters (See Figure).

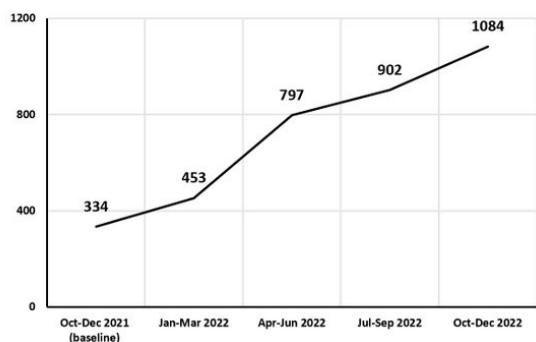


Figure: TB case notification in the intervention areas.

**Conclusions:** Our results showed that the Peer-Network Hub strategy improved TB case detection among men and TB notification in the intervention areas. This strategy needs to be scaled to other states in Nigeria to improve TB case-finding.

### OA17-333-16 The impact and effectiveness of artificial intelligence in the search for missing TB cases in Osun State, Nigeria: EPCON and CAD4TB as case studies

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**Background and challenges to implementation:** A significant public health concern is finding missing tuberculosis (TB) cases, particularly in low-resourced areas. The USAID-funded TBLON3 project has utilized artificial intelligence (AI) to improve the precision and efficiency of TB case finding. Epidemic Control (EPCON) and Computer-Aided Detection for Tuberculosis (CAD4TB) are the primary platforms used in this study to highlight the effectiveness of AI in identifying missing TB cases.

**Intervention or response:**

	TRADITIONAL METHOD (NNS 71, NNT 11)			AI SUPPORTED (NNS 39, NNT 6)		
	Total Screened	Presumptives Identified	TB Cases	Total Screened	Presumptives Identified	TB Cases
Quarter 1	49030	7639	756	2514	433	85
Quarter 2	54786	8683	735	6066	1319	212
Quarter 3	50419	8620	755	7637	1000	187
Quarter 4	57180	8122	721	6987	843	112
Total	211415	32704	2967	23204	3595	596

Table. Comparative Quarterly Data showing the TB Cascade for both AI Supported and Traditional Methods of Location Choices and TB Screening.

A comparative study determined the accuracy and efficiency of the AI tools (EPCON and CAD4TB) deployed in mapping hotspots, screening activities, and identi-

fying presumptive TB cases. This study reviewed data generated in 12 months, from February 2022–January 2023 across the 30 LGAs in Osun State. It compared the screening outcomes from both AI-suggested locations and the conventional methods of location choices in Osun State, Nigeria.

**Results/Impact:** For the AI-supported screening activities, 23,204 people were screened, and 3,595 (15.5%) were identified as presumptive TB cases and evaluated. A total of 596 (16.6%) TB cases were diagnosed. The NNS and NNT calculated were 39 and 6, respectively. Of the 211,415 people screened for TB using conventional methods, 32,704 (15.5%) were identified as presumptive TB cases and evaluated. 2,967 (9.0%) TB cases were diagnosed. The NNS and NNT calculated were 71 and 11, respectively.

**Conclusions:** The AI-supported method of location choices and TB screening in the community is more effective and helps in utilizing minimal resources to achieve great results. In conclusion, AI can improve TB case-finding by enhancing the process' accuracy and effectiveness. Hence, there is a need to encourage the use of AI in the search for missing TB cases not just in Osun state but in Nigeria at large

### OA17-334-16 Understand the spaces to curb the cases: using individual activity space data to inform TB prevention in KwaZulu-Natal, South Africa

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**Background:** Access to TB screening services remains a critical challenge for TB care and prevention efforts, and an estimated 40% of incident TB cases still go undiagnosed. Individual-level activity space data, capturing locations where people spend time daily, has yielded new insights into the locations where TB transmission can occur. Better understanding the differences in overall mobility, among the diverse groups of individuals affected by TB, can help inform precision public health strategies for TB screening.

**Design/Methods:** We enrolled individuals recently diagnosed with TB at two primary healthcare clinics in Tongaat, KwaZulu-Natal, South Africa. We conducted

structured interviews to capture the residences, locations, and transit hubs that participants visited in the 12 months before TB diagnosis and mapped the GPS coordinates of these locations.

We used this data to calculate the convex hull (the smallest convex polygon containing all coordinates) of each participant's activity space and used linear regressions to examine preliminary associations between clinical and demographic characteristics and the area of the activity space convex hull (in km<sup>2</sup>).

**Results:** Between July 2022 – March 2023, the study enrolled 181 individuals with newly diagnosed (GeneXpert-positive) TB, of whom 95 had activity spaces with three or more total locations within an 11.72 km<sup>2</sup> community. Prior TB disease was associated with smaller activity space area, controlling for age ( $\beta$ : 1.87, 95% CI: 0.34, 4.08). Alcohol use was associated with larger activity space area (Figure 1,  $\beta$ : 2.81, 95% CI: 0.92, 4.71). Demographic characteristics were not associated with activity space.

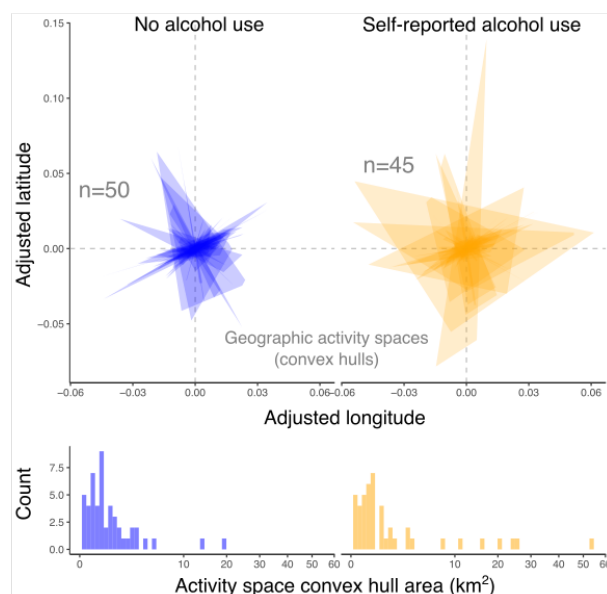


Figure 1.

**Conclusions:** Highly detailed, GPS-mapped activity space data revealed heterogeneous mobility patterns among individuals with newly diagnosed TB. Our findings are informative for understanding the geographic spaces over which TB transmission occurs and identifying individuals at higher risk of exposure and secondary transmission. Combined with *M. tuberculosis* genomic data, these insights can inform new strategies for TB screening.

### OA17-336-16 Systematic screening for TB disease using a combination of the WHO 4-symptom screening and chest X-ray with computer-aided detection in identified TB hotspot communities in Nigeria

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**Background and challenges to implementation:** Nigeria has the highest TB burden in Africa with an estimated incidence of 219/100,000 and accounts for 6.3% of the gap of unidentified TB cases globally. This gap between notified and estimated cases is largely due to underreporting and under diagnosis. To address these two factors, KNCV Nigeria USAID-funded TB LON 1 and 2 project introduced Systematic screening in TB hot spot communities.

**Intervention or response:** TB Hot spot communities were identified using Early Warning Outbreak Recognition System (EWORS), advocacy and community mobilization done, Trained community teams conducted combined symptom and chest Xray screening. WHO 4 symptom screening (W4SS) checklist was used while chest Xray screening was done using Portable digital X ray with Computer aided detection for TB(CAD4TB). Presumptive TB cases were identified as those who screened positive to W4SS and or a CAD4TB score of  $\geq 50$ . All identified presumptive TB were tested with GeneXpert or TB LAMP.

**Results/Impact:** A total of 516,048 clients were screened from January - December 2022 across hotspot communities. A total of 55,583 presumptive TB were identified, 4062 cases diagnosed (TB yield of 7%) an average Number Needed to Test (NNT) of 14 and Number Needed to Screen (NNS) of 127.

Disaggregating by screening method, a total of 247,093 clients were screened with W4SS, of those 26,414 presumptive TB were identified 1,327 TB cases diagnosed (5% TB yield) NNT was 20 and NNS as 186.

While 268,955 clients were screened with a combination of W4SS and Chest X ray screening, 29,169 identified presumptive TB were evaluated, 2,735 TB were diagnosed (TB yield of 9%) NNT was 11 and NNS was 95.

Screening method	Screened	Presumptive	Diagnosed	TB Yield	NNT	NNS
W4SS and Chest Xray	268,955	29,169	2,735	9%	11	95
W4SS	247,093	26,414	1,327	5%	20	186
Total	516,048	55,583	4,062	7%	14	127

Table.

**Conclusions:** There was a higher TB yield and better TB cascade efficiency with the combined chest Xray and W4SS compared to W4SS only. We recommend the use of combined screening methods to improve TB case yield in communities.

### OA17-337-16 Integrating active TB case-finding interventions in outpatient departments of two chest disease hospitals in Bangladesh

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**Background and challenges to implementation:** Tuberculosis (TB) remains a major public health concern in Bangladesh. About 18% of estimated TB cases remain undetected in Bangladesh. We sought to demonstrate whether the integration of an active case finding (ACF) strategy in 2 chest disease hospitals (CDHs) in Bangladesh can lead to more individuals being identified with TB/ DR-TB.

**Intervention or response:** We screened all individuals (age  $\geq 15$  years) verbally for symptoms of TB who visited the outpatient department of selected 2 CDHs in Khulna and Chattogram using an Android-based digital screening App with a standardized quick questionnaire. Individuals identified as TB presumptive were referred to the facility doctor for further evaluation and diagnostic tests. Diagnosed TB/DR-TB patients were initiated on TB/DR-TB treatment as per the National guidelines.

**Results/Impact:** We screened 43,145 individuals for possible TB between January 2022 and March 2023. The majority of those individuals were either patient who came to the facilities with other health problems or was accompanying with other patients.

Out of all screened, 13,277 (30.8%) were identified as possible TB, and 12,637 (95.2%) were further evaluated for TB. Of all evaluated/tested, 1,046 (8.3%) were diagnosed with DS-TB and 218 (1.7%) were diagnosed with DR-TB and all were enrolled for treatment. The mean age of those diagnosed was 47 years, and the majority (68.3%) were male.

**Conclusions:** The yield of the ACF approach that screens and tests individual regardless of their TB symptoms status was high in our intervention sites. Integrating ACF into existing care delivery platforms of health facilities has demonstrated the potential for additional TB case detection. The NTP should consider the incorporation of ACF intervention in high-volume facilities across the country.

## OA18 Genome sequencing and new diagnostics research

### OA18-338-16 Discordant results in drug susceptibility testing using whole-genome sequencing and phenotypic method under routine conditions in Peru

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**Background:** Drug susceptibility tests are essential to define an individualized treatment scheme for patients with drug-resistant TB, however, these tests can present discordant results.

The objective of this study is to analyze the discordant results obtained in the evaluation of susceptibility to anti-TB drugs using Whole Genome Sequencing (WGS) and BACTEC MGIT system in strains of *M. tuberculosis* that arrived, under routine conditions, at the National Reference Laboratory for Mycobacteria of the National Institute of Health of Peru.

**Design/Methods:** 100 solid cultures were routinely and simultaneously processed for Drug Susceptibility Test through WGS and BACTEC MGIT 960 methodologies according to routine laboratory workflow.

First and second line drugs were evaluated in order to analyse the discordant results. Using WGS, the mutations present were detected, which were also compared with the resistance categories established by the WHO. Resistance-associated variants were identified with TB-Profler v4.1.1 using the catalogue of mutations published by the World Health Organization (WHO).

**Results:** All compared drugs (except amikacin) presented discordant results.

For rifampicin, two strains were discordant showing sensible results by BACTEC MGIT but resistant by WGS. For isoniazid, only one strain was discordant with sensible result by WGS.

For pyrazinamide, we obtained 5 discordant results, of which one was determined as resistant by WGS.

Among second line injectables only capreomycin had one discordant result which was sensible by WGS. Respect to moxifloxacin, there were 6 discordant results with all of them presenting resistant pattern by WGS.

Overall, mutations detected by WGS in these discordant results are mostly catalogued as “associated with resistance,” whereas only 2 catalogued as “associated with resistance – interim” (Table 1)

**Conclusions:** In Peru, under routine conditions, the evaluation of mutation-associated resistance to anti-TB drugs was better detected by WGS compared to phenotypic testing. All these discordant mutations were correctly defined in the WHO mutation catalogue.

Fármaco	BACTEC	WGS	Mutación WGS	Categoría WHO
<b>Rifampicina</b>				
PER-TB-030	S	R	rpoB_Q432L	Assoc w R
PER-TB-092	S	R	rpoB_I491F	Assoc w R
<b>Isoniacida</b>				
PER-TB-075	R	S	-	
<b>Pirazinamida</b>				
PER-TB-015	S	R	pncA_K48T	Assoc w R - Interim
PER-TB-022	R	S	*	
PER-TB-029	R	S	-	
PER-TB-036	R	S	-	
PER-TB-067	R	S	-	
<b>Capreomicina</b>				
PER-TB-062	R	S	-	
<b>Moxifloxacina</b>				
PER-TB-013	S	R	gyrA_A90V gyrA_D94N, gyrB_N499D	Assoc w R Assoc w R, Assoc w R - Interim
PER-TB-015	S	R	gyrA_A90V	Assoc w R
PER-TB-041	S	R	gyrA_A90V	Assoc w R
PER-TB-068	S	R	gyrA_A90V	Assoc w R
PER-TB-080	S	R	gyrA_D94A	Assoc w R
PER-TB-095	S	R	gyrA_A90V	Assoc w R

**WHO:** World health organization, **WGS:** Whole genome sequencing, **R:** resistant, **S:** sensible. **Assoc w R:** Associated with resistance, **Assoc w R – Interim:** Associated with resistance – Interim.

Table 1. Discordant results obtained for each drug using WGS and BACTEC MGIT.

### OA18-339-16 Remote management of a TB sequencing diagnostic accuracy clinical trial during the COVID-19 pandemic

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**Background:** The Unitaid-funded Seq&Treat project led by FIND aims to transform the detection of drug-resistant tuberculosis using targeted next-generation sequencing (tNGS). In 2020, FIND planned a multicentre clinical evaluation in three countries to assess the performance of multiple tNGS solutions; the COVID-19 pandemic hit before the trial could be initiated. Amidst lockdowns and travel restrictions, we developed a strategy to remotely set-up and manage this complex clinical evaluation.

**Design/Methods:** Standard setup activities were conducted remotely following a stage-gated procedure. Processes were developed for remote site management, including tools for remote Site Assessment (rSA), remote Site Initiation Visit (rSIV) and remote monitoring. Following a conventional site feasibility assessment pre-pandemic, short-listed sites underwent rSA to verify their capacity to perform the trial in compliance with the protocol, standard operating procedures, and international quality standards. The assessment required sites to submit videos of routine procedures for sample collection, storage, processing, standard and comparator testing, as well as assessments of their quality man-

agement systems. Once the sites were confirmed, the rSIV included training on Good Clinical Practice (GCP), study protocol, laboratory testing, and electronic data capture. Centralized monitoring and review of data were established.

**Results:** The remote site set-up strategy permitted effective site assessments, activation and monitoring. On-site monitoring and close-out visits were carried out after travel restrictions were lifted as per recommendations of the European Medicines Agency Guidance on the Management of Clinical Trials During the COVID-19 Pandemic.

**Conclusions:** An effective remote trial management strategy allowed the Seq&Treat project activities to take place successfully during the pandemic and limited delays in implementation. Data gathered during on-site monitoring and audits indicate that remote trial management did not compromise study protocol adherence or GCP compliance. Further, the experience offers learnings for future remote site setup activities that could be effective and efficient in similar circumstances.

### OA18-340-16 Effects of oral hygiene, food intake and patient characteristics on oral swab quantitative polymerase chain reaction results in South African patients with TB

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**Background:** Oral swabs (OS) have shown promise as novel patient samples for detecting *Mycobacterium tuberculosis* DNA. We evaluated the effect of oral hygiene (OH), food/drink intake (FD), and patients' characteristics on OS signal strength and sensitivity.

**Design/Methods:** One hundred sputum Xpert Ultra-confirmed TB patients were enrolled within 72 hours of TB treatment from clinics in Worcester. OS was collected over three days under three different OH and FD conditions.

OS was analysed by qPCR. Before sample collection, patients in Case 1 did not have FD or OH (OH-, FD-). In Case 2, OH was allowed but not FD (OH+, FD-). In Case 3, FD was allowed but not OH (OH-, FD+).

We compared the sensitivity of OS relative to sputum testing and mean Cq values under different conditions and patients' characteristics using a 2-sided paired t-test and linear regression.

**Results:** We are presenting results for 93/100 TB patients. At Cq=38 cut-off, OSA was positive in 68/93 patients (sensitivity 73.1%) for Case 1 (OH-, FD-), in

75/93 patients (sensitivity 80.6%) for Case 2 (OH+, FD-), and 70/93 (sensitivity 75.3%) for Case 3 (OH-, FD+). The Mean (SD) Cq value for Case 1 was 27.9 (4.2); Case 2, 28.4 (5.7); Case 3, 29.2 (5.1). Case 1 (OH, FD-) had a lower mean Cq (stronger qPCR signal) than Case 3 (OH-, FD+),  $p=0.03$ . Cq values did not differ significantly in other comparisons between Cases.

In the multivariate model, mean Cq was affected by: Diabetes Mellitus (DM) ( $p=0.01$ ) and night sweats ( $p=0.05$ ) in Case1. Within Case 2, Cq values were significantly higher (weaker signal) for DM ( $p=0.001$ ) and alcohol ( $p=0.02$ ).

**Conclusions:** Food/drink intake and oral hygiene did not affect the sensitivity of OS testing for TB; however, qPCR signal strength was significantly correlated with food/drink intake, DM, smoking, and drinking habits.

### OA18-341-16 Diagnostic accuracy of Xpert MTB/RIF Ultra and TrueNat in a high HIV and TB burden setting

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**Background:** Truenat is a molecular test endorsed by the World Health Organization (WHO) as a smear microscopy replacement test. It utilizes chip-based real-time PCR technology for *Mycobacterium tuberculosis* (*Mtb*) detection in sputum in less than 60 minutes.

**Design/Methods:** We evaluated the diagnostic accuracy of the Truenat MTB Plus (Plus), Truenat MTB Ultima (Ultima) and Xpert MTB/RIF Ultra (Ultra) tests for the detection of *Mtb* in sputum samples using sputum culture as a reference standard. We performed Truenat testing on biobanked sputum samples from 385 participants who had actionable culture, smear and Ultra results available. Adults (aged  $\geq 18$  years) self-presenting with presumptive tuberculosis symptoms were sequentially enrolled at Scottsdene and Wallacedene clinics in Cape Town, South Africa between March 2015 and February 2021.

**Results:** Ultima demonstrated higher sensitivity 85% (95% CI 78-90) versus 80% (72-86) and lower specificity 83% (78-87) versus 94% (90-96) when compared to Plus, regardless of HIV and smear status. Among PLHIV with smear-negative result, sensitivity point estimates were higher in Ultima compared to Plus 83% (63-93) versus 57% (34-74), and Ultra 83% (63-93) versus 79% (59-89). Ultima's overall specificity was lower than that of Ultra 83% (78-87) versus 95% (92-97) and Plus 83% (78-87)



versus 94% (90-96). However, the specificity point estimates for Ultima were higher among PLHIV than HIV-negative individuals.

**Conclusions:** Truenat assays met the WHO set minimal sensitivity threshold for sputum-based assays for smear-negative culture-positive TB with Ultima having higher specificity estimates in PLHIV. However, Ultima's potential decrease in specificity requires further evaluation.

### OA18-342-16 Alternative specimens for *M. tuberculosis* complex detection – feasibility of oral tongue swabs

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**Background:** Recent studies report the promising use of oral tongue swabs (OTS) for the detection of *Mycobacterium tuberculosis* complex (MTBC) for diagnosing pulmonary tuberculosis.

In this study, we aimed to investigate the feasibility of testing OTS compared to sputum on two automated WHO-recommended moderate-complexity molecular assays: cobas® MTB (Roche, Basel, Switzerland) and BD MAX™ MDR-TB (Becton Dickinson and Company, Sparks, MD, USA) in a clinical setting.

**Design/Methods:** We consented and enrolled 322 participants who met eligibility criteria at the Hillbrow Community Health Centre, Johannesburg, South Africa. Four OTS (collected either dry or in 1mL Tris-EDTA (TE) buffer) and four sputum specimens were collected per participant over two visits.

OTS collection was randomized at each visit and performed either before or after sputum collection. All specimens were transported at 2-8°C to the laboratory. Two swabs and a single raw sputum were tested on each assay and compared to the standard of care (SOC) Xpert Ultra (Cepheid, Sunnyvale, CA, USA). Ultra sputum semi-quantitative categories was also used as a guide for mycobacterial load.

**Results:** OTS yielded good but reduced detection on both molecular assays compared to sputum (Figure 1). Both molecular assays detected 75% (18/24) MTBC in OTS down to the Xpert Ultra sputum semi-quantitative “medium” category with some detection in the “low” category.

Collection and transport of OTS in TE buffer appears to offer better performance compared to a dry swab tested on BD MAX™ MDR-TB assay.

Preliminary results on the cobas® MTB assay demonstrates that there is no difference in MTBC detection between OTS collected before or after sputum.

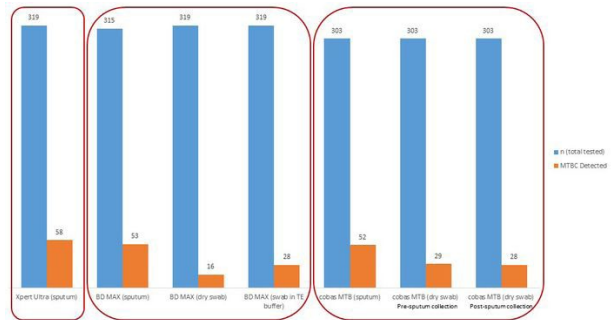


Figure 1. Summary of sputum and oral tongue swab results, per assay.

**Conclusions:** These preliminary findings indicate the feasibility of OTS testing on multiple molecular assays, but also suggest protocol optimization to improve MTBC detection especially in paucibacillary disease.

### OA18-343-16 Utility of whole-genome sequencing in the detection of fabG1 mutations for isoniazid resistance

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**Background:** fabG1 mutations are known to be associated with isoniazid resistance and can be detected through whole genome sequencing (WGS) or rapid molecular tests, though not routinely applied across all isolates. It is therefore necessary to await the phenotypic drug susceptibility testing (pDST) from the culture to determine if there is isoniazid resistance. We reviewed if WGS could provide additional benefit beyond routine pDST in detecting fabG1 mutations, and the impact on treatment.

**Design/Methods:** A retrospective review of all WGS results of MTC isolates carrying fabG1 mutations from 1 November 2020 to 31 October 2022, analysing the types of fabG1 mutations detected and comparing the timing of the WGS result to that of the pDST to examine which was detected first. For isolates where WGS preceded the pDST, we assessed if this led to a change in treatment.

**Results:** Out of approximately 3,900 isolates, 71 had fabG1 mutations. After excluding cases which had rifampicin and/or isoniazid resistance on molecular tests and additional mutations on WGS, 53 cases had solo fabG1 mutations. Two types of solo fabG1 mutations were observed, fabG1\_c.-15C>T (83.0%) and fabG1\_c.609G>A (3.8%).

Correlation with pDST for isoniazid resistance was 100%. Median duration of time to pDST (70 days; IQR 57-86 days) was significantly shorter compared to WGS (41 days; IQR 32-49 days) (p<0.01). WGS results preceded pDST for 5 isolates, while pDST results preceded

WGS for the remaining 48 isolates. For the 5 isolates where WGS preceded pDST, three had isoniazid stopped based on WGS, one died and one left the country. Median duration of treatment did not differ significantly (pDST:242 days; WGS 240 days). No relapse was observed.

**Conclusions:** Solo fabG1 mutations demonstrate 100% correlation with the pDST. A decrease in turnaround time for WGS can impact treatment by initiating a switch earlier to the appropriate regimen.

### OA18-344-16 Metabolomic analysis reveals potential biomarkers involved in TB

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**Background:** Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), continues to be a major public health epidemic around the world. Misdiagnosis and late detection of the disease increase the risk of *Mycobacterium tuberculosis* transmission and infection. Progress in controlling TB and mitigating its consequences can be expedited through early diagnosis and treatment.

**Design/Methods:** Patients and controls were recruited from Beijing Chest Hospital. This research was approved by the Ethics Committee of Beijing Chest Hospital, Capital medical university. All the methods and research protocol in this research were conducted by the Ethics Committee's existing guidelines.

We used the ultra-high performance liquid chromatography-quadrupole/exactive Orbitrap mass spectrometry/mass spectrometry (UPLC-Q-Exactive-Orbitrap-MS/MS) to provide a broader range of applications in TB diagnosis.

**Results:** In the study, urine from 40 cases of tuberculosis, 40 cases of pneumonia, 40 cases of lung cancer, and 39 healthy controls were collected. During the entire experiment, variables with VIP value >1.0, P value <0.05, and |FC| >1.5 were considered to be potential differential metabolites.

Based on the rank of the mean decrease in accuracy, we selected the top 10 metabolites in the urine data. In this study, we identified that compared with tuberculosis, the top 10 different metabolites in urine were in healthy control, pneumonia and lung cancer, with AUC values of 0.953 (95%CI 0.885-1), 0.959 (95%CI 0.863-1) and 0.921 (95%CI 0.772-0.988), respectively.

Here, MetaboName. 1-Methylnicotinamide, Mucic Acid, Glycolic Acid, Prolylproline, CDP were significantly different in tuberculosis compared to pneumonia, lung cancer and healthy controls.

**Conclusions:** Metabolomics is a valuable tool for discovering novel TB biomarkers, and we have identified a five-metabolite host biosignature that had accuracy to distinguish TB from lung cancer, pneumonia, and healthy controls. Further work is needed to optimize the model and understand the role of these metabolites in TB pathogenesis.

### OA18-345-16 The benefit of targeted next-generation sequencing for the treatment of patients diagnosed with drug-resistant TB in Eswatini

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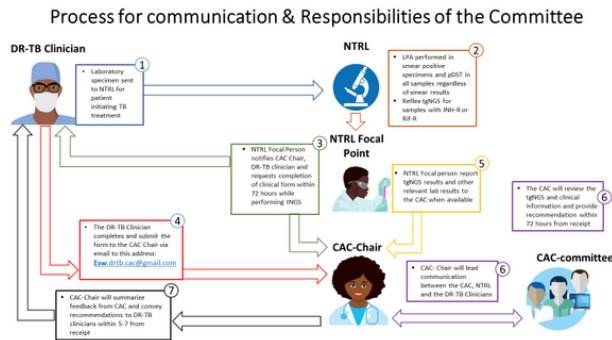
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**Background and challenges to implementation:** National TB Drug Resistance Surveys (TBDRS) conducted in Eswatini in 2009/2010 and 2018 revealed transmission of a rifampicin resistant (RR) *Mycobacterium tuberculosis* complex (Mtb) strain harboring the *rpoB* I491F mutation. This strain increased in prevalence from 30% in the 2009/2010 survey to 58% in the 2018 survey.

Current commercial molecular rapid diagnostics (MRD) and phenotypic drug susceptibility testing (pDST) by MGIT do not detect RR caused by this mutation, leading to a diagnostic gap and suboptimal DR-TB treatment.

**Intervention or response:** The Eswatini National Tuberculosis Program in collaboration with key partners implemented a pilot project, utilizing targeted next generation sequencing (tNGS) for molecular drug susceptibility testing (mDST) of clinical Mtb strains from November 2021 to December 2022. A clinical Advisory committee (CAC) was formed to guide optimization of treatment incorporating tNGS results. This team has clinical, laboratory and public health expertise. Terms

of reference, standard operating procedures, feedback templates and process flow algorithms were developed to guide the committee on interpretation and reporting of the mDST results.



**Results/Impact:** A total of 85 samples were sequenced and 61 RR strains were identified. Out of these, 38 (62%) had *rpoB* I491F mutation with 29 (76%) of the I491F strains having an additional resistance to Bedaquiline and Clofazimine. 40 cases were submitted to the CAC for treatment guidance. The mDST-guided treatment regimen was adapted for 14 (35%) of the 40 submitted cases. The interim outcomes of 40 DR-TB cases were 5 cured, 5 completed, 3 died, 1 loss to follow-up and 26 still on treatment.

**Conclusions:** Without using tNGS in DR-TB diagnosis in Eswatini, a substantial proportion of DR-TB cases would not benefit from an optimal treatment regimen. Detection of the I491F *rpoB* mutation and drug resistance mutations for new and repurposed drugs should be considered when developing MRDs. Newer medicines are needed, bedaquiline resistance is becoming more common.

## OA19 New Diagnostics in DRTB

### OA19-346-16 Two-stage TB diagnostics from a single sample at the point-of-care

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**Background:** An easy, decentralized, two-step molecular workflow could revolutionize DR-TB diagnostics in peripheral areas of high-prevalence countries. 1<sup>st</sup> step: Rapid detection of *M.tb* in clinical samples including genetic resistance markers of both Rif and Inh; 2<sup>nd</sup> step: targeted next generation sequencing (tNGS) for the determination of the complete resistance pattern. The assay should provide purified DNA for tNGS; so far, only centralized WHO-endorsed platforms do that, but are not suitable for small labs. To overcome these gaps, we demonstrate the concept of two-stage DR-TB diagnostics at the point of care (PoC) based on a single sample using a novel centrifugal-microfluidic cartridge (CMC) technology.

**Design/Methods:** qPCR detection of *M. tuberculosis* (*M.tb*) including Inh & Rif resistance markers is realized in a CMC run on the Rhonda qPCR cycler (Dialunox, Konstanz) developed for PoC testing. A geometrical multiplex qPCR design in ten integrated microchambers is applied. The CMC provides purified *M.tb*-DNA in a detachable sample vial. This is applied to Deeplex-tNGS (Genoscreen, France) for the determination of the resistance profile. The system was validated with sputum samples.

**Results:** The CMC and the two step diagnostic workflow are presented in figure 1. The assay uses centrifugal microfluidics to purify DNA and to mix it with PCR reagents. Proof-of-concept testing revealed an analytical sensitivity of 44.2 CFU/ml, a diagnostic sensitivity of 96%, and specificity of 100%. tNGS resistance profiling from purified DNA was successfully demonstrated. The complete diagnostic process chain takes two to three days.

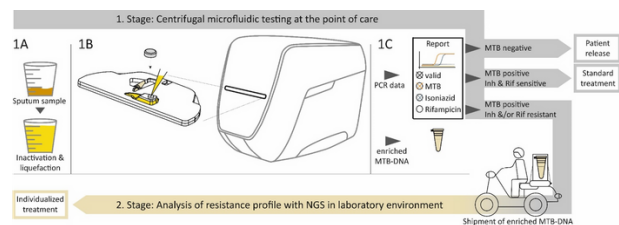


Figure 1: Two-stage TB diagnostic workflow based on a single sputum sample. Top: Centrifugal microfluidic testing at the point of care with 1A) sampling, inactivation and liquefaction of the sputum sample; 1B) sample transfer into the cartridge, followed by an automated sample preparation and qPCR analysis in the cartridge; 1C) qPCR data and a detachable sample tube containing enriched MTB-DNA as output, followed by the decision strands according to the results. Bottom: Shipment of the enriched MTB-DNA to a more centralized laboratory environment (right) followed by the generation of a comprehensive resistance profile via NGS.

**Conclusions:** We demonstrate a fully automated, centrifugal-microfluidic, geometric-multiplex qPCR-cartridge that could be applied at the PoC. It reliably detects *M.tb* and *Inh* & *Rif* resistance-markers. In a detachable micro-vial, it provides purified DNA of sufficient quality and quantity for downstream tNGS for the determination of the complete resistance profile.

### OA19-347-16 Pooled tongue swab testing for the diagnosis of pulmonary TB using Xpert MTB/RIF Ultra shows higher sensitivity than single swab testing

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**Background:** Pulmonary tuberculosis (PTB) diagnosis relies mainly on sputum examination. Acknowledging that sputum production can be challenging in sputum-scarce patients, alternative non-invasive oral sampling methods have been suggested. We aimed to determine whether pooled tongue swab samples (TSS) are an effective alternative to sputum samples (SS) for diagnosing PTB by Xpert MTB/RIF Ultra (Ultra).

**Design/Methods:** In a prospective study, sputum-smear microscopy (SM+) confirmed PTB patients were recruited in two TB Center of Conakry, Guinea. Eleven TSS and one additional SS were collected from each patient for Ultra testing at the National Reference Laboratory of Mycobacteriology in Conakry.

Ultra testing was done on a single TSS (1TSS), three pooled TSS (3TSS) and the additional SS. On a weekly basis, the following order of assigning sampled TSS to one of the test methods (1TSS/3TSS-Ultra), was alternated to minimize bias.

**Results:** From February to March 2023, 101 patients were recruited, of which 99 SM+ could be retained.

Among the 99 confirmed PTB patients, *Mycobacterium tuberculosis* (MTB) was detected by Ultra in 87 (87.9%) and in 91 (91.9%) cases respectively from 1TSS and 3TSS with 0.001 p-value while from sputum, MTB was detected in 96 (96.9%) cases.

The highest positivity grade for sputum was “MTB detected high” (n=31) with no “Trace” results, while for any TSS the maximum grading was “Medium” with majority having a “Low” result (n=56 for 1TSS and n=69 for 3TSS) and some “Trace” results.

Xpert MTB positivity grading from TSS appeared not to be associated with sputum-smear grading, opposite to sputum-Xpert MTB grading. The TSS positivity grade was not impacted by the sample swab number tested.

**Conclusions:** Our findings demonstrate that pooled TSS may reach a slightly higher sensitivity for Ultra testing compared to single TSS and that up to 10 TSS can yield MTB DNA.

### OA19-348-16 Applying COVID-19 technology to TB control: Rapid detection of *M. tuberculosis* DNA in oral swab samples using a fully automated, point-of-care molecular testing platform

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**Background:** Many people with tuberculosis (TB) cannot routinely produce sputum for testing, especially in community settings and at point-of-care (POC). We pioneered an alternative approach called oral swab analysis for TB (TB-OSA). In TB-OSA, the dorsum of the tongue is gently scraped with a disposable swab and the collected material is tested for *Mycobacterium tuberculosis* (MTB) DNA by quantitative PCR (qPCR).

To date, the most promising TB-OSA results have been generated by using manual, lab-based qPCRs. There remains a need for automated TB-OSA methods that can be implemented at POC and in community settings.

**Design/Methods:** We adapted the DASH (Diagnostic Analyzer for Specific Hybridization) COVID-19 testing platform (Minute Molecular Diagnostics, Inc.), to the task of detecting MTB DNA in oral swabs. DASH is rapid and explicitly designed for swab testing without manual liquid handling. It concentrates and purifies target DNA by hybridization-based capture, followed by qPCR. It is CLIA-waived and battery-powered.

For the present study, SARS-CoV-2 detection reagents in DASH were replaced with reagents for capturing and detecting MTB DNA.

**Results:** DASH consistently detected contrived samples with  $\leq 50$  MTB bacilli/swab, similar to manual and GeneXpert methods for TB swab testing. We then applied TB-OSA-DASH to clinical FLOQSwab samples (N = 30) collected from people with possible TB in South Africa.

The set included swabs from strongly TB-positive, weakly TB-positive, and TB negative donors. Blinded samples were tested using a very simple protocol in which swabs were placed directly into the DASH cartridge, followed by fully automated analysis (total time to result, 20 minutes).

Within this set, DASH detected 12/20 samples from people with TB and 0/10 samples from people without TB, nearly identical to the performance observed with manual qPCR methods (13/20 and 0/10, respectively).



**Conclusions:** With further optimization, TB-OSA-DASH could become an exceptionally user-friendly, POC platform for TB testing using oral swabs.

### OA19-349-16 Portable, battery-operated lab-in-tube detection of active TB and drug resistance

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**Background:** Tuberculosis (TB) remains a leading cause of global mortality, and despite the urgent need for accurate and reliable case identification, 4.2 million (39.6%) of active TB cases were missed in 2021 and only 57% of diagnosed cases are confirmed by gold-standard TB tests.

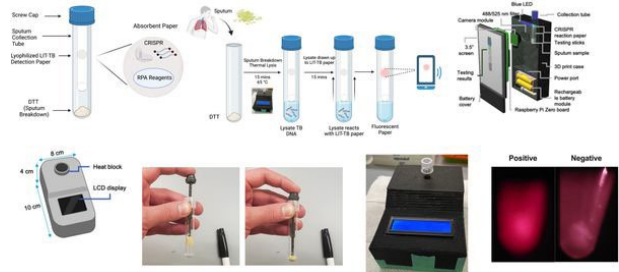
Rapid and reliable assays are needed at the point-of-care (POC) to accomplish TB diagnosis at sites of patient care and sample collection in resource-limited settings without the need for sample transportation, specialized personnel, and expensive, bulky equipment.

**Design/Methods:** Here, we develop a Lab-in-Tube TB (LIT-TB) diagnostic device: a low-cost, ultraportable, battery-operated device that mediates CRISPR-based TB diagnosis and drug-resistance detection in a single sputum collection tube. The lyophilized detection reagents do not require cold-chain storage or transportation and the smartphone readout allows for automated fluorescence intensity analysis and diagnostic result reporting. The complete protocol is performed in a single-tube, closed-system protecting users from TB contamination without the need for external power supply.

**Results:** The lab-in-tube and battery-powered device can diagnose TB infection and detect drug resistant mutations from patient sputum samples following a protocol

than can be performed without highly skilled technicians. Utilizing DNA isolation-free approach, the LIT-TB system displayed 89% sensitivity and 100% specificity in patient sputum samples.

With specific design of CRISPR gRNAs to detect SNPs, rifampicin-resistant mutation S450L of the *rpoB* gene is accomplished to inform clinicians on treatment choice.



**Conclusions:** The LIT-TB device is a lightweight, field-deployable microincubator and smartphone imager, that can be transported to sites of sample collection and performed by individuals with minimal training at the point-of-care.

We believe the enhanced portability and inexpensive equipment will improve accessibility to TB healthcare in developing countries.

### OA19-350-16 Quantitation of differentially culturable tubercle bacteria retrieved from tongue swabs improves detection of TB in people living with HIV

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**Background:** Historically, TB diagnosis relies on sputum as a testing sample but it can be difficult to produce, or may yield equivocal results in those with paucibacillary TB. Alternative specimen types, such as tongue/oral swabs, which are non-invasive, safer and easier to collect, has gained traction for TB testing in both adults and children with pulmonary TB, albeit with varied sensitivities. In this study, we aimed to assess the diagnostic utility of tongue swabs relative to sputum,

and also considered the contribution of differentially culturable tubercle bacilli (DCTB) that are missed when using routine clinical tests, to further improve diagnostic pickup.

**Design/Methods:** We performed a prospective study recruiting TB patients in primary healthcare settings in Soweto, South Africa. Sputum and tongue swabs from participants with Xpert MTB/RIF ultra or smear-confirmed TB were further tested using the Mycobacterial Growth Indicator Tube (MGIT) assay and the Most Probable Number (MPN) assay supplemented with growth factors to detect DCTB.

**Results:** From 89 eligible participants, 83 (93.3%), 79 (88.8%) and 66 (74.2%) were sputum positive by MGIT, Ultra, and smear respectively; tongue swabs had lower sensitivity with 39 (43.8%), 2 (2.2%) and 18 (20.2%) participants, respectively, for the same tests. DCTB assays provided a greater yield in sputum compared to tongue swabs with 82/89 (92.1%) and 36/89 (40.4%) positivity, respectively.

Interestingly, for tongue swabs taken from people living with HIV, DCTB positivity increased significantly relative to MGIT culture.

**Conclusions:** Our data demonstrate that while tongue swabs yield lower bacterial numbers for diagnostic testing compared to sputum, the use of growth supplementation can improve detection over standard MGIT culture, particularly in participants with TB and HIV coinfection.

### OA19-351-16 Evaluation of Deeplex-MycTB using clinical specimens in Japan

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**Background:** Targeted next generation sequencing (tNGS)-based *Mycobacterium tuberculosis* drug resistance prediction test kit, Deeplex-MycTB (Deeplex, GenoScreen), can predict resistance to 15 different anti-tuberculosis (TB) drugs using specimens from active TB cases in a few days. It is a promising management tool for drug-resistant TB patients. Using multidrug-resistant tuberculosis (MDR-TB) isolates in Japan, we showed that Deeplex could predict drug resistance with

high accuracy (The 52nd UNION World Conference, 2021). In this study, we evaluate Deeplex using clinical specimens in Japan.

**Design/Methods:** DNA is extracted from NALC-NaOH treated sputum from patients with active pulmonary TB and molecular drug susceptibility testing (DST) is performed using Deeplex. AMR predictions are compared with the results of phenotypic DST (pDST) using MGIT AST and whole genome sequencing analysis using Illumina sequencer.

**Results:** To date, 79 specimens are registered and 53 of them are completely tested. Deeplex could analyse all smear-positive specimens; 22 resistance-predicting single nucleotide variants (SNVs) are detected for Rifampicin (RFP), Isoniazid, Streptomycin (SM), Fluoroquinolone, and Ethionamide (TH), and discrepancies with the pDST results are observed in the prediction of RFP (*rpoB*: H445L) and SM (*gidB*: S70N) resistance. 34 SNVs with unreliable mutation information are detected, with 24 SNVs (70.5%) for TH. For smear-negative and  $\pm$  specimens, several SNVs with a few % variants are found, but all were judged susceptible by pDST.

**Conclusions:** Although Deeplex is highly useful tool, it also detects many SNVs of unknown susceptibility and the variant ratios of clinical relevance are unknown. Further studies are required using clinical specimens.

### OA19-352-16 Feasibility and acceptability of stool-based TB diagnosis: perspectives from healthcare providers in Manhica District, southern Mozambique

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**Background:** Stool-based TB diagnostics (SbTBD) are reported to contribute to increased rates of bacteriological confirmation in children and people living with HIV. However, there is a lack of evidence on perceived feasibility and acceptability of SbTBD in TB high burden

countries. Within the Stool4TB project, this study aimed to assess healthcare providers' (HPs) perspective on the feasibility and acceptability of SbTBD.

**Design/Methods:** A qualitative study was conducted across five health facilities and four communities within the Manhiça District (Mozambique). Twenty-one semi-structured interviews were conducted with HPs, from February 2022 to March 2023. The interviews were transcribed, coded, entered in a matrix and analyzed using the Diffusion of Innovation and symbolic power theories.

**Results:** According to HPs, the SbTBD can be suitable for diagnosis of TB in people who have difficulty in producing sputum, especially children; the approach is considered simple, non-traumatic, and feasible supporting sample capture across all age groups.

However, according to respondents, the acceptability of this technique might vary among the patients. Refusals might be due to delays in receiving assistance; lack of awareness about the technique; fear and disgust of touching stool; the association of stool with witchcraft and local beliefs about TB transmission.

On the other hand, acceptability could depend on: feeling obliged to comply with government recommendations; the experience and trust in the health services, and the expectation of being cured.

**Conclusions:** HPs view Stool-based TB diagnostics as a more advantageous approach in terms of feasibility compared to other diagnostic strategies, such as sputum-based approaches.

However, patient acceptability may be compromised due to existing health services challenges and perceptions about stool and TB. Acceptability could be promoted by the dissemination of information about the SbTBD, enforcement of awareness raising about TB and SbTBD, and increasing experience and trust in the health services.

## OA20 Meaningful engagement of CSO's in delivering quality TB services

### OA20-353-16 Engaging local stakeholders to co-develop gender-responsive community TB interventions

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**Background:** In Nigeria, men constitute over half of the people notified with TB, experience longer delays before reaching care, and are estimated to account for two-thirds of people who miss out on care. Reaching men earlier with TB services will likely reduce onward transmission in households, communities, and workplaces. The aim of this research was to co-develop a gender-responsive intervention for men in peri-urban communities in Nigeria.

**Design/Methods:** Between March and November 2022, we engaged 13 local TB stakeholders comprising TB programme implementers, survivors, and advocates in a participatory intervention design process involving two iterative cycles of Delphi research online, and an in-person workshop. In the first cycle, participants described the likely impact of 15 listed interventions. In the second cycle, they prioritized combinations out of nine high-impact interventions. We analyzed responses using a qualitative framework approach, assisted by NVivo software. We then facilitated stakeholder consensus on a preferred intervention package during a participatory workshop.

**Results:** Following the identification of key gendered challenges, a complex intervention package comprising three synergistic activities was developed (Figure). Intervention activities included: targeted awareness creation among men in communities; TB screening in male-dominated congregate settings; and the use of digital chest X-ray screening. Anticipated immediate outputs of the intervention included reduced TB-related costs and TB stigma, and improved TB knowledge, care-seeking, and diagnosis amongst men in Nigeria (Figure). Anticipated longer-term outcomes included increased TB case notification, health service access use, and improved socio-economic and clinical outcomes amongst men in Nigeria.

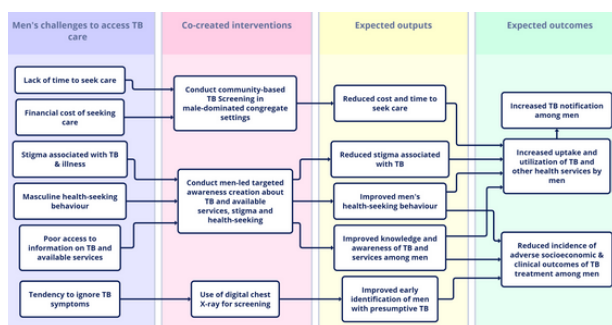


Figure: Change pathway for co-created intervention.

**Conclusions:** Engagement with local stakeholders yielded consensus on the design of a gender-responsive TB intervention for community settings in Nigeria. The intervention was perceived to be locally appropriate and suitable for future implementation and evaluation.

### OA20-354-16 Community health workers - an efficient last-mile delivery mechanism to improve diagnosis

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**Background and challenges to implementation:** In India, private health facilities providing TB care largely rely on x-ray for diagnosis. In Bhilwara and Nagaur, Rajasthan, mechanisms to link people seeking care in the private sector to public sector CBNAAT facilities do not exist and many people with TB are missed and lack microbiological confirmation of the disease, likely leading to both over and under diagnosis.

**Intervention or response:** In 2021 (July-Dec), we sensitized the private health facilities on the importance of microbiological confirmation and appointed 18 CHWs to act as a link between private health facilities and CBNAAT centres. CHWs collected sputum specimens from the private health facilities and transported them to the CBNAAT centres. CHWs also coordinated the timely examination of specimens and communicated results back to the private facilities and the persons seeking care to link to treatment.

**Results/Impact:** Before the intervention, in Bhilwara 27% of people with TB notified in the private sector (323 of 768) received any bacteriological test, 27% (209 of 768) were tested with a CBNAAT. During the intervention those figures rose to 77% (631 of 815) and 38% (308 of 815).

In Nagaur 12% of people with TB had any type of bacteriological test (49 of 411) and all 12% were tested with a CBNAAT before the intervention. During the inter-

vention, 49% of people with TB who were notified got a bacteriological test (202 of 416) while 33% (137 of 416) received a CBNAAT test.

**Conclusions:** Interventions that promote improved quality of TB diagnosis in the private sector are needed and can be highly successful. CHWs are a critical link between the accessibility gap between the services and the people needing them. CHWs can play a pivotal role in coordination between the private health facilities and the NTEP for the achievement of the goal of TB free India.

### OA20-355-16 Community accountability framework: Improving the quality of TB care and services in India by leveraging community action as an ally

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**Background and challenges to implementation:** The TB response in India has evolved over the years, in keeping with the ambitious National Strategic Plan, adopting a data-driven, multi-sectoral and community-led approach. National TB Elimination Programme (NTEP) calls for strong community participation, real-time feedback to the health system by communities and an increased focus in enhancing the quality of care and services.

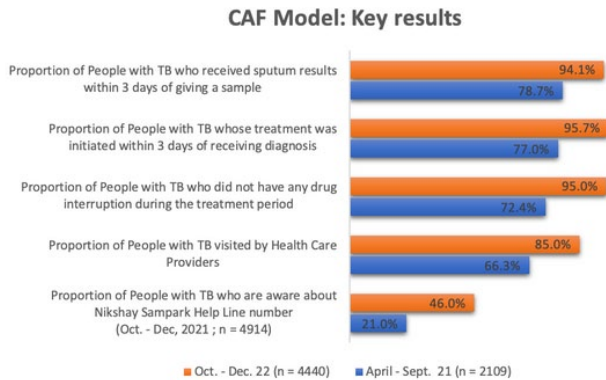
**Intervention or response:** The Community Accountability Framework (CAF) model implemented under the Accountability Leadership by Local communities for Inclusive, Enabling Services project by REACH, supported by USAID, is a community-led monitoring mechanism that focuses on result-based outcomes.

Currently being implemented in 139 TB Units across 15 districts of 4 states in India, TB Champions use a structured CAF tool, with questions on Quality of Care and Quality of Services parameters - timeliness, access, quality of information, attitudes of care providers, families and communities to get feedback from people with TB (PwTB). Identified gaps and challenges translate into Block Action Plans which are then discussed with NTEP and addressed, at the individual level or at the systemic level.

**Results/Impact:** The CAF process showed improvement in the indicators that can be attributed to the combined efforts of NTEP staff and TB Champions, in identify-



ing and addressing gaps at the family, community and health system levels. As in the graph below, over a period of 18 months, CAF has resulted in significant improvement in timely declaration of sputum results, early treatment initiation and regular drug intake.



**Conclusions:** The CAF model has shown for the very first time a combination of community-led monitoring along with a solution-based approach. The 18+ months of CAF implementation and joint efforts of community and program together have shown that a solution-oriented, bottom-up community-led monitoring approach can lead to tangible change and help foster an enabling environment for TB elimination in India.

**OA20-356-16 Supporting civil society organisations to develop strong organisational systems to implement quality health interventions**

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**Background and challenges to implementation:** Despite availability of sufficient evidence in favor of civil society organizations (CSO) strengthening for better outcomes and impact in the health sector; there is limited documented, standardized, systematic, and replicable process.

It is against this backdrop that Amref developed a dynamic and outcome based participatory process known as organizational development and system strengthening (ODSS) that emphasized on capacity development and organizational ownership through the support from Global Fund.

**Intervention or response:** Between May 2022 to March 2023, 1018 CSOs in 24 Counties were mapped and subjected to assessment using the organization capacity assessment (OCA) tool, out of which 851 organizations were selected and trained/mentored on ODSS.

The assessment and mentorship of the CSOs was based on nine thematic areas. Scoring, selection and performance was based on five broad categories including:

Embryonic, Emerging, Growing, Well developed and Mature. The aim was to identify CSOs who would advocate for and participate in quality community health service delivery.

**Results/Impact:** From the mapped CSOs, only 15% had annual implementation plans, while most relied on donor/county work plans. Financial procedures were in place for 45%, and 53% compiled financial reports only when required by third parties. CSOs lacked performance tracking systems, hindering assessment of intervention efficiency. Two thirds of CSOs lacked basic TB knowledge. Over 57% lacked funds and technical know-how for knowledge management, while sustainability was poor, with only 19% financially viable and over 90% reliant on a single source of funds. ODSS mentorships are ongoing to address these gaps.

**Conclusions:** The use of the ODSS approach revealed significant gaps in organizational capacity. There is ongoing mentorship to address these gaps. It is clear that building the organizational capacity of CSOs is crucial for them to efficiently utilize technical skills, implement project objectives, and achieve sustainability. Standardized and replicable processes, such as ODSS, can support this essential work.

**OA20-357-16 Tajikistan Ministry of Health invests in civil society organisations to improve TB outcomes**

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**Background and challenges to implementation:** In Tajikistan, social support for People with Tuberculosis (TB) (PWTB)—including counseling, home-based nursing care, subsistence packages, and one-off monetary support—forms an important aspect of case management and encourages adherence to treatment.

A recent decline in donor funding to civil society organizations (CSOs) to provide such services has left a gap in non-medical TB services.

**Intervention or response:** To address the gap, the USAID Eliminating Tuberculosis in Central Asia (ETICA) Activity and the National TB Program (NTP) advocated for the Ministry of Health (MOH) to pilot “social contracting” funding to a CSO in 2021. As a result, the MOH competitively awarded a grant of 80,000 TJS (around 8,000 USD) to the CSO Avesto.

Avesto used the grant to support 60 PWTB in 2022. In implementing the grant, Avesto worked closely with the Dushanbe city TB Center, which shared lists of patients on outpatient care, assisted in conducting a patient fo-

cus group to identify priority areas for social support, and helped Avesto with clinical aspects related to TB case management. Avesto's services to PWTB included psychological assistance, legal consultations, and home visits by social workers and volunteers.

**Results/Impact:** No interruptions in treatment were registered in Avesto's 60 person target group. In a 2022 MOH grant evaluation, Avesto earned high performance ratings. As a result, the MOH extended its contract with Avesto, allocating 160,000 TJS for provision of services to around 80 additional PWTB in Dushanbe city in 2023.

**Conclusions:** Successful implementation of the first grant resulted in allocation of additional state funds for provision of non-medical TB services. This is a significant first step in building sustainable government-CSO cooperation for improved TB care. Based on this initial experience, the MOH intends to increase its annual funding for TB social contracting, pending Ministry of Finance approval.

### OA20-358-16 Engaging civil society organisations in support for people with TB to improve treatment adherence in Kyrgyzstan

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**Background and challenges to implementation:** In Kyrgyzstan, the 2019 cohort treatment success rate was 81% for drug-sensitive TB and 72% for drug-resistant TB. The lost-to-follow-up rate was 18%.

Economic and social issues, such as financial or family problems, stigma, and neglect of health, make treatment adherence difficult.

Treatment interruption is one of the most significant challenges for the Kyrgyz TB program.

**Intervention or response:** The USAID Cure Tuberculosis project, led by JSI in collaboration with the National TB Program (NTP), implemented a person-centered approach to TB care in six pilot oblasts through primary health care (PHC) facilities, local civil society organizations (CSOs), and community leaders.

We designed patient support programs using targeted training and tools to build CSOs' capacity in psychosocial support and resource mobilization for TB patients at risk of treatment interruption.

Project-trained CSOs and over 30,000 community leaders provide food and hygiene packages, psychological and legal support, individual and peer-to-peer counsel-

ing, directly observed treatment and patient support group services, and local funding based on the specific needs of persons receiving TB care. These community-level interventions help people with TB adhere to treatment.

**Results/Impact:** Since 2020, we've helped over 2,100 people with TB. Of these, 91% showed improved treatment adherence: 47% completed treatment, 41% continue treatment with regular community-based support, and 3% with improved adherence continue treatment at a PHC facility without further need for assistance. Some former patients become volunteers to help the CSOs that provided them with psychosocial support to assist new TB patients at risk of treatment interruption.

**Conclusions:** Community-based treatment support for people with TB is crucial for person-centered care and an effective approach to addressing treatment adherence in Kyrgyzstan. This approach should be adopted nationally to improve treatment adherence and prevent treatment interruption.

### OA20-359-16 The Gujarat model to end TB through an innovative community participatory approach: A learning for public health programme in India

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**Background and challenges to implementation:** The National Tuberculosis (TB) Elimination Program is providing financial incentives to address malnutrition, however, its effective utilization by TB patients is uncertain and undetermined. To address social determinants such as malnutrition and social stigma, an initiative named Pradhan Mantri TB Mukta Bharat Abhiyaan (PMTBM-BA) was launched in India. With an objective to provide additional patient support, augment community involvement and leverage corporate social responsibility (CSR) activities, the state of Gujarat implemented three different models for ensuring doorstep delivery of nutrition kits to TB patients.

**Intervention or response:** To ensure social mobilization and community participation, a strong advocacy campaign was conducted by the highest level of state and district administration. An appeal was also made by the Minister of Health and Family Welfare to all the elected representatives for their active participation. This was followed by identification and sensitization of various stakeholders who were engaged as either

donors (Ni-kshay Mitra - NM) or procurement partner or distribution agency. The engaged NM provides nutritional support to the consented TB patients for a period ranging from six months up to three years based on the three models as described in the given figure.

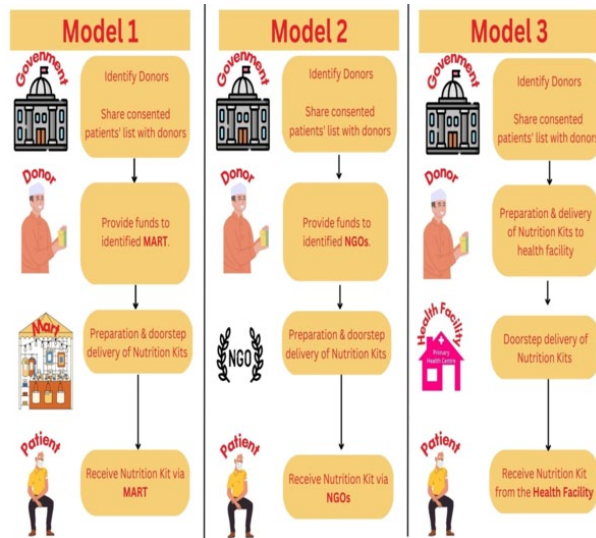


Figure. Gujarat model on community participation for nutritional support.

**Results/Impact:** The intervention led to nearly two-fold increase in overall engagement of NMs (from 1344 to 2353). The intervention also resulted in three-fold and two-fold increase in enrolment among corporates and elected representatives, respectively. Due to implementation of three different models, there was a huge leap in average monthly delivery of nutrition kits to TB patients (from 2730 to 9945).

**Conclusions:** This intervention demonstrated a self-sustaining model of doorstep delivery of nutrition kits to TB patients with effective collaboration and partnerships with different stakeholders. This model is easily replicable, addresses social stigma, reduces out of pocket expenditure, and promotes community participation.

### OA20-360-16 Increasing TB care-seeking behaviour through religious leaders in Nigeria: The critical role of non-clinical community stakeholders

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**Background and challenges to implementation:** Religion and faith are integral factors that influence lifestyles, attitudes and decision making. Many people trust religious leaders' (RL) opinions when making important decisions, including about their health. While other health areas regularly work with RL to promote health behaviours, the Nigeria National Tuberculosis Control Programme (NTBLCP) had not adequately engaged this group to bridge the gap between TB knowledge and case finding.

We examined the impact of engaging RL to improve TB awareness and generate demand for TB services in their places of worship.

**Intervention or response:** Beginning in 2020, Breakthrough ACTION Nigeria (BA-N) organized TB co-design workshops for Christian and Islamic RLs. The workshops addressed fears, myths and misconceptions about TB, equipped RLs with basic facts about TB (causes, transmission, symptoms, prevention) and invited the leaders to suggest the best strategies to engage their audiences, using their platforms to create awareness, reduce stigma, and encourage positive health seeking behaviours.

A simplified referral system was designed to facilitate referral of their congregants for TB tests.

**Results/Impact:** BA-N has engaged 1,500 RL in seven states. From January 2021 to December 2021, RLs reached 299,294 people with TB messages and referred over 12,906 people to health facilities for testing. BA-N started tracking positive TB cases in late 2021; from January 2022 to December 2022, 401,428 people were reached, 20,121 were referred for testing, out of which 585 were diagnosed with TB. The RLs have been making remarkable contribution to TB case finding in the country.

**Conclusions:** Enlisting religious leaders as advocates and referral agents in the End TB Strategy is a proven effective intervention. Their roles in changing norms and addressing stigma should be explored, while maintaining their current role of increasing correct knowledge of TB and facilitating referral for TB testing.

## OA21 Breathe Easy: Lung function and quality of life

### OA21-361-16 Causative agents of community-acquired pneumonia: A prospective multicentre cohort study from South Africa

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**Background:** *Streptococcus pneumoniae* and viral respiratory pathogens are generally noted as the most common organisms causing community-acquired pneumonia (CAP) globally. However, there is a paucity of data on causative agents of CAP in HIV- and TB-endemic areas. Furthermore, the rate of acute tuberculous pneumonia presenting as CAP is unknown.

We investigated the aetiology of acute CAP in ambulatory patients in Cape Town, South Africa.

**Design/Methods:** 334 symptomatic ambulatory participants were consecutively screened for ~14 months across 3 primary care clinics and one emergency room of a tertiary hospital. Only patients with mild to moderate CAP (those who did not meet hospital inclusion criteria) were enrolled. CAP was further defined as the presence of respiratory symptoms and appropriate signs within ≤14 days of symptom onset with or without infiltrates on a chest x-ray.

A multiplex polymerase chain reaction platform, the Biofire FilmArray Pneumonia *plus* Panel, was performed in combination with standard-of-care testing (gram stain and culture) and TB microbiology. Definite TB was defined as GeneXpert Ultra and/or TB MGIT culture positive.

**Results:** 209/334 fitted the definition of CAP. The most commonly detected organisms were *Mycobacterium tuberculosis* (n=66/209, 31.6%), *Haemophilus influenzae* (n=63/209, 30.1%), *Streptococcus pneumoniae* (n=22/209, 10.4%), *Moraxella catarrhalis* (n=10/209, 4.7%) and Coronavirus (6/209, 2.9%).

Those with acute TB were significantly younger (34(27-43) versus 45(33-56), p<0.001) and more likely to be living with HIV (28/69 [40.6%] versus 34/144 [22%], p=0.01). Polymicrobial infection was detected in 23/69 (33.3%) participants.

**Conclusions:** In endemic countries, and contrary to teaching and popular dogma, TB must be considered in the differential for CAP and when symptom duration is < 14 days. These data inform the diagnosis and management of CAP in resource-poor settings.

## OA21-362-16 Pulmonary function testing in healthy young Bangladeshi infants, a pilot study

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**Background:** Innovations delineating the impact of early life insults on the lungs are critical to understanding lung development and future pulmonary health. To date, paediatric pulmonary function tests (PFT) in low-income and middle-income countries have been hampered by a lack of expertise and suitable devices, and logistical challenges.

We sought to determine the feasibility of establishing an infant PFT laboratory in rural Bangladesh and report on the first 50 infants measured.

**Design/Methods:** A nested longitudinal birth cohort study at the Zakiganj Upazila Health Complex (UHC), a sub-district hospital, in the Projahnmo Research Foundation (PRF) surveillance area in the Sylhet District, Bangladesh, enrolled pregnant women in their second trimester and their offspring.

A PFT laboratory was established in November 2021 by experts with extensive experience in infant PFTs, who facilitated laboratory set-up and trained local staff. Infants enrolled in the birth cohort study were eligible for PFT measurements, including tidal breath flow-volume loops (TBFVL) and SF<sub>6</sub> multiple breath wash-out (MBW) using an Exhalyser D and accompanying Spiroware 3.3.1 software (EcoMedics AG, Duernten, Switzerland), and following American Thoracic Society/European Respiratory Society guidelines, at two and six months of age, from November 2021 until October 2022, during clinically defined natural sleep.

**Results:** Measurements from 50 infants were analyzed. 58% were male, mean age of 78.7 days (standard deviation (SD), 10.2), mean weight of 5.0 kg (SD 0.7), median height of 56.8 cm (interquartile range (IQR), 54.5-58.1), and median birthweight of 2.9 kg (IQR, 2.6-3.0). Environmental tobacco smoke exposure was frequent (48.9%).

Final TBFVL and MBW success rates were 94% and 96%. Repeat testing for unsuccessful measurements was required in 24%. Quality PFT results were obtained in those with successful tests (Table 1):

	Total cohort (N=50)	TBFVL: 47/50 (94%)	MBW: 48/50 (96%)
<b>General Demographics</b>			
Age (days)(Mean (SD), Range)	78.7 (10.2), 60-106	78.3 (1.04), 60-106	78.4 (10.3), 60-106
Gender (Male) (n/%)	29 (58)	29 (61.70)	29 (60.42)
Weight (kg) (Mean (SD), Range)	5.00 (0.77), 3.3-6.5	4.99 (0.73), 3.3-6.5	4.99 (0.75), 3.3-6.5
Height (cm) (Median (IQR), Range)	56.8 (54.5-58.1), 48.3-62	56.5 (54.5-58.1), 48.2-60.5	56.7 (54.6-58.0), 48.3-60.5
Mid-upper arm circumference (Mean (SD), Range)	12.4 (1.2), 9.5-14.3	12.4 (1.1), 9.5-14.3	12.3 (1.1), 9.5-14.3
<b>Birth and Social History</b>			
Gestational age (weeks) (Median (IQR), Range)	38 (33-39), 30-51	39 (33-39), 30-51	38 (33-39), 30-51
Birthweight (kg) (Median (IQR), Range)	2.9 (2.6-3.0), 1.4-3.7	2.8 (2.6-3.0), 1.4-3.7	2.9 (2.6-3.0), 1.4-3.7
Previously admitted (n/%)	1 (2.0)	1 (2.1)	1 (2.1)
Previous wheezing (n/%)	1 (2.0)	1 (2.1)	1 (2.1)
Underlying medical condition (n/%)	0 (0)	0 (0)	0 (0)
Environmental tobacco smoke exposure* (n/%)	22 (48.9)	20 (47.6)	22 (51.2)
<b>Pulmonary function Indices</b>			
Oxygen saturation (%) (Median (IQR), Range)	98 (97-99), 92-100		
RR <sup>1</sup> (b/min) (Mean (SD), Range)	42.93 (7.02), 30.30-61.86		
Vt/kg (Mean (SD), Range)	7.31 (1.32), 4.64-10.45		
TI <sup>3</sup> (s) (Median (IQR), Range)	0.68 (0.59-0.75), 0.51-0.90		
TE <sup>4</sup> (s) (Mean (SD), Range)	0.77 (0.15), 0.46-1.15		
TI/TE (Median (SD), Range)	87.30 (82.02-96.46), 69.02-142.76		
MTIF <sup>5</sup> (ml/s) (Mean (SD), Range)	49.35 (8.95), 27.83-65.53		
MTEF <sup>6</sup> (ml/s) (Median (IQR), Range)	50.98 (48.17-55.60), 31.25-82.35		
PTIF <sup>7</sup> (ml/s) (Mean (SD), Range)	66.30 (12.59), 37.27-89.21		
PTEF <sup>8</sup> (ml/s) (Median (IQR), Range)	73.30 (67.08-82.85), 44.23-121.25		
TPEF/TE <sup>9</sup> (Median (IQR), Range)	33.35 (29.36-37.99), 19.45-64.69		
FRC <sup>10</sup> (ml) (Mean (SD), Range)	84.1 (18.5), 50.6-124.6		
LCI <sup>11</sup> (Mean (SD), Range)	7.40 (6.65-7.86), 4.92-10.20		

\*Contact in same household; <sup>1</sup>Respiratory rate; <sup>2</sup>Tidal volume; <sup>3</sup>Inspiratory time; <sup>4</sup>Expiratory time; <sup>5</sup>Mean tidal inspiratory flow; <sup>6</sup>Mean tidal expiratory flow; <sup>7</sup>Peak tidal inspiratory flow; <sup>8</sup>Peak tidal expiratory flow; <sup>9</sup>Time to peak tidal expiratory flow as a percentage of the expiratory time; <sup>10</sup>Functional residual capacity; <sup>11</sup>Lung clearance index.

OA21-362-16 Table.

**Conclusions:** Establishing an infant PFT laboratory and performing quality TBFVL and MBW measurements in a rural population of young infants in Bangladesh is feasible.

**OA21-363-16 Factors associated with lung function differences in young adults in Karachi, Pakistan**

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**Background:** Most studies of lung dysfunction and chronic airflow obstruction (CAO) have been conducted among adults aged 40 years or older. The aim of this study was to determine the socio-demographic and environmental factors associated with differences in lung function in young adults in Karachi, Pakistan.

**Design/Methods:** A community-based cross-sectional survey was conducted in 75 randomly selected clusters in Karachi using an interviewer-administered questionnaire and post-bronchodilator spirometry among 919 adults aged 18 years or older. Post-bronchodilator forced expiratory volume in the first second to the forced vital capacity ratio (FEV<sub>1</sub>/FVC) was used as a proxy for CAO. Multivariable linear regression was conducted to identify factors associated with a lower FEV<sub>1</sub>/FVC.

**Results:** The mean (±SD) value of FEV<sub>1</sub>/FVC was 0.79 (± 0.07). Lower FEV<sub>1</sub>/FVC was associated with increasing age, illiteracy (-0.02, 95% CI: -0.03 to -0.004), mosquito coil use (-0.01, 95% CI: -0.02 to -0.002), increasing pack-years of smoking, a history of allergy (-0.02, 95% CI: -0.03 to -0.01) and family history of asthma (-0.02, 95% CI: -0.03 to -0.01), and being 'elementary worker' (-0.026, 95% CI: -0.046 to -0.006). People living in a house with a ventilated kitchen showed better FEV<sub>1</sub>/FVC (0.01, 95% CI: 0.002 to 0.02).

**Conclusions:** Several modifiable risk factors of CAO were identified in this study, which support the urgent need to implement measures to reduce tobacco smoking and eliminate common causes of indoor and workplace exposures.

## OA21-364-16 Lung function outcomes after TB treatment completion in Gambian children and adolescents

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**Background:** A growing body of evidence suggests that post-tuberculous lung disease (PTLD) significantly contributes to the burden of chronic pulmonary disease in adults. However, there remains limited knowledge about the sequelae of childhood pulmonary TB (PTB). This study aims to investigate the pattern and evolution of sequelae in children and adolescents aged 19 years and below following PTB *treatment completion or cure* in The Gambia.

**Design/Methods:** This is an ongoing cohort study where participants with microbiologically confirmed and unconfirmed, clinically diagnosed PTB are recruited after successful treatment and followed up for at least 12 months. At each study visit, we collect demographic and clinical data, including symptoms, spirometry, chest x-ray, and other relevant data.

The presented data collected at the time of recruitment after TB treatment completion show the prevalence and severity of associated lung function impairment using Global Lung Initiative (GLI) and American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines and reference standards.

Spirometry Variable	Total (N = 77)	Confirmed TB (n = 47)	Unconfirmed TB (n = 30)	P-value (from independent samples t-test)
FEV <sub>1</sub> z-score mean (SD)	-1.88 (1.47)	-1.79 (1.18)	-2.04 (1.84)	0.466
FVC z-score mean (SD)	-1.95 (1.37)	-1.91 (1.11)	2.04 (1.71)	0.690
FEV <sub>1</sub> /FVC ratio z-score mean (SD)	-0.10 (1.16)	0.07 (0.92)	-0.38 (1.42)	0.092
<b>Pattern of spirometry</b>				
Normal, n (%)	43 (55.8)	26 (55.3)	17 (56.7)	
Restrictive, n (%)	33 (42.9)	21 (44.7)	12 (40.0)	
Mixed, n (%)	1 (1.3)	0	1 (3.3)	

Table: Lung function parameters at the end of TB treatment stratified by prior tuberculosis status.

**Results:** Overall, 77/78 (98.7%) participants eligible for spirometry produced valid results. Among them, 40 (51.9%) were female, and the median age was 15.6 years (IQR: 12.0-17.9). The TB diagnosis was confirmed in 47 (61.0%) participants; 2 (2.6%) had multiple TB episodes, while 8 (10.4%) were HIV positive. Lung volume measurements (FEV<sub>1</sub> and FVC) showed mean z-scores that fell below the lower limit of normal, which is -1.64 (see table). Normal lung function was observed in only 43 (55.8%) of the participants, whilst 33 (42.9%) exhibited a restrictive pattern, and 1 (1.3%) had a mixed pattern of ventilation on spirometry.

**Conclusions:** Preliminary data from the ongoing *Childhood TB Sequel* study suggests that even after successful TB treatment, a large proportion of children and adolescents have impaired lung function. Early assessment and follow-up strategies for childhood TB survivors are imperative to enhance their health and well-being following TB treatment.

## OA21-365-16 Domains and items to standardise holistic health-related quality of life assessment for children aged 0-5 years with respiratory illnesses, including pulmonary TB

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**Background:** Morbidity, measured through the health-related quality of life (HRQoL), is a key policy-informing outcome. However, there is a lack of appropriate HRQoL measures for the youngest children (0-5-years-old) most affected by respiratory illness, including pulmonary tuberculosis, especially in low- and middle-income countries (LMICs).

We aimed to correct this gap by developing key domains and items within these to inform a disease-specific measure.

**Design/Methods:** We created an initial long list of domains (n=7) and items (n=110) from a previously completed scoping review. To refine the list, we completed a Delphi consensus review of this list among local and international experts (paediatric respiratory illness and health-related quality of life measurement; n=18).

We then conducted cognitive interviews with caregivers of children with TB, pneumonia, or bronchitis (n=30) in Cape Town, South Africa to further refine the list and item phrasing.

**Results:** Experts reached a consensus on all the items after two Delphi rounds. Experts' recommendations for refinement were related to 1) adjusting item wording to the developmental stages of the children by developing two versions of the measure; for 0-2-year-olds and 3-5-year-olds, 2) Using Likert-type response options, and 3) having a consistent recall period.

Overall, caregivers felt that the domains were appropriate and most items were easy to understand. An alternative phrasing for a minority of items was suggested (Table 1). Caregivers preferred 3-point, preference-based Likert scale response options and a recall period of in the preceding month.

Our final draft measures reflect these preferences with a 7-domain, 65-item version for 0-2-year-olds, and a 7-domain, 82-item version for 3-5-year-olds.

Symptoms participants found difficult to understand	Alternative phrasing from participants
Difficulties feeding	Difficulties eating
Wheezing	Chest making whistling noises
Upset stomach	Runny tummy
Loss of energy	Tiredness
Quality of life items participants found difficult to understand	Alternative phrasing from participants
My child was fussy	My child was difficult
My child was defiant	My child was naughty
My child was irritable	My child was impatient
My child was more withdrawn	My child was more distant

**Conclusions:** Experts and caregivers provided valuable input in developing version 1.0 of a holistic, disease-specific HRQoL measure for youngest children affected by respiratory illness, including TB from an LMIC context. Subsequent research will evaluate the psychometric properties of this draft measure.

### OA21-366-16 Health-related quality of life measures for children with respiratory illnesses - review and evidence synthesis

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**Background:** Limited data is available on HRQoL in young children affected by respiratory illnesses including tuberculosis (TB), especially in high-burden low- and middle-income countries (LMICs).

We charted the available measures and synthesized key components to inform better, standardized monitoring of this key outcome among young children with respiratory illnesses in LMICs, including TB and post-TB lung disease.

**Design/Methods:** We conducted a scoping review in PubMed, EBSCOhost, and PsycArticles databases.

Our keywords included a variation of the following terms ‘quality of life’, ‘health-related quality of life’, ‘wellbeing’, ‘questionnaire’, ‘instrument’, ‘measure’, ‘children’, ‘toddler’, ‘paediatric’, ‘child\*’, ‘develop’ or ‘validation’. We then applied thematic analysis deductively to organise the measures and synthesize cross-cutting components.

**Results:** After screening 1571 articles, we extracted data from 68 articles that reported on 37 discrete measures; 17 generic, 20 disease-specific. Key dimensions of existing HRQoL measures included physical health and functioning, emotional health, social support, and school functioning. Challenges to using existing HRQoL measures among children, <5-years-old with respiratory illnesses in LMIC settings are:

1. Age ranges that are often too old or do not map with disease burden needs,
2. A broad range of domains and items with inconsistent definitions,
3. Developmentally inappropriate domains and items,
4. Parent/caregiver or researcher proxy responses lacked standardization, and;
5. Challenges with cultural translation from higher-income countries from which the measures originated.

Five measures (4 generic; 1 disease-specific) had some validation for children <5-years-old, but these lacked detailed understanding of HRQoL in this age group.

**Conclusions:** There is an urgent need for a HRQoL tool in young children that is holistic, takes the developmental stages of young children into account and is suitable for use in low-resource settings.

### OA21-367-16 Quality of life among TB patients in Viet Nam: A longitudinal EQ-5D-5L study

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**Background:** Health-Related Quality of Life (HRQoL) is a patient-reported health outcome used to understand the impact of interventions, such as tuberculosis (TB) treatment. The aim of the study was to assess the HRQoL of TB patients in Viet Nam throughout their treatment phases.

**Design/Methods:** A longitudinal cohort study was used through consecutive recruitment of TB patients from four different cities across Viet Nam. EQ-5D-5L, a validated HRQoL instrument, was used to collect data at the beginning, middle and at the end of TB treatment. The Vietnamese EQ-5D-5L value set was used to generate the utility scores in the cohort.

**Results:** The study cohort included 467 patients, average age of 50 years old, 76% of them were men. A high percentage of TB patients reported problems at the begin-

ning of the treatment in most EQ-5D domains: Mobility, Usual Activities, Pain/Discomfort, Anxiety/Depression. Reported problems decreased significantly throughout the treatment phases in all these domains. The utility and VAS scores have also significantly decreased, reaching comparable values to the Vietnamese general population by the end of treatment.

		Start of treatment	Middle of treatment	End of treatment
Percentage of patients scoring problem in each EQ-5D dimension	Mobility	26,34%	21,84%	14,56%
	Self Care	7,92%	9,85%	7,28%
	Usual Activities	30,62%	23,34%	11,99%
	Pain/Discomfort	47,75%	41,54%	27,19%
	Anxiety/Depression	31,26%	26,12%	20,99%
Utility scores	Mean (SD)	0,85 (0,19)	0,87(0,18)	0,91 (0,17)
	Median (IQR)	0,91 (0,8;1)	0,93(0,84;1)	1(0,91;1)
VAS scores	Mean (SD)	68 (18,47)	70(16,8)	80 (15,36)
	Median (IQR)	70 (52;80)	70 (60;85)	80 (70;90)

EQ-5D, euroqol-5 dimensions instrument; IQR, inter-quartile range; SD, standard deviation.

**Conclusions:** TB treatment improved the HRQoL of patients in Viet Nam and decreased health concerns among them. However, problems with Pain/Discomfort and mental health need to be addressed beyond the treatment timeline. A utility score improvement of 0.06 could be attributed to completion of susceptible TB treatment; this value could be used in future health economic evaluations in Viet Nam.

## OA21-368-16 Integrated TB and lung cancer screening in Viet Nam

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**Background and challenges to implementation:** Lung cancer is the second leading cause of cancer-related mortality in Viet Nam, and lung cancer incidence is expected to increase substantially as Viet Nam's population grows and ages. We piloted an integrated service delivery model which uses computer-aided detection (CAD) software to indicate people who were initially

screened for TB in the community using chest X-ray (CXR), for further lung cancer screening using computerized tomography (CT).

**Intervention or response:** Between October 2022 and February 2023, CXR DICOM files were collected from TB screening events hosted in Ho Chi Minh City and Hai Phong and processed using qXR v3 CAD software (Qure.ai, India) in order to identify participants with potentially malignant lung nodules. These individuals were then contacted by pilot staff over the phone and were referred to a Provincial Lung Hospital for a CT scan to better assess the nodule's malignancy risk using the Lung-RADS classification system.

**Results/Impact:** 31,297 people initially assessed for TB had their CXR processed by qXR CAD software, resulting in the detection of 212 (0.7%) people with a potentially malignant lung nodule. Of those who were eligible, 59.0% were reached over the phone and verbally agreed to the CT referral. 91 CT scans were performed (72.8% of those agreeing), resulting in the detection of 19 people having malignant nodules with a Lung-RADS score of 4 or 5.

	Ho Chi Minh City	Hai Phong	Total
CXR screens for TB	29,999	5,527	35,526
Processed by qXR CAD software	27,702 (92.4%)	3,585 (64.9%)	31,297 (88.1%)
Eligible for a CT scan	152 (0.5%)	60 (1.7%)	212 (0.7%)
Agreed to participate	90 (59.2%)	35 (58.3%)	125 (59.0%)
CT scan performed	64 (71.1%)	27 (77.1%)	91 (72.8%)
Lung-RADS score $\geq 4$	12 (18.8%)	7 (25.9%)	19 (20.9%)

**Conclusions:** This pilot successfully established a model for early lung cancer detection through CAD-assisted CT referrals. Further research should be conducted on the reasons for refusal, in order to tailor outreach messages and enabler packages.

In addition, the CAD threshold for a potentially malignant nodule on CXR should be assessed in order to optimize yields among those referred for a CT scan.



## OA22 Nothing about us without us!

### OA22-369-16 TB stigma assessment in Ukraine

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**Background:** TB stigmatization is among the most significant social factors hindering equal access to the health care services for people with tuberculosis (PWTB), preventing them from seeking care and continuing treatment and resulting in poor health outcome and human rights violation.

Personal factors, family, health care, community settings and legal environment were studied to assess how stigma affects people-centered care in Ukraine being amongst the thirty countries with high MDR TB burden.

**Design/Methods:** Mixed-methods study was conducted June 2020-March2021 using StopTBP Partnership TB Stigma assessment guidelines adopted to Ukrainian context.

Representative sample of 1101 PWTB (36% female and 64% male), 45 PWTB family members, 43 community members and 248 health care workers (HCW) providing services to PWTB were interviewed with semi-structured questionnaires designed for each group to assess self-stigma, anticipated, perceived stigma at different stages of TB care pathway.

Data was collected remotely due to COVID-19 by trained PWTB interviewers; triangulated and analyzed using Qualtrics, MS Excel to present the aggregated stigma scale. Policy and law environment desk review was made and 15 stakeholders participated in 2 focus groups to validate law and policy environment stigma scale.

**Results:** 97% PWTB experienced self-stigma, which diminishes post-treatment but never gone. Self-stigma among women and elderly PWTB is higher. 39% PWTB reported stigma prevented them from entering TB care.

Anticipated stigma in community and health-care settings appeared to be high reaching 70% and 63% while PWTB reported stigma experience to be lower 11-19%. Anticipated stigma of HCW was leveled 63%, while 30% HCW experienced stigma. Harmful policy environment level was scaled 81% See diagram 1 for Stigma radar results.



Note: An indicator is assessed on a scale from 0 to 100%. The larger the radar web, the more likely PWTB will face barriers in seeking and accessing TB services due to stigma and discrimination.  
Diagram 1. Stigma radar in Ukraine

**Conclusions:** Rights-based TB awareness campaigns, PWTB empowerment and economic integration interventions should be developed to support people entering care. Legal environment improvement is needed to protect PWTB rights. TB stigma is a complex barrier to be addressed comprehensively.

### OA22-370-16 Prevalence and determinants of TB-related stigma experienced by nurses in Ghana: A cross-sectional survey

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**Background:** The nurses who care for tuberculosis patients often experience serious violations of their human rights due to stigma, which can make them vulnerable and negatively impact their mental health and productivity. However, the extent and determinants of this stigma in Ghana are not well known.

Therefore, this study aimed to estimate the prevalence of tuberculosis-related stigma and identify its determinants among nurses.

**Design/Methods:** To achieve this, a facility-based cross-sectional study was conducted involving 295 nurses who provide tuberculosis services in eight administrative regions. Nurses were selected using a systematic sampling approach and interviewed using semi-structured questionnaires. Logistic regression models were used to

establish the determinants of experienced tuberculosis stigma. The results were presented as odds ratios (OR) with 95% confidence intervals (CI) at a significance level of 5%.

**Results:** The findings revealed that overall, 57% (CI: 51%–63%) of nurses experienced high levels of stigma due to their work with tuberculosis patients. More than a quarter (26.1%) reported being avoided by health-care workers in other departments of the health facility, while nearly a quarter (23.7%) reported being gossiped about and 13.2% reported being verbally or physically abused.

The study also found that male nurses had a higher likelihood of experiencing tuberculosis stigma (OR=1.63; 95% CI: 1.02, 2.60), and being within the age group of 30 to 40 years increased the likelihood of experiencing tuberculosis stigma (OR=1.73; 95% CI: 1.07, 2.90).

**Conclusions:** This study highlights the high levels of tuberculosis-related stigma experienced by nurses in Ghana, with male and middle-aged nurses at a higher risk. To address this issue, stigma reduction interventions that are sensitive to gender and age should be implemented, monitored, and evaluated in health facilities and communities.

### OA22-371-16 Consequences of TB-induced self-stigmatisation on access to TB services among people with TB in Ghana

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**Background:** Self-stigmatization among individuals diagnosed with Tuberculosis (TB) is linked with negative health outcomes such as delay in seeking and following treatment. However, little is known about the extent of self-stigmatization and how situational factors affect access to TB services in Ghana.

Therefore, this study aimed to investigate the impact of TB-induced self-stigmatization on access to TB services in Ghana.

**Design/Methods:** This study employed a mixed-methods approach to conduct a cross-sectional study among 1,025 individuals who currently have or previously had TB across eight administrative regions in Ghana. Both quantitative and qualitative data were collected on self-stigmatization and its effects on access to TB services. The collected data were analyzed using descriptive statistics, logistic regression, and thematic analysis.

**Results:** Out of the people with TB or people who have had TB surveyed, 707 (69%) reported experiencing self-stigmatization due to their TB diagnosis. Of those who experienced self-stigmatization, 10.8% stated that it prevented them from accessing TB services.

Additionally, 51.3% of the participants whose access to TB services was limited due to self-stigmatization were female. Being female (adjusted Odds Ratio, aOR=2.28, 95% CI: 1.37, 3.78), having attained tertiary education (aOR=3.00, 95% CI: 1.26, 7.16), and living with HIV (aOR=3.09, 95% CI: 1.67, 5.71) were found to be significantly associated with limited access to TB services due to self-stigmatization. The thematic analysis revealed that self-stigmatization led to feelings of shame and the distancing of TB patients from others.

**Conclusions:** The study findings suggest that self-stigmatization negatively impacts access to TB services in Ghana. Interventions targeting female TB patients should be implemented to ensure they have equitable access to essential TB care services, without interference from their roles in the home. Furthermore, the importance of social support and health education among TB patients should be emphasized.

### OA22-372-16 Equity of access is a critical factor to consider for placement of rapid molecular TB diagnostics: Lessons from Zambia

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**Background and challenges to implementation:** Since the adoption of Xpert MTB/RIF as the first line diagnostic test in 2016, placement of GeneXpert machines in Zambia has prioritized test demand and disease burden. An integrated specimen courier system is available and complements the laboratory network to optimize access to Xpert testing. However, facilities in rural areas without road network, lower disease burden and those not connected to national electricity grid present questions of equitable access to Xpert testing. We assessed the diagnostic network to evaluate current coverage and identify approaches for further optimization.

**Intervention or response:** We profiled the diagnostic network and performed a spatial analysis to determine access and coverage of the current network. Data on test demand, GeneXpert utilization and machine functionality, and population estimates were used in a decision-making model to inform interventions to optimize access, improve population coverage and address the issue of equity of access to rapid molecular diagnostics.

**Results/Impact:** 47% of GeneXpert machines were concentrated in the three high burden provinces. Areas with more sparse road network have low coverage of GeneXpert machines. Only 44.7% of the population had access to a GeneXpert service facility within a 5km walking distance. With the inclusion of courier services pegged at a 35km distance to a GeneXpert service facility, only 75% of the population was covered.

**Conclusions:** Continued prioritization of disease burden and test demand is a barrier to achieving equity of access to molecular diagnostic services in Zambia.

Further efforts to optimize the diagnostic network should prioritize increasing population coverage, bringing the test closer to people in rural areas and including newer molecular tools, suitable for rural settings with lower test demand and poor electricity supply.

We argue that further investment is pivotal in providing equitable access to molecular diagnostics in rural settings and should address challenges with sparse road network and poor electricity supply.

### OA22-373-16 Activating law and human rights to end TB: An empirical assessment of the fulfilment of UN commitments by ten countries

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**Background:** The UN General Assembly held the first-ever High-Level Meeting on TB in 2018. In the Political Declaration, Heads of State made ambitious pledges to end TB by 2030. Among these were pioneering legal and human rights commitments on the right to health (para. 37), non-discrimination (para. 37), and access to medicines (para. 19). In 2020, the UN Secretary-General and WHO released reports examining countries' progress toward the UN pledges. They contain data for key targets, such as reductions in TB incidence and deaths, but they do not empirically evaluate progress toward the legal and human rights commitments.

This assessment begins filling this gap by evaluating over 150 legal instruments from ten countries with high DR-TB burdens.

**Design/Methods:** This assessment develops the TB UNHLM Legal Rights Index, a novel empirical methodology modeled on the UN Human Development Index. The Legal Rights Index measures countries' fulfillment of the TB UNHLM legal and human rights commitments. The TB UNHLM Legal Rights Indicator (LRI) is a country's overall score between 0 and 1 calculated from the arithmetic mean of its three UNHLM commitment indicator scores (right to health (RtH), non-discrimination (ND), and access to medicines (A2M)):  $LRI = (I_{RtH} + I_{ND} + I_{A2M}) / 3$ . The assessment evaluates constitutions, legislation, and executive branch directives in ten high DR-TB burden countries.

**Results:** None of the ten countries has fulfilled all three TB UNHLM legal and human rights pledges. The assessment produced four ranked indexes, including the overall TB UNHLM Legal Rights Index:

		Right to Health	Non-Discrimination	Access to Medicines	LRI
1	Russia	1.0	1.0	0.90	0.97
2	Vietnam	1.0	1.0	0.70	0.90
3	China	1.0	0.75	0.80	0.85
4	Indonesia	1.0	0.50	0.90	0.80
5	Philippines	1.0	0.35	1.0	0.78
6	DRC	1.0	0.25	0.60	0.62
7	India	0.75	0.10	0.95	0.60
8	Myanmar	1.0	0.25	0.50	0.58
9	Nigeria	0.75	0.35	0.55	0.55
10	Pakistan	0	0	0.50	0.17

**Conclusions:** Although none of the countries fulfilled all three legal and human rights pledges, several fulfilled one or two. These countries provide concrete examples of legal instruments that fulfill the TB UNHLM pledges.

Countries should consider constitutionally recognizing the right to health, explicitly prohibiting TB-based discrimination, and enshrining TRIPS flexibilities in intellectual property legislation.

### OA22-374-16 Tracking progress against United Nations High-Level Meeting targets in select countries in humanitarian crisis and supported through a regional Global Fund grant

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**Background and challenges to implementation:** The United Nations General Assembly (UNGA) will hold the second high-level meeting on the fight against tuberculosis in September 2023. Global leaders had met in the first such meeting in 2018 and resolved to "unite to End TB" and endorsed global targets to monitor progress and outcomes.

UNHLM indicator (2018-2022)	Iraq (% achievement) achievement/target	Jordan (% achievement) achievement/target	Lebanon (% achievement) achievement/target	Palestinian Territories (% achievement) achievement/target	Syria (% achievement) achievement/target	Yemen (% achievement) achievement/target
TB treatment targets (Notified and treated cases)	(57%) 31,297/55,100	(71%) 1,544/2,180	(77%) 2,551/3,300	(92%) 123/133	(118%) 15,081/12,800	(84%) 48,333/57,700
MDR-TB treatment target	(23%) 565/2,460	(14%) 15/110	(85%) 23/27	(150%) 3/2	(35%) 107/303	(27%) 248/908
Childhood TB (<=14 years) treatment targets	(57%) 2,443/4,300	(57%) 108/189	(114%) 243/213	(143%) 20/14	(111%) 1,114/1,000	(116%) 5,814/5,000
TPT targets <5 years household contacts	(74%) 7,717/10,390	Achieved 60 No target defined.	Achieved 398 No target defined.	Achieved 12 No target defined.	(144%) 3,278/2,270	(1%) 119/10,014
TPT targets >=5 years household contacts	(6%) 675/11,718	Achieved 497 No target defined.	Achieved 1,052 No target defined.	Achieved 166 No target defined.	(124%) 5,411/4,365	(1%) 134/17,574

OA22-374-16 Table 1: Achievement by MER countries against select UNHLM targets.

The Stop TB Partnership (STP) had detailed country-level breakdown of these targets to drive local commitment and progress and to facilitate monitoring.

**Intervention or response:** UN Migration Agency (IOM) has supported National TB Programmes in six countries (Iraq, Jordan, Lebanon, Palestinian Territories, Syria, and Yemen) categorized as ‘challenging operating environments’ through the Global Fund’s Middle East Response grant (MER), although the grant prioritizes essential services (prevention, diagnosis, treatment) and key affected populations: TB remains a public health threat in these countries, due to the context of humanitarian crisis, damaged health systems and limited or no domestic budgets for TB services.

We reviewed the Global TB Report 2022 to measure progress against select country-level targets set out by the STP. (Presented in Table 1)

**Results/Impact:** Overall, the six MER countries notified and treated 98,929 (75%) TB case including 9,742 children (91%) against UNHLM targets with Syria exceeding both targets despite the conflict. Yemen seems to have done well with children, while Iraq, with a significant TB burden has grossly underperformed in meeting the country’s UNHLM target. Only, one-fourth of the target MDR TB cases were notified across these countries.

**Conclusions:** Monitoring progress against UNHLM targets has helped identify gaps in TB service delivery in these countries. Achieving UNHLM targets was necessary in context of conflict, displacement, and humanitarian crisis settings to ensure ‘no one is left behind’. Differentiated approaches backed with additional funding are needed to help countries End TB.

### OA22-375-16 The future of TB after UN High-Level Meeting: a collaborative effort involving pandemic prevention, preparedness and response and universal health coverage

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**Background and challenges to implementation:** The second UNHLM on tuberculosis will be conducted in September 2023, following the first in September 2018. The COVID-19 pandemic showed how TB platforms and interventions can serve any other airborne pandemics and reminded the country of the significance of a health system with primary health care as a foundation that can ensure reaching UHC. During 2020-2021 tuberculosis was one of the most severely impacted programs, with about 1.6 million TB deaths globally in 2021

**Intervention or response:** The COVID-19 pandemic has disrupted the majority of TB services in Indonesia as most of its resources were allocated for COVID-19. The DR-TB hospitals with isolation were being used for COVID-19 isolation, healthcare workers in primary level focused on tracing the COVID-19 cases, and the community were unable to provide its full service due to mobilization restrictions in the country.

Despite the disruptions observed in 2020, TB case notification in Indonesia exponentially increased from 54% in 2021 to 74% in 2022. The presidential decree 67/2021 on TB Control, enables the TB program to have a multisectoral approach and secure support from ministries and institutions other than health. Based on lessons learned from COVID 19 response, the government increased the active case finding in/at the primary level, strengthened the monitoring network, and implemented

a public private partnership approach and managed to diagnose and treat 635.840 people with TB in 2022, a record number

**Results/Impact:** TB is the oldest airborne pandemic and the investments in TB response during COVID-19, demonstrating how an investment in tuberculosis may contribute not just to the TB program, but also the goal of universal health care and prepare the country for pandemic or emergency scenarios.

**Conclusions:** Ensuring access for all people to quality diagnosis, treatment and care is the key to achieve all TB, UHC and PPPR targets.

### OA22-376-16 Supporting access to COVID-19 vaccination and other health-related services among internally displaced persons in Ukraine during the war

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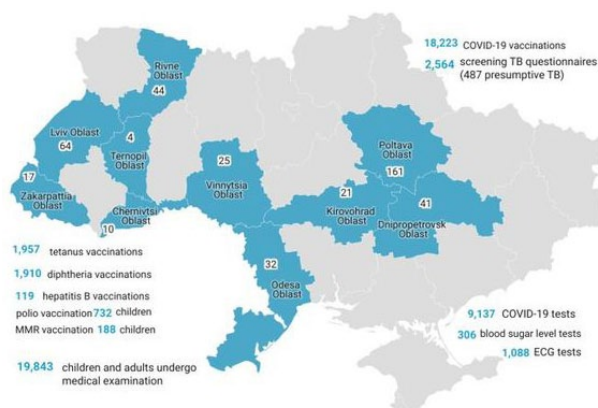
**Background and challenges to implementation:** Russia's military intervention in Ukraine came at the peak of the wave of COVID-19 caused by the Omicron strain. War significantly impeded COVID-19 pandemic control. For example, the number of new cases and vaccination history were no longer being monitored.

In addition, the health system, including primary health care, screening, and immunization programs, is strained by large numbers of internally displaced persons (IDPs). According to the IOM, at the end of August 2022, nearly 16 % of Ukraine's population (7 million people) were internally displaced.

**Intervention or response:** Support TB Control Efforts in Ukraine (STBCEU) project responded to these war-related challenges by organizing field visits to IDP shelters and dormitories to provide COVID-19 testing, vaccination, and other health services. The field visits were conducted by multidisciplinary teams (MDTs) consisting of representatives from the Regional Centers of Diseases Control and Prevention, epidemiologists, primary health care providers, and infection diseases doctors. The MDTs conducted risk assessments, provided information on infectious disease prevention in temporary shelters, COVID-19-specific prevention measures, and vaccination.

**Results/Impact:** From March 25, 2022, to February 28, 2023, MDTs conducted 419 visits in Poltava (161), Lviv (64), Rivne (44), Dnipro (41), Odesa (32), Vinnytsia (25), Kirovohrad (21), Zakarpattia (17), Chernivtsi (10), and Ternopil (4) regions. A total of 36,209 people received health-related information, including information on COVID-19 prevention and vaccination. 18,223 persons (50.3%) received COVID-19 vaccinations during the

visits. Specific services provided during these visits depended on the region but generally included: COVID-19 vaccinations, tetanus vaccinations, diphtheria vaccinations, and medical examination, and other patient-specific services.



*Figure. Number of field visits to IDP locations and services provided, March 2022 - February 2023.*

**Conclusions:** The MDTs approach increased access to COVID-19 vaccination among IDPs as well as enhanced access to medical services in conditions of limited medical care. This approach could be used in the de-occupied territories where many medical facilities have been destroyed.

## OA23 Validation of diagnostics

### OA23-377-16 Validating the WHO-integrated treatment decision algorithms for pulmonary TB in high-risk children from three African countries

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**Background:** The World Health Organisation (WHO) endorsed integrated treatment decision algorithms for childhood tuberculosis (TB), including two new algorithms with and without chest x-ray (CXR). However, these have not been externally validated, especially among high-risk children (<2 years old, children living with HIV [CLHIV], or with severe acute malnutrition [SAM]).

**Design/Methods:** We included data on children under 2 years, CLHIV, or with SAM enrolled in prospective pulmonary TB (PTB) diagnostic cohorts in South Africa, Uganda and The Gambia. Clinical data were collected, and CXR, HIV and TB microbiological testing (Xpert MTB/RIF Ultra and culture) performed. Children were classified according to NIH consensus definitions, and a TB treatment decision score calculated based on Algorithm A (with CXR) and B (without CXR). A score >10 was defined as PTB; we determined diagnostic accuracy according to composite (CRS) and microbiological reference standards (MRS).

**Results:** We included 385 children with presumptive TB: 87.3% were <2 years, 23.1% were CLHIV, and 21.3% had SAM. 17.4% had Confirmed TB, 53.0% Unconfirmed TB and 29.6% Unlikely TB. 42.1% had a known

TB exposure, where the algorithms recommend treating for PTB without requiring a clinical/radiological score. Of these children, 15.4% were classified as Unlikely TB. Compared to the CRS, sensitivities of Algorithms A and B were 92.6% and 94.8% respectively, and specificities 24.6% and 11.4%. Diagnostic accuracy was similar among children <2 years old, CLHIV, and children with SAM. By following the algorithm and excluding children with TB exposure, sensitivity decreased and specificity improved, albeit minimally for Algorithm B (Table 1), with a further reduction in sensitivities when Xpert was disregarded (representing settings where Xpert is unavailable).

	Composite Reference Standard <sup>a</sup>				Microbiological Reference Standard <sup>b</sup>			
	Algorithm A (with CXR)		Algorithm B (without CXR)		Algorithm A (with CXR)		Algorithm B (without CXR)	
	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)
<b>Overall (n=385)</b>	92.6 (88.8-95.4)	24.6 (17.0-33.5)	94.8 (91.5-97.1)	11.4 (6.2-18.7)	98.5 (92.0-99.9)	14.8 (11.1-19.2)	98.5 (92.0-99.9)	8.2 (5.4-11.8)
<b>Children under 2 years (336/385)</b>	93.6 (89.7-96.4)	24.8 (16.7-34.3)	95.3 (91.8-97.6)	10.9 (5.6-18.7)	98.3 (90.9-99.9)	14.1 (10.2-18.7)	98.3 (90.9-99.9)	7.6 (4.8-11.4)
<b>Children living with HIV (89/385)</b>	89.4 (79.4-95.6)	21.7 (7.4-43.7)	95.5 (87.3-99.1)	13.0 (2.8-33.6)	91.7 (61.5-99.8)	14.3 (7.4-24.1)	100.0 (73.5-100.0)	7.8 (2.9-16.2)
<b>Severe Acute Malnutrition (82/385)</b>	90.0 (79.5-96.2)	22.7 (7.8-45.4)	96.7 (88.5-99.6)	13.6 (2.9-34.9)	93.3 (68.1-99.8)	14.9 (7.4-25.7)	100.0 (100.0)	7.5 (2.5-16.6)
<b>Excluding children with TB exposure (n=221)</b>	85.7 (78.6-91.2)	31.8 (22.3-42.6)	90.2 (83.9-94.7)	14.8 (8.1-23.9)	97.0 (84.2-99.9)	24.5 (18.5-31.3)	97.0 (84.2-99.9)	13.3 (8.8-19.0)
<b>Excluding children with TB exposure, disregarding Xpert result (n=221)</b>	78.9 (71.0-85.5)	32.9 (23.3-43.8)	87.2 (80.3-92.4)	15.9 (9.0-25.2)	75.8 (57.7-88.9)	26.1 (19.9-33.0)	93.9 (78.2-99.3)	15.4 (10.6-21.4)

Table 1. Diagnostic Accuracy of the World Health Organization Integrated Treatment Decision Algorithms among High-Risk Children from South Africa, Uganda, and the Gambia.

<sup>a</sup> Accuracy based on a composite reference standard of Confirmed or Unconfirmed TB vs. Unlikely TB according to NIH consensus definitions.

<sup>b</sup> Accuracy based on a microbiological reference standard.

**Conclusions:** WHO integrated treatment decision algorithms have high sensitivity but very low specificity for PTB, likely leading to over-treatment if consistently applied. Further study of algorithm implementation and modifications to increase diagnostic accuracy is required.

### OA23-378-16 Evaluation of the Lung Flute ECO to assist in sputum collection among people with presumptive TB: A randomised cross-over trial

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**Background:** The Lung Flute ECO is a low-cost, self-powered, oscillatory positive expiratory pressure (OPEP) device. We evaluated the performance of the Lung Flute ECO to aid in sputum collection in people with presumptive tuberculosis, who often have difficulties producing adequate sputum for diagnostic testing.

**Design/Methods:** This randomized, two-period cross-over study assessed the efficacy and tolerability of the Lung Flute ECO at eight hospitals in Cameroon from March to May 2022.

In intervention A, participants received 3 minutes of video instruction on sputum collection for TB testing in one of four languages.

In intervention B, participants were provided with the Lung Flute ECO device together with video instruction. Participants were randomised 1:1 to sequence A-B or sequence B-A. The primary outcome was the proportion of people who produced sputum >1mL, as assessed by a blinded external reader.

**Results:** 1,271 people were randomly assigned, 1,172 completed both interventions, and 1,097 had data available for inclusion in the primary analysis. A sputum volume of >1mL was obtained from more participants after the use of the Lung Flute ECO only versus after video instruction only (117/1,097 (10.7%) vs 46/1,097 (4.2%); OR 2.6, 95% CI 1.9-3.7, p<0.001; Table 2); in addition, sputum was collected from 78.6% (862/1,097) of participants by both interventions.

Among 212 people reporting ≤1 symptom, 13.2% (28/212) produced >1mL sputum after the use of the Lung Flute ECO versus 4.7% after video instruction only (OR 3.0, 95% CI 1.4-6.5, p=0.006). New symptoms or symptom aggravation events after use of the Lung Flute ECO were mild and rare (<8% of participants), and participants reported satisfaction with the use of the device.

**Conclusions:** More people to be evaluated for TB were able to produce >1mL sputum for diagnostic testing after the use of the Lung Flute ECO versus after video instruction only, and the device was well-tolerated.

### OA23-379-16 Integrated TB and COVID-19 community intervention, a tool for improved TB case detection and COVID-19 vaccine uptake - the Bauchi State (Nigeria) experience

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**Background:** Tuberculosis remains a major global public health problem with a current data showing that everyone living in The Gambia is at risk of contracting TB with an incidence rate of 149 case per 100000 as of 2021, however there is still significant undetected cases within the country. Close TB contacts are generally at greater risk.

The study aims to advance understanding in predicting progression time and diagnosis of early active TB disease and the need for preventive actions.

**Design/Methods:** In this ongoing prospective study, we are recruiting individuals aged between 12 and 70 years who are close contacts with a recently diagnosed TB patient (within 6weeks) from greater Banjul and following them up for 60 weeks. A three-monthly study contact session is made to check for TB symptoms and signs.

At the baseline visit, chest x-ray, sputum culture (MGIT) and GeneXpert ultra is collected to confirm /rule out TB. In subjects who were diagnosed with PTB, time to TB diagnosis was measured as time in days from date of first study visit.

**Results:** Among the 421 participants enrolled in the study from July 2021, 184 (43.7%) were male and 237 (56.3%) were female. A preliminary result of 11(2.6%) were found to turn positive within the study timeframe with an overall mean diagnostic time of 216.6days and SD of 161.62. From the 11, 2 were prevalent cases. However, 9 (2.1%) were found to be living with HIV and 1 out of the 11 positive TB (9%) lives with HIV which was among the fastest to turn positive.

**Conclusions:** The study from exposure to active disease is a corner stone to inform decision for policy as the population is in continual risk.

The most important finding is with those living with HIV having a turnover of 107 days with a need for prophylaxis isoniazid among them.

### OA23-380-16 Clinical and microbiological predictors of TB disease in children – a multi-centre prospective study in low- and middle-income countries

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**Background:** Diagnosis of TB disease in children, relying on non-specific clinical and radiological features, remains an obstacle to reduce associated mortality. Current WHO-recommended Treatment Decision Algorithms (TDAs) are based on low certainty of evidence.

**Design/Methods:** RaPaed-TB was a multi-centre prospective diagnostic validation study including five countries. Children (<15 years) with presumptive TB provided at least two (induced) sputum samples at enrolment and one nasopharyngeal aspirate if <5 years. Standardised microbiological, radiologic, and clinical data were used to define TB status, following published consensus criteria for diagnostic studies.

**Results:** Of 976 children enrolled, 842 met criteria for diagnostic classification with 28.4% (239/842) being microbiologically confirmed TB [46.0% (110/239) by both Xpert®/MTB/RIF-Ultra (Ultra) and culture, 18.0% (43/239) by culture only, and 36.0% (86/239) by Ultra only; 26.4% (63/239) were confirmed by Ultra Trace alone. Of all participants, 34.6% (293/842) were unconfirmed TB and 37.3% (316/842) unlikely TB. Microbiological yield was 44% (239/ 532) amongst those with TB. Children with confirmed TB were older (6.2 years [IQR 1.8-1.6] vs 4.8 years [IQR 2.1-7.2]), with lower weight-for-length (<5 years)/BMI-for-age (>5 years) z-scores (-0.6 [SD 1.6] vs -0.1 [SD 1.5]). Symptoms were similar amongst all groups. The confirmed group had higher prevalence of positive Tuberculin Skin Tests (TSTs) (61.2% [134/239] vs 41.9% [125/315]) and chest radiograph (CXR) consistent with TB compared to unlikely TB (45.2% [108/239] vs 13.0% [41/315]).

Regression analysis supported an associations between confirmed TB and TST-positivity (OR 6.36, 95% CI 3.52-11.50), CXR-findings attributable to TB (OR 2.57, 1.33-

4.97), and number of symptoms (OR 1.27 per symptom count, 1.05-1.52). On multivariate binomial regression, older age (RR 0.56, 95% CI 0.35-0.89), positive TST (RR 0.42, 0.27-0.65), or CXR consistent with TB (RR 0.52, 0.32-0.84) remained significantly less likely for children confirmed by Trace alone.

**Conclusions:** This is one of the largest cohorts described in recent years, with high rates of microbiological confirmation and findings reflecting the well-described symptomology of paediatric TB.

This data can be used to inform the development of novel TDAs and externally validate currently recommended TDAs.

### OA23-381-16 Utility of point-of-care C-reactive protein in HIV-positive adult inpatients screened for TB

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**Background:** WHO has endorsed C-reactive protein (CRP) as a screening tool for outpatient tuberculosis (TB) in adults living with HIV. The role of inpatient CRP screening after testing for urine lipoarabinomannan (LAM) has not yet been established.

**Design/Methods:** We determined the utility of the Nycocard point-of-care (POC) CRP assay as a TB screening test in HIV-positive adult inpatients enrolled on the PROVE TB study in KwaZulu-Natal, South Africa.

Participants were symptomatic, over the age of 16 years, hospitalised for <72 hours at enrolment and on anti-TB therapy for <48 hours. All were screened with the Alere urine LAM test. TB was defined as a positive Xpert-Ultra, culture or LAM result.

**Results:** 831 patients were screened and 471 met inclusion criteria (median age 41.3 years (IQR 33.5; 50.2); median CD4 count 158 cells/microL (IQR 40; 427). 53.5% were male; 49.2% were taking antiretroviral therapy, and 5.1% tested COVID-19 positive. 54 (11.5%) tested urine LAM positive. 70 (19.5%) were diagnosed with TB (5 on LAM only), and 83 (16.6%) were started on empiric therapy.

Median CRP (IQR) was 170 (73; 200) mg/L for confirmed TB, 120 (40; 200) mg/L for empirically treated TB, and 56 (18; 153) mg/L for those without TB (p < 0.0001). Median CRP was higher for LAM positive TB than LAM negative TB (199 [IQR 133; 200] vs. 132 [IQR 33; 198] p = 0.004). The negative predictive value (NPV) was >90% at three POC CRP cut-offs, irrespective of urine LAM status (Table).



		Including LAM positive	Excluding LAM positive
CRP ≥50 mg/L	Sensitivity	0,80 (0,69; 0,88)	0,68 (0,53; 0,81)
	Specificity	0,44 (0,39; 0,50)	0,44 (0,39; 0,50)
	Negative predictive value	0,91 (0,86; 0,94)	0,92 (0,88; 0,95)
CRP ≥30 mg/L	Sensitivity	0,90 (0,81; 0,95)	0,81 (0,67; 0,91)
	Specificity	0,33 (0,28; 0,39)	0,33 (0,28; 0,39)
	Negative predictive value	0,94 (0,88; 0,97)	0,93 (0,88; 0,96)
CRP ≥10 mg/L	Sensitivity	0,97 (0,90; 0,99)	0,95 (0,83; 0,99)
	Specificity	0,19 (0,15; 0,24)	0,19 (0,15; 0,24)
	Negative predictive value	0,97 (0,88; 0,99)	0,97 (0,88; 0,99)

Table: Performance of POC CRP as TB screening test: Confirmed TB vs. Not TB.

Conclusions: POC CRP may have a role in ruling out further TB testing after initial urine LAM testing.

### OA23-382-16 Yield and operational challenges of including urine LAM testing in intensified TB case-finding among outpatients with HIV: Experience from the TB-SCRIPT trial

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**Background:** Scaling-up urine lipoarabinomannan (LAM) as a confirmatory TB test may improve outcomes among outpatient PWH undergoing intensified case-finding (ICF). However, distinguishing positive Grade 1 from negative tests can be difficult, and misinterpretation can lead to inappropriate initiation of anti-TB therapy. We assessed the benefits and challenges of LAM testing among PWH undergoing ICF.

**Design/Methods:** TB SCRIPT is an ongoing randomized trial evaluating point-of-care C-reactive protein (CRP)-based TB screening among ART-naïve PWH attending four clinics in Uganda (ClinicalTrials.gov NCT04557176).

We performed TB screening (CRP or symptom-based), and confirmatory TB testing (urine LAM ± sputum Xpert [Ultra], if indicated) on participants who screened positive by their randomization assignment (CRP ≥5mg/L or ≥1/4 symptoms).

LAM tests were interpreted by two nurses using a standard reference card; positive results were later reviewed by a TB lab expert who made the final determination using the same reference.

We determined the:

1. Proportion of screen-positives diagnosed with TB by LAM and Ultra,
2. Days-to-treatment initiation for LAM and Ultra, and;
3. Proportion of ‘positive’ LAM tests re-classified as negative.

**Results:** Of 871 participants who screened positive (53% female, median 33 years-old, 55% with pre-ART CD4+ <200 cells/μL), 862 (99%) underwent LAM testing, and 793 (99.6%) underwent Ultra testing after a negative LAM result. Overall, 147 (17%) were diagnosed with TB, including 66 (7.7%) by LAM (37/66 [56.1%] Grade 1) and 81 (9.4%) by Ultra. Nine (24%) Grade-1 positive LAM tests were re-classified as negative by the expert reader. LAM-positive participants initiated anti-TB treatment earlier than Ultra-positive participants (0 vs 1 days, p<0.001).

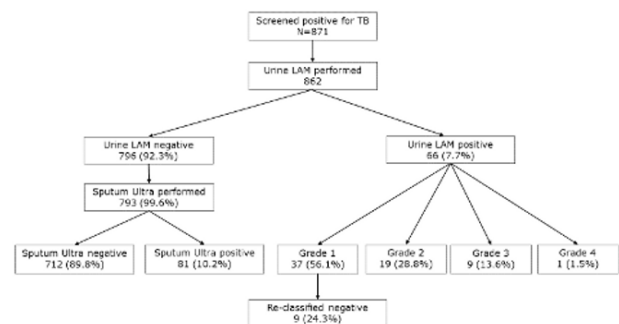


Figure. Time to TB treatment initiation: LAM 0 days vs Xpert 1 day, p<0.001.

**Conclusions:** Although LAM detected more than one-third of PWH with active TB, 24% of Grade-1 positive LAM tests were re-classified as negative after expert review. LAM can improve TB/HIV outcomes by shortening time-to-treatment initiation, but careful interpretation of Grade 1 results is required.

### OA23-383-16 Integrated TB and COVID-19 community intervention, a tool for improved TB case detection and COVID-19 vaccine uptake - the Bauchi state experience

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**Background and challenges to implementation:** The outbreak of coronavirus (COVID-19) pandemic came with a negative setback on TB care and prevention. Progress made in the years up to 2019 has slowed down and global TB targets are off track (WHO, 2022 TB report). This makes TB stakeholders to explore innovative ways to increase TB case detection in the countries with

high burden and reduce the cause of death by TB infection. In a bid to mitigate this twin challenge, KNCV Nigeria through funding from USAID adopted a strategy of integrating TB community screening and Covid-19 vaccine intake in hard-to-reach communities.

**Intervention or response:** KNCV Nigeria is currently implementing a twin USAID funded projects TB LON region 1&2 and Glovax project. To improve TB case detection and increase Covid-19 vaccine coverage in Bauchi state an integrated community intervention was adopted where mobile teams were constituted leveraging on the existing structure of community TB outreaches. The mobile team were segmented into two; Covid-19 vaccination team and TB screening team. These activities were carried out simultaneously in the field when a person is vaccinated for Covid-19.

**Results/Impact:** During the period of the intervention from July 2022 to October, 2022 a total of 5,948 persons were screened for TB, 1,649 presumptive identified, and 87 TB cases diagnosed after implementation. And a total of 201,139 people were vaccinated. Following the intervention, there was a 108% increase in the TB case finding as shown in the chart below.

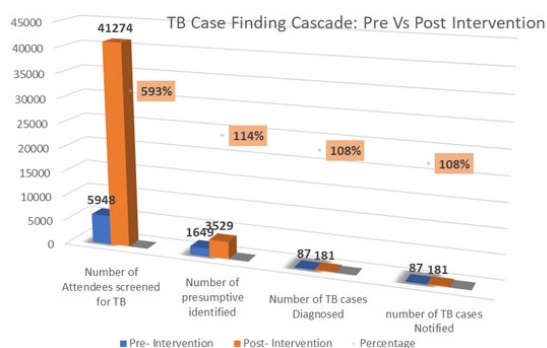


Figure: Cascade of integrated Covid - 19 /TB case finding in Bauchi state from July to October 2022.

**Conclusions:** It is recommended that to improve Covid-19 vaccine uptake and TB case detection in hard-to-reach communities the integration of Covid-19 vaccine and community TB screening should be adopted and sustained.

## OA23-384-16 Enhancing diagnostic accuracy of slide microscopy using MagnaSlide: Preliminary results from a study in Chennai, India

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**Background:** Despite the roll-out of molecular diagnostics, sputum smear microscopy remains the first-line test for the majority of people with presumptive TB. In 2022, smear microscopy, a test with ~50% sensitivity compared to culture, was used to diagnose approximately two-thirds of people with TB globally. We evaluated the effectiveness of MagnaSlide, a low-cost (~USD 2/test) microscopy-based proprietary polymer technology in improving the performance of smear microscopy.

**Design/Methods:** MagnaSlide, a microscopy slide with proprietary polymer technology acts as a sample concentration tool for smear microscopy. From May to December 2022 (study ongoing) at an infectious disease lab in Chennai India, sputum samples were collected from people living with HIV and tested using GeneXpert (GX) MTB/RIF Ultra.

Thereafter, de-identified samples were tested using traditional smear microscopy, and MagnaSlide smear microscopy; results were compared. The lab technicians were blinded to patient identifiers and GX results.

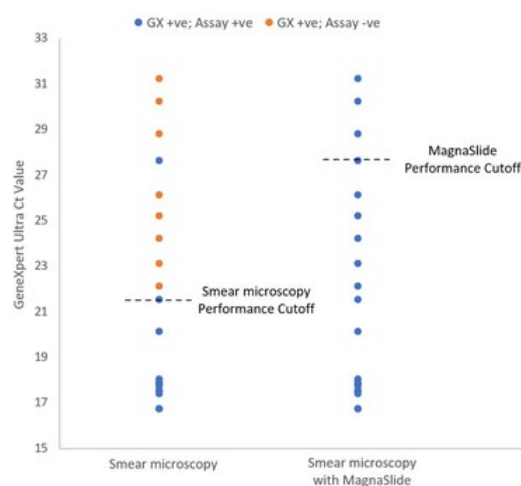


Figure. The distribution of Ct values for 23 of 25 positive samples are plotted on number lines. The lowest rpoB Ct values from GeneXpert Ultra are used. Smear microscopy has a performance cutoff at ~Ct 21.5 corresponding to ~10k CFU/mL. While the MagnaSlide has a performance cutoff at ~Ct 27.6 corresponding to ~500 CFU/mL (Chakravorty et al., 2017)

**Results:** Among sputum samples from 58 unique patients, 25 were identified as GX-positive, and 33 were GX-negative. 15 (60%) samples were smear-positive. Smear microscopy with MagnaSlide detected all 25 GX positives (100% sensitivity) and correctly identified all negative samples (100% specificity); cycle threshold (Ct) values ranged from 16.7 (high load) to 31.2 (low load).

**Conclusions:** The MagnaSlide is a low-cost sustainable solution that improves the sensitivity of smear microscopy, which could be pivotal to the elimination of TB given the reliance on smear microscopy globally for the diagnosis of TB.

## OA24 Changing policies through advocacy and community based interventions

### OA24-385-16 Using the lived experience of an HIV-TB clinician to reduce stigma, inspire patients and create demand for TB services

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**Background and challenges to implementation:** Stigma associated with TB affects people infected negatively with many experiencing stigma and shame because of the disease. Many end up hiding and failing to seek early care, support and treatment; which often leads to preventable deaths and increased new infections. The problem could be common among health service providers who get infected with TB, with many unable to use their lived experiences to help their patients and others infected with TB have better treatment outcomes.

**Intervention or response:** Between 1988 and 2003 I suffered from TB, including MDR-TB five times. After being treated successfully, I realised that as a TB survivor, I could use my lived experience plus my knowledge as a clinician to inspire others live positively, take their medicine with good adherence and have better treatment outcomes.

**Results/Impact:** At the beginning many people did not accept me as one of them; another TB survivor and a person living with HIV (PLHIV). However, when they realised I had gone through what they were going through, it gave them courage, hope and inspiration to live positively as they went through the treatment.

The act of sharing my experience with others also helped me overcome self-stigma, which I had at the beginning. As I endeavored to explain the cause, effects and treatment of TB to others in a bid to empower them; I realised I no longer lived in fear, shame and did not need to hide the fact that I am a PLHIV and a TB-survivor.

**Conclusions:** TB survivors, especially health care providers with lived experiences should be supported and if able and willing to be open; they should be helped to acquire advocacy and communication skills, which they could use to create demand for TB services if we are to realise the TB goal of reducing TB deaths by 2030.

### OA24-386-16 Improving linkage and retention of multidrug-resistant TB patients through differentiated service delivery and community engagement: a case of Namisindwa District, Uganda

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**Background and challenges to implementation:** In November-December 2022, Magale Health Centre IV (HCIV), in Namisindwa district diagnosed twenty (20) multi drug resistant (MDR) Tuberculosis (TB) patients through TB hotspots outreaches in Bumbo and Bukokho sub-counties. When the first four of these patients were taken to Mbale regional referral hospital, 49Km away, for treatment initiation, two of them ran away within three days. Community members were scared of being diagnosed with MDR TB and being taken away from their community for treatment.

Uganda Protestant Medical Bureau with funding from USAID through the Local Service Delivery for HIV/AIDS Activity (USAID/LSDA) adapted community interventions to improve linkage and retention of the MDR TB patients.

**Intervention or response:** Multi-stakeholder meetings were held with the Ministry of Health, Namisindwa district health leadership, political leaders, community opinion leaders and health managers from Bungoma community in Kenya. Community dialogue meetings were held to sensitize the community on MDR TB. An MDR TB satellite clinic was set up at Bumbo HCIII, at the centre of hotspots. Health workers at Bumbo HCIII were trained in management of MDR TB. Contact investigations were conducted. The two patients at Mbale RRH were transferred back to their community to continue treatment at the new satellite clinic.

**Results/Impact:** All the 20 (100%) MDR TB patients accepted to be started on treatment at the satellite clinic in their community. Even the 2 patients who had escaped returned to care. All patients have been retained in care to-date.

**Conclusions:** Setting up a community satellite clinic and community dialogue meetings improved linkage and retention of patients on care. Multistakeholder engagement with consistent public health information messages increases MDR TB service uptake and reduces stigma.

### OA24-387-16 *Jan Andolan* for TB Elimination (People's Movement for TB Elimination), India

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**Background and challenges to implementation:** Under-nutrition is a known risk factor for active tuberculosis infection. On September 9, 2022, the Indian Government launched a novel initiative “*Pradhan Mantri TB Mukh Bharat Abhiyan*” – a people's movement, to bring together citizens to provide people affected by TB with increased nutritional, diagnostic, and vocational support.

**Intervention or response:** The PMTBMBMA initiative invites individuals and organizations to register as “Ni-kshay Mitra”. Ni-kshay Mitras can choose to provide people with TB with food baskets, diagnostic, and vocational support. Each Ni-kshay Mitra can choose the geography and number of TB clients for a period ranging from 6 months to 3 years.

The National Programme conducted a nationwide drive to get consent from active TB clients for community support through Ni-Kshay Mitra. Community stakeholders were also registered as Ni-Kshay Mitras, who were then linked by the programme to TB clients.

While the initiative is led by the Government of India, technical support for the rollout of the program was provided by USAID through the TIFA Project implemented by JSI Research & Training Institute, Inc.

**Results/Impact:** From Sept'22 to March'23, >75000 Nikshay Mitras were registered who were linked to >1 million TB clients, which amounted to >96% of the consented TB clients. The Ni-kshay Mitras, comprised of 49,567 individuals, 1249 corporations, 6657 political parties and elected representatives, 2675 NGOs, 780 co-operatives, and 8910 other institutions. Together, these donors donated 470,000 food baskets to 334,437 people affected by TB.

**Conclusions:** This ambitious and innovative crowd-sourcing TB nutrition and support initiative of Indian government is showing excellent promise. It has gener-

ated tremendous response, raised TB awareness, contributed to the reduction in stigma, and led to better nutrition and improved treatment outcomes among people with TB. Though still in its early days, this initiative can be replicated in other high burden countries to achieve the *End TB* goal.

### OA24-388-16 The role of civil society in the Universal Health Care Law of the Philippines: challenges, impact and opportunities

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**Background and challenges to implementation:** In 2019, the Philippines passed a landmark legislation that aims to provide universal health care (UHC) services to all its citizens and reform the country's health system. The approval of the Law has been largely popular among policymakers and the public. However, prior to its passage, civil society observed that discussions only centered on the financing and curative aspect of the health system. Knowing that there is a high political support for public health measures, civil society groups mobilized to put forward to Congress a people's UHC proposal to ensure government accountability and a whole of society action to achieve UHC.

**Intervention or response:** In 2017, upon learning that a Universal Health Care (UHC) bill is being prioritized by Congress, civil society mobilized to discuss a comprehensive proposal that will ensure that UHC is pro-people, achievable, and sustainable.

Civil society did the following to improve the UHC bill:

1. Conduct learning sessions on the concept of UHC,
2. Consultation meetings with stake holders on the existing challenges and what solutions work,
3. Dialogue with government officials from the Department of Health and the Office of the President,
4. Advocacy with legislators,
5. Engagement with the media, and;
6. Participation in the crafting of the implementing rules and regulations.

**Results/Impact:** The active involvement of civil society resulted to inclusion of key provisions to the UHC Law such as representation of CSOs in various UHC-related offices such as the health technology assessment council and funding of 1% of the total health budget for health promotion.

**Conclusions:** Civil society is an important sector in bridging the gap between the government and its people in policy discussions. It is instrumental in bringing the policy discussion closer to communities, facilitate dialogues with the government, and ensure that critical mechanisms that allow citizen participation are enshrined in a policy.

### OA24-389-16 The impact of war-related challenges in Ukraine on the capacity of the National TB Programme: Is it possible to ensure TB care continuity?

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**Background:** In 2022, the National TB Program of Ukraine (NTP) faced unprecedented challenges related to the war: the destruction of facilities, active hostilities, temporary occupation, migration, and limited funding. According to the World Health Organization's forecasts, war can cause the anticipated loss in progress toward ending TB not only in Ukraine but in the European Region.

**Design/Methods:** Since the beginning of the war, the NTP has constantly been monitoring war-related challenges, making operational decisions, and periodically conducting online surveys of the TB centers' management.

**Results:** 475 (4 %) people with TB have become internally displaced, about 300 (2,5 %) people with TB may remain in the temporarily occupied territories, 152 (1,2%) people with TB remain abroad, and almost 12,000 (96,3 %) people with TB in Ukraine receive TB medical care. Out of 25 regional TB centers coordinating TB response at the regional level, only 8% (2 facilities ) do not provide complete services, and 4% (1 Luhansk center) have been relocated to another region.

Among the main war-related challenges identified by the TB centers' management: 44% (11 centers) are related to complicated logistics and transportation, 40% (10 centers) to migration, and only 20% (5 centers) complain about the lack of staff.

The NTP, with the support of WHO EURO, has created all possible conditions for the continuity of TB care: data exchange on people with TB between regions and with doctors abroad has been established; recommendations for responding to urgent problems have been implemented; regulations have been updated by the latest WHO research; and intersectoral cooperation has been introduced.

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**Conclusions:** The most significant challenges were the direct destruction of infrastructure and migration processes among people with TB. Several measures allowed the NTP to coordinate the TB response and ensured the sustainability of the TB response across the country.

### OA24-390-16 Transitioning funding of TB care to sustainable social health insurance: An implementation case study from Vietnam

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**Background and challenges to implementation:** TB care in Vietnam was funded by the national program of targeted diseases until July 2022, when funding moved to social health insurance (SHI). This integrated TB within the health system and required major policy updates.

In Vietnam, TB care is managed at district facilities, but people obtain medicine at commune health stations (CHS). Many district-level TB facilities were not

eligible to provide SHI TB care due to their classification as “preventive” facilities, while drug dispensing at community-level CHS was at risk due to unclear guidance. We aimed to ensure continuous care at all levels of the health system.

**Intervention or response:** Throughout 2021, we provided national-level policy assistance for guidelines specifying SHI requirements: facility classification, staffing, service integration, and procedures for prescribing and dispensing TB drugs. We provided technical assistance through 2022 in seven provinces comprising provider trainings, facility checklists, tools, and convening meetings of health authorities. In December 2022 we supported the MoH to issue additional guidance on dispensing SHI covered TB drugs at CHS and coordinated local health and social security agencies.

**Results/Impact:** By July 2022, 98/99 (99%) district facilities in seven provinces met criteria and began billing SHI for first-line TB drugs; in the first quarter 76.2% (4,071/5,344) of DS-TB drugs in these provinces were dispensed using SHI and this rose to 84.4% (3,831/4,541) the following quarter. By December 2022, the remaining facility met criteria and dispensed TB drugs using SHI. Drug dispensing under SHI at commune level took more time and effort; four out of seven supported provinces were dispensing TB drugs at CHSs by year end, ranging from 17%-43% of CHS.

Province	July - September 2022			October - December 2022		
	# people initiating DS-TB treatment	# people who received DS-TB drugs using SHI	% of DS-TB drugs dispensed using SHI	# people initiating DS-TB treatment	# people who received DS-TB drugs using SHI	% of DS-TB drugs dispensed using SHI
An Giang	1,724	1,540	89.3%	1,295	1,157	89.3%
Can Tho	690	11	1.6%	576	336	58.3%
Dong Thap	687	520	75.7%	636	463	72.8%
Nghe An	565	552	97.7%	477	471	98.7%
Tay Ninh	750	600	80.0%	644	550	85.4%
Thai Binh	377	363	96.3%	377	363	96.3%
Tien Giang	551	485	88.0%	536	491	91.6%
<b>Total</b>	<b>5,344</b>	<b>4,071</b>	<b>76.2%</b>	<b>4,541</b>	<b>3,831</b>	<b>84.4%</b>

Table. Provision of DS-TB drugs using social health insurance in 7 provinces of Vietnam, July - December 2022.

**Conclusions:** Moving TB funding to SHI is the pathway towards sustainable universal health coverage for Vietnam. Support and coordination at the national and grassroots levels is key for continuous, accessible, affordable care during a funding transition to SHI.

## OA24-391-16 A strategy to engage ethnic minority populations in the design of TB education materials

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**Background and challenges to implementation:** Ethnic minority communities in Viet Nam often lack access to localized information sources, as many do not speak Vietnamese, and vernacular languages are not taught in schools. This can lead to healthcare access barriers.

**Intervention or response:** This intervention engaged four ethnic minorities to develop a package of TB education materials which could be used for advocacy, education and participant mobilization for active TB case finding. Ethnic minority communities were selected based on demographic statistics and willingness of local healthcare facilities.

Draft education materials in Vietnamese were shared with the Directors of four Provincial Lung Hospitals for their comments on the accuracy of the TB information. Clothing and background settings were developed for a series of cartoon characters to best reflect the communities they represent.

Focus group discussions were conducted whereby key populations were asked, “Describe who this person is?” Based on their perceptions, the materials were modified. We engaged the Provincial Committees of Ethnicity Minority Affairs to finalize the content.

**Results/Impact:** Materials were developed for people in the H’mong, La Hu, Co Tu, and Gia-Rai communities. Final materials included a TB handbook and animated videos. Voice overs were completed in the vernacular languages by Provincial Television and Radio Stations’ professional broadcasters.

These materials were then used by community advocacy volunteers in 49 villages in remote, mountainous communities to sensitize community members about TB and

to refer them for TB screening. Ultimately, 20 people were diagnosed with TB from these referrals, leading to a detection rate of 8,065 per 100,000 people screened. This value is 45x higher than Viet Nam's national incidence rate.



Figure. The characters featured in printed and animated communications materials for four ethnic minority groups in Viet Nam.

**Conclusions:** Our intervention demonstrates one successful way of engaging target populations when developing TB education materials.

**OA24-392-16 The CC-TATA project and the use of EduClowns by the Blossom Trust to enhance TB awareness in Tamil Nadu, India**

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**Background and challenges to implementation:** Tuberculosis (TB) is a public health challenge worldwide. More than 90% of global cases and deaths occur in the developing world and India has the highest burden of TB. Despite being an infectious disease, Tuberculosis represents the biological expression of strong social inequalities in the country. Lack of formal health services and social support, malnutrition, and pollution expose high numbers of people to infection, progression to disease and late or inappropriate diagnosis.

**Intervention or response:** Blossom Trust, a leading NGO working in the area of TB eradication, works on the CC-TATA project focusing on TB-affected communities among three districts in Madurai - Tamil Nadu. It targets socially and economically marginalised people infected or affected by the disease.

The project objective is to create a civil society network on TB to transform disease response at the national level by amplifying community voices to foster more inclusive and stigma-free access to health services. In this framework, community engagement is one of the key-factors for the project. During World TB Day 2022, Blossom organised EduClown Theatre Performances in three villages in Madurai District.

The EduClowns are non-professional actors, coming from the communities and affected by TB. Dressed up as clowns, they provided information about TB symptoms, treatment and nearby treatment facilities to the public.

**Results/Impact:** More than 1000 people participated in the programme, including high-society members. TB messages were disseminated and the performances had a great impact on the targeted communities. The activities were recognized at the state and national level and District NTEP supported Blossom to implement all the planned activities.

**Conclusions:** Through the activities, Blossom team uses advocacy as a tool to demand the rights of TB patients and engages prominent stakeholders in the process. In this way, Blossom has contributed to the outlined output of mobilising and empowering TB communities.

**OA25 Breaking down silos: Bidirectional TB and COVID screening**

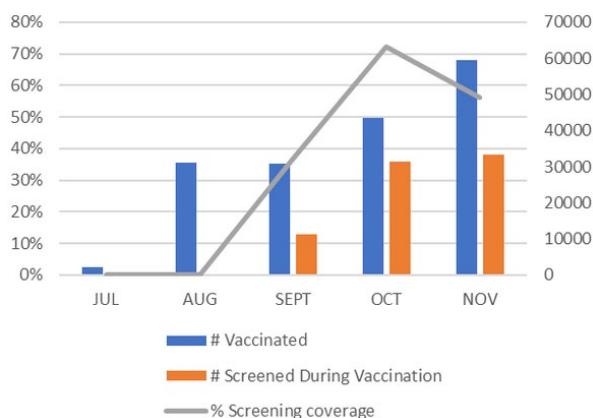
**OA25-393-16 Reducing missed opportunities in strengthening TB awareness in communities: leveraging COVID-19 vaccination campaigns in Taraba State, Nigeria**

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**Background and challenges to implementation:** The lack of awareness for Tuberculosis and poor health seeking behavior are the key drivers of TB transmission in communities. The 2012 National TB prevalence survey report states that the TB prevalence rate of over 80% was due to low community awareness about TB services. The COVID-19 pandemic brought a lot of investment opportunities especially in community structures to improve vaccination campaigns. The vaccination campaigns provided an opportunity to increase TB disease awareness, screening and testing for TB. This paper aims to show how TB screening increased during the COVID-19 vaccination campaigns.

**Intervention or response:** In 2022, the USAID funded GLOVAX COVID19 vaccination project under KNCV Nigeria piloted a community-based intervention where health workers go to rural communities to administer COVID 19 vaccines. During such campaigns, an integrated service approach model was introduced where social mobilization, and community awareness on emerging health concerns were prioritized. We leveraged on this to strengthen the awareness of TB and even more importantly, TB screening & services.

**Results/Impact:** The chart below shows a significant increase in the percentage of TB screening in Taraba state Nigeria.



**Conclusions:** TB on-the-spot screening awareness is an essential service that should be maintained during public health campaigns to help find more missing TB cases and reaching the overall aim of curbing the spread of TB and the impact of the disease on individuals and communities.

### OA25-394-16 Leveraging active TB case-finding using the Wellness-on-Keke intervention in the community to improve COVID-19 vaccine uptake in Nigeria

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**Background and challenges to implementation:** In March 2020, WHO announced the COVID-19 pandemic, and that marked the beginning of a new normal way of life. In 2022, KNCV Nigeria received a USAID grant to improve COVID-19 vaccination uptake among targeted populations in seven TB LON 1 & 2 Project supported states. The integrated TB/COVID-19 WoK intervention was introduced to efficiently cover hard-to-reach difficult-terrain areas. This abstract assesses opportunities provided by innovative community-based hard-to-reach TB program interventions to improve COVID-19 vaccination uptake with minimal cost.

**Intervention or response:** The TB/COVID-19 WoK intervention involves the deployment of a one-stop-shop vehicle (tricycle) with an AI-enabled portable digital x-ray for TB screening and a Truenat platform for TB diagnosis. The WoK also contains a solar-powered vaccine carrier, relevant consumables for COVID-19 vaccination, and a first aid kit. From October 2022 to January 2023 every week, the WoK team goes to hard-to-reach & difficult terrain areas to provide the integrated services it renders, such as BP monitoring, serum glucose, and malaria testing, & dispensing over-the-counter medicines when available. Data from the field are captured on paper-based tools & electronically transferred via google forms daily when the team returns to where the internet is available.

**Results/Impact:** The WoK intervention contributed 7,199 more vaccinations to the overall effort. This accounts for a 1% contribution of 719,371 vaccinations from various interventions including Community-based outreaches, Fixed sites & Mass vaccination sites. The same WoK intervention identified 1,811 presumptive TB, with 100% evaluation linkage and a TB yield of 25% in October – December 2022.

COVID-19 Services		3 Wellness on Wheels Vehicles	TB Services	
Community-base outreach site	476,497		# persons screened	15,769
Fixed Sites	7,466	# presumed to have TB	1,270	
Mass vaccination sites	228,209	# evaluated for TB	1,270	
Wellness on Wheels (WoK)	7,199	# TB patients detected	329	
Grand Total	719,371	# TB (all forms) put on treatment	325	
WoK Contribution	1%	TB yield	25%	

**Conclusions:** The WoK intervention can be a useful tool to provide integrated point-of-care TB services, including COVID-19 vaccination in a cost-efficient manner, especially in hard-to-reach or rural areas. There are more opportunities to provide expanded medical services such as surveillance and control of non-communicable diseases like hypertension & diabetes using the WoK intervention.

### OA25-395-16 Implementation of integrated mobile case-finding for TB, HIV and COVID-19 in rural mining communities in Ghana

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**Background and challenges to implementation:** The COVID-19 pandemic disrupted health service delivery in Ghana, making it necessary to adopt innovative strategies, including the integration of COVID-19 testing with diagnostic services for other respiratory diseases and comorbidities. We describe results of an integrated case finding approach for COVID-19, TB, and



HIV in rural Ghana leveraging existing mobile testing infrastructure of the National Tuberculosis Programme (NTP) to expand access to quality diagnostics to remote mining communities.

**Intervention or response:** We deployed a mobile clinic to implement simultaneous screening and testing for TB, HIV and COVID-19 across 58 mining communities in the Western, Eastern and Ashanti Regions of Ghana between October 2022 and March 2023. High-risk community members and those experiencing presumptive symptoms, targeted through focused demand generation by district health officials, first underwent integrated symptom screening for TB, HIV and COVID-19 using a standardized checklist collaboratively developed with the NTP.

Clients were subsequently screened for TB using onboard digital x-ray and CAD4TB, with GeneXpert testing for clients meeting symptom-based criteria or CAD4TB > 60. Antigen-detecting rapid diagnostic tests were used for COVID-19 and HIV testing. Clients with positive diagnoses were linked to confirmatory testing (HIV) or care at district hospitals.

**Results/Impact:** Overall, we reached 5475 individuals; 5409 (98.79%), 4971 (90.79%), and 5208 (95.12%) completed screening and testing for TB, HIV, and COVID-19, respectively. We identified 104 COVID-19 cases and 109 HIV infections, 30 of which were previously diagnosed. Sputum samples were collected from 596 (11.02%) clients, yielding 36 MTB+ cases. Client's age was inversely correlated with odds of positive diagnoses for all 3 conditions ( $p < 0.001$ ), while relative risk of MTB+ diagnosis was 65.64% lower for males [95% CI: 58.80% - 71.34%,  $p < 0.001$ ].

**Conclusions:** The deployment of integrated diagnostic services proved effective in identifying cases of TB, HIV, and COVID-19, partly owing to germane symptom presentations, and may benefit similar resource-limited settings.

## OA25-396-16 Bi-directional screening strategies for TB and COVID-19 in Nigeria and the Philippines: case studies of two best practices

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**Background:** Given the commonalities between TB and COVID-19, integrated managed is proposed as a strategy to mitigate the pandemic's negative impact on TB care. We assessed the facilitators and barriers of implementing and scaling up integrated screening in Nigeria and the Philippines.

**Design/Methods:** We conducted two case studies in Nigeria and Philippines between August-December 2022. We selected one project from each country for in depth analysis of both qualitative and quantitative data. Qualitative data sources included a desk review of guidelines, standard operating procedures, project reports, peer-reviewed publications, and in-depth interviews with 20 stakeholders. We used routine project data for the quantitative analysis.

**Results:** In Nigeria, the pilot screening of 1,931 people (900 males and 1,028 females) in the Kano State yielded three people with TB and 183 people tested positive for SARS-COV-2, and 12 had HIV. During scale-up in Imo State, 11 TB and 59 COVID-19 cases were identified after screening 1767 and 1798 persons respectively. In the Philippines, of 3,729 and 3743 people screened, 37 and 38 people were tested positive for TB and COVID-19 respectively. The numbers needed to screen (NNS) and test (NNT) were 101 and 13 respectively in swabbing facilities. In isolation wards, the yield rate was 2.7%, and the NNS and NNT equal, 36.

The momentum of urgency created by the COVID-19 pandemic, commitment of the local leadership, similarities of disease manifestations, trainings and logistic support, digital technologies and efficiencies gained through multi-disease screening facilitated implementation. Competing priorities, security concerns, fear of testing positive, low participation of clients, and shortage of trained personnel were some of the challenges.

**Conclusions:** Bi-directional screening for COVID-19 and TB is a high yield strategy that should be considered for further scale-up. The experience can be leveraged to address the growing challenges of non-communicable diseases and broader pandemic preparedness challenges.

## OA25-397-16 Implementation of bidirectional screening for COVID-19 and TB to increase TB case-finding in the context of the COVID-19 pandemic in Lao PDR

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**Background and challenges to implementation:** TB testing in Lao PDR fell 31% from 2020 to 2021, largely due to pandemic interruption of active case finding and other testing services.

The introduction of antigen rapid tests (AgRDT) in 2022 expanded COVID-19 testing to all health facilities, but patients testing negative for COVID-19 were often sent home without further assessment or care.

A growing body of evidence pointing to the relationship between COVID-19 and TB, including similarity of symptoms, shared co-morbidities/behaviours, and TB as a risk factor for severe COVID-19, suggested that a more intensive intervention was required.

**Intervention or response:** Lao PDR designed and rolled out bidirectional screening to increase TB testing and case finding in eleven hospitals across two provinces starting September 2022.

All patients were screened at key entry points using a checklist of COVID-19 and TB symptoms (n=6,156). Patients meeting the COVID-19 case definition were tested using AgRDT. Those meeting the TB case definition were tested using GeneXpert.

All patients with a confirmed diagnosis were linked to appropriate care. Select patients testing negative for COVID-19 and TB, but suffering from severe respiratory symptoms, were tested using the Xpert Xpress SARS-CoV-2/Flu/RSV (4plex).

Workflows were unique to each hospital, collaboratively developed to accommodate hospital infrastructure and protocols, and revised in a continuous improvement process in response to operational findings.

**Results/Impact:** In pilot sites, TB tests increased 31% and TB cases found increased 55% above pre-pandemic levels (Sept22-Jan23 versus Sept20-Jan21) [Figure 1]. COVID-19 testing only decreased by 32% in pilot sites (Aug22 to Feb23), versus a 79% decrease nationally.

Total costs were estimated to be \$68,000, primarily from pre-existing infrastructure (58%, \$39,500), with additional costs (42%, \$28,500) for start-up (trainings, supervision) and commodities (AgRDT, 4plex).

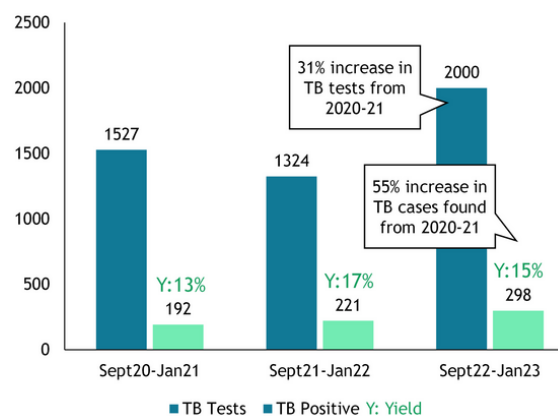


Figure 1. TB testing numbers in all pilot sites for the intervention period Sept 2022 to Jan 2023, and corresponding historical periods (Sept 20 - Jan 21 and Sept 21 - Jan 22).

**Conclusions:** Bidirectional screening is a low-cost intervention that relies primarily on existing infrastructure and offers an opportunity to sustain COVID-19 testing and increase TB case finding.

## OA25-398-16 TB and COVID-19 bi-directional screening is one way of improving TB case detection efforts and notifications in the COVID-19 era

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**Background and challenges to implementation:** The covid-19 pandemic had major impact on TB case-detection efforts and notifications in Malawi and in South West Zone (SWZ) in particular. Number of presumptive and confirmed TB patients in SWZ decreased from 44,672 to 30,839; and from 6,150 to 5,188 between 2019 (pre-covid-19 period) and 2020 (during covid-19) respectively.

**Intervention or response:** As one way of improving the gains lost during to covid-19 period, SWZ of National TB and Leprosy Elimination Program (NTLEP), with funding from Global Fund, conducted a 4-days training in TB and Covid-19 bi-directional screening. The training targeted different cadres of health care workers in 9 high-volume TB sites to implement TB and Covid-19 screening. The training aimed at equipping participants with knowledge and skills of screening patients for both

TB and Covid-19 on entry to health facility using symptomatic screening. Implementation started in June, 2022 in all sites.

Person with presumed TB or Covid-19 or both were registered in an improvised TB/Covid register and upon laboratory investigation(s), a final diagnosis of either TB or Covid-19 or both was made or ruled out. All patients diagnosed were linked to treatment.

We, therefore, analyzed presumptive and confirmed TB patients registered from 1<sup>st</sup>July-31<sup>st</sup>December, 2022 from all implementation sites. Existing data for 2021 from the same sites was used as a control.

**Results/Impact:** The number of presumptive TB patients from the 9 sites increased from 5,178 in July-December 2021 to 7,106 in July-December 2022 (37% increase). Similarly, number of notified TB patients increased from 1,041 to 1,172 in the same periods (11% increase).

**Conclusions:** Implementation of TB and Covid bi-directional screening can greatly improve TB case detection and notification in the era of Covid-19 in resource limited settings like Malawi. NTLEP needs to put in place measures to implement similar interventions during any pandemics that may have an impact on TB case detection efforts.

### OA25-399-16 COVID-19 vaccination during a market storm: an opportunity for improving TB case-finding in Southwestern State, Nigeria

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**Background and challenges to implementation:** The COVID-19 pandemic has caused significant disruptions to routine healthcare services, including tuberculosis (TB) case finding, diagnosis, and treatment. The importance of curbing the pandemic justifies the focus of resources on vaccination, however, finding TB cases should not be placed on hold. The two infectious diseases require prompt attention and infusing the two processes provided an opportunity for TB screening. This paper aimed to assess the impact of COVID-19 vaccination on TB case finding in Oyo State.

**Intervention or response:** In Oyo State, Nigeria, the COVID-19 vaccination team carried out outreaches in the markets and other large gatherings. Screening outreach was carried out in 21 communities from 1st August to 11th August 2022. All individuals provided with the COVID-19 vaccine were simultaneously screened for TB

using WHO TB symptomatic method. Sputum samples were collected from presumptive TB individuals identified for laboratory diagnosis while those who could not produce sputum samples were referred for Chest Xray.

**Results/Impact:** A total of 6379 people were screened, from which 774 were presumptive. All presumptive evaluated for TB. Sixty-one positive TB cases were diagnosed and 98.4% (60) of them were placed on TB treatment.

**Conclusions:** The COVID-19 vaccination campaign provided an opportunity to improve TB case finding in Oyo State. We recommend that TB programs leverage the existing vaccination programs to enhance TB case finding as the intervention demonstrated an increase in TB case finding as a result of the COVID-19 vaccination.

### OA25-400-16 Yield of integrated TB screening at COVID-19 care and prevention events in Viet Nam

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**Background:** Viet Nam's fourth wave of the COVID-19 pandemic led to a sharp spike in the number of infections and deaths. The government responded with strict lockdowns and substantial repurposing of TB care infrastructure, raising insuperable access barriers for people with TB.

**Design/Methods:** Between 2021-Q3 and 2022-Q2, the National TB Program and Friends for International TB Relief (FIT) advocated and coordinated with five provincial health authorities to integrate TB screening activities into COVID-19 quarantine centers and vaccination sites. All attendees at these sites were screened using AI-supported chest X-ray (CXR) interpretation, followed by testing with the Xpert MTB/RIF Ultra assay. Individuals diagnosed with TB were linked to care at the provincial lung hospitals.

**Results:** 49,000 persons (53.5% female) underwent CXR screening and sputum was tested from 4.1% (2,025/49,000) of participants. The events detected 132 persons with bacteriologically-confirmed TB and another 44 individuals were clinically diagnosed. 90.3%

(159/176) were initiated on treatment. The TB detection rate was 359/100,000, which was comparable to Viet Nam's estimated prevalence rate (322/100,000). Disaggregated by sex, the rates were 654/100,000 among men and 103/100,000 among women. This male-to-female ratio (MFR) of 6.3 was substantially higher than the MFR of 4.0 measured on the prevalence survey and the MFR of 2.5 among notified TB patients in Viet Nam.

	All Provinces	Ha Noi	Ho Chi Minh	Hai Phong	Can Tho	Quang Nam
0.1 Days of screening	116	51	43	14	7	1
0.2 Screening locations	136	59	54	15	7	1
1.1 Verbally screened in ACIS	53,487	27,833	14,032	9,456	1,879	287
1.2 Screened by chest X-ray (CXR)	49,000	27,780	13,862	5,196	1,878	284
1.3 Abnormal CXR	2,019	680	938	286	112	3
1.4 Sputum test after abnormal CXR	1,966	680	902	269	112	3
1.5 Bac(+) TB detected after abnormal CXR	131	66	35	13	17	0
1x1 Sputum testing outside Double-X	59	16	36	7	0	0
1x2 Bac(+) TB detected outside Double-X	1	1	0	0	0	0
1.6 Clinically diagnosed TB	44	19	3	6	16	0
1.7 All Forms of TB detected (1.5 + 1x2 + 1.6)	176	86	38	19	33	0
... TB prevalence rate (per 100,000)	359	310	274	366	1,757	0
1.8 All Forms of TB linked to treatment	159	79	34	17	29	0
1.9 All Forms of TB successfully treated	-	-	-	-	-	-

**Conclusions:** The rate of persons with TB detected during integrated screening events was similar to the prevalence survey, likely due to the broad cross-section of society encountered at the COVID-19 care and prevention sites. Nevertheless, this intervention offered the only avenue for individuals with TB to be found and treated during these lockdowns and provides a blueprint for continuity of care in future pandemics. The substantially higher rate of men with TB may also offer a strategy to reach more of the missing men with TB.

## OA26 Lessons learnt from the use of new technologies for TB prevention and care

### OA26-401-16 Programme benefits of using a localised performance tracker at the start of a project: TB-HIV integrated services in Lagos State, Nigeria

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**Background and challenges to implementation:** Once project implementation starts, it is sometimes difficult to start monitoring performance and achievement at the initial time due to unavailability of data, which is as

result of unstable database and unavailability of tools for reporting. The implication is that, as the project progresses, we see that challenges and gaps that would have been identified early and closed immediately tend to pose a big problem for the project. There is need to create a local system where one can routinely monitor progress and achievement once implementation starts, and while waiting for a more stable database and reporting tools.

**Intervention or response:** In April 2022, KNCV Nigeria under ACE 6 project developed a localized performance tracker to monitor TB/HIV integrated services across 11 LGAs in Lagos State, Nigeria. Field staff were trained on how to use the tracker and tracker was deployed to 55 supported facilities. The tracker was populated from facility registers by project facility ad hoc staff and sent back to State team for collation and review on weekly basis. Data was generated and reported using the excel-based weekly tracker.

**Results/Impact:** Comparing TB/HIV data 6 months before tracker was introduced and 6 months after, there was a massive increase in performance across all TB/HIV indicators as seen in (fig 1) below:

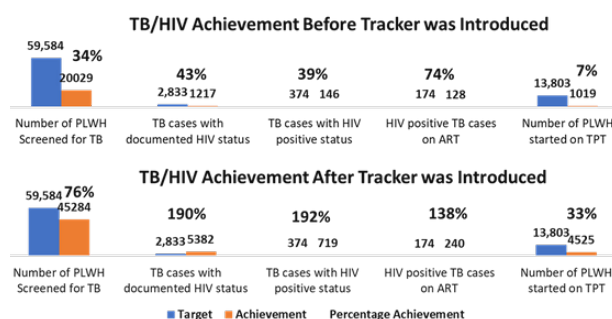


Fig 1: TB/HIV achievement before and after tracker introduction.

**Conclusions:** An increased performance is seen across all the TB/HIV indicators due to the routine monitoring of data using the localized TB/HIV tracker. The introduction of the tracker helped in timely identification and closing of gaps, development of strategies to improve performance, review of achievement and feedback to field staff.

**OA26-402-16 Role of patients' support package on pre-treatment loss to follow-up among patients with drug-resistant TB in Afghanistan**

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**Background and challenges to implementation:** Pre-treatment lost to follow-up (PTLFU), and dropout after diagnosis before treatment registration is a major gaps in tuberculosis (TB) care in Afghanistan. Centralized drug-resistant (DR) -TB services, economic factors, long travel times from hard-to-reach areas, weak referral systems, and cultural barriers all reduce adherence to treatment enrollment in programmatic management of drug-resistant TB (PMDT) sites. Researchers used routine data to assess the role of patient support in PTLFU in Afghanistan

**Intervention or response:** In 2022, with the support of the United States Agency for International Development's Urban Health Initiative project, the National Tuberculosis Program (NTP) began the implementation of patient support packages including local transport, food baskets, and initial lab exam costs for DR TB patients. The activity was coordinated with all GeneXpert sites and health facilities to refer people after being diagnosed as Rifampicin Resistant (RR)/DR-TB cases to PMDT sites. A WhatsApp group network was established among all GeneXpert sites to inform provincial teams and PMDT staff to track the people with TB and inform them about the availability of support packages before they were referred to PMDT sites for treatment enrollment.

**Results/Impact:** In 2021, 459 DR-TB cases were diagnosed in Afghanistan; 392 (85.7%) of them enrolled for treatment in five PMDT sites and 67 (15%) were pre-treatment lost to follow-up.

In 2022, 639 DR-TB cases were diagnosed in the GeneXpert sites, 596 (93%) of them enrolled for treatment and only 43 (6.7%) lost to follow-up before starting the DR-TB treatment.

Loss to follow-up during the treatment was 14 % until the end of 2021 and 12% until the end of 2022 (Table 1).

Years	Total RR/multi DR-TB cases	Total cases enrolled	PTLFU rate	Lost to follow-up during treatment
2018	452	327	28%	21%
2019	486	396	19%	19%
2020	442	348	21%	17%
2021	459	392	15%	14%
2022	639	596	7%	12%

Table 1: Trend of DR-TB cases diagnosed vs treatment enrollment in Afghanistan (2018-2022) and PTLFU.

**Conclusions:** Patient support packages significantly reduced PTLFU and increased adherence to enrollment. Treatment was significantly improved by providing this package and close coordination with GeneXpert sites.

**OA26-403-16 Benchmarks for TB control that incorporate routine whole-genome sequencing**

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**Background:** Routine whole genome sequencing of *Mycobacterium tuberculosis* has been implemented with increasing frequency. However, its value for enhanced tuberculosis (TB) control and novel benchmarks to assess this, have not been explored.

**Design/Methods:** We analysed routine sequencing data of culture-confirmed TB cases notified between 1<sup>st</sup> January 2017 and 31<sup>st</sup> December 2021 in New South Wales, Australia. Genomic surveillance included drug-resistance conferring mutations and evidence of local TB transmission, defined by single nucleotide polymorphism (SNP) clustering over a variable (0-25) SNP threshold.

**Results:** *M. tuberculosis* sequences from 1831 patients were analysed, representing 64.8% of all notified TB cases and 96.2% of culture-confirmed cases. Genotypic drug susceptibility testing (DST) was highly concordant with phenotypic DST, facilitated surveillance of drug resistance mutations and provided a 6.6% 'value add' for antimycobacterial resistance detection. Beijing strains were more likely to be drug resistant (p=0.04) and locally transmitted if drug resistant (p=0.01). The application of a traditional 5-SNP cluster threshold identified 62 clusters with 183 clustered cases and an estimated rate of recent transmission (RRT) of 6.8%. Of these clustered cases 104/183 (56.8%) had 0 SNP differences, which is highly indicative of person-to-person transmission. A lineage-specific 5-year cluster assessment provided a comprehensive overview of recent transmission within Australia.

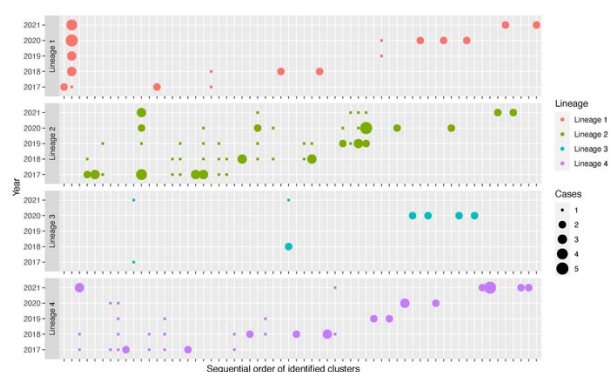


Figure: All *M. tuberculosis* transmission clusters\* identified over the 5-year study period. Y-axis indicates the study year (2017-2021) and the X-axis the sequential clusters identified in that year.

\*Using a five single nucleotide polymorphism (SNP) distance cut-off; programmatically the focus should be on larger and/or multi-year clusters that indicate failed containment.

**Conclusions:** Routine WGS offers an opportunity to implement new benchmarks for TB control, such as using a rolling 5-year cluster assessment, as an indicator of effective epidemic containment. Genomic DST also provides valuable information for clinical care and drug resistance surveillance.

### OA26-404-16 Using drug sales data to estimate the number of TB cases managed by the private healthcare sector in India

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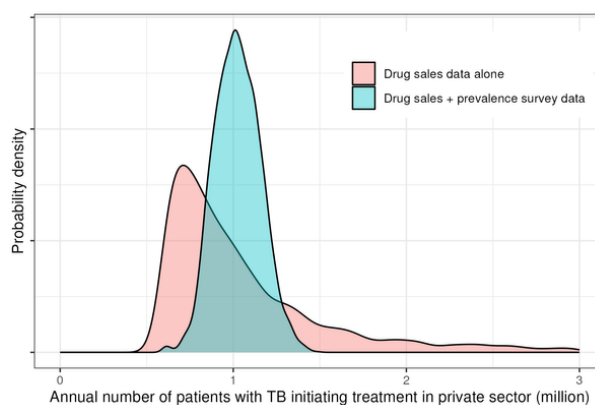
**Background:** In countries with a strong private healthcare sector, it is important to estimate the number of patients managed by this sector. In the absence of universal notification, a key source of evidence is commercial data for the volume of anti-TB drugs sold through the private sector: if this volume in a given year is  $V$ , then the number of TB patients  $N$  is:  $N = Vp/d$ , where  $p$  is the proportion of patients receiving TB treatment who genuinely have TB (the 'positive predictive value', or PPV, of receiving private TB treatment), and  $d$  is the average duration of treatment in the private sector.

However, a major challenge is that both  $p$  and  $d$  are typically unknown. In India, data from a recent national prevalence survey now provides an opportunity to estimate these key unknowns.

**Design/Methods:** We developed a Bayesian model of TB care, distinguishing the public sector; the notifying private sector; and the non-notifying private sector. We fitted the model to data from the prevalence survey;

national-level data for the volume anti-TB drugs sold in the private sector; and notifications. Using this model, we sought to estimate the key parameters  $p$  and  $d$  described above.

**Results:** In India, model estimates suggest that the average duration of TB treatment in the private sector is 13.4 months (95% CrI 5.0 – 22.3) and the PPV of private sector diagnosis is 59% (95% CrI 24 – 84). Applied to recent drug sales data, these estimates suggest that in 2019, 1.0 (95% CrI 0.7 – 1.3) million people with TB received treatment in the private sector (see Figure).



**Conclusions:** While estimates may vary by country, our analysis shows how prevalence survey data can be combined with drug sales data, to estimate key parameters for monitoring the TB caseload being managed by the private sector through time.

### OA26-405-16 Strengthening the laboratory network: A demonstration of the DataToCare laboratory connectivity solution strategy in the Philippines

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**Background and challenges to implementation:** Laboratories play an important role in diagnosing TB in the Philippines by providing fast and accurate diagnostic test results using Xpert MTB/Rif. Challenges include limited accessibility, delayed test result release, and late reporting which lead to delay in treatment initiation.

To boost ongoing efforts of case finding activities and strengthen the laboratory network of the Department of Health (DOH)-National TB program (NTP), key stakeholders adopted laboratory connectivity solutions (LCS) in Xpert laboratories of the three biggest regions of the country.

**Intervention or response:** From June 2020 to October 2021, DataToCare (DTC) was installed in 49 Xpert laboratories and the Research Institute for Tropical Medicine-National TB Reference Laboratory. Training was conducted among super-users and data managers on the installation, access, and interpretation of data on the web. A series of orientations and job aids were developed for healthcare providers to increase understanding of the system. A DOH issuance was disseminated, and joint monitoring to sites was conducted by USAID's TB Innovations and Health System Strengthening together with regional/provincial authorities to solicit participation and ensure guideline compliance.

**Results/Impact:** Baseline turnaround-time from collection of specimens to initiation of treatment was 5.9 days ( $p=0.1763$ ) which is within NTP recommended TAT of 7 days. When LCS was introduced, TAT significantly decreased to 4 days in 2021 ( $p<0.0001$ ) and 4.7 days in 2022 ( $p=0.0089$ ). Real-time notification of results was same day in most sites, but variation was noted from release of results to initiation of treatment due to geographic and network challenges. While the healthcare

provider was immediately notified through the LCS, delay from release of results to initiation of treatment was noted in sites with patients in far-flung areas.

TAT from collection of specimen to initiation of treatment	Baseline	2021	2022
Mean+ SD	5.91 + 4.28	4.03 + 3.18	4.7 + 5.13
Min (in days)	1	1.5	within the day
Max (in days)	17.5	14	23
p-value	0.1763	<0.0001	0.0089

**Conclusions:** TAT from release of results to treatment initiation can be improved with introduction and utilization of DTC for GeneXpert. LCS allows real time surveillance and monitoring by program managers.

### OA26-406-16 The involvement of the national health insurance body to increase TB case notification in Indonesia

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**Background and challenges to implementation:** Indonesia is the second-highest country with TB burden globally (GTBR, 2022). In 2017-2019, there was a 30% gap between reported and estimated TB cases in the country. A Public-private mix approach is essential to engage all health facilities and stakeholders, including the National health insurance body, in the TB control program. Presidential Decree No. 67/2021 for TB Control mandated TB financing for individual health services is covered by universal health insurance, which is managed by the Social Security Agency of Health (BPJS Kesehatan). BPJS Kesehatan provides capitation financing for primary health facilities and INA CBG's package payment for secondary health facilities. The information systems (IS) used by BPJSK (pCare/vClaim) and NTP (SITB) are different and not integrated with each other.

**Intervention or response:** In response to the Presidential decree, BPJS Kesehatan circulated an official letter in 2022 to mandate all secondary health facilities input the TB patient unique code reported in SITB as a mandatory variable in vClaim for TB claim disbursement. In addition, NTP and BPJS Kesehatan compared TB data in both ISs (SITB and vClaim) to find the underreported TB cases in secondary health facilities.

**Results/Impact:** TB case notification is exponentially increased from 54% in 2021 to 74% in 2022 after the implementation of mandatory variable for TB unique code

in SITB for TB claim disbursement as one of the interventions to accelerate the TB case notification. From the data matching between SITB and vClaim, 95,571 potentially underreported TB cases were found in secondary health facilities within the BPJS Kesehatan information system (January - December 2022). 47% of them are eligible to be inputted into SITB.

**Conclusions:** Strengthening the surveillance system through the mandatory variable for TB in the BPJS Kesehatan information system and bridging both platforms is very important to ensure no under-reporting of TB cases in the health facility.

### OA26-407-16 Implementation of airborne infection control measures to prevent cross TB transmission at HIV care settings in India, 2022: a mixed-methods study

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**Background:** This mixed method study was done to assess the status and challenges faced to implement Airborne Infection Control (AIC) measures in HIV care settings in India to prevent cross-transmission of tuberculosis.

**Design/Methods:** After multi-stage sampling, 37 Anti-retroviral treatment centers, and 58 linked ART centers were selected (2022). At each facility, AIC measures pertaining to administrative, environmental, and personal protective measures (PPE) were assessed by trained researchers with the help of a pre-tested questionnaire based on AIC guidelines. AIC Measures that need to be adopted were discussed with each center and a detailed report was also shared with them. Feedback was obtained at the end of 9 months.

Data pertaining to the status of recommended measures were captured in a pretested questionnaire and analyzed with SPSS 28.0. In-Depth Interviews (23) and focus group discussions (2) were conducted among different stakeholders to identify challenges to AIC measures implementation.

**Results:** Out of 819 administrative recommendations (infection committees, training, fast tracking, etc), 67.9% were implemented, 20% weren't implemented and 12.1% were in implementation.

Out of 957 Environmental recommendations (changes in seating arrangements, obstructed furniture, exhaust fans installation, etc), 63% were implemented, 29.6%

weren't implemented and 7.4 % of sites were in process. Out of 236 Biomedical waste recommendations (waste disposal practices, record-keeping, training, etc), 69.1% were implemented, 20.8% weren't implemented and 10.2 % were in process.

Out of 74 PPE recommendations ( use of masks, staff immunization, etc.), 79.7% were implemented, 18.9% were not implemented and 1.4 % of sites were in process.

Qualitative findings revealed challenges for AIC measures implementation like inadequate infrastructure, overcrowding, workload, and less manpower. *"we have a problem .....our patient load per day is 150 ....we are facing the problem in fast-tracking"(FGD NE)"*

**Conclusions:** AIC measures can be improved in HIV care settings for the prevention of TB cross-transmission

### OA26-408-16 Integration of drug-resistant TB information systems to implement active TB drug safety monitoring and management

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**Background and challenges to implementation:** South Africa is implementing active TB-drug safety monitoring and management (aDSM), in line with World Health Organization recommendations, using the electronic Pharmacovigilance Information Management System (PViMS) as a tool to actively manage adverse drug reactions. The country utilises a standardised electronic DR-TB recording and reporting system (EDRWeb). Integration of these two systems was key to facilitating aDSM uptake and acceptance. We discuss our initiative in support of systems integration.

**Intervention or response:** We placed emphasis on advocacy and strategic engagement with multiple stakeholders to drive systems integration. These included the National Department of Health, the South African Health Products Regulatory Agency, donor agencies and implementing partners supporting the DR-TB programme. Initial efforts focussed on understanding every stakeholder's interest, while identifying areas of commonality for systems integration around which to coalesce.



Further, we utilised the multi-stakeholder platform to identify opportunities for strengthening adverse event (AE) reporting. This led to the development of a pre-populated online AE reporting form on EDRWeb that drew relevant information from both systems, thereby simplifying the AE reporting process for frontline clinicians and obviating a need for reporting on multiple systems.

**Results/Impact:** This approach to systems integration yielded a single recording and reporting system for DR-TB. It makes available all relevant information for identification of AEs by clinicians and provides a communication mechanism with national pharmacovigilance specialists to determine and actively manage causality. In time, this integrated system will also facilitate signal detection while strengthening AE reporting.

**Conclusions:** This recently completed systems' integration will accelerate aDSM in South Africa's implementation of the 6-month DR-TB regimens.

Understanding these drugs' toxicity profiles will assist with clinical care and more broadly, programme management. There is potential for deployment in treatment programmes for other diseases such as HIV.

### OA26-409-16 Lessons learnt from the SMS/USSD project implementation in Nigeria: the KNCV TB LON Regions 1 and 2 experience

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**Background and challenges to implementation:** Through the USAID TB LON 1 & 2 project in Nigeria, KNCV implemented a Short Message Service (SMS) and Unstructured Supplementary Service Data (USSD) intervention, which aimed to promote the early detection and treatment of TB and improve medication adherence among patients receiving treatment.

**Intervention or response:** The intervention involved sending out a USSD application code via SMS instructing recipients to dial the code if they have symptoms of TB such as cough lasting 2 weeks or more, fever, weight loss or drenching night sweats. Users who responded yes to any of these symptoms were further contacted and evaluated for TB, and those who were diagnosed as TB patients were placed on treatment.

This intervention also included monitoring patients who were already receiving TB care and sending them periodic SMS via the USSD application to ensure medication adherence. Data from the USSD transactions were mined and stored on a web application dashboard to provide real-time analysis and reporting.

**Results/Impact:** From December 2020 to December 2022, a total of 25,407 people were reached via SMS broadcasts, of which 1,997 (8%) self-screened for TB using the USSD application. The number of presumptive cases identified and contacted by a healthcare worker were 939 (47%), and 624 (66%) were further evaluated. Of these, 10 (1.60%) persons were diagnosed with TB and placed on treatment.

Of the 14,069 in-care patients reached through SMS broadcast only 5.5% (781) of them responded to the USSD application, of which 21% (164) responded yes to medication adherence, while 9 persons responded to not adhering to their medication and reported barriers to non-adherence to their medication.

**Conclusions:** Mobile technologies have the potential to increase access to TB diagnosis and care, but it requires local players and stakeholders to engage target audiences during planning and development phases and capacity building among organizations for a deeper knowledge.

### OA27 TB diagnostics – Operational and clinical studies

#### OA27-410-16 The diagnostic performance of unstimulated interferon-gamma (IRISA-TB™) for pleural TB: A prospective study in South Africa and India

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**Background:** Tuberculous pleural effusion (TPE) is the most common form of extrapulmonary tuberculosis (EPTB) in many settings. The diagnostic performance of frontline rapid nucleic acid amplification tests, such as GeneXpert®MTB/RIF, remains suboptimal (sensitivity of ~30%).

However, a more sensitive version (GeneXpert®MTB/RIF Ultra), and alternative newer assays, are now available. We therefore evaluated the diagnostic performance of Xpert Ultra and the newer interferon-gamma-rapid-immunosuspension-assay (IRISA-TB), a rapid (same-day) diagnostic test, in patients with presumed TPE (the pleural fluid sample remains unprocessed and there is no overnight stimulation step, and thus this is not an IGRA).

**Design/Methods:** In this multicenter, observational study, a total of 218 participants with suspected TPE were recruited (110 and 108 from South Africa and India, respectively). Participants underwent routine diagnostic testing and pleural biopsy. IRISA-TB testing was concurrently performed. Performance was compared to other available same-day diagnostic tests (adenosine deaminase [ADA] and Xpert Ultra). The reference standard for TB was microbiological and/or histopathological confirmation of TB using the fluid and/or pleural biopsy sample.

**Results:** Results for this preliminary analysis were available for 133/218 (61.0%) participants. The sensitivity of IRISA-TB (cut-point of 20.5pg/ml) was significantly better than Xpert Ultra (81.9% vs 34.6% [25.2-45.5],  $p < 0.001$ ). The specificity of IRISA-TB was significantly higher than that of ADA (97.5% vs 84.7% [76.5-90.4],  $p = 0.029$ ) but was similar to Xpert Ultra (97.5% vs 99.1% [94.9-99.9]). The NPV of IRISA-TB (88.4% [80.0-93.7]) was higher than that of ADA (86.3% [78.3-91.7]) and Xpert Ultra (66.7% [59.1-73.6],  $p = 0.036$ ). The PPV of IRISA-TB was 88.4% (80.0-93.6).

**Conclusions:** Xpert Ultra has poor sensitivity for the diagnosis of pleural TB. IRISA-TB, by contrast, demonstrated high sensitivity, specificity, NPV, and PPV for the diagnosis of TPE in TB-endemic settings.

### OA27-411-16 Decentralising childhood TB diagnostics in health districts in high TB burden, low-income countries: fidelity, feasibility and acceptability of implementation strategies

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**Background:** Decentralizing childhood TB diagnosis in Primary Health Centres (PHC) and District Hospitals (DH) relies on key implementation strategies such as training, regular site support supervision with national TB programs and clinical mentoring by paediatricians. In the context of the TB-Speed Decentralization study, we described the acceptability, perceived feasibility, and fidelity of these implementation strategies.

**Design/Methods:** We did a mixed method implementation research study (2020-21) in 12 DH and 47 PHCs of Cambodia, Cameroon, Cote d'Ivoire, Mozambique, Sierra Leone, and Uganda. We analysed feasibility and fidelity data extracted from training logs, supervision and mentoring reports. We conducted individual interviews with 130 Health Care Workers (HCWs) and six project managers to explore acceptability and perceived feasibility.

**Results:** Of 2197 HCWs involved in childcare, 221 (10%) were trained on childhood TB and diagnostic tools before study start – 47.5% of trainees were nurse/midwives, 26.2% physicians, 20.8% radiographers. Training was conducted off-site following a “cascade model” (international coordination team, national teams, facility in-charges, colleagues). HCWs shared frustrations on the “once-off training model” and called for refresher trainings, specifically tailored to their responsibilities in childcare.

Overall, 65.5% of the planned site support supervision visits (2 to 6 visits per site over 12 months) were effectively carried out. Clinical mentoring visits were mostly combined with support supervision.

HCWs described site support supervision and clinical mentoring as effective, appreciating continuous learning and guidance from experts. Many planned site visits were not done due to distance, lack of time and Covid.

Mitigation strategies included remote support visits through teleconference, and problem solving within chat applications.

**Conclusions:** Decentralised services are by essence implemented in challenging contexts, in terms of access to facilities, or limited staff availability and stability. Innovative ways to deliver new interventions, and to support HCWs and implementers through change, in context of limited resources, should be further investigated.

### OA27-412-16 Increased TB case detection using African giant pouched rats among children and adults in Tanzania

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**Background:** African giant pouched rats (*Cricetomys ansorgei*), trained by Anti-Persoonsmijnen Ontmijnende Product Ontwikkeling (APOPO) to identify tuberculosis (TB) by smell, have demonstrated their ability to detect TB from sputum.

We evaluated rat-based case detection and compared mycobacterium bacillary load (MB-load) among children and adults.

**Design/Methods:** Sputum samples were collected from presumptive TB patients in 69 (58 Dar es Salaam, 11 Dodoma) outpatient health facilities from Jan-Dec 2022. Samples from sputum-smear microscopy (smear)-negative presumptive TB patients at Directly Observed Therapy (DOT) facilities were re-evaluated at APOPO using 10 detection rats.

Rat-positive samples (samples indicated by at least one rat) were confirmed using concentrated light-emitting diode microscopy. Using Chi-square test, we analyzed the yield of rats' TB case detection over DOTs facility diagnosis and compared the increase in case detection by MB-load.

**Results:** A total of 46,048 samples from 35,766 patients were screened by rats, 3,929 TB cases were detected, and 52% (2029/3929) were additional TB cases contributed by APOPO rats that were missed by routine program smear testing. Compared to DOTs clinics, the APOPO

rats were six times more likely to detect TB among Acid Fast Bacilli (AFB) smear +1 or scanty, [90% (1829/2029) versus 60% (1139/1900), Odds ratio, OR=6.11, 95% confidence interval, CI: 5.14-7.26]. The odds of identifying additional TB cases by rat among children were two times higher than adults, [71% (91/129) versus 51% (1795/3542), OR=2.3, 95% CI: 1.59-3.42].

Furthermore, the odds of identifying additional TB cases by rats among children with AFB +1 or scanty were two times higher than adults with the same MB-load range, [75% (86/114) versus 61% (1617/2656), OR=2.0, 95% CI: 1.28-3.03].

**Conclusions:** Rats contributed for over half of the additional TB cases in a high TB burden setting. Increased TB detection was higher among children, especially among patients with lesser bacillary load.

### OA27-413-16 Decentralisation of multidrug-resistant TB surveillance services through placement of molecular line-probe assays: Kenya's experience

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**Background and challenges to implementation:** Kenya has been adopting WHO-approved molecular diagnostics (mWRDs) for TB diagnosis. However, besides line probe assay, most assays do not detect resistance to isoniazid. The country decentralized first and second-line LPA to four additional regional laboratories to increase access and early detection and treatment of DR TB, while reducing workload at the National Tuberculosis Reference Laboratory (NTRL). The intervention was aimed at sharing the Kenyan experience with MDR TB surveillance implementation.

**Intervention or response:** The country developed a road map for the decentralization of LPA services. Key activities conducted were; planning meetings with stakeholders; engaging the relevant subnational Health team; developing a quality assurance plan; remapping of sample referral system; developing a monitoring and evaluation framework plan; procurement and installation of LPA machines; data connectivity; training six people two per site; Commissioning of the LPA machines; training of health care workers; weekly meetings; quarterly mentorship program; enrollment of the sites to External Quality Assurance (EQA) program.

**Results/Impact:** Three sites were identified considering the geographical representation and were renovated to have three PCR rooms. Implementation of testing took three months, weekly meetings were conducted with the lab staff; quarterly mentorship was performed to address the gaps identified during implementation. Out of the 8,116 samples subjected to LPA in the country 10% (837) were from these sites.

Challenges noted were slow uptake which was addressed by training the healthcare workers in the facilities on DR TB to create demand. Three additional lab staff were trained to address staffing challenges. LPA EQA performance was above 80%.

**Conclusions:** Decentralizing DST services had an impact by reducing the number of samples to be sent to the national lab by 10%.

Improved prompt initiation of treatment for MDR patients due to near testing. A detailed implementation plan determines the operationalization of services across the TB diagnostic network.

### OA27-414-16 Latent TB infection diagnosis: Correlation between molecular and immunological biomarkers

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**Background:** A quarter of the world's population is estimated to play host to *Mycobacterium tuberculosis* (Mtb) in the form of Latent TB infection (LTBI) without any clinical manifestation of active disease. The diagnosis of LTBI can be performed using either Tuberculin skin test (TST) or IFN- $\gamma$  release assay (IGRA), which are either subjective or expensive.

The objective of the present study was to identify transcriptomic and circulating small non-coding RNAs (sn-cRNAs) based biomarkers and their correlation with immunological markers for diagnosis of LTBI cohort.

**Design/Methods:** Around 80 household contacts (HHCs) of bacteriologically confirmed active pulmonary TB cases (drug sensitive and drug resistant) were recruited for the study. Whole blood and sera samples were collected from the subjects. Chest X-ray (CXR)/

GeneXpert was used to rule out active TB in the HHCs. The HHCs were screened using QuantiFERON-TB Gold Plus (QFT-Plus) to perform IGRA and categorize LTBI and uninfected cohorts. Total RNA extracted from whole blood was used to quantitate expression levels of six genes known to be associated with LTBI.

For each individual, small RNA libraries were prepared using sera samples. These libraries were sequenced using Illumina HiSeq and differentially expressed miRNAs were identified using DeSeq analysis [fold change ( $\geq/\leq 2$ ) and p-value ( $<0.05$ )].

**Results:** *FCGR1B*, *GBP1* and *GBP5* transcripts differentiated LTBI from uninfected among HHCs using Livak method. ML and ROC (Receiver Operator Characteristic) analysis validated this transcript signature to have a specificity of 72.7%. DeSeq analysis identified a set of five miRNAs, which distinguish LTBI cases from uninfected among the HHCs.

**Conclusions:** In this study, we assessed the potential of a quantitative transcript signature and circulating sn-cRNAs to diagnose LTBI among HHCs of a high-TB burden population.

The study identified a transcript and sn-cRNA signature which can be used as a biomarker for rapid screening of large populations.

### OA27-415-16 Improving utilisation of TB-lipoarabinomannan testing using data-driven quality improvement approaches in Uganda

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**Background and challenges to implementation:** In 2017, Uganda adopted the use of urine lateral flow lipoarabinomannan assay (LF-LAM) to assist in detection of active TB among people living with HIV (PLHIV) with Advanced HIV Disease (AHD).

However, since its adoption, the test utility has been sub-optimal. About 44% and 50% of the eligible PLHIV accessed LF-LAM test in 2020 and 2021 respectively. This study aimed to explore if evidence based continuous

quality improvement (CQI) approaches can be utilized to improve the uptake of the LF-LAM test at poorly performing health facilities in Uganda.

**Intervention or response:** The study utilized both qualitative and quantitative CQI interventions to increase utilization of LF-LAM test at randomly selected 14 intervention and 16 control health facilities from August-2022 to October-2022. Prior to implementation, baseline data review was conducted to identify the barriers to sub-optimal LF-LAM utilization at health facilities. The most frequently noted challenges included: training related barriers, documentation gaps, workflow inefficiencies, and poor stock management. To address these barriers, sites implemented interventions such as refresher trainings and mentorships, revised LF-LAM workflows and improved documentation and stock management practices. The paired t-test was used to summarize the means in LF-LAM utilization before and after the CQI intervention.

**Results/Impact:** The mean uptake of LF-LAM at the intervention health facilities significantly increased from 70% to 95% after the implementation of the CQI intervention (p-value=0.03), whereas the mean uptake at the control health facilities remained at 79% (p-value=0.82). The intervention facilities showed a consistent month-over-month improvement in LF-LAM uptake compared to the control facilities.

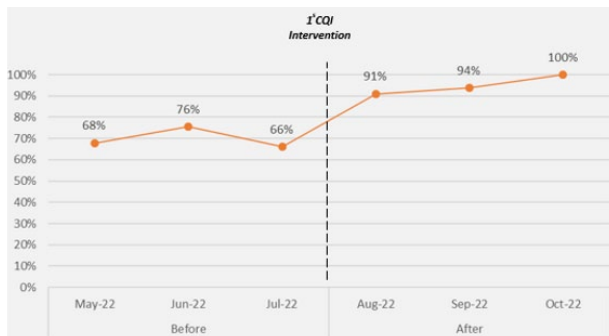


Figure 1. Showing mean LF-LAM uptake before and after CQI intervention among newly enrolled AHD clients at intervention sites (N=14).

**Conclusions:** The results demonstrate that CQI methodology can be utilized to increase uptake of LF-LAM test at poorly performing health facilities. As a recommendation, CQI interventions can be adapted by TB and HIV programs globally to improve not only the utilization of LF-LAM testing but also all AHD point of care screening tests.

### OA27-416-16 Impact of laboratory turnaround time on pre-treatment loss to follow-up among drug-resistant TB cases in rural Bihar, India

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**Background and challenges to implementation:** DR-TB is difficult to diagnose. The turnaround time (TAT) is very critical for ensuring timely diagnosis and treatment initiation for PwDRTB. An estimated 74% of people are lost in the diagnostic phase. Overburdened DST labs, high TAT and poor diagnostic reports communication channels are among the reasons for a worrisome rate of PTLFU in Samastipur, Madhubani and Begusarai districts of Bihar.

**Intervention or response:** We compared the TAT from sample submission to results received for LPA and Xpert MTB/XDR. We also evaluated the impact of TAT on the treatment regimen change status and subsequent pre-treatment outcomes among PwDRTB following high TAT (defined as days between sample submission and results received). FL-LPA detects resistance of Rifampicin (R) and Isoniazid (H), whereas SL-LPA detected resistance to Levofloxacin (Lfx), Moxifloxacin (Mfx), Amikacin (Am), Capreomycin (Cm), and Kanamycin (Km). Xpert MTB/XDR detects resistance similar to FL and SL-LPA along with additional resistance of Ethionamide (Eto).

**Results/Impact:** Of 1145 LPA samples tested, the median TAT from sample submission to results received was 26 days, with a range of 1 to 84 days. Out of 1145, 244 (21%) samples were of PwRR diagnosed through NAAT. The median TAT of LPA for PwRR was 18 days. For the total 843 samples tested in Xpert XDR, the range was 0-13 days, with median of 0 day, the results are similar for all 652 PwRR samples tested. The TAT of LPA is leading to high PTLFU. Out of 153 PwDRTB, only 107 (70%) persons' treatment regimen was changed, causing 30% of PTLFU.

**Conclusions:** When using LPA, TAT is very high compared to TAT of Xpert XDR. For PwRR, with Xpert XDR, the median TAT is 18 days shorter compared to LPA. If proper treatment for DR-TB is not initiated on time, it leads to poorer outcomes and poses a high threat to society.

### OA27-417-16 The proportion of potential TB misdiagnoses among clinically diagnosed TB patients during the COVID-19 pandemic in Lusaka, Zambia

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**Background:** Definite diagnosis of tuberculosis (TB) clinically is still difficult and poses a challenging dilemma. While some patients have paucibacillary TB that is not detected using available diagnostics, there is also evidence that many do not have TB disease and are misdiagnosed. We conducted a prospective cohort study to determine the extent to which clinically diagnosed TB may be misdiagnosed.

**Design/Methods:** Consecutive patients with a clinical TB diagnosis were enrolled from two public health facilities in Lusaka, Zambia with a high proportion (55%) of clinically diagnosed TB notifications between December 2021 and January 2023. Patients were subjected to a second sputum examination using Xpert Ultra, a rapid COVID antigen test, chest X-ray (CXR) interpretation using computer-aided diagnosis (CAD; qXR), and a second CXR review by an experienced radiologist.

**Results:** A total of 179 patients with clinically diagnosed TB were included in the analysis; the median age was 39 (IQR 29-47) years, 133 (76%) were male, 71 (39.7%) were HIV positive and 47 (26.6%) had a history of prior TB.

All patients had a positive WHO symptom screen, cough being the commonest 68 (95.7%) and fever the least common (33.8%). COVID antigen positivity was 0.6%. Radiologist review showed 164 (91.6%) CXR images were abnormal of which 74 (41.3%) were active TB, 6 (3.4%) previous TB, 25 (14%) COVID-19 and 45 (25.1%) other respiratory conditions. CAD analysis of 80 (44.6%) determined 73 (91.5%) to be abnormal of which 40 (50%) were TB presumptive and the other 40 (50%) were not suggestive of TB. On repeat Xpert examination only 6 (3.4%) had a positive result.

**Conclusions:** More than half of persons with clinically diagnosed TB in this study were likely misdiagnosed, in part reflecting front-line clinicians' inexperience interpreting CXRs. Strategies to address inappropriately high rates of clinically diagnosed TB are needed to mitigate TB misdiagnoses.

### OA28 Into the unknown: gender, TB and pregnancy

#### OA28-418-16 Enrolment of pregnant women with rifampicin-resistant TB into the BEAT Tuberculosis Randomized Clinical Trial: Early outcomes

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**Background:** Pregnant women do become sick with RR-TB but have historically been excluded from clinical trials of new treatments leaving an evidence gap.

The BEAT Tuberculosis Study was a phase III, open-label, pragmatic, randomized, controlled strategy trial to evaluate the efficacy and safety of a 6-month all-oral delamanid containing regimen compared to the South African all oral standard of care. Enrolment was open to pregnant women irrespective of their HIV status and duration of gestation.

Women that became pregnant while in the study were counselled about treatment options and were allowed to stay in the trial. Enrollment to the trial was completed in October 2022 (400 participants).

**Design/Methods:** In addition to routine clinical safety monitoring, a fetal anomaly scan was done prior to starting TB treatment. Adverse event follow-up was conducted at scheduled visits at 2-week intervals for a month and monthly thereafter until treatment completion.

All participants living with HIV were on antiretroviral as per National Guidelines. In addition, PK samples were collected at week 2 and again after delivery. Breast milk samples if available were collected

**Results:** Ten pregnant women were enrolled. Most women had been diagnosed with RR-TB in their local Antenatal Clinics during TB symptoms screening. Nine were pregnant when enrolled and one became pregnant on trial. Most women presented for care in their second or third trimester.

All women had a singleton pregnancy. None of the participants had a poor obstetric outcome, all pregnancies resulted in safe delivery of live infants (see Table).

All the women were cured at the end of treatment and are still in study follow up. There were no SAEs in the group.

Site	Patient number	Age in Years	HIV status and Cd4+	ART Regimen	Gestational age	Randomized strategy	Timing of delivery	Birth weight (grams)	Outcome at the end of treatment
Site 1	1	19	Negative	N/A	36/40	Study	Term Normal vaginal delivery (NVD)	UNK	Cured
	2	30	Positive: 87	TDF/FTC/LPVr → TLD	20/40	Control	28+5/40 due to Premature rupture of membranes	1500	Cured
	3	38	Positive: 78	TLD	20/40	Control	Term NVD	2400	Cured
	4	32	Positive: 159	TLD	19/40	Study	Term NVD	2600	Cured
	5	25	Positive: 100	TLD	2/40	Control	Term NVD	2570	Cured
	6	21	Positive: 24	TDF/FTC/LPVr(DRVr) → TLD	20/40	Study	Term NVD	3300	Cured
	7	42	Positive: 362	TLD	2/40	Control	Term Caesarean section (C/S)	2850	Cured
Site 2	8	27	Positive:	TLD	0/40	Study	Term NVD	3340	Cured
	9	34	Positive: 716	TLD	16/40	Control	Term C/S	2840	Cured
	10	37	Positive: 234	TLD	28/40	Study	Term NVD	3020	Cured

**Conclusions:** This study has shown that it is possible and feasible to enroll women who are pregnant that are infected with RR-TB and co-infected with HIV in clinical trials.

**OA28-419-16 Improving early screening, identification and management of TB during pregnancy: experience from Assam, India**

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**Background and challenges to implementation:** India contributes to 21% of global active Tuberculosis (TB) cases among pregnant women. TB during pregnancy increases the risk for adverse maternal and fetal outcomes including maternal morbidity, miscarriage, pre-term and low-birth-weight, and perinatal deaths. To address this, the Indian Government released a guideline “Management of TB in Pregnant women” to integrate TB and

maternal health services, yet its implementation remains limited. The guideline focuses on improving the overall treatment outcome of pregnant women with TB by ensuring bidirectional screening and referral between NTP and Maternal Health (MH) Division. Given the high maternal mortality rate in the state of Assam (195 vs 97 per 100,000 live births in India), screening and managing TB in pregnant women there is crucial.

**Intervention or response:** Jhpiego, through USAID-funded NISHTHA program, assisting Assam government in implementing the guidelines across the state via Community Health Officer(CHO)-led Health and Wellness Center’s (HWC) and TB Units since April 2022. Jhpiego is involved in conducting collaboration meetings between Maternal Health and State TB cell divisions; capacitating CHOs and government officials on framework roll-out; establishing a reporting mechanism on TB MIS (NIKSHAY); mobilizing provision of sputum collections essentials at HWCs; and community awareness. Various facility-based & community-based platforms are leveraged for screening.

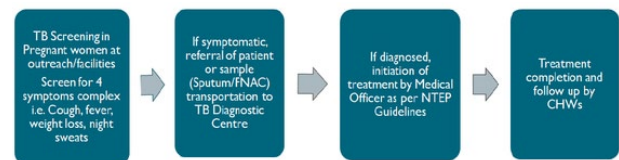


Figure. Service delivery pathway for TB in pregnant women.

**Results/Impact:** More than 1000 CHOs and district/block officials of both Maternal and TB cells were trained. Between 2022-23, ~40,000 pregnant women were screened for TB in their ANC check-ups, of which 5,862 were identified as presumptive and 17 diagnosed with active pulmonary and extra-pulmonary TB. Among these, five completed treatment and 12 are currently availing care.

**Conclusions:** The TB screening program for pregnant women was effective but needs improvement in reach. This can be done by using data for programmatic decision-making, intensive community awareness, streamlined reporting, empowering Frontline workers, and better coordination between TB and MH divisions.

### OA28-420-16 Evaluating the implementation and uptake of targeted universal TB sputum testing using Xpert Ultra in HIV-positive pregnant women in Cape Town, South Africa

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**Background:** Targeted Universal TB Testing (TUTT) using GeneXpert Ultra was endorsed in 2019 by the South African National Department of Health for HIV positive pregnant women and was thereafter adopted by the Western Cape Government in 2020, to address the high rates of maternal mortality attributed to TB. This analysis aims to evaluate the pre and post TUTT implementation diagnosis of TB in primary health care (PHC) facilities among this vulnerable population.

**Design/Methods:** This was a retrospective before-and-after analysis to compare TB screening, testing and diagnosis of TB in HIV positive pregnant women (15-50 years of age) at their first antenatal visit, pre and post TUTT implementation (2018-2019 versus 2020-2021). Multivariate logistic regression analysis was conducted to determine the association between TB testing, clinical and demographic characteristics.

**Results:** Initially 7235 records of HIV positive women were identified of which 3332 and 3903 were in the pre and post TUTT implementation cohorts. Symptom screening at the first antenatal visit were relatively the same pre and post TUTT implementation (16.8% versus 15.9%). The total sputum testing per cohort increased significantly by 13-fold from 1.26% (n=42) to 14.3% (n=557) pre and post TUTT implementation. There was also a significant increase in women that were tested for TB specifically at their first antenatal visits from 17% (n=7 of 42) to 78% (n=432 of 557) (p<0.01). Additionally, sputum samples sent for GeneXpert Ultra testing increased from 2.4% to 15%, pre and post TUTT implementation.

**Conclusions:** Implementation of TUTT in PHC facilities in Cape Town resulted in significantly more HIV positive pregnant women tested for TB; however, testing rollout remains low with less than 15% of the eligible cohort receiving access to a TB test. Further scale-up is required to ensure all HIV positive pregnant women are tested according to TUTT to meet the ENDTB TB incidence and mortality reduction targets

### OA28-421-16 High prevalence of antepartum and postpartum depressive symptoms and their association with active TB: Findings from a prospective longitudinal cohort of pregnant and postpartum Indian women

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**Background:** To estimate the prevalence and persistence of depressive symptoms in a cohort of pregnant and postpartum women in India with a high prevalence of TB infection. We also examine risk factors for the same.

**Design/Methods:** We enrolled 234 HIV +/- pregnant women with and without TB infection (TBI) into a prospective observational cohort study, Pregnancy Associated CHanges In Tuberculosis immunology, in Pune, India. Enrolled women were screened for depressive symptoms with Patient Health Questionnaire-9 (PHQ-9) during pregnancy, at 6 months and 12-18 months postpartum. Fischer exact test and logistic multivariate regression identified the risk factors for depression; variables with a p<0.1 were included in the multivariate analysis.

	N=234	AP Depressive symptoms			N=211	PP Depressive symptoms		
		Depressive symptoms n(%)	OR (95% CI)	aOR (95% CI)		Depressive symptoms n (%)	OR (95% CI)	aOR (95% CI)
Median age >= 23	128	77 (60%)	1.2 (0.7 - 2.0)	1.2 (0.6 - 2.1)	117	36 (31%)	1.1 (0.6 - 2.0)	0.9 (0.4 - 1.9)
HIV positive	79	51 (65%)	1.5 (0.9 - 2.6)	1.5 (0.8 - 2.8)	73	30 (41%)	2.2 (1.2 - 4.1)	2.1 (1.0 - 4.4)
Active Tuberculosis	10	7 (70%)	1.7 (0.5 - 8.1)	1.3 (0.3 - 7.0)	8	6 (75%)	7.7 (1.7 - 53.5)	7.2 (1.2 - 58.6)
IPV- In the 12 months before pregnancy	39	33 (85%)	4.9 (2.1 - 13.5)	3.4 (1.3 - 10.2)	35	19 (54%)	3.6 (1.7 - 7.6)	2.1 (0.8 - 5.2)
Personal financial instability	50	43 (86%)	6.0 (2.7 - 15.2)	5.0 (2.1 - 13.2)	48	24 (50%)	3.2 (1.6 - 6.3)	2.2 (1.0 - 5.0)
Substance abuse by someone close to the patient in the 12 months before pregnancy	26	21 (81%)	3.4 (1.3 - 10.5)	2.8 (1.0 - 9.1)	26	14 (54%)	3.2 (1.4 - 7.6)	4.1 (1.5 - 11.4)
Moderate to severe food insecurity	25	15 (71%)	1.9 (0.7 - 5.5)	0.8 (0.2 - 2.8)	12	9 (75%)	7.9 (2.3 - 36.6)	7.9 (1.9 - 40.3)
Cannot read a newspaper, magazine, etc.	40	26 (65%)	1.4 (0.7 - 2.9)	1.0 (0.5 - 2.3)	37	19 (51%)	3.1 (1.5 - 6.5)	2.5 (1.1 - 6.1)

**Results:** Of the 234 enrolled women, 136 (58%) reported at least one depressive symptom during pregnancy; 27% (64/234) were more than minimal. Adjusted for age and



parity, intimate partner violence (aOR 3.4 (1.3 – 10.2)) and personal financial insecurity (aOR 5.0 (2.1 – 13.2)) were significantly associated with antepartum depressive symptoms. There was no significant difference in proportion with antepartum depressive symptoms in women with and without TBI.

Overall, 30% (63/211) had postpartum depressive symptoms: 48 (39%) with persistent symptoms from pregnancy. Women with active TB had significantly higher risk of postpartum depressive symptoms (aOR 7.2 (1.2 – 58.6)). Living with HIV (aOR 2.1 (1.0 – 4.4)) , illiteracy (aOR 2.5 (1.1 – 6.1)) and severe food insecurity (aOR 7.9 (1.9 – 40.3)) were also associated with postpartum depressive symptoms.

**Conclusions:** We found high prevalence of depressive symptoms in pregnant and postpartum women in India, but risk factors differed between antepartum and postpartum. Because active TB is a significant predictor of postpartum depression, effective TB prevention could decrease postpartum depressive symptoms, especially for women with HIV. Interventions to address social and financial predictors would help alleviate both antepartum and postpartum depressive symptoms.

**OA28-422-16 Adverse pregnancy outcomes and isoniazid exposure during pregnancy: Systematic review and individual participant data meta-analysis of women living with HIV**

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**Background:** To evaluate the association between exposure to isoniazid (INH) during pregnancy and adverse pregnancy outcomes (APO), we conducted an individual participant data meta-analysis (IPD-MA) of available data on pregnant women living with HIV from published randomized TB prevention trials.

**Design/Methods:** Following PRISMA guidelines, we conducted a systematic review for published data on women who were/became pregnant during randomized TB prevention trials. Four studies with available IPD

met eligibility criteria. We excluded ectopic pregnancies and therapeutic abortions. We used a generalized mixed model with random treatment and study effects to estimate the odds ratio (OR, 95% CI) of composite and individual APO associated with INH exposure during pregnancy, adjusting for participant characteristics (Table). Heterogeneity of treatment effect was assessed using R values (>1 implies more heterogeneity).

**Results:** We obtained IPD for 1483 women from 13 countries: 128 from BRIEF-TB, 196 from BOTUSA, 233 from TEMPRANO, 926 from TB-APPRISE.

Some participant characteristics during pregnancy (age, ARV regimen/use, CD4) differed across studies. Mean (SD) age and CD4 count were 30(6) years and 513(236) cell/mm<sup>3</sup>, respectively.

Most (1429, 96%) were on ARVs during pregnancy, including 929 (62%) on EFV-based regimens.

There were 631 (42.5%) women exposed to INH during pregnancy, including 170 (11.5%) during first trimester.

From the IPD-MA, we observed increased odds of fetal demise if INH-exposed (adjusted aOR=1.58 (95%CI: 0.78-3.22) but was not significant, with R=1.34 (Table); this was observed in TB-APPRISE (OR=2.37, 95%CI: 0.96-5.84), TEMPRANO (OR=4.29, 95%CI: 0.53-36.41) and was significant in BRIEF-TB (OR=2.92, 95%CI: 1.19-7.17), but decreased odds in BOTUSA (OR=0.68, 95%CI: 0.25-1.89).

Outcome	Total n/N (%)	INH-unexposed n/N (%)	INH-exposed n/N (%)	Unadjusted OR (95%CI)	Unadjusted p-value	Unadjusted R	Adjusted* OR (95%CI)	Adjusted* p-value	Adjusted* R
Any Adverse pregnancy outcome (fetal demise, low birth weight, preterm delivery) <sup>a</sup>	369/1362 (25.8%)	204/768 (26.6%)	165/594 (27.8%)	1.30 (0.77, 2.19)	0.41	2.00	1.10 (0.59, 2.07)	0.79	2.17
Fetal demise <sup>**</sup>	97/1429 (6.8%)	55/808 (6.8%)	42/621 (6.8%)	1.63 (0.94, 2.82)	0.19	1.17	1.58 (0.78, 3.22)	0.30	1.34
Low birth weight (<2500 gms) <sup>a</sup>	174/1287 (13.1%)	94/721 (13.0%)	80/566 (14.1%)	1.24 (0.65, 2.33)	0.63	1.87	1.15 (0.57, 2.33)	0.76	2.69
Preterm delivery (<37 wks) <sup>a</sup>	175/1286 (13.1%)	99/723 (13.7%)	76/563 (13.5%)	1.07 (0.65, 1.77)	0.82	1.47	0.98 (0.67, 1.42)	0.93	1.00

\*Adjusted for maternal age, CD4 count, ARV use, TB infection status, and multiple gestation  
<sup>a</sup>Denominators (in n/N columns) exclude ectopic pregnancies and therapeutic abortions  
<sup>\*\*</sup>Denominators (in n/N columns) exclude ectopic pregnancies and therapeutic abortions, and relevant missing data on preterm delivery and low birth weight

*Table: Summary of Adverse Pregnancy Outcomes and IPD-MA Regression Results of Adverse Pregnancy Outcomes vs. INH Exposure during Pregnancy.*

**Conclusions:** Our meta-analysis did not find a significant effect of INH exposure during pregnancy on composite and individual APO, but possibility of increased odds of fetal demise deserves further study. We should explore potential modification effect of participant characteristics, given generally notable heterogeneity in treatment effects.

### OA28-423-16 TB infection in infertile women: Interim results from a multi-centre study in China (TB-PRIME study)

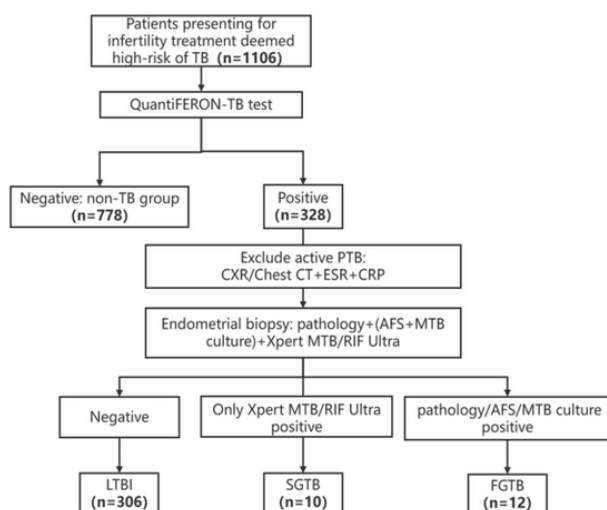
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**Background:** Female genital tuberculosis (FGTB) is an important cause of women infertility in high TB burden areas. There is subclinical/latent genital tuberculosis infection as well, defined as the detection of pathogens but asymptomatic. However, guidelines to identify those with female genital tuberculosis or latent tuberculosis in fertility centers are lacking. Our TB-PRIME study aims to establish a multi-center cohort to characterize the epidemiology of TB infection and its impact on pregnancy in Chinese infertile women.

**Design/Methods:** This is a prospective cohort study. From November 2021 to February 2023, infertile women from 13 reproductive centers were assessed for risk factors for TB infection and eligible participants underwent screening using QuantiFERON-TB Gold (QFT) assay. Participants with positive QFT results underwent further testing for genital tuberculosis (ClinicalTrials.gov: NCT05311423).

**Results:** This study presently recruited 1,106 infertile women and formed 4 groups (Figure below).



CXR, chest X-ray; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; PTB, pulmonary tuberculosis; AFS, acid-fast staining; MTB, Mycobacterium tuberculosis; LTBI, latent tuberculosis infection; SGTB, subclinical genital tuberculosis; FGTB, female genital tuberculosis

A total of 328 (29.6%) participants were QFT positive. Among the QFT-positive patients, the prevalence of genital tuberculosis infection was 6.7% (22/328), among which 10 (3.05%) were recognized as subclinical/latent genital TB infection by positive Xpert MTB/RIF

Ultra but negative pathology results of the endometrial biopsy, and 12 (3.66%) were diagnosed as FGTB. BMI, duration of infertility, chest imaging abnormalities, previous TB history, non-BCG vaccination, and repeated implantation failure were identified as risk factors for QFT positivity in this population.

Moreover, the previous positive IGRA results was identified as a risk factor for genital tuberculosis infection in QFT-positive patients.

**Conclusions:** The prevalence of female genital TB in infertile women in China seems to be high, and this study indicates that all at-risk women seeking infertility care should be screened for TB infection before infertility treatments are initiated.

### OA28-424-16 Female genital TB: A diagnostic conundrum

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**Background:** Diagnosing extrapulmonary tuberculosis including female genital tuberculosis (FGTB) is challenging. We aimed to assess diagnostic value of Douglas pouch aspirates cytology with utility of Cytospin-preparation for diagnosing FGTB.

**Design/Methods:** We conducted a retrospective study among persons with presumed FGTB from 2020 to 2022 at the National Center for Tuberculosis and Lung Diseases (NCTL). Complex of investigations for diagnosing FGTB included Douglas pouch fluid samples cytology by Cytospin-preparation.

**Results:** During the study period, 18 patients were screened for suspected FGTB in NCTL. Cytology of Douglas pouch aspirates revealed a predominance of mesothelial cells and lymphocytes in 13 (72%) specimens, although in 2 (11%) cases, mesothelial cells mimicked malignancy. These two patients underwent laparoscopy with ovarian biopsy and histomorphology revealed tuberculous granuloma in both cases. In 11 (61%) patients, PCR examination of vaginal samples revealed MTB, but the growth of the MBT culture was seen in one (5.5%) person.

A total of 13 (72%) patients were diagnosed with FGTB, 1 (6%) patient was diagnosed with ovarian cancer, and 4 (22%) patients had nonspecific bacterial inflammation. All patients with FGTB successfully completed TB treatment.

**Conclusions:** Douglas pouch aspirates' cytology with the utility of Cytospin-preparation showed high diagnostic value, although complex investigations are necessary for diagnosing FGTB.

### OA28-425-16 Sex differences in TB infection and disease in people with HIV in Brazil

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**Background:** Males experience an excess burden of TB compared to females, likely due to differences in biological, socioeconomic, and behavioral factors that influence risk of infection and prognosis. However, data on sex differences in TB among people with HIV (PWH) are limited.

We therefore compared risk of TB infection and disease in males and females with HIV in Brazil.

**Design/Methods:** We analyzed data from THRio, a cluster-randomized trial conducted in 29 clinics in Rio from 2005-2012 that increased tuberculin skin testing (TST), with TB preventive therapy (TPT) for those who were TST-positive.

We included PWH newly registered at participating clinics during the study period, following patients from entry into care until TB diagnosis, death, or administrative censoring.

We compared TB infection prevalence and TB incidence rates (IR) per 100 person-years (pys) between males and females. Analyses of TB incidence were stratified by TST, TPT, and ART status.

**Results:** Among 4,606 PWH entering care, 2,867 (62.2%) were male and 2,989 (64.9%) received TST (65.0% males vs. 64.8% females,  $p=0.87$ ). Of these, 670 (22.4%) were TST-positive, including 415 (22.3%) males and 255 (22.7%) females ( $p=0.81$ ).

A total of 300 (6.5%) were diagnosed with incident TB, including 204 (7.1%) males and 96 (5.5%) females. TB incidence rates were higher among males than females overall (1.51 vs. 1.14 per 100pys, IRR 1.33, 95% CI 1.04-1.69), among those who did not receive TPT (1.58 vs. 1.22 per 100 pys, IRR 1.30, 95% CI 1.01-1.67), and among those on ART (1.69 vs. 1.03 per 100 pys, IRR 1.64, 95% CI 1.17-2.29, Table).

	IR per 100 pys, total (95% CI)	IR per 100 pys, male (95% CI)	IR per 100 pys, female (95% CI)	IRR (95% CI)
Total	1.37 (1.22-1.53)	1.51 (1.32-1.74)	1.14 (0.93-1.39)	1.33 (1.04-1.69)
TST-negative	0.84 (0.69-1.04)	0.97 (0.76-1.24)	0.64 (0.43-0.93)	1.53 (0.97-2.41)
TST-positive	2.46 (1.95-3.12)	2.50 (1.86-3.38)	2.40 (1.63-3.52)	1.04 (0.64-1.70)
TST-unknown	1.68 (1.42-1.98)	1.89 (1.55-2.31)	1.35 (1.00-1.81)	1.40 (0.98-2.00)
No TPT	1.44 (1.28-1.62)	1.58 (1.37-1.82)	1.22 (0.99-1.50)	1.30 (1.01-1.67)
Initiated TPT	0.82 (0.54-1.25)	0.98 (0.59-1.62)	0.62 (0.29-1.30)	1.58 (0.64-3.87)
No ART	1.27 (1.06-1.52)	1.28 (1.02-1.61)	1.26 (0.95-1.66)	1.01 (0.71-1.45)
Initiated ART	1.45 (1.25-1.68)	1.69 (1.42-2.00)	1.03 (0.77-1.38)	1.64 (1.17-2.29)

**Abbreviations:** IR, incidence rate; pys, person-years; CI, confidence interval; IRR, IR ratio; TST, tuberculin skin test; TPT, TB preventive therapy; ART, antiretroviral therapy  
TST, TPT, and ART were treated as time-varying

**Conclusions:** TB incidence rates were higher among men than women with HIV in Rio, despite similar prevalence of TB infection, especially in those receiving TPT and ART. This suggests that biologic sex differences in host responses to infections may decrease the risk of TB in females with HIV.

### OA29 Imaging in tuberculosis

#### OA29-426-16 Can artificial intelligence be used to detect subclinical pulmonary TB in the Philippines?

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**Background:** Chest X-ray (CXR) screening is used to identify clients with presumptive pulmonary tuberculosis (TB); however, issues of scarcity of radiologists and substantial variations among human-readers impede efforts in TB diagnosis and treatment. As computer-aided detection (CAD) may be used to screen TB disease, artificial intelligence (AI) creates an opportunity for early diagnosis, including subclinical TB, which is operationally defined as having radiologic and/or bacteriologic evidence of TB but not TB-symptomatic ( $\geq 2$  weeks of cough, fever, night sweats, or weight loss among HIV-negative or unknown HIV status). This study aimed to evaluate the agreement between CAD with AI (CXR-AI) and human-reader, assess CAD performance in detecting subclinical TB, and estimate its prevalence within the study population.

**Design/Methods:** We conducted a secondary analysis of 2019-2022 project data, wherein participants were screened using CXR-AI and symptoms. A portion of the CXR scans were independently assessed by radiologists. Clients with presumptive TB were tested for presence of TB bacilli using Xpert MTB/Rif.

**Results:** Among (N=48,486) participants (mean age 42.57±15.36, unknown HIV status), 1.42% had bacteriologic evidence of TB. Of these patients, 32% were symptomatic and 68% were subclinical. Among 4,306 CXR assessed by human-reader, Cohen's Kappa coefficient (K) between CXR-AI and radiologist reading was 0.71 (SE=0.0152), with near perfect agreement of 93.85% (p<0.0001). Our results showed that CXR-AI had 74.4% sensitivity, 96.6% specificity, 73.7% positive predictive value, and 97.0% negative predictive value. While 7.83% of all TB symptomatic clients were detected with bacteriologic evidence of TB, CXR-AI was able to identify 1.03% subclinical TB cases among clients who were not TB-symptomatic which would otherwise be missed using conventional methods (p<0.001).

Characteristics of the Population	(n = 48,486)	
Age	42.57±15.36	11 to 93 years old
Gender	56% Female, 44% Male	
TB yields	689 (1.42%)	
Clinical	220 (7.83%)	p<0.001 (statistically significant using Pearson's chi-test)
Subclinical	469 (1.03%)	
<b>Measures and predictive values of CAD powered by AI</b>		
Sensitivity	74.7%	
Specificity	96.4%	
Positive Predictive Value	73.7%	
Negative Predictive Value	96.6%	
<b>Cohen's Kappa (K)</b>	<b>0.7070 (SE=0.0152)</b>	<b>p&lt;0.001</b>
<b>Agreement</b>	<b>93.85%</b>	

**Background and challenges to implementation:** Chest X-ray (CXR) screening is used to identify clients with presumptive pulmonary tuberculosis (TB); however, issues of scarcity of radiologists and substantial variations among human-readers impede efforts in TB diagnosis and treatment.

As computer-aided detection (CAD) may be used to screen TB disease, artificial intelligence (AI) creates an opportunity for early TB diagnosis, including subclinical TB, which is operationally defined as having radiologic and/or bacteriologic evidence of TB but not TB-symptomatic (≥2 weeks of cough, fever, night sweats, or weight loss among HIV-negative or unknown HIV status).

This study aimed to evaluate the agreement between CAD with AI (CXR-AI) and human-reader, assess CAD performance in detecting subclinical TB, and estimate its prevalence within the study population.

**Intervention or response:** We conducted a secondary analysis of 2019-2022 project data, wherein participants were screened using CXR-AI and symptoms. A portion of the CXR scans were independently assessed by radiologists. Clients with presumptive TB were tested for presence of TB bacilli using Xpert MTB/Rif.

**Results/Impact:** Among (N=48,486) participants (mean age 42.57±15.36, unknown HIV status), 1.42% had bacteriologic evidence of TB. Of these patients, 32% were symptomatic and 68% were subclinical. Among 4,306 CXR assessed by human-reader, Cohen's Kappa coefficient (K) between CXR-AI and radiologist reading was 0.71 (SE=0.0152), with near-perfect agreement of 93.85% (p<0.0001).

Our results showed that CXR-AI had 74.4% sensitivity, 96.6% specificity, 73.7% positive predictive value, and 97.0% negative predictive value. While 7.83% of all TB symptomatic clients were detected with bacteriologic evidence of TB, CXR-AI was able to identify 1.03% subclinical TB cases among clients who were not TB-symptomatic which would otherwise be missed using conventional methods (p<0.001).

Characteristics of the Population	N = 48,486	
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<b>Measures and predictive values of CAD powered by AI</b>		
Sensitivity	74.7%	
Specificity	96.4%	
Positive Predictive Value	73.7%	
Negative Predictive Value	96.6%	
<b>Cohen's Kappa (K)</b>	<b>0.7070 (SE=0.0152)</b>	<b>p&lt;0.001</b>
<b>Agreement</b>	<b>93.85%</b>	

**Conclusions:** CXR-AI can be used to detect subclinical TB, as evidenced by high sensitivity and specificity. Near-perfect agreement between CXR-AI and human-reader shows that it offers advantage in Philippine settings with limited access to radiologists.

### OA29-427-16 18F-fluorodeoxyglucose PET-CT imaging in the ROSETTA trial: the impact of adjunctive rosuvastatin in rifampicin-susceptible TB treatment

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**Background:** The randomised phase 2b ROSETTA trial tested adjunctive rosuvastatin in the treatment of rifampicin-susceptible Tuberculosis. We report results from a nested, exploratory PET-CT sub-study, investigating changes in metabolic and structural lung disease parameters.

**Design/Methods:** A subset of participants from the ROSETTA trial, identified via convenience sampling, underwent <sup>18</sup>F-fluorodeoxyglucose (18F-FDG) PET-CT scans at baseline and at 8 weeks. Avid lesion segmentation was performed by two readers using Osirix and through a semi-automated method (Syngo.via VB50MM, Siemens). Total lesion glycolysis [TLG; mean Standard Uptake Value (SUV) X volume of lesion], cavity diameter and SUVmax are presented here. Rosuvastatin versus control groups were compared using a quantile regression model. Interclass correlation coefficients between readers and software platforms were derived from a random effects model.

**Results:** Twenty-four out of 137 (17.5%) participants underwent two PET-CT scans; 19/24 (79.2%) were male, median age of 30 years and baseline characteristics between groups were similar. Within eight weeks of tuberculosis treatment, TLG reduced by >60% in both rosuvastatin and control groups, whilst changes in SUVmax were less substantive.

Reduction in cavity diameter in the rosuvastatin group was greater than the control group, but differences between groups were not significant for any outcomes measured. Inter-class correlation between the two readers was very high at 0.999, and 0.829 between the software platforms.

	Rosuvastatin (N=12)	Control (N = 12)	Difference**, median (95% CI) <sup>A</sup>	P value
<b>Total Lesion Glycolysis (TLG),</b>				
Baseline, median (IQR)	328.2 (884.3)	804.7 (1175.6)		
Week 8, median (IQR)	79.8 (441.4)	308.5 (679.0)		
Percentage change*, median (Q1, Q3)	-69.5 (-99.0, -41.6)	-64.3 (-81.7, 20.0)	9.4 (-63.6, 82.4)	0.79
<b>Cavity Diameter (mm),</b>				
Baseline, median (IQR)	48.1 (100.7)	49.8 (47)		
Week 8, median (IQR)	17.9 (64.1)	34.2 (47.8)		
Percentage change* of median (Q1, Q3)	-55.0 (-64.4, 6.0)	-27.1 (-73.8, 23.6)	-34.4 (-130.3, 61.5)	0.45
<b>SUVmax</b>				
Baseline, median (IQR)	8.3 (5.0)	10.3 (7.0)		
Week 8, median (IQR)	6.8 (5.3)	7.9 (4.2)		
Change from baseline, median (IQR)	-0.8 (1.3)	-1.9 (9.1)	-0.5 (-4.5, 3.4)	0.77

\*Baseline to week 8, \*\* rosuvastatin - control, <sup>A</sup>Based on quantile regression model.

Table 1: Outcomes of PET-CT sub-study

**Conclusions:** Results from this exploratory PET-CT study are consistent with the main trial findings; adjunctive rosuvastatin does not show benefit over standard treatment for tuberculosis. PET-CT metrics which combine volumetric and metabolic parameters, such as TLG, characterise treatment induced metabolic and structural lung changes better than semi-quantitative measures, such as SUVmax. More data are need to determine whether PET-CT has a role in evaluating responses to drug treatment within clinical trials.

### OA29-428-16 Quality assurance of computer-aided detection to improve chest X-ray interpretation in facility- and community-based TB screening: experience from Vietnam

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**Background and challenges to implementation:** In Vietnam, chest X-ray (CXR) triages GeneXpert (Xpert) testing to diagnose TB, demonstrating high yield TB disease detection but variable CXR interpretation. Computer-aided detection (CAD) artificial intelligence can standardize and improve CXR interpretation quality. We integrated CAD into TB screening to support physicians on CXR interpretation and triage for Xpert testing.

**Intervention or response:** Retrospective CAD (qXR) analysis with Xpert as reference was performed on 51,441 CXR from community TB screening in 2020.

With the resultant CAD framework, we integrated real-time CAD into community screening in 2021 (17,078 CXR) and 2022 (28,112 CXR) and expanded to 11 facilities in 2022 (24,945 CXR). The CAD-parallel model (qXR threshold  $\geq 0.60$ ) incorporated physician and CAD interpretation for all CXR; the CAD-first model (qXR threshold  $\geq 0.40$ ) selected only abnormal “TB-presumptive” CXR for physician interpretation.

For both models, physicians made the final decision for Xpert testing and also triaged individuals with positive symptom screen for Xpert, independent of CXR.

**Results/Impact:** At three months, CAD-parallel integration in facility-based screening resulted in 47.3% CXR with concordant TB interpretation by CAD and physician (Kappa=0.30 SE 0.01), 11.0% Xpert positivity; increasing at six months to 69.1% concordant CAD-physician TB interpretation (Kappa=0.44 SE 0.01), 21.1% Xpert positivity; and at nine months to 76.1% concordant CAD-physician TB interpretation (Kappa=0.56 SE 0.01), 22.0% Xpert positivity.

In community screening, CAD-first integration decreased Xpert testing for normal CAD CXR from 33.3% (2021) to 8.8% (2022); however, the proportion of “missed” Xpert testing for CAD TB-presumptive CXR increased over the same period (13.7% and 22.0%).

Facility ICF: CAD-parallel model	April-June 2022 (N=5826)	July-Sept 2022 (N=9696)	Oct-Dec 2022 (N=9423)
No. (%) CXR with CAD TB + Doctor TB reading	227/480 (47.3%)	522/755 (69.1%)	796/1046 (76.1%)
No. (%) CXR with CAD Normal + Doctor TB reading	253/480 (52.70%)	233/755 (30.9%)	250/1046 (23.9%)
No. (%) Xpert positive	50/455 (11.0%)	148/703 (21.1%)	199/903 (22.0%)
<b>Community ACF: CAD-first model</b>	<b>2020 (N=51,441)</b>	<b>2021 (N=17,078)</b>	<b>2022 (N=28,112)</b>
No. valid Xpert results	7205	3722	4297
No. (%) tested with Xpert for normal CAD CXR	2827/7205 (39.2%)	1241/3722 (33.3%)	378/4297 (8.8%)
No. (%) Xpert positive for normal CAD CXR	36/2827 (1.3%)	6/1241 (0.5%)	2/378 (0.5%)
No. (%) without Xpert testing for CAD TB CXR	2496/6934 (36.0%)	396/2892 (13.7%)	1109/5033 (22.0%)

*Table. Computer-aided detection (CAD) implementation results from 11 facilities in 2022 and at community TB screening campaigns in 2020-2022.*

**Conclusions:** CAD integration into community and facility TB screening supported physicians to improve triage decisions for Xpert testing. Using quality assurance, CAD-first and CAD-parallel models impacted decision-making at different steps in the workflow. Selection of the model and threshold score and physician concordance with CAD interpretations are important to optimize CAD performance and TB yield.

## OA29-429-16 Feasibility of computer-aided detection to improve chest X-ray interpretation: results from district-level health facilities in a high TB burden country

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**Background and challenges to implementation:** Vietnam’s TB screening algorithm prioritizes chest radiography (CXR) to triage GeneXpert testing (the Double X strategy). CXR is known for inter-reader variability, high sensitivity, and lower specificity for detecting TB abnormalities. The WHO recommends models for integrating computer-aided detection (CAD) but there is limited guidance on programmatic implementation.

**Intervention or response:** From April-December 2022, CAD (qXR) was installed to interpret CXRs of outpatients and inpatients in seven district health facilities across four provinces. CAD was implemented as quality assurance through a CAD-parallel model: CAD and physicians interpreted all CXR, and physicians incorporated CAD readings into the triage decision for GeneXpert testing. CAD facilities were selected for high patient volume, adequate infrastructure, and leadership interest. A protocol was developed to guide CAD installation, CAD platform user guidelines, TB screening algorithm, CAD-integrated clinical workflow, and data reporting. In the same four provinces, 23 facilities implemented Double X without CAD.

**Results/Impact:** CAD sites had more CXRs read as “TB-presumptive” (19.9%) compared with non-CAD sites in the same provinces (8.9%) with similar GeneXpert positivity rates and higher yield for detecting TB disease (4,635/ 100,000 CXR versus 2,352/ 100,000 CXR). TB-presumptive CXRs and TB yield increased in CAD sites compared to pre-CAD installation (10.7% and 3,538/100,000 CXR during April – December 2021). In CAD sites, 85.9% of 3,352 patients triaged for GeneXpert testing were tested, lower than non-CAD sites and the pre-CAD period.

	Evaluated with CXR	# (%) TB-presumptive CXR	# (%) tested with Xpert	Total TB diagnosed	# (%) initiated treatment	TB case Yield/100,000 CXR
Pre-implementation: April – December 2021						
Facilities selected for CAD (n=7)	12,351	1,322 (10.7%)	1,320 (99.8%)	437	424 (97%)	3,583
Post-implementation: April – December 2022						
CAD Facilities (n=7)	19,289	3,884 (19.9%)	3,352 (85.9%)	896	816 (91.1%)	4,635
Facilities without CAD (n=23)	81,245	7,269 (8.9%)	7,029 (96.4%)	1,915	1,729 (90.3%)	2,352

Table. TB Screening results at CAD sites and sites with physician interpretation only, 4 provinces of Vietnam.

**Conclusions:** CAD integration in district general health facilities increased the CXR triage rate for GeneXpert testing with higher yield for detecting TB disease compared with non-CAD facilities and the pre-CAD installation period. CAD improves the quality of CXR interpretation, which is advantageous for decentralized TB screening in non-TB specialized facilities or units. Successful CAD implementation requires a detailed protocol, user support, and collaboration between health facility departments to ensure confirmatory diagnostic testing for TB-presumptive CXR.

### OA29-430-16 Lessons learnt during the implementation of digital chest X-ray with computer-aided detection software screening for TB in primary healthcare facilities in South Africa

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**Background and challenges to implementation:** TB remains a major clinical and public health issue in South Africa. Despite progress made in reducing the TB incidence in recent years, the TB burden is still very high. The national TB prevalence survey conducted in 2018 estimated the TB prevalence at 737/100,000. Notably 58% of the bacteriologically positive cases in the survey were asymptomatic and only identified through DCXR. This highlighted the need for chest X-Ray based screening at primary healthcare facilities (PHCs) and community level.

**Intervention or response:** The National Department of Health with support from Global Fund to Fight Aids, Tuberculosis and Malaria, implemented a DCXR TB screening pilot project in 2019. Fifteen containerized DCXR units, equipped with computer-aided detection

(CAD) software and an integrated M&E system, were placed at 23 high TB burden PHC facilities in 6 districts between 12 November 2020 and 31 March 2022. Each container was staffed with a Radiographer, Enrolled Nursing Assistant (ENA) and data capturer.

PHC attendees presenting at the container, were interviewed by the ENA using a structured questionnaire which included the WHO-recommended four-symptom screening tool. Symptomatic clients were collected sputum sample for investigation and those asymptomatic or could not produce a sputum were referred for chest x-ray screening. DCXR films were interpreted by CAD software and findings and reports automatically populated into patient’s profile in the M&E software.

**Results/Impact:** 77 876 visits were made to DCXR containers, and the results were as per the table below.

TB screening modality	Number screened	Screened positive	Xpert test positive	TB yield	NNT
Symptoms alone <sup>a</sup>	77,113	26,001	949	949/77,113 1,2%	26,001/949 27
DCXR alone <sup>b</sup>	74,200	7,053	1,021	1,021/74,119 1,4%	7,053/1,021 7
Symptoms and/or DCXR screening	74,119	28,374	1,216	1,216/74,119 1,6%	28,374/1,216 23

<sup>a</sup> Excludes 763 clients without a symptom screening result

<sup>b</sup> Excludes 3,676 clients without a valid DCXR result

### Conclusions:

- Screening for TB using DCXR has a better yield at 1,4% compared to symptom screening alone at 1,2%.
- The number needed to test after screening using X-rays was lower (7) compared to symptom screening (27).
- Combining symptom and DCXR screening had a better yield at 1,6%

### OA29-431-16 Parallel chest X-ray and symptom screening for TB among marginalised and key populations in Malawi: an effective TB screening and diagnostic strategy

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**Background and challenges to implementation:** Malawi still faces significant challenges in diagnosing tuberculosis (TB), with one-third of cases remaining undiagnosed and missed in communities. Marginalized and key populations are particularly affected due to struc-

tural, geographical, and gender-related barriers to TB services. Hence the need for NTLEP to come up with an innovative strategy to minimize and mitigate these aforementioned barriers.

**Intervention or response:** To address this problem, the NTLEP introduced an outreach TB screening intervention using a chest X-ray and symptom screening approach and targeted marginalized and key populations in poor urban communities. The healthcare workers were trained on the screening and diagnostic algorithms, the community mobilization activities were undertaken before the outreach program to increase demand for TB screening and diagnosis services.

**Results/Impact:** In 2022, 30,225 individuals were screened for TB using digital CXR and symptoms of which 1,993 (7%) were identified as presumptive TB. Of those screened, 165 were diagnosed with TB, with an overall yield of 546 per 100k individuals screened which is four times higher than the TB incidence in the general population (132 cases/100k). The highest yield was observed among refugees (957 cases per 100k), followed by internally displaced persons (567 cases per 100k), prisoners (523 cases per 100k), and healthcare workers (510 cases per 100k).

**Conclusions:** The findings highlight the need for targeted TB screening and diagnostic strategies for each specific risk group. However, the parallel CXR and symptom screening approach used in this intervention has proven to be effective and provides valuable insights that can help in the scale-up of more effective TB screening and diagnostic strategies in similar settings.

### OA29-432-16 Ultra-portable X-ray with artificial intelligence for TB screening and facilitating TB preventive therapy in Bangladesh

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**Background and challenges to implementation:** To address the scarcity of X-ray facilities for tuberculosis (TB) screening in Bangladesh, the National TB Control Programme (NTP) introduced ultra-portable chest X-ray (CXR) system equipped with Artificial Intelligence (AI) namely Computer Aided Detection for TB (CAD4TB). This new intervention is aimed to aid NTP to improve TB case detection in remote areas and facilitate roll-out of TB Preventive Therapy (TPT) in Bangladesh.

**Intervention or response:** From January-March 2023, six units of ultra-portable CXR were deployed at six districts of Rajshahi division, covering 45 sub-districts. Participants were divided into two groups: household contacts of index TB cases; and TB presumptive identified by clinicians. CAD4TB cut-off score was determined at 50. All TB presumptive identified by X-ray screening and symptom screening were referred for bacteriological confirmatory tests and clinical evaluation.

**Results/Impact:** A total of 5,137 TB presumptive were tested by ultra-portable CXR machines. Of them, 85.75% had <50 score where we identified 0.43% (15/3484) bacteriologically confirmed (B+) persons with TB and 0.79% (21/2633) were clinically diagnosed (CD) with TB. The rest 14.25% had ≥50 score from where we found 7.22% (43/595) B+ TB and 22.92% (119/519) CD TB. We observed significant difference in TB case detection using AI software ( $P < 0.0001$ ) among <50 and ≥50 CAD4TB (AI) scores. Among 552 household contacts tested, 92.4% (510/552) had <50 score and 7.6% (42/552) had ≥50 score. Total 9.5% (4/42) B+ case and 5.2% (2/38) CD case were found from contacts with ≥50 score. No TB was found from contacts with <50 score. Among contacts, 546 individuals were referred for TPT eligibility evaluation.

INDICATORS	TOTAL	CAD4TB SCORE (≥50)	CAD4TB SCORE (<50)
<b>TB presumptive tested by X-ray</b>	5137	732 (14.25%)	4405 (85.75%)
Bacteriologically confirmed(B+)	58	7.22% (43/595)	0.43% (15/3484)
Clinically diagnosed (CD)	140	22.92% (119/519)	0.79% (21/2633)
<b>Household contact tested by X-ray</b>	552	7.6% (42/552)	92% (510/552)
Bacteriologically confirmed(B+)	04	9.5% (4/42)	00
Clinically diagnosed (CD)	02	5.2% (2/38)	00

**Conclusions:** Ultra-portable X-Ray system with AI (CAD4TB) can be a gamechanger in facilitating early diagnosis of missing TB cases and ensuring equitable access to quality care in peripheral settings. NTP can scale-up this technology to diagnose missing TB cases in remote locations, as well as for nationwide TPT roll-out.



**OA29-433-16 Implementation of the ultra-portable chest X-ray with artificial intelligence and TrueNAT testing: screening and testing strategies during active case-finding activities in Tarlac, the Philippines**

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**Background and challenges to implementation:** The Global TB report 2022 estimates there were 741,000 TB cases in the Philippines in 2021, however only 321,564 were notified. Despite implementation of community- and facility-based case-finding strategies, challenges remain including implementation inefficiencies, geographic restrictions, and long turnaround times (TAT) for TB services.

**Intervention or response:** USAID's TB Platforms for Sustainable Detection, Care and Treatment Activity supported the demonstration of new TB diagnostic tools under the Introducing New Tools Project (iNTP) in select project sites in Tarlac province to accelerate TB elimination efforts in 2022. Through iNTP, the Activity conducted one-stop-shop community active case-finding (ACF) activities using ultra-portable chest x-rays (UP-CXR) with computer-aided detection (CAD) and TrueNAT machines to enable same-day screening and testing among community members in target sites.

**Results/Impact:** After seven months of implementation in Tarlac Province, 6,372 individuals were screened for TB. Fifteen percent (933) were presumed to have TB. Of those, 87% (815) were tested and 60 bacteriologically diagnosed with TB. The Number Needed to Screen (NNS) to detect one TB case is 106. The average testing rate using CAD and TrueNAT was significantly higher than that of case finding activities without CAD or on-site sputum collection/testing, (56% vs 35%, *p-value* <0.001). The average TAT from screening to release of test results was less than a day, an improvement from the seven-day average in traditional active case-finding approaches.

**Conclusions:** Using the UPCXR/CAD and TrueNAT provided an innovative approach to active case-finding activities. An understanding of the acceptability of these new tools in the community, especially in lieu of traditional screening tools, will prove essential in designing implementation strategies and increasing buy-in from local partners.

**OA29-434-16 Using ultra-portable chest X-ray screening for TB in nomadic communities of Northeast Nigeria**

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**Background and challenges to implementation:** Despite having the highest tuberculosis (TB) burden in Africa, Nigeria missed 59% of the people estimated to develop TB in 2022. Nomads are an important Key Population who contribute to the people with TB who are missed in Nigeria due to their limited access to health services, overcrowded and poorly ventilated living condition, and distrust of public health services. Chest x-ray (CXR) can detect many people with TB that symptom screening misses but is not widely available in health facilities.

**Intervention or response:** From July to December 2022, TB screening camps were organized in Nomadic communities of Adamawa and Gombe States. Consenting individuals ≥ 15 years were screened for TB symptoms (cough, fever, night sweats, and weight loss) and received a CXR using an ultraportable system interpreted by artificial intelligence (AI) (qXR V3). Sputum samples were collected from individuals with an abnormality score of 0.3 or higher or if they reported any TB symptoms and tested with Xpert MTB/RIF (Xpert). The TB screening cascade was documented, and screening performance evaluated.

**Results/Impact:** 107 screening days were held in 95 Nomadic communities across 15 LGAs in Gombe and Adamawa States. 6,461 people were screened; 2,739 (51%) were females. A total of 1,119 sputum samples were collected, transported, and tested by Xpert, 91 were found to be Bac+ including 36 (42%) females.

In addition, 170 TB people were clinically diagnosed, totalling 261 individuals with all forms of TB. Bacteriologically confirmed and all forms notifications increased by 30% and 41% respectively when compared to previous quarters in the targeted LGAs.

**Conclusions:** Use of ultra-portable CXR for TB screening in Nomadic communities led to increased TB notifications in both Bac+ and all forms. Scaling this approach can potentially the treatment coverage gap.

## OA30 Models of Active Case Finding and Contact Investigation

### OA30-435-16 Strengthening intensified case-finding in public facilities without diagnostic tools using the healthcare worker model: an experience from Kano State, Nigeria

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**Background and challenges to implementation:** Access to health care services in public facilities in Kano State, Nigeria is across the tertiary, secondary, and primary level facilities. While primary health centers (PHCs) mostly serve the underprivileged population with a higher prevalence of tuberculosis, they are often without diagnostic tools.

The scope of the National Program's commissioned sample movers is limited as they move samples twice a week with priority on ART sites, creating challenges of sample wastage, increased diagnostic turn-around-time, and delayed treatment.

**Intervention or response:** The KNCV USAID-funded TB-LON project designed a hub-and-spoke model of healthcare worker sample transportation. Healthcare workers in each of the LGAs were trained on infection prevention and control, triple packaging of samples, and provided with cold boxes to routinely move samples from 112 spoke sites (PHCs) to hub sites (higher capacity facilities) to address diagnostic gaps. Generated samples from screening officers domiciled at the spokes sites are stored in cold boxes.

The laboratory or DOT officer engaged, routinely retrieves these samples, and moves them to the lab. The results are returned on the next visit for sample retrieval. The screening officer then contacts the patients.

Quarter	Type of facility	Hospital attendees	# of clients screened for TB	# presumed to have TB	# sent for evaluation	# evaluated for TB	# diagnosed with TB	# started on TB treatment
Jan to March 2022 (Q1)	Spoke	163,783	120,503	17,427	12,986	11,120	450	450
April to June 2022 (Q2)	Spoke	126,452	105,988	8,460	8,291	7,734	1,036	1,033
July to Sept 2022 (Q3)	Spoke	322,485	253,989	16,049	15,029	14,366	619	618
Oct to Dec 2022 (Q4)	Spoke	108,634	86,279	4,634	4,549	4,458	181	180
	Hub	555,517	463,663	32,366	31,279	29,498	2,567	2,561
Total (Q1-Q4)	Spoke	721,354	566,759	46,570	40,855	37,678	2,286	2,281
% Contribution	Spoke		55%	59%	57%	56%	47%	47%

Table 1. TB cascade results across the spoke sites.

**Results/Impact:** Out of the 140 facilities, spoke sites represent 80% of the public facilities with the ICF intervention. Between January to December 2022, 88% of the samples generated at the spoke sites were successfully transported for evaluation, with 92% evaluated, yielding 6% TB cases. The proportion of sample transported increased from 75% in Q1 to 98% in Q4, and

the evaluation rate from 86% to 98%. Altogether spoke sites contributed 47% of diagnosed and notified cases in the ICF intervention.

**Conclusions:** Utilizing the healthcare worker model for sample movement can bolster TB case finding in public facilities through increased timely sample transportation and evaluation, ensuring that TB cases that pass through PHCs without diagnostic capacities are not missed.

### OA30-436-16 TB in times of COVID-19: specificities and lessons learnt from Brazilian clients

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**Background:** Brazil, a high TB burden country, has the 3rd highest poll death from COVID-19. We conducted a mixed methods study among patients and caregivers to understand their perspectives on TB service disruptions and lessons learned from the pandemic.

**Design/Methods:** This was conducted in six Brazilian capitals, with patients/caregivers who underwent treatment for drug-susceptible or, drug-resistant TB or preventive during the pandemic. In phase 1 - quantitative, we applied an objective questionnaire; in phase 2 - qualitative, we applied a face-to-face semi-structured interview. The questions sought to compare services before and during the pandemic and the access barriers faced during this period. In phase 1, we used descriptive statistics, and in phase 2, content analysis in the thematic mode.

**Results:** 202 participants answered the questionnaire, 53% were women and 79% were patients, of whom 46% were undergoing susceptible TB treatment. Fifteen people were interviewed: 13 patients and 2 caregivers, 8 men. The diagnosis was delayed because of the patients' fear of accessing services (46%) and the limitations of travel. In the thematic category "diagnosis", participants reported delays in access to laboratorial tests and TB services even with positive results. Some were diagnosed with TB during the COVID-19 investigation. Participants found that TB services have been the most affected by COVID-19. In the "treatment" category, participants perceived being well attended, especially when DOT was realized. Participants also suggested there are lessons from the COVID-19 response that can be transferred to the TB program: a better understanding of the importance of contact tracing and of wearing masks, the possibility of remote care, and better dissemination of information about TB.

**Conclusions:** Patients/caregivers have noticed the decline of TB services and the prioritization of COVID-19 in services, especially regarding the diagnosis. Understanding of contact mapping is an opportunity. The need for more social visibility of TB is clear.

### OA30-437-16 Strategic integration of active TB case-finding into the COVID-19 vaccination programme - experience from the KNCV Nigeria GLOVAX Project in Anambra and Imo State, Nigeria

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**Background and challenges to implementation:** The most lethal infectious disease in the globe prior to the emergence of COVID-19 was tuberculosis (TB). Increasing amounts of evidence indicate that COVID-19 occurs whether or not TB occurs, whether it does so before, during, or after an active TB diagnosis. Due to reluctance, it became urgent to raise the uptake of the COVID-19 vaccine in Nigeria. Strategic integration of active TB case search into the COVID-19 vaccination program (GLOVAX Project) is required to support TB case finding activities. Hence, this study is aimed at assessing the strategic integration of active TB case finding into covid-19 vaccination program.

**Intervention or response:** KNCV Nigeria is implementing the GLOVAX Intervention in Nigeria. Two south-east states, Anambra and Imo were selected. Were amongst the 7 states implementing the GLOVAX project. Between July to December 2022 people in the community were vaccinated for COVID-19. These patients that were vaccinated were also screened symptomatically for TB. Presumptive clients were identified and evaluated clinically or bacteriologically for TB. Data from KNCV Nigeria intervention data base was obtained. Information on number of Persons screened, number Presumptive identified, number of presumptive evaluated and number of diagnosed TB cases was extracted and used for this study. Analysis was done using descriptive statistics.

**Results/Impact:** A total of 250,650 clients were vaccinated for COVID-19 and 100% (250650) of these clients were screened symptomatically for TB. There was a 3% (n=250650; 6821) presumptive yield and 96% (n=6821; 6553) were evaluated. The TB yield from this evaluation was 3% (n=6553; 161).

**Conclusions:** In the result, 161 (3%) clients were identified to have TB in the GLOVAX project within the period. This strategic integration shows potential to detect

the missing TB cases in Nigeria. However, if more emphasis is put into quality screening and gaps in evaluation is closed there are possibilities to improve the TB yield.

### OA30-438-16 Universal testing for TB investigation among household TB contacts in three sub-Saharan African countries

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**Background:** A reliance on symptom-based screening, followed by complicated testing and referral algorithms, have limited the impact of tuberculosis (TB) contact investigation in high-burden settings. Consequently, alternative approaches such as universal TB testing, where household contacts (HHCs) are tested regardless of symptoms, has gained interest. We piloted a universal Test-and-Treat strategy among HHCs, complemented by linkage to appropriate TB treatment or TB preventive therapy (TPT).

**Design/Methods:** We conducted a cross-sectional pilot study in South Africa, Lesotho and Tanzania. Index patients  $\geq 18$  years, with microbiologically-confirmed TB diagnosed within  $\leq 6$  weeks were enrolled. Among all consented HHCs, we aimed to collect sputum samples regardless of whether symptoms were reported or not. In HHCs  $< 10$  years, we also followed an algorithm based on WHO pediatric guidelines, where all symptomatic contacts were referred for further evaluation. Sputa was tested using Xpert MTB/Rif (Xpert).

As indicated, persons were referred for TB treatment initiation, further investigation or TPT depending on country guidelines.

**Results:** We enrolled 342 index patients and 964 HHCs. The median age of HHCs was 18 years (8-39 years) and HIV status was known among 57%; 16% self-reported being HIV infected. Among the 964 HHCs, 147(15.2%) had any symptoms.

The proportion with successful sputum collection was similar in symptomatic and asymptomatic patients. In total, 25(2.5%) HHCs had a positive Xpert; 11(7.4%)

among symptomatic and 14(1.7%) among asymptomatic. Of those eligible for TPT according to country guidelines (n=277), 208(75%) were started on TPT. Country differences are shown in Table.

	South Africa	Lesotho	Tanzania	Total
Index patients	152	100	90	342
HHC (n, % female)	300 (174, 58%)	321 (211, 66%)	343 (212, 62%)	964 (597, 62%)
HHC<10 years	31	96	155	282
HHC>=10years	269	225	188	682
Sputum collected	290 (96.6%)	219 (66.2%)	243 (70.8%)	752 (78.0%)
Xpert+ve (% of HHC)	11 (3.7%)	5	9 (2.6%)	25 (2.5%)
TB Treatment started	5	9	9	23
TPT started	10	156	42	208

Table. Universal testing study results by country.

**Conclusions:** Universal testing for TB among household contacts was feasible and yielded PWTB among contacts who were asymptomatic. Variations in study findings by country suggest the effect of the intervention may vary by setting; a planned cluster randomised trial is underway which will further evaluate the yield of TB and TPT uptake in a larger scale implementation.

### OA30-439-16 Rapid training and deployment of nurse-led community-based TB contact investigation teams in five rural districts in Mozambique: a promising new model for community-based services

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**Background and challenges to implementation:** Mozambique is one of 30 WHO high burden countries for TB, TB/HIV and drug-resistant TB (DR-TB) and had an estimated TB incidence of 361 per 100,000 in 2021. ADPP with JSI and USAID support through a 12-month TB Commitment Grant demonstration project, recruited, trained, and deployed nurse-led outreach teams in five mostly rural districts in Nampula Province (Nampula City, Monapo, Nacala Porto, Angoche, and Moma).

**Intervention or response:** Between July 2022 and September 2022, the five teams with two nurses each were established to provide comprehensive, community-based

TB contact investigations (TBCI) in the five districts to locate and screen household and other close contacts (HCCs) who were exposed to active TB and who may have acquired TB. Beginning in November 2022, all eligible contacts 15 years old or younger and without evidence of active TB disease were offered and initiated on TB preventive treatment (TPT).

**Results/Impact:** Between November 2022 and March 2023, 584 persons with TB (572 DS-TB and 12 DR-TB) reported 3,224 (3,149 DS-TB and 75 DR-TB) household or other close contacts (HCC) or an average of 5.5 per index case; 2,022 (62.7%) contacts were <15yrs and 1,202 (37.3%) >15 yrs.

Overall, 81/3,224 (2.5%) of contacts were diagnosed with TB (all DS TB), however 57/81 (70%) of those newly diagnosed were less than 15 years; 1,928/2,022 (95%) were eligible for TPT, 57/2,022 (3%) had DS TB and 37/2,022 (2%) were not eligible. From all eligible contacts less than 15 years, 1911/1928 (99%) were started on TPT (1,870 for DS TB and 41 for DR TB). Completion rates being monitored.

**Conclusions:** Nurse-led TBCI teams can be rapidly recruited, trained and deployed and are highly effective in identification of close contacts, finding persons with active disease, and initiating TPT with high acceptance among eligible persons 15 years old or younger, both for DS and DR TB.

### OA30-440-16 An assessment of the effectiveness of community-based mobile chest X-ray TB screening in a state in Southwest Nigeria

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**Background and challenges to implementation:** Nigeria is ranked sixth in TB burden in Africa with a 40% gap in TB case notification. There has been a progressive decline in the gap between estimated and notified cases from 2017 till 2022 due to the deployment of several innovative strategies such as the Computer Aided Detection enabled mobile x-ray for mass screening.

**Intervention or response:** This was a collaboration between the USAID TBLON 3 and the Global Fund Grant Management Unit of the Lagos State Ministry of Health. Active case-finding targeted at hotspots for TB key and

vulnerable populations (TB KVP) were conducted using a computer-aided detection enabled digital x-ray, fitted in a van for ease of movement and operation. The x-ray van has on-site 2 radiographers and other support staff for logistics support while a radiologist remotely reviews the digital radio-graphs as necessary.

Prior engagement and mobilization of the target populations was done to ensure good turnout and acceptance. All clients were screened using a parallel screening algorithm that included the WHO four-symptom screening (W4SS) and CAD4TB score with threshold set at 50. All identified persons presumed to have TB were evaluated with GeneXpert, and bacteriologically negative results had their digital x-ray films and symptoms sent for radiologist review for clinical diagnosis.

**Results/Impact:** A total of 16 LGAs and average of 77 communities in each quarter were covered between July 2022 to March 2023. 18,628 persons were screened during this period while 1,029 persons were presumed to have TB were evaluated. A total of 269 TB cases were diagnosed out of which about two-thirds were clinically diagnosed. The number-needed-to screen and number-needed -to test were 69 and 4 respectively.

**Conclusions:** This intervention was found to be very efficient as evidenced by the low NNS and NNT compared to W4SS only from other studies. The proportion of sub-clinical TB detection also increased.

### OA30-441-16 Engaging private pharmacies for TB case detection in major cities of Nepal

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**Background and challenges to implementation:** Nearly 14% of participants of the national TB prevalence survey 2018 presented with cough for two weeks or more, sought medical treatment in private health facilities including pharmacies. Pharmacies are always first points of contact because of accessibility and extensive utilization by communities.

A pharmacy referral program was established with the aim to empower private pharmacies to identify and refer individuals with TB symptoms to the nearest health facility for diagnosis, and to bring these pharmacies to active participation in the National Tuberculosis Program surveillance system.

**Intervention or response:** Close to 400 pharmacies in seven high TB burden cities of Nepal were selected as TB screening points for communities that access care from

them. This approach was done in collaboration with the Nepal Chemist & Druggist Association (NCDA). All received orientation from the NTP on identification and referral of TB presumptive to health facilities for diagnosis and treatment. These pharmacies were linked to performance-based incentive scheme for each patient referred to a health facility and additional incentive if the referred patient was diagnosed with TB. The pharmacy personnel received regular onsite mentorship visits to assure their knowledge of TB screening and referral procedures.

**Results/Impact:** Out of the 24,937 patients referred by 188 pharmacies, 2,229 (M:1313, F:916) patients were diagnosed with TB from January-December 2022. This identification of TB at a primary level has contributed significantly to increased quality of care for community members.

**Conclusions:** Pharmacies hold huge potential to contribute meaningfully to TB PPM efforts. Orientation and continuous mentorship of pharmacy owners and workers on screening for TB will enable early detection and access to treatment by community members. The successful outcome of the pharmacy referral program targeting less than 8% of the nearly 5,000 pharmacies in seven cities suggests that similar innovations should be initiated and evaluated in other major cities.

### OA30-442-16 Systematic investigation of hospital-based TB transmission in two hospitals of the Kyrgyz Republic, Central Asia

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**Background:** Although control of TB transmission dynamics in the community and in hospitals is considered an important key to the control the whole TB epidemic, systematic progressive studies investigating frequencies and risk factors of transmission in TB hospitals are so far missing. In this longitudinal cross-sectional study, a cohort of 563 TB patients were systematically investigated over 20 months from 2017 to 2019 at two TB hospitals in the Kyrgyz Republic.

**Design/Methods:** Patients were tracked with regards to their rooms and room-mates during hospitalization. Whole genome sequencing was performed on 708 *Mycobacterium tuberculosis* complex (*M.tbc*) isolates, including 563 early (grown from samples collected within  $\leq 6$  weeks of hospitalization), 10 late (grown from samples collected  $>6$  weeks post admission), and 135 serial isolates (grown from follow-up samples).

**Results:** The cohort of participants represented  $>90\%$  of all patients hospitalized at the study sites during the follow-up period of 53,372 hospitalization days in total. The 563 early isolates belonged into three phylogenetic *M.tbc* lineages, i.e., L2 (Beijing; 70.7%, 398/563), L3 (Delhi/CAS; 1.1%, 6/563), and L4 (Euro-American; 28.1%, 158/563), and into *M. bovis* (0.2%, 1/563). Genome-based cluster analysis revealed that 30.7% (173/563) of isolates fell into 56 clusters ( $<5$  SNPs) with 50.3% of clustering isolates being drug-resistant. Based on genome-analysis of all 708 isolates, two proven (0.04%), and nine potential (1.6%) nosocomial TB transmission events were identified.

**Conclusions:** Within-community transmission of *M.tbc* is highly active in Kyrgyzstan. Drug resistance is one of the drivers of the TB epidemic. When extrapolating observed transmission events to the country level, 21.0 and 94.5 hospitalized Kyrgyz TB patients would be struck by proven and potential, respectively, nosocomial TB transmissions per year.

## OA31 Evidence based intervention to influence the policies

### OA31-443-16 Quality of governance, domestic TB spending and TB control programme outcomes in sub-Saharan Africa: a panel data regression analysis

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**Background:** This study investigates the influence of institutions on the impact of domestic tuberculosis spending on TB case detection rates and treatment success rates in a panel of 15 high TB burden African countries.

**Design/Methods:** The panel data comprised the independent, dependent, and moderating variables for the period, 2016-2021. The independent variables were domestic TB expenditures. The dependent variables were TB case detection and treatment success rates. The moderating variables, governance indicators, comprised voice and accountability index, political stability index, government effectiveness index, regulatory quality in-

dex, rule of law index, and control of corruption index. Ordinary least square (OLS), pooled OLS, fixed effects and random effects estimators were used in this study. The baseline model is from the random effects estimators given the insignificant Hausman test results.

**Results:** Domestic spending mainly impacts positively and significantly TB treatment: control of corruption ( $\beta=0.0481$ ,  $\rho = 0.027$ ), government effectiveness ( $\beta=0.0434$ ,  $\rho=0.117$ ), political stability ( $\beta=0.0483$ ,  $\rho=0.059$ ), regulatory quality ( $\beta=0.0656$ ,  $\rho < 0.001$ ), rule of law ( $\beta=0.0532$ ,  $\rho=0.009$ ), and voice and accountability ( $\beta=0.0616$ ,  $\rho=0.218$ ).

Nonetheless, the moderating role of institutional quality on this effect remained mainly adverse: control of corruption ( $\beta=-0.0163$ ,  $\rho=0.047$ ), government effectiveness ( $\beta= -0.0112$ ,  $\rho=0.067$ ), political stability ( $\beta=-0.0096$ ,  $\rho=0.196$ ), regulatory quality ( $\beta=-0.0177$ ,  $\rho < 0.001$ ), rule of law ( $\beta=-0.01161$ ,  $\rho=0.012$ ), and voice and accountability ( $\beta=-0.0138$ ,  $\rho=0.277$ ).

The effect of domestic spending on the case detection rate is predominantly negative and statistically insignificant throughout. The role of institutions as a channel of transmission also remained muted throughout.

**Conclusions:** Domestic expenditure enhanced TB treatment success rate but did not improve case detection. Our findings suggest that institutions in Africa have not been a channel for improving the TB control-domestic spending relationship. Sub-Saharan African countries must build strong institutions to ensure efficient and effective domestic spending on TB control.

### OA31-444-16 TB knowledge and practices among private practitioners in Varanasi, India: implications for ending TB

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**Background and challenges to implementation:** This study found suboptimal knowledge and practice patterns among private practitioners treating TB in Varanasi district of Uttar Pradesh. The research highlights the need for contextual strategies to improve private sector engagement and enhance appropriate TB management practices in high-burden settings.

**Intervention or response:** The mixed-methods study used purposive sampling to select 120 private practitioners across Varanasi district zones in 2022. A structured questionnaire collected quantitative data on practitioners' TB management knowledge and practice patterns based on factors like age, gender, speciality and TB program training. In-depth interviews provided qualitative insights. Results were analysed on MS excel and transcripts annotated with Transcribear tool.

**Results/Impact:** The study had 65% of participants from urban, and 35% rural. Knowledge and practice patterns were found to be suboptimal, especially among elder age, rural, and stand-alone clinicians. Urban practitioners scored 9.2 points higher than rural peers, and younger age respondents scored 3.1 points higher than older age ones ( $p=0.000643119$ ). More clinical experience correlated with a 12.4-point knowledge decrease ( $p=0.031$ ), while TB program training led to a 10.8-point knowledge increase ( $p=0.02$ ).

Practice competency was low at 13.6 points out of 20 (35.6%,  $SD=2.44$ ). A positive relationship between knowledge and practice was observed ( $p=0.0004$ ). Respiratory physicians outperformed stand-alone clinicians in practice scores ( $p=0.009$ ) while urban doctors scored 2.77 higher than rural peers ( $p=0.033$ ). Gender had no significant practice score impact.

Qualitative data suggested interventions for enhancing private sector engagement in TB elimination, such as continued medical education, engaging physicians from allied system of medicine and addressing training gaps.

**Conclusions:** The study highlights the need for strong policy inducement to adopt a strategic framework focused on strengthening private sector engagement in high burden settings.

### OA31-445-16 Strengthening of results-based financing to ensure person-centred TB care in the Kyrgyz Republic

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**Background and challenges to implementation:** In 2017, the Kyrgyz Republic adopted results-based financing to motivate primary health care (PHC) workers to provide quality care and counseling to persons receiving TB care. Payments are made following provider submission of successfully treated TB cases into an information system developed for the Mandatory Health Insurance Fund (MHIF) with USAID support. Payments for successful treatment of drug-resistant tuberculosis are

twice as high as for drug-sensitive TB. However, documents submitted for payment often failed to meet successful TB treatment outcome criteria.

**Intervention or response:** The USAID-funded Cure Tuberculosis project, led by JSI, examined 300 TB cases submitted for payment in Chui and Jalal-Abad oblasts from the 2018 cohort (20% of total TB cases). We assessed clinical criteria for the categorization of TB cases, criteria for verification of successfully treated TB cases submitted for payment, and payments made in 2019 and 2020.

**Results/Impact:** TB cases were categorized properly as drug-sensitive or drug-resistant, and 90% met the definition of a successfully treated TB case. However, compliance with the diagnostic algorithm was found in only 29% of cases. Noncompliance included testing samples after the start of treatment or failing to conduct drug susceptibility testing, leading to a high rate of clinically diagnosed cases. Due to the lack of guidelines, errors occurred in recording and reporting transferred cases and cases with failed treatment outcomes. The assessment also revealed poor clinical case management and treatment monitoring.

**Conclusions:** Study findings have led to strengthening the verification system, including through developing clinical criteria for verification and regular review of individual successfully treated cases by TB Concilia. This has resulted in improved adherence to the diagnostic algorithm and a decrease by 30% in erroneously reported successfully treated cases.

### OA31-446-16 Child and adolescent TB policy and governance in the sub-Saharan Africa region, 2021

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**Background and challenges to implementation:** The Sub-Saharan Africa Regional Child and Adolescent TB Centre of Excellence (COE) is a virtual platform established in 2019 by The International Union Against TB and Lung Disease, U.S. Centers for Disease Control and Prevention and nine founding member countries: Eswatini, Ethiopia, Kenya, Malawi, Mozambique, Tanzania, Uganda, Zambia, and Zimbabwe. The COE aims to bridge policy-practice gaps in management of child and adolescent TB (C&A TB) by fostering south-to-south learning and partnerships.

**Intervention or response:** In April 2021, the COE assessed C&A TB policy and governance through an online, cross-sectional survey completed by child TB focal points of the nine member countries. The objective was to better understand the current structure of management, financing, and training for C&A TB. Analysis was restricted to de-identified data and aggregated results.

**Results/Impact:** While interventions and targets for child TB were included in all countries' (n=9) national strategic plans (NSP) and guidelines, only four (44%) included adolescent TB in NSPs, while 78% included them in guidelines. Only four (44%) countries captured all WHO-recommended disaggregated age categories. Eight (89%) countries have C&A TB Technical Working Groups (TWGs), though stakeholder representation varied. All reported dedicated funding for C&A TB, but only five (56%) received funding from their government with most or all funding coming from external donors for most countries. All countries had an existing training curriculum for child TB, but only four (44%) included adolescents and only five had a strategy for training relevant staff.

**Conclusions:** Most countries included C&A TB in governance, strategic, and technical documents that guide TB programming and have functional TWGs to provide guidance. However, many programs rely on donor funding, leaving them vulnerable to external forces. Training curricula don't cover all relevant topics, especially adolescent TB. Many countries are not following WHO-recommended age-disaggregated reporting, limiting their ability to track key indicators.

### OA31-447-16 Accelerating patient-centric approach through multi-sectoral convergence in the state of Himachal Pradesh, India

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**Background and challenges to implementation:** Tuberculosis (TB) is not just a health problem; but a socio-economic problem. To achieve Country's goal of eliminating TB by 2025, a coordinated effort across multiple sectors is necessary, to bolster the country's response against tuberculosis. However, due to limited resources, the States require technical assistance and expertise to reinforce collaboration and implement strategies effectively at the grassroots level. The Union's Axshya Plus initiative strives to foster collaboration across multiple sectors to mobilize resources for strengthening the National Tuberculosis Elimination program.



**Intervention or response:** In partnership with The Union, the Himachal Pradesh State Government evaluated gaps, planned strategies and implemented a multi-sectoral approach to eliminate tuberculosis (TB). The strategy entailed targeted advocacy efforts with policymakers and the creation of a novel framework for collaboration across various sectors, including government departments and non-governmental organizations (NGOs). The dedication exhibited by politicians and policymakers acted as a stimulus, inspiring stakeholders to increase their efforts towards enhancing the program.



**Results/Impact:** Under the chairmanship of the esteemed Governor of Himachal Pradesh, two top-level multi-sectoral meetings took place over the course of one year. This led to:

1. 19 departments solidified their partnership by crafting state action plans for TB elimination efforts.
2. Civil societies i.e. Rotary, Lions clubs adopted approximately 2000 TB patients by providing additional nutritional support, vocational support etc.
3. Around 600 government officials (District Magistrates, Chief Medical officers, Block Medical officers, Panchayati Raj representatives, Vice chancellors, etc.) engaged in 35 community outreach initiatives and social media campaigns, effectively reaching out to approximately 150,000 community members on TB awareness.

**Conclusions:** Multi-sectoral engagement requires commitment, persistent advocacy, and regular follow-ups. Implementing this approach will provide psychosocial support to TB patients leading to improved health outcomes and demand generation from the community. It is a scalable intervention which can be adopted by the National Tuberculosis Program of different countries.

### OA31-448-16 From policy to implementation: planning for the implementation of targeted universal TB testing in the Western Cape, South Africa

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**Background and challenges to implementation:** The South African National Department of Health (NDoH) endorsed Targeted Universal TB Testing (TUTT) as a strategy to find more persons with TB in 2023.

This strategy aims to mitigate some of the negative impacts of COVID-19 on the TB programme and improve TB diagnosis among at risk populations. Operational planning is critical as it impacts successful implementation of new policies.

**Intervention or response:** TUTT recommends Xpert MTB/RIF testing to be used among the following groups regardless of TB symptoms: newly diagnosed HIV positive, known HIV positive (annual) and HIV positive pregnant women; all close contacts of persons newly diagnosed with TB; all individuals who completed TB treatment in the preceding 2 years.

Using routinely collected data the number of tests required among the different groups were calculated in order to inform sub-district level planning. The following assumptions were made: HIV positivity rate of 20% in antenatal clients; 30% of TUTT eligible clients unable to expectorate; on average, four close contacts tested per person diagnosed with TB.

**Results/Impact:** Assuming 70% coverage of TUTT, a more than two-fold increase in Xpert MTB/RIF testing demand (Table) is predicted. The Cape Town Metropole district will experience the largest increase in testing volume.

	Routine programmatic data for Western Cape 1 April 2021-31 March 2022*						Scenario: assume 4 contacts tested per person diagnosed with TB**		
	Notified with TB 21/22 (N)	Total Xpert Tests 21/22 (N)	Positivity rate (%)	Xpert MTB/RIF positive (N)	On ART 21/22 (N)	New HIV positive 21/22 (N)	Deliveries 21/22*** (N)	Projected total Xpert MTB/RIF tests at 70% TUTT target plus routine testing (N)	Projected Increase in Xpert testing volume (%)
Western Cape	45,185	232,087	15.9	36,902	294,080	30,290	96,319	561,152	242
Cape Winelands	7,730	40,016	15.2	6,082	28,133	4,048	13,393	79,468	199
Central Karoo	646	3,329	16.9	563	2,026	223	945	6,298	189
Cape Metro	25,239	126,999	15.8	20,066	212,932	20,141	63,350	349,256	275
Garden Route	5,263	28,723	16.4	4,711	24,942	2,625	8,873	59,066	206
Overberg	2,355	12,833	14.6	1,874	13,262	1,179	4,298	27,936	218
West Coast	3,952	20,187	16.7	3,371	12,785	2,074	5,460	39,129	194

\*Data Sources: Provincial Health Data Centre, Sinjani. Data presented per district and sub-district (not shown in table)

\*\*Multiple scenarios were modelled; only one is displayed due to display limitations

\*\*\*Approximately 20% (HIV pos) eligible for TUTT at pregnancy diagnosis, however eligibility for screening with Xpert MTB/RIF may be tallied under newly diagnosed HIV pos or annual test. Therefore inclusion of this data in estimate may result in modest over-estimation.

**Conclusions:** TUTT implementation will require additional physical resources, such as sputum booths and waiting spaces, guidelines, standard operating procedures, training, and human resources. Community based testing strategies will be required to engage with groups of persons infrequently in contact with the healthcare system, such as contacts of persons diagnosed with TB. Clinics will have to accommodate increasing numbers of persons accessing TB treatment. The use of routine data as a tool for modelling TUTT implementation will enable informed and appropriate planning at district, sub-district, and facility level for capacitation and resource allocation.

### OA31-449-16 The current condition and possible mechanisms of social security for people affected by drug resistance TB in Indonesia - a convergent parallel study

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**Background:** Medication and treatment costs for drug-resistant TB (DR TB) are covered by the government of Indonesia (GoI) through the Indonesian National Health Insurance (JKN). However, indirect costs, direct non-medical costs, and income loss caused a catastrophic financial burden to people affected by DR TB, which are not covered by the existing scheme of national health insurance. A catastrophic financial burden may worsen the TB treatment outcomes. Therefore, this study explores existing social safety net policies and the perceived need for social security for DR-TB patients in tackling the effects of DR-TB treatment.

**Design/Methods:** A mixed-method approach with a convergent parallel study design was utilized in this study. The data were collected through in-depth interviews, FGD, policy analysis, and surveys to 322 respondents selected purposively from December 2021 to February 2022.

**Results:** 50% of the respondents experienced side effects and 36% of the respondents complained about their living cost during the TB treatment. About 81% of the respondents have received support during their treatment. However, the support was varied and not routine. Only 23% of DR-TB respondents accessed the GoI cash transfer mechanism (PKH), wherein 77% of respondents' level of income positions them vulnerable to poverty. Conditional cash transfer (CCT) was an appropriate option for providing social security. Several existing schemes of social security which fit with CCT are "The Health Indonesian Program," "PKH," "Sembako Program," "Social Entrepreneurship Program," and "Social Rehabilitation of Uninhabitable Homes" (RS-RTLH). Those social measures can be tailored for DR-TB patients to prevent catastrophic consequences and multidimensional effects.

**Conclusions:** Access to the security for people with DR-TB remains limited. However, there is a viable policy option to protect people affected by DR-TB from its multidimensional consequences and improve patients' recovery. It requires multi-sectoral (MoH and MoS) synergy to integrate DR TB into social security mechanisms.

### OA31-450-16 How should national public institutions provide health communication to the general public in a health crisis? Lessons learnt from managing COVID-19 pandemic communication in Finland

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**Background:** The COVID-19 pandemic was a challenge for health care and health communication. In Finland the pandemic was managed well. However, there were challenges in public communication. This study analysed how Finnish public institutions organised health communication and what lessons can be learned.

**Design/Methods:** The study was conducted as individual interviews via video conferences. Representatives of Finnish institutions providing health communication to the general public were interviewed (n=33, leading specialists with media visibility, representing directorship, medical and/or communication expertise). The interviews were conducted between 10/2022 and 03/2023, recorded, transcribed and pseudonymised. The closed and open-ended questions were identical for all participants (partly adapted from "Assessment tool for crisis communication during pandemics").

Participants received written information on the study and gave consent before the interview.

**Results:** According to the participants there was an enormous demand for knowledge among the public and they were resolved to meet this demand by providing multi-channel communication in several languages. They stated that the media reported and elaborated their information releases, which was seen as a major factor in improving information distribution. Most participants did not want a national communication coordination group in a possible future pandemic. Instead, each organisation should have a stand-by infrastructure for coordinating communication with relevant institutions. Several participants stated that institutional roles should be more clearly defined to avoid conflicting information from different institutions. Institutions should internally agree on their statements before publication. Information materials and their translations should be created in a centralised way to save resources. Legislation should be updated based on legal controversies faced during the pandemic.

**Conclusions:** This study showed that COVID-19 pandemic served as a tool to envisage a good communication strategy for future pandemics. These findings suggest that a more coherent and synchronised communication model should be developed. Generally, trust in public institutions in Finland is high.

## OA32 Pharmacokinetics and treatment of TB

### OA32-451-16 Rifampicin underexposure as a potential cause of unfavourable outcomes among children with TB: an individual participant meta-analysis and new dosing recommendations

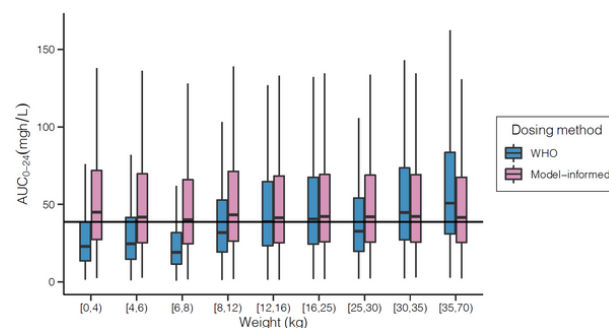
R. Miyakawa,<sup>1</sup> B. Perez Solans,<sup>2</sup> S. Floren,<sup>2</sup> R. Ruslami,<sup>3</sup> A. Mukherjee,<sup>4</sup> P. Denti,<sup>5</sup> J. Tarning,<sup>6</sup> A.C. Hesselning,<sup>7</sup> A. Turkova,<sup>8</sup> A. Kwara,<sup>9</sup> H. McIlleron,<sup>10</sup> R. Savic,<sup>2</sup> <sup>1</sup>University of California San Francisco, Pediatrics, San Francisco, United States of America, <sup>2</sup>University of California San Francisco, Bioengineering and Therapeutic Sciences, San Francisco, United States of America, <sup>3</sup>Universitas Padjadjaran, Biomedical Sciences, Bandung, Indonesia, <sup>4</sup>All India Institute of Medical Sciences, Pediatrics, New Delhi, India, <sup>5</sup>University of Cape Town, Pharmacometrics, Cape Town, South Africa, <sup>6</sup>University of Oxford, Centre for Tropical Medicine and Global Health, Oxford, United Kingdom of Great Britain and Northern Ireland, <sup>7</sup>Stellenbosch University, Desmond Tutu Tuberculosis Centre, Cape Town, South Africa, <sup>8</sup>University College London, Medical Research Council Clinical Trial Unit, London, United Kingdom of Great Britain and Northern Ireland, <sup>9</sup>University of Florida, Medicine, Gainesville, United States of America, <sup>10</sup>University of Cape Town, Clinical Pharmacology, Cape Town, South Africa. e-mail: rada.savic@ucsf.edu

**Background:** Rifampicin is a first-line drug to treat drug-susceptible tuberculosis (DS-TB). Previous studies suggest that the current World Health Organization (WHO) dosing recommendation may result in lower exposure in children compared to adults. Individual participant data meta-analysis helps identify patient factors affecting rifampicin pharmacokinetics (PK) and evaluate their association with treatment outcomes.

**Design/Methods:** We identified PK studies of rifampicin in children with DS-TB and obtained individual participant data. PK characteristics were quantified using nonlinear mixed-effects modelling. AUC was derived from the model and compared against the adult median (38.7 mg/L). Logistic regression was used to analyse the association between rifampicin exposure and treatment outcomes. Different dosing strategies were explored to resolve underexposure.

**Results:** Steady-state PK data of 950 participants from 11 PK studies published 2010-2021 were analyzed. Median age was 5 years (range 0-17 years), and 24% were children living with HIV. A one-compartment model with first-order absorption better fitted the PK data. Study-level random effects were applied to account for inter-study differences. Allometric scaling by weight and a maturation function influenced clearance, and HIV infection and nutritional status impacted bioavailability. Of 321 children receiving daily doses for pulmonary TB, 15% experienced death or treatment failure, and

rifampicin AUC was associated with these unfavourable outcomes (odds ratio 0.91 (95% CI 0.85-0.99)). The median AUC under the current WHO dosing guideline was lower than the target in those weighing <12 kg and 25-29 kg. Model-informed dosing strategy indicated doses as high as 30 mg/kg for children <6 kg and resulted in improved exposures in these groups as shown in the Figure.



**Conclusions:** Current WHO dosing recommendation results in rifampicin underexposure in younger children with DS-TB, and doses as high as 30 mg/kg are necessary for those <6 kg to achieve exposure comparable to adults. An increase in rifampicin exposure has the potential to improve outcomes.

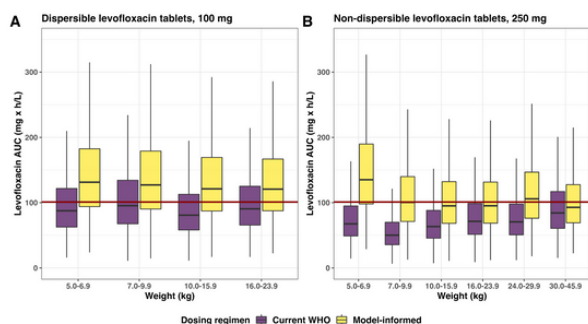
### OA32-452-16 Pharmacokinetics and optimal dosing of levofloxacin in children: an individual participant data meta-analysis

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**Background:** Levofloxacin is a fluoroquinolone with increasing importance as a component of rifampin-resistant/multidrug-resistant tuberculosis (RR/MDR-TB) treatment and prevention in children. Existing data on levofloxacin pharmacokinetics in children is limited to individual regional studies. Previous studies have shown that levofloxacin exposure in children may be lower than in adults receiving a 750 mg dose. Individual participant data from four distinct pediatric studies were used to conduct a meta-analysis, identify characteristics affecting exposure, evaluate exposure with revised 2022 WHO-recommended doses, and calculate optimal dosing regimens.

**Design/Methods:** Available plasma concentration data from 217 intensively sampled children from four studies were analyzed using nonlinear mixed effects modeling in NONMEM. Model-informed optimal dosing was calculated targeting exposure matched to adults following a standard 750 mg once-daily levofloxacin dose with 250 mg tablets (median  $AUC_{24,SS}$  of 101  $mg^*h/L$ ). Steady-state pharmacokinetics were simulated with current WHO dosing guidance and model-informed dosing.

**Results:** The pharmacokinetic data were well described by a one-compartment model with linear elimination. Inclusion of age through a maturation function ( $HILL = 3.4$ ,  $PMA_{50} = 8.9$  months; approximately 50% mature at birth and 95% mature at 1 year of age), allometric scaling by weight, and formulation (37% decrease in apparent oral bioavailability with adult-formulation non-dispersible 250 mg tablets) affected levofloxacin pharmacokinetics. Current WHO-recommended dosing resulted in exposures below the median adult exposure for all weight bands. Per-kilogram model-informed optimized doses decreased with increasing patient weight and ranged from 22-38 mg/kg of levofloxacin non-dispersible 250 mg tablets and 14-24 mg/kg of levofloxacin 100 mg dispersible tablets for children weighing 5-34 kg.



**Figure.** Simulated levofloxacin  $AUC_{24}$  at steady state with weight band dosing of 250mg non-dispersable tablets (A) or 100mg dispersible tablets (B) according to current WHO recommendations and with model-informed optimized doses. Data are based on 500 simulations. Solid line represents target  $AUC_{24}$ .

**Conclusions:** Updated weight-based dosing guidelines are needed in order to reach target levofloxacin exposure in children with consideration of formulations.

## OA32-453-16 Pharmacokinetics and pharmacogenomics of isoniazid in children worldwide: an individual participant data meta-analysis

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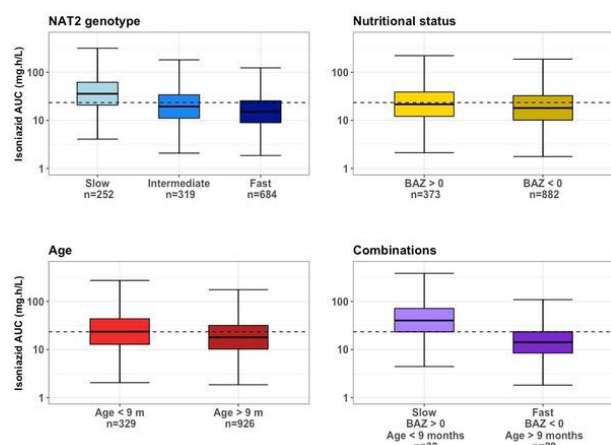
**Background:** Between 2018 and 2021, 1.9 million children (aged <15 years) received treatment for tuberculosis (TB). In 2021, 220,000 children died from TB. Younger children (aged <6 years), children living with HIV, malnourished children, and fast N-acetyl transferase 2 (NAT2) metabolizers are known to be underexposed to isoniazid.

We aimed to characterize the pharmacokinetic (PK) and pharmacogenomic (PG) properties of isoniazid in children through an individual participant data meta-analysis (IPD-MA).

**Design/Methods:** For this IPD-MA, we searched PubMed for eligible studies and asked for individual patient level data to be contributed to this analysis. The PK properties and the influence of PG were quantified using nonlinear mixed-effects modeling. The final PK model was used to simulate optimal dosing regimens to achieve a target  $AUC_{24hr} \geq 23.4$   $mg.h/L$  (equivalent to that of the median adult target).

**Results:** We collected data from 17 studies, from 8 countries, published between 2012 and 2021. Observed isoniazid concentrations were available in 1255 children ( $n=6601$  samples). At the time of sampling, children had a median (range) postnatal age of 3.5 (0.01-17.8) years (313 children < 1 year old) and weight of 12.5 (0.9-57) kg. NAT2 genotype was available in 606 (48%) patients (171 slow, 320 intermediate and 115 fast metabolizers). Allometric scaling by weight, a maturation function (half of the adult maturation attained at one postna-

tal month) and NAT2 genotype significantly influenced isoniazid clearance. The current dosing recommendations allow more than 40% of the children to reach the adult target. In the 663 children with known clinical outcomes, predicted isoniazid AUCs were not significantly different across outcomes.



**Conclusions:** The World Health Organization guidelines provide an adequate exposure for the majority of the children. However, a PG-based dosing regimens would be the most powerful approach to achieve balanced isoniazid exposure in children worldwide.

### OA32-454-16 In-vitro evaluation of crushed pretomanid tablet (200 mg) for delivery and stability via enteral feeding tubes

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**Background:** In-Vitro testing is recommended by the United States (US) Food and Drug Administration (FDA) for seeking labeling extension for administration of pretomanid tablet via enteral tube by crushing method. The present study aims to explore the feasibility of delivering an extemporaneously compounded pretomanid suspension via enteral feeding tube and check the physical/chemical stability of the same.

**Design/Methods:** Using mortar and pestle, one tablet of Pretomanid was crushed, 50 mL of water was added, and stirred for 60 seconds. This suspension was drawn into an oral syringe (60 mL capacity) and delivery was evaluated using two enteral feeding tubes [Nasogastric tube (16 Fr) with Poly Vinyl Chloride (PVC) material and Gastric tube (8 Fr) with silicone material]. The recovery was checked 12 times at 0 and 15 min (soaking at 25°C ± 2). The physical and chemical stability assessments were performed at 0, 15, 30, and 120 min, in apple puree and water mediums.

**Results:** The recovery of pretomanid after delivery through the nasogastric and gastric tube was >95% (Table 1). No clogging or adherence in the oral syringe, nasogastric tube, and gastric tube was observed and the recovery of the suspension of crushed pretomanid tablet was found to be satisfactory.

The physical and chemical observations over 120 min showed that the suspension of crushed pretomanid tablet retained the initial light brown in apple puree and white color in water media, with no significant pH changes in both media, and all impurities were found below the threshold limit.

	Nasogastric tube		Gastric tube	
	0 min	15 min	0 min	15 min
Time	0 min	15 min	0 min	15 min
Mean (%)	98.10	97.3	96.80	96.7
Relative Standard Deviation (%)	1.59	1.30	0.79	0.26

Table 1. Recovery of pretomanid after delivery through nasogastric tube and gastric tube at 0 and 15 min

**Conclusions:** The study presents a convenient procedure for the preparation of a stable suspension of pretomanid using crushed pretomanid tablets, for administration via enteral feeding tubes.

### OA32-455-16 Improving access to child-friendly formulations of medicine to treat drug-resistant TB in South Africa

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**Background and challenges to implementation:** Major changes are taking place in the drug resistant tuberculosis (DR-TB) environment with the introduction of novel all-oral treatment regimens that include new and repurposed medicine. Lack of child friendly formulations threaten to erode the perceived benefits of the all-oral treatment regimen in children. Children received adult medications that must be cut, crushed and mixed, making bioavailability questionable.

This was the accepted standard for many years, in the absence of alternatives however children, healthcare workers and caregivers experienced mental, physical and emotional trauma when taking adult medicines.

**Intervention or response:** In 2017, dispersible child friendly formulations became available on the global market with the Global Drug Facility (GDF) proposing a pooled procurement model and a donation to encourage countries to gain programmatic experience with the medication. Initial access in South Africa was via Kwa-zulu Natal. The need was presented to the Pharmacy and Therapeutics Committee, authorization to use the unregistered medicine was obtained from the regulatory body and the donation was accepted by the Head Of Health. An agreement and procurement request form was completed.

**Results/Impact:** In 2019, dispersible tablets of clofazimine 50mg, ethambutol 100mg, levofloxacin 100mg and pyrazinamide 150mg was delivered. Healthcare workers were trained on standardized processes for ordering and administration. Informed consent and 6 monthly progress reports were completed. 24 children received the paediatric formulations with excellent outcomes and minimal adverse events reported.

Based on this experience a further donation was offered for expanded use in South Africa. Updated guidelines were reviewed and the need identified for delamanid 25mg, levofloxacin 100mg, clofazimine 50mg and linezolid 150mg dispersible tablets. Quantification and forecasting was done and processes repeated with delivery expected in 2023.

**Conclusions:** Lack of evidence in children is a barrier to access however political will and perseverance enabled access to child friendly formulations in South Africa. Sustainability of supply must be prioritized.

### OA32-456-16 Higher rifampicin doses to shorten TB prevention treatment: results from the controlled, randomised, partially blind, 2R<sup>2</sup> trial

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**Background:** TB preventive treatment (TPT) is a key component of the EndTB strategy. To improve completion and reduce burden for people and health systems, short, safe and effective TPT regimens are needed.

**Design/Methods:** Controlled, randomized, partially blind, phase 2b trial, including persons 10yrs old or older in Canada, Indonesia or Vietnam, with positive TST or IGRA. Randomization was 1:1:1 to standard treatment with 10mg/kg/day of rifampin for 4 months (4R10), 20mg/kg/day for 2 months (2R20) and 30mg/kg/day (2R30) for 2 months. Participants and investigators were blind to high dose. Co-primary outcomes were adverse events (AE) of grade 3 or higher (and allergic reactions of any grade), requiring permanent treatment discontinuation, and judged possibly or probably due to study drug by an independent, blinded panel, and treatment completion.

**Results:** Between September 2019 and December 2022, 1368 participants were enrolled and 1302 took at least one dose of treatment. Fifty (3.9%) stopped for an AE: 22 grade 3 AE (3 (0.7%) in standard arm, 5 (1.1%) in 2R20 and 14 (3.3%) in 2R30) and 28 for grade 1-2 allergies (8 (1.8%) in standard arm, 4(0.9%) in 2R20 and 16 (3.8%) in 2R30). Five had grade 3 hepatotoxicity (1 in 2R20, 4 in 2R30). Rate of AE was not different for 2R20 compared to standard arm (aRD 0.15, 95% CI -0.09 to 0.45) but was higher for 2R30 (aRD 1.16, 95% CI 0.62 to 1.70). Completion was lower for 2R20 (aRD -7.4 (95% CI -13.3 to -1.5) and 2R30 (aRD -14.4 (95% CI -20.5 to -8.3) compared to standard.

	Standard arm (10mg/kg/day for 4 months), N(%)	2R20 (20mg/kg/day for 2 months) N(%)	2R30 (30mg/kg/day for 2 months) N(%)	2R20 vs Standard aRD* (95% CI)	2R30 vs Standard aRD* (95% CI)
Safety Population (took ≥1 dose)	439 (100)	440 (100)	423 (100)		
Grade 1-2 AE attributed to drug	4(0.9)	9(2.0)	15(3.6)		
Grade 1-2 rash/ allergy or Grade 3-4 AE attributed to drug	11(2.5)	9(2.0)	30(7.0)	- 0.5 (- 2.4; 1.5)	4.6 (1.7; 7.4)
Completed per protocol (MITT population)	355 (78)	313 (68)	277 (61)	-7.4 (-13.3; -1.5)	-14.4 (-20.5; -8.3)
Completed but not per protocol	17(4)	17 (4)	15 (3)		
Never started	15 (3)	21 (5)	30 (7)		
Stopped for patient decision	48(10)	88(19)	85 (17)		
Stopped for Adverse event	18(4)	19(4)	46(10)		
Died** or active TB	1(0.2)	3(1)	0		

\* Risk Differences adjusted for clustering.

**Conclusions:** In this controlled trial, 30 mg/kg/day of rifampin was less safe than standard rifampin dose and therefore not a future option for TPT. 2R20 appeared to be as safe as standard treatment, but completion was worse, although reasons for this difference are unclear.

### OA32-457-16 Safety and feasibility of a 3-month bedaquiline regimen for TB preventive treatment among contact persons exposed to pre-extensively drug-resistant TB

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**Background:** Tuberculosis preventive treatment (TPT) is a key intervention to achieve the End TB Strategy targets. Despite significant breakthroughs in TPT for drug-sensitive TB, there is not yet strong evidence for the safety and effectiveness of TPT for drug-resistant TB. Since 2019 we have been conducting a study to evaluate the safety and feasibility of a 3-month bedaquiline (3Bdq) TPT regimen in three Russian cities: Vladimir, Murom, and Kovrov.

**Design/Methods:** We enrolled persons 18 and over years old exposed to pre-extensively drug-resistant tuberculosis (pre-XDR-TB). Prior to the TPT initiation, active TB was ruled out, and TB infection was confirmed by Diaskintest. All eligible persons were offered TPT with 3Bdq. TPT was administered under direct observation. Patients who expressed complaints were screened for adverse drug reactions (ADRs) at each TB drugs in-take. A physician examined patients weekly. If no complaints were reported, biochemical markers and ECG tests were conducted at least once a month. The ADRs grading was based on the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. Observational cohort of enrolled persons was used to assess ADRs, treatment completion, and zero active TB disease rates during 2 years after the TPT initiation. Data collection was conducted using MS Access.

**Results:** From January 1, 2019 to December 31, 2022, 41 (87%) persons out of those 47 eligible for TPT have started treatment. Few adverse events were reported, including one moderate, and one medically significant but not immediately life-threatening ADRs. TPT with 3Bdq showed high adherence and low non-completion rates (Table 1). There have been no active TB disease cases documented among those persons who completed TPT.

Number of individuals	Vladimir city	Kovrov city	Murom city	Total
Eligible for TPT	27	7	13	47
Initiated TPT	26	7	8	41
Completed TPT	25 (96%)	7 (100%)	8 (100%)	40 (98%)
Discontinued TPT due to adverse events (lab findings, clinical decision)	1* (4%)	0	0	1 (2%)
Discontinued TPT due to patient decision	0	0	0	0
Covered with chest X-Ray in a 12-month follow-up	70% (16 of 23)	86% (6 of 7)	85% (11 of 13)	77% (33 of 43)

\*Bedaquiline was canceled in patient having taken 75% of doses and was associated with diabetes decompensation and related symptoms.

Table 1. Outcomes of TPT with 3Bdq in 41 contact persons (January 1, 2019 - December 31, 2022).

**Conclusions:** This is the first use of bedaquiline for TPT in program settings. We found that TPT in contact persons with pre-XDR-TB exposure is both safe and feasible.

### OA32-458-16 Attributable fractions for unfavourable treatment outcomes among adults with drug-susceptible pulmonary TB in India

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**Background:** The population-level impact of risk-factors for unfavorable tuberculosis treatment outcomes depends on their relative prevalence in a given population. We calculated unadjusted and adjusted attributable fractions (AF) to estimate the proportion of unfavorable

tuberculosis treatment outcomes that can be indirectly and directly attributed, respectively, to potentially modifiable risk-factors in India.

**Design/Methods:** Adults with drug-sensitive pulmonary tuberculosis were enrolled at treatment initiation and prospectively evaluated for 24 months in the ongoing multi-site RePORT-India Consortium. The primary outcome was a composite unfavorable treatment outcome of failure, recurrence, or all-cause mortality. For potentially modifiable risk-factors, we estimated the unadjusted AFs as  $P(RR-1)/[P(RR-1)+1]$  where  $P$  is the prevalence of exposure and  $RR$  is its risk-estimate, and adjusted AFs as  $(O-E)/O$  where  $O$  is the observed number of outcomes and  $E$  the expected number of outcomes in a hypothetical counterfactual scenario if the exposure were completely removed with all other confounders remaining unchanged.

**Results:** 2931 participants contributed 10.6 mean person-years of follow-up; 129 failed treatment, 80 had recurrence, 101 died. The median age was 43 (IQR 18-82) years, 2137 (72.9%) were male, 1132 (39.1%) were undernourished (BMI<18.5kg/m<sup>2</sup>), 1182 (40.4%) ever smoked, 956 (32.8%) had diabetes (HbA1c>6.5% or a physician diagnosis), 437 (14.9%) reported alcohol misuse (AUDIT>10 points), and 65 (2.2%) were HIV positive. After adjusting for confounders, undernourishment, alcohol misuse and HIV accounted for 25.1% (95% CI 17.1-32.3%), 7.4% (95% CI 2.3-12.2%) and 2.1% (95% CI 0.9-3.4%) of all unfavorable treatment outcomes, respectively. Contrary to unadjusted AF estimates, we did not find statistically significant adjusted AF estimates for ever-smoking (Table). These findings were consistent in a sex-stratified analysis.

Exposures	Unadjusted AF, % (95% CI)	Adjusted AF, % (95% CI)
Undernourishment	26.2 (18.8, 32.9)	25.1 (17.1, 32.3)
Alcohol misuse	9.1 (4.7, 13.3)	7.4 (2.3, 12.2)
HIV coinfection	1.8 (0.6, 3.0)	2.1 (0.9, 3.4)
Ever smoking	14.1 (5.0, 22.3)	6.3 (-7.2, 18.3)
Diabetes	1.2 (-6.6, 8.5)	-2.4 (-12.3, 6.5)

Adjusted AF models include age, sex, symptom duration prior to treatment initiation, smear grade at treatment initiation, undernutrition, alcohol misuse, HIV co-infection, ever-smoking, and diabetes.

*Table: Unadjusted (indirect) and adjusted (direct) attributable fractions (AFs) for unfavorable tuberculosis treatment outcomes in India.*

**Conclusions:** Undernourishment, alcohol misuse and HIV together accounted for nearly a third of all unfavorable treatment outcomes and may present high-yield intervention targets among adult pulmonary tuberculosis cases in India.

## OA33 Covid A-to-Z

### OA33-459-16 Poor performance of point-of-care tests on severe acute respiratory syndrome coronavirus-2 samples with low viral load

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**Background:** The emergence of SARS-CoV-2 has seen an avalanche in the development of diagnostic assays. The COVID-19 antigen tests (Ag-POCTs) have been recommended for use by the WHO to circumvent the limitations of the reference diagnostic assay reverse-transcriptase polymerase chain reaction (RT-PCR). The RT-PCR assay is expensive, require specialised infrastructure, and highly trained staff, thus, rendering the assays impractical in most developing countries. The Ag-POCTs assays provide bed-side detection, lower costs detection than PCR, and require little and no training for staff to perform.

However, the performance of Ag-POCTs in samples with low viral load has not been evaluated in Limpopo province, South Africa. Thus, the aim of the study was to evaluate the accuracy of three WHO-EUL certified Ag-POCTs in comparison to the RT-PCR technique.

**Design/Methods:** A total of 272 SARS-CoV-2 nasopharyngeal samples were retrieved from the National Health Laboratory Service repository. All samples had RT-PCR results, with cycle threshold (CT) values ranging from 13 to 45. A total of 143 samples had CT values above 35.

The samples underwent testing on Ag-POCTs provided from Abbott Panbio, Roche SARS-CoV-2 antigen detection test (Roche RDT), and SD Biosensor (Standard Q) according to manufacturers' instructions. Results of RT-PCR technique and Ag-POCTs were compared and correlated.

**Results:** Of the 129 samples with CT values less than 35, the three Ag-POCTs had 100% sensitivity and specificity. Lower CT values correlated with higher band intensities.

However, with regards to samples with CT values above 35, only 21/143 (14.7%) tested positive on at least one Ag-POCTs kit. The SD Biosensor Standard Q solely detected 32/272 (12%) of the positive specimens.

**Conclusions:** The performance of all three Ag-POCTs was low on samples with low viral load. Of the three Ag-POCTs, the SD Biosensor Standard Q antigen test showed greater sensitivity of detection.



### OA33-460-16 Evaluating the impact of viral load on the effectiveness of COVID-19 sample pooling for RT-PCR detection of COVID-19

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**Background:** In resource limited settings, sample pooling for COVID-19 testing is considered a cost-effective approach for rapid expansion of access to Real time (RT) PCR tests.

The risk of missing out a positive sample in a pool is likely to be affected by the number of samples in a pool and the viral load of each sample. In our context, there is no guidance for the optimal number of samples to be included in a pool for effective identification of all positives.

This study examined the effect of viral load on the maximum number of samples that can be safely pooled for PCR diagnosis of COVID-19

**Design/Methods:** Five confirmed positive COVID-19 samples of known Cycle threshold (Ct) values were selected with the following Ct values:  $\leq 20$ ,  $\leq 25$ ,  $\leq 30$ ,  $\leq 35$  and  $\leq 40$  to represent decreasing viral load with ' $\leq 20$ ' as highest and ' $\leq 40$ ' lowest.

Similarly, 1,217 confirmed negative samples were selected for the pooling to create different pools of varying dilution factors.

Each selected positive sample was pooled with the negative samples in an increasing dilution factor of 1:4 until the Ct value of the pool with the highest dilution factor was above 40 and still positive. The Ct values of each pool for each positive sample were documented.

POS Ct Value	Pools of varying dilution factors																Ct value of POS with highest dil.
	1:4	1:8	1:12	1:16	1:20	1:24	1:28	1:32	1:36	1:40	1:44	1:48	1:52	1:56	1:60	1:64	
$\leq 20$	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	31.6
$\leq 25$	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	38.3
$\leq 30$	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	+ve	-ve	-ve	-ve	-ve	40.2
$\leq 35$	+ve	+ve	+ve	+ve	+ve	+ve	+ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	41.1
$\leq 40$	+ve	+ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve	41.4

Table 1. Positivity across different pools of varying dilution factors based on Ct value of a single positive among 4 to 64 negative samples.

**Results:** As shown in the table, a single positive sample with a presumed Ct value of  $\leq 20$  can be pooled with up to 64 negative samples to give a positive pool, while a single positive sample with Ct value  $\leq 40$  can only be pooled with a maximum of 8 negative samples to give a positive pool.

**Conclusions:** This research reveals that Ct value is a determining factor in choosing the maximum number of samples to be pooled for effective RT-PCR detection of COVID-19 and provides a guide for covid-19 sample pooling.

### OA33-461-16 Characteristics of people with TB reported to the WHO Global Clinical Platform of COVID-19 and their associations with clinical outcomes

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**Background and challenges to implementation:** Tuberculosis (TB) is a leading infectious cause of death worldwide. The advent of coronavirus (COVID-19) led to concerns that the burden of TB disease and death would increase due to synergy between the two conditions.

**Intervention or response:** Since 2020, the World Health Organization (WHO) encouraged contribution of individual-level clinical and demographic data to its Global Clinical Platform for COVID-19 to improve the clinical characterization of COVID-19.

By November 2022, 62 countries reported anonymized data for 430,890 persons hospitalised for COVID-19 and with known TB status. We explored associations of TB with in-hospital mortality using multivariable logistic regression.

Forest plot of the results (log10 scale)

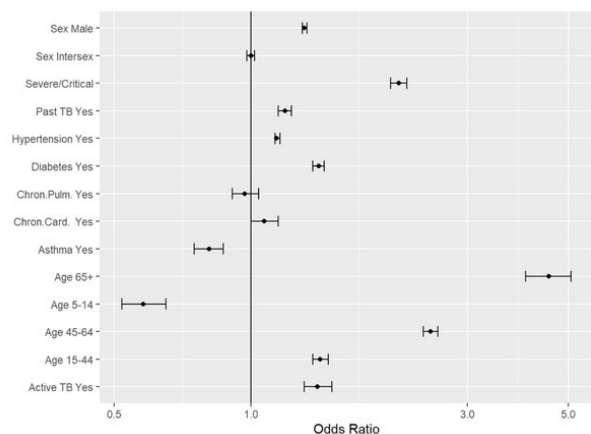


Figure. Adjusted odds ratio of in-hospital mortality among COVID-19 patients, WHO Global Clinical Platform for COVID-19 (from multivariable logistic regression of pooled data, 2020-2022).

**Results/Impact:** Among people hospitalised with COVID-19 with known outcome, 4,687 with current TB only, 7,583 with past TB only and 3,354 with both were reported by 48 countries, mostly Africa (94%): 53% were male; median age was 45 years. In people with current TB, 28.8% were admitted with severe illness and 23.5% died. Current TB (adjusted OR=1.32, [95%CI=1.23-1.41]) and past TB only (aOR=1.24, [95%CI=1.21-1.28]) were independently associated with higher mortality when adjusted for age, sex, HIV status, illness severity at hospital admission, and underlying conditions (Figure).

Among those dying, time to death was shorter in people with current TB (median 5 days, [IQR 2-12]) than those without TB (7, [3-14])

**Conclusions:** In people reported to the WHO Clinical Platform for COVID19, current or past TB were independent risk factors for in-hospital mortality regardless of illness severity at hospital admission. Findings should be interpreted considering variations in viral strains over time, vaccination coverage, sampling criteria for case reporting and geographical distribution. The WHO Platform exemplifies how timely collection of global data can help public health decision-making (acknowledging all data contributors to the Platform).

### OA33-462-16 Lung impairment, COVID-19 risk perception and preventive behaviours among TB survivors in three African countries

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**Background:** TB survivors may experience lung impairment which could influence risk perceptions and behavior in response to emerging respiratory infections. In addition, individuals' risk perception can negatively impact health-seeking behavior if they fear seeking healthcare. In a cohort of TB survivors, we assessed the association between lung impairment and perceived risk of, and preventive behavior against, COVID-19.

**Design/Methods:** We conducted a cross-sectional study of adult TB survivors (n=966) returning for TB Sequel follow-up visits at 3, 6 or 12 months after TB treatment completion between 12/2020-01/2022. Lung impairment was defined as forced vital capacity and forced expiratory volume levels less than lower limit of normalcy, based on age, height, and sex. Perceived probability, susceptibility, and severity of COVID-19 and COVID-19 preventive behaviors were assessed using the WHO Behavioral Insights on COVID-19 questionnaire by country and impairment status among those with spirometry conducted at the same visit.

**Results:** 358 TB survivors were included (South Africa: 98; The Gambia: 174; Mozambique: 86). The median (IQR) age was 33 (26-41), 68% were male, and 40% were living with HIV. Overall, 69% had lung impairment (South Africa: 42%; The Gambia: 83%; Mozambique: 71%).

A higher percentage of participants with lung impairment indicated that they were likely or extremely likely to be infected with COVID-19 compared to those without (33% vs 25%; p=0.13, OR=1.47; 95% CI: [0.89, 2.44] and indicated that their infection would be severe or extremely severe if contracted (22% vs 13%; p=0.07, OR=1.78; 95% CI: [0.95, 3.31]. We observed no difference in adopting preventive behavior—mask-wearing, physical distancing—by impairment status, although this varied by country (Table I).

	Total (n=358)		The Gambia (n=174)		South Africa (n=98)		Mozambique (n=86)	
	Impairment	No Impairment	Impairment	No Impairment	Impairment	No Impairment	Impairment	No Impairment
	246 (69%)	112 (31%)	144 (83%)	30 (17%)	41 (42%)	57 (58%)	61 (71%)	25 (29%)
<b>Risk Perception</b>								
Perceived probability of being infected with COVID-19 (likely or extremely likely)	81 (33%)	28 (25%)	53 (37%)	15 (50%)	13 (32%)	8 (14%)	15 (25%)	5 (20%)
Perceived susceptibility to COVID-19 infection (very or extremely susceptible)	26 (11%)	14 (13%)	15 (10%)	7 (23%)	6 (14%)	5 (9%)	5 (8%)	2 (8%)
Perceived severity of COVID-19 infection if contracted (very or extremely severe)	53 (22%)	15 (13%)	43 (29%)	8 (26%)	6 (15%)	7 (12%)	4 (7%)	0 (0%)
<b>Preventive Behaviors</b>								
Wore a mask in public (very much or extremely)	156 (63%)	82 (73%)	72 (50%)	15 (50%)	36 (88%)	46 (81%)	48 (79%)	21 (84%)
Ensured physical distancing in public (very much or extremely)	79 (32%)	57 (51%)	31 (22%)	9 (30%)	31 (76%)	41 (72%)	17 (28%)	7 (28%)

Table I: Risk perception and COVID-19 preventive behaviors stratified by country (The Gambia, South Africa, and Mozambique) and lung impairment status.

**Conclusions:** We observed an association between lung impairment and COVID-19 risk perception but not preventive behaviors. Further research is needed to understand timing of COVID-19 waves and prevention policies to inform prevention efforts for future respiratory-infection pandemics.

### OA33-463-16 COVID-19 severity in Africa is inversely correlated to intestinal parasite co-infections

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**Background:** COVID-19 symptomatology in Africa appears significantly less serious than in the industrialized world. We and others previously postulated a partial explanation for this phenomenon, being a different, more activated immune system due to parasite infections. We investigated this hypothesis in an endemic area in sub-Saharan Africa.

**Design/Methods:** A prospective observational cohort study was conducted between July 2020 and March 2021, at Kuyha (Mekelle University College of Health Sciences, Mekelle), and Eka Generalized Hospital COVID-19 isolation and treatment centers, Ethiopia. SARS-CoV-2 infection was confirmed by RT-PCR on samples obtained from nasopharyngeal swabs, while direct microscopic examination, modified Ritchie concentration and Kato-Katz methods were used to identify parasites and ova from fresh stool sample.

Ordinal logistic regression models were used to estimate the association between parasite infection, and COVID-19 severity. Models were adjusted for sex, age, residence, education level, occupation, body mass index, and comorbidities.

**Results:** A total of 751 SARS-CoV-2 infected patients were enrolled, of whom 284 (37.8%) had intestinal parasitic infection. Only 27/255 (10.6%) severe COVID-19 patients were co-infected with intestinal parasites, while 257/496 (51.8%) non-severe COVID-19 patients appeared parasite positive ( $p < 0.0001$ ).

Patients co-infected with parasites had lower odds of developing severe COVID-19, with an adjusted odds ratio (AOR) of 0.14 (95% CI 0.09–0.24;  $p < 0.0001$ ) for all parasites, AOR 0.20 ([95% CI 0.11–0.38];  $p < 0.0001$ ) for protozoa, and AOR 0.13 ([95% CI 0.07–0.26];  $p < 0.0001$ ) for helminths.

When stratified by species, co-infection with *Entamoeba spp.*, *Hymenolopis nana*, and *Schistosoma mansoni* implied lower probability of developing severe COVID-19. There were 11 deaths (1.5%), and all were among patients without parasites ( $p = 0.009$ ).

**Conclusions:** Parasite co-infection is associated with a reduced risk of severe COVID-19 in African patients. Parasite-driven immunomodulatory responses may mute hyper-inflammation associated with severe COVID-19.

### OA33-464-16 Effect of restrictions due to the SARS-CoV-2 pandemic on social and geospatial networks of TB in Kampala, Uganda

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**Background:** In 2020, the SARS-CoV-2 (COVID-19) entered Uganda. To limit the spread of SARS-CoV-19, the government-imposed restrictions on travel, social gatherings, and curfews. These restrictions may have affected tuberculosis transmission, since tuberculosis is transmitted via the airborne route.

We examined the effect of SARS-CoV-2 restrictions on the social and geo-spatial networks of tuberculosis in Kampala, Uganda.

**Design/Methods:** Between 08/22/2019 and 05/24/2022 we enrolled 307 adults with culture-confirmed pulmonary tuberculosis from public health clinics in Kampala. These individuals were interviewed to ascertain their social network and to list the locations where they spent time before diagnosis.

We constructed a bipartite network to show how network members (i.e., social network) were connected through locations and how the locations (geo-spatial network) were connected via network members.

We compared network statistics before (08/22/2019 to 06/24/2020), during (06/25/2020 to 01/31/2022), and after restrictions (02/01/2022 to 05/24/2022) were imposed.

**Results:** 307 participants with tuberculosis reported 5,344 social network members and 7,355 locations where they visited during the 6 months before tuberculosis diagnosis. Network characteristics of social networks, such as average degree, average path length, and diameter were similar across periods of COVID-19 restrictions (Table).

Characteristics of geo-spatial networks, however, varied across periods of COVID-19. The median number of meeting locations dropped from 13 before COVID-19 restrictions to 10 during COVID-19. During the CO-

VID-19 restrictions, the geo-spatial network was disaggregated into many components, had a smaller average degree and larger diameter, and greater clustering.

	No. nodes	No. edges	Average degree	Average path length	Diameter	Generalized clustering coefficient	No. components	
Social network	Overall	4435	91171	23	3.5	8.0	0.60	7
	Before COVID-19	1406	6304	15	4.3	8.0	0.54	6
	During COVID-19 restriction	2554	16326	17	3.8	8.5	0.55	5
	After COVID-19 restriction	475	2260	16	4.3	8.3	0.61	1
Geo-spatial network	Overall	6278	38640	34	2.3	5.0	0.27	7
	Before COVID-19	2032	34315	40	2.4	5.0	0.55	3
	During COVID-19 restriction	3587	38895	24	4.9	11.3	0.87	43
	After COVID-19 restriction	659	5797	22	1.7	2.5	0.99	36

Table. Characteristics of social network and geo-spatial network by before, during and after COVID-19 restrictions.

**Conclusions:** During the restrictions imposed to control SARS-CoV-2 epidemic in Kampala, Uganda, the social network of individuals with tuberculosis remained intact whereas the geo-spatial network was disrupted, by separating individuals with tuberculosis into a greater number of highly clustered groups. We inferred that transmission of *M. tuberculosis* continued among social network contacts but may have been reduced to incidental contacts.

### OA33-465-16 Formation of community-led rapid response teams to mitigate TB and COVID-19 in India

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**Background and challenges to implementation:** The COVID-19 pandemic revealed gaps in the provision of health services that calls for system strengthening on several fronts, including the engagement of communities to work in tandem with the health system. There is a consensus among the global TB community and public health professionals on the need for substantial value in integrating care, prevention, and rehabilitation of diseases that affect people in large proportions, such as TB and potentially COVID-19.

**Intervention or response:** In 2022, the Unite to ACT (UTA) project trained, engaged, and strengthened TB Champions (TBC) to provide person-centered care services telephonically to people with TB (PwTB). Representatives from the District TB cell (DTC) and District National Health Mission (NHM) were sensitised to be an integral part of the community-led response team, which aimed to mitigate the effects of TB and COVID-19 while identifying and leveraging points of intersection between the responses to the two diseases.

Community-led Rapid Response Teams (RRT) were formed from October 2022 onwards to address the needs and challenges of PwTB, to encourage TB and COVID-19 testing, and to promote health-seeking behavior.

#### Results/Impact:

No. of States	No. of TBCs engaged		PwTB who received services between Oct 2022 and Feb 2023						
	Male	Female	Total	Gender			Age group		
				Female	Male	Trans-gender	0-14	15-59	60 and above
10	117	149	40986	16134	24836	16	1923	32307	6756

States of Delhi, Bihar, Uttarakhand, Uttar Pradesh, West Bengal, Punjab, Haryana, Gujarat, Rajasthan, Madhya Pradesh

More than 160 RRTs have been formed in 80 districts across 10 states of India. 266 TBCs and 103 nominated persons from DTC/NHM are closely working together to provide comprehensive services to PwTB. Between October 2022 and February 2023, 40,986 PwTB received person-centered care through the RRTs. 1919 PwTB identified a range of issues like limited drug dispensation, delay in diagnosis, and stigma, out of which 1258 (66%) were resolved by TB Champions through effective counseling and 661 (34%) were resolved with the support of DTC/NHM.

**Conclusions:** The concept of RRT creates a forum for integrated communication between the health system and the participation of the community which aligns with India's commitment to community empowerment.

### OA33-466-16 Supporting people with long COVID: policy recommendations derived from patient experience

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**Background:** Twenty percent of adults with COVID-19 develop Long COVID, leading to prolonged symptoms and disability. Understanding the supportive needs of persons with Long COVID is vital to enacting effective policies for Long COVID research and social support systems.

**Design/Methods:** This qualitative sub-study explored the experiences of people with Long COVID and their unmet needs. Participants enrolled in a larger study on the post-acute cardiovascular impacts of COVID-19 were invited to participate in subsequent in-depth interviews. Participants were enrolled purposively until saturation at 24 participants. Data was analyzed using modified grounded theory.

**Results:** The sample was 54% female with median age of 46.5 years. Participants focused on adaptations to life with Long COVID, and their unmet needs in different life spheres. Three domains, 1) occupational & financial; 2) healthcare-related; and 3) social & emotional support, emerged as areas that affect quality of life. Although participants were motivated to return to work for financial and personal reasons, Long COVID symptoms often resulted in unemployment and inability to perform tasks required by their existing jobs. Those who maintained employment through employer accommodations still were inadequately supported. Within the healthcare system, participants encountered diagnostic challenges, scarce specialty appointments, insurance loopholes, high healthcare costs, and medical skepticism. Existing social networks provided support completing daily tasks; however, those with Long COVID typically turned to others with similar lived experience for emotional support. In all three domains, participants found government support programs inadequate and difficult to access.

**Conclusions:** We propose a five-pronged policy approach to meet the support needs identified by persons with Long COVID. These overarching recommendations are (1) improve public awareness of Long COVID; (2) improve clinical care quality and access; (3) implement additional school and workplace accommodations; (4) strengthen socioeconomic benefits and social services; and (5) improve research and data collection on Long COVID.

### OA34 New developments in DR TB diagnostics

#### OA34-467-16 Cross-border whole-genome sequencing TB clusters in Aruba, Curacao, the Netherlands, Sint Maarten and Suriname

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**Background and challenges to implementation:** Aruba, Curacao, Sint Maarten and Suriname were Dutch (Netherlands) colonies. Suriname became independent in 1975. Aruba (since 1986), Curacao and Sint Maarten (both since 2010) are constituent countries within the Kingdom of the Netherlands. These five countries have strong economic and cultural ties with frequent movement of people between the countries. Previously, a cluster of rifampicin mono-resistant tuberculosis was reported, on the basis of whole genome sequencing (WGS), involving patients in Suriname and the Netherlands.

**Intervention or response:** Since 2019, the National Institute for Public Health and the Environment types *Mycobacterium tuberculosis* complex isolates with WGS from all five countries. We studied the frequency and characteristics of patients diagnosed in 2019-2022 and WGS clusters with isolates from >1 country (cross-border WGS clusters).

**Results/Impact:** Most patients in Aruba (80%), Curacao (77%) and the Netherlands (74%) had unique WGS types, while WGS types of patients in Sint Maarten (67%, only

3 types) and Suriname (82%) were mostly in country clusters; the latter suggesting in-country transmission. WGS of patient isolates from the five countries identified six cross-border clusters. Four clusters shared only one or two cases from a second country. Two large clusters had  $\geq 2$  patients in  $\geq 2$  countries, with the majority of the cases identified in Suriname. Eight of the 12 patients from the Netherlands in cross-border clusters were first- or second-generation migrants from Aruba, Curacao, Sint Maarten or Suriname, two were born in African countries and two were born in the Netherlands as well as their parents.

	Aruba	Curacao	Netherlands	Sint Maarten (Dutch part)	Suriname
Total population*	106,537	190,338	17,501,696	44,042	612,985
Estimated TB incidence per 100,000 population*	6.5	8.3	4.4	2.6	29.0
<b>Notified patients per year</b>					
2019	2	2	754	5	139
2020	1	3	621	1	110
2021	6	5	673	1	93
2022	5	5	635	1	127†
Total notified 2019-2022	14	15	2,683	8	469
Bacteriologically confirmed‡	14	15	1,848		350
WGS result available	10	13	1,826	3	218
Unique	8	10	1,344	1	34
In country clusters	2	3	482	2	178
<b>Cross-border clusters</b>					
A.	1		4		53
B.			4		29
C.			2		1
D.	2		1		
E.	2		2		
F.			1	2	

\* Data from Global Tuberculosis Report 2022 (2021 data), World Health Organization, Geneva, 2022

† WGS of *Mycobacterium tuberculosis* isolates of the last two months 2022 not yet available

‡ Xpert MTB/RIF or culture positive

**Conclusions:** Our study identified six cross-border TB clusters. Four of them, were small, suggesting travel-related (family clusters) with limited local spread. Two large cross-border clusters were identified which should be further explored jointly by the countries concerned, including initiatives to optimise cross-border TB contact investigation and outbreak management.

### OA34-468-16 Analysis of the cross-study replicability of TB gene signatures using 49 curated transcriptomic datasets

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**Background:** Tuberculosis (TB) is the leading cause of infectious disease mortality worldwide. Many blood-based gene signatures predicated on gene expression have been proposed as alternative tools for diagnosing TB infection. However, the generalizability of these signatures to different patient contexts is not well-characterized. There is a pressing need for a well-curated database of TB gene expression studies for the systematic assessment of existing TB gene signatures.

**Design/Methods:** We built *curatedTBData*, a manually-curated database of 49 TB transcriptomic studies available as an R Bioconductor package. It allows users to perform meta-analysis without the challenges of harmonizing heterogeneous studies. We describe the process of curating these datasets (Figure 1) and use them for cross-study comparisons of 72 TB gene signatures. We also explore ensembling methods for averaging predictions from multiple gene signatures to improve diagnostic ability beyond any single signature. The area under the curve (AUC) value is used to measure performance in both analyses.

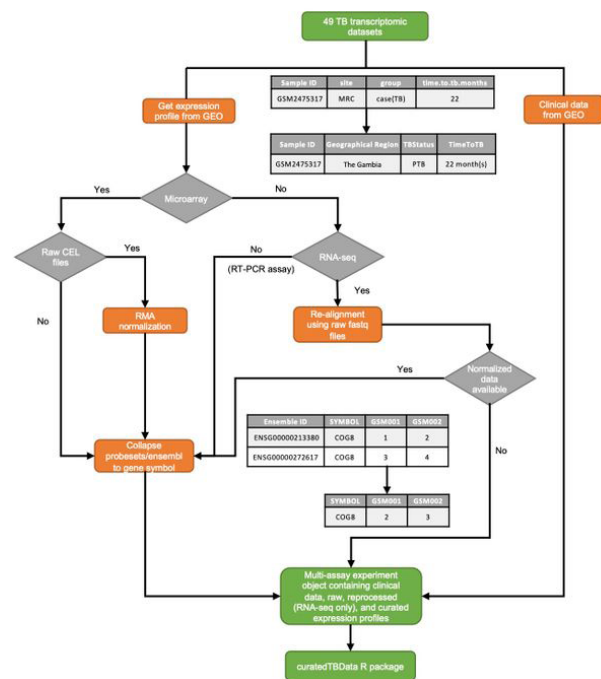


Figure 1. Flowchart of processing steps for curating TB transcriptomic datasets.

**Results:** For the comparison of subjects with active TB from healthy controls, 19 gene signatures showed weighted mean AUC of 0.90 or higher, with a maximum of 0.94. In active TB vs. latent TB infection, 7 gene signatures had weighted mean AUC greater than or equal to 0.90, with a maximum of 0.93. Ensemble techniques for combining TB gene signatures outperformed individual gene sets with up to 3% AUC gains.

**Conclusions:** The *curatedTBData* database offers a comprehensive resource of gene expression and clinically annotated data. It can be used to identify robust TB gene signatures and to perform comparative analysis of existing TB gene signatures. We demonstrated that these blood-based gene signatures could potentially distinguish patients with distinct TB subtypes; moreover, the combination of multiple gene signatures could improve the overall predictive accuracy in differentiating these subtypes, which highlights a crucial factor in the translation of genomics to clinical practice.

### OA34-469-16 Targeted sequencing of cerebrospinal fluid for rapid diagnostics of drug resistance in tuberculous meningitis

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**Background:** Up to 30% of tuberculosis meningitis (TBM) patients die, most within 2 months of starting treatment. Isoniazid and multi-drug resistance increase the risk of death further.

Diagnosing of drug resistance (DR) in TBM by culture-based drug susceptibility testing (DST) is time-consuming whereas most molecular methods are insensitive or insufficiently comprehensive.

**Design/Methods:** We evaluated the performance of targeted next-generation sequencing (tNGS) using the Deeplex® Myc-TB assay for detecting DR from stored cerebrospinal fluid (CSF) specimens of 73 patients with culture-confirmed TB from a clinical trial. The DR profiles by tNGS were compared to a composite reference standard of phenotypic DST (MGIT) and whole genome sequencing from culture.

The effect of DR on time to CSF culture conversion defined by patients having two consecutive negative cultures after treatment initiation was also examined.

**Results:** Deeplex detected *Mycobacterium tuberculosis* (*Mtb*) complex DNA in 25 of 73 (38%) CSF samples with full drug resistance reports generated for 23/25 (92%). Hetero-resistance for first-line drugs was detected to be highly prevalent, particularly for rifampicin (35%).

Using a threshold of  $\geq 20\%$  allele frequency, above which reads representing a resistant allele could predict resistance, Deeplex had 100% concordance with the reference standard for 1<sup>st</sup>- and 2<sup>nd</sup>-line drugs, except for pyrazinamide (96%) and streptomycin (91%) (Figure).

Among 21/23 patients whose culture converted after 30 days of treatment with standard regimens, two had isoniazid resistance by MGIT and Deeplex.

The other 2/23 patients culture converted at 60 days. MGIT and Deeplex identified isoniazid resistance in both with Deeplex identifying a further unsuspected minority population of rifampicin resistant alleles in one.

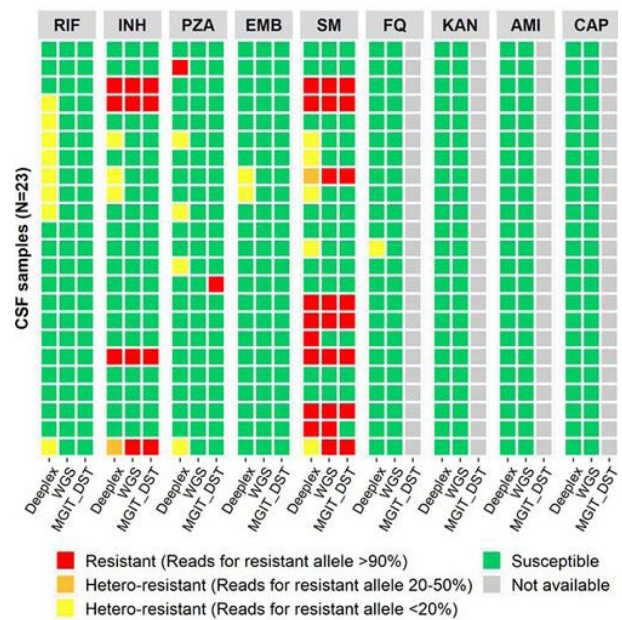


Figure. Concordance in 1st- and 2nd- line drug resistance profiles between Deeplex from 23 CSF specimens and whole genome sequencing (WGS) and phenotypic DST (MGIT-DST) from their cultures. RIF: Rifampicin, INH: Isoniazid, PZA: Pyrazinamide, EMB: Ethambutol, SM: Streptomycin, FQ: Fluoroquinolones, KAN: Kanamycin, AMI: Amikacin, CAP: Capreomycin

**Conclusions:** tNGS from direct CSF samples promises to rapidly and accurately detect drug resistance with faster turnaround than culture-based methods. Its advantage in identifying hetero-resistance and drug resistance early could be very important for the management of patients with TBM.

### OA34-470-16 Efflux pump gene variants in multidrug-resistant TB strains with discrepant phenotype-genotype correlations may further guide drug resistance interpretation

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**Background:** Whole genome analysis of *Mycobacterium tuberculosis* (MTB) is an increasingly important method of identification of multi-drug resistance (MDR) in clinical isolates. It is based on the identification of single nucleotide variants (SNVs) in genes associated with resistance. However, there remain gaps in our understanding of phenotype – genotype correlation between strains. Efflux pumps contribute to drug resistance and here we studied SNVs in key efflux pump genes (EP) to investigate their association with resistance.

**Design/Methods:** Whole genome data of 2221 MTB isolates comprising 1432 susceptible and 789 drug resistant strains were downloaded from ReSeqTB database. MTB lineage and resistance genotyping analysis was performed using an in-house bioinformatics pipeline, MTB-VCF. SNVs in 47 EP genes were categorized according to their SIFT/Polyphen scores.

**Results:** We identified variants unique to EP in DR isolates. SIFT/Polyphen effect analysis determined 38 high impact SNVs across twenty EP genes (EP) to be present in these 789 genomes. SNVs were not associated with MTB lineages. The EPs with SNVs in DR isolates were *Rv1819*, *Rv0194*, *Rv0507*, *Rv2333c*, *Rv3728*, *Rv3823*, *Rv1250*, *Rv1273*, *Rv1458*, *Rv1634*, *Rv1217*, *Rv1218*, *Rv0450*, *Rv0676c*, *Rv0191*, *Rv3008*, *Rv3756*, *Rv2688*, *Rv1704* and *Rv1877*. Examination of 52 isolates with discrepant phenotype-genotypes resistance comprising, MDR, pre-XDR and XDR strains revealed SNVs in EP associated with RIF and INH (*Rv0194*, *Rv1217\_1218*, *Rv1819*, *Rv0450*, *Rv1458*, *Rv0507*), and those associated with fluoroquinolone (*Rv1634* and *Rv2688*) resistance.

**Conclusions:** We identified SNVs in efflux pumps which could contribute to resistance in MTB strains. It may be important to consider these as part of MTB genome-based resistance interpretation. Functional studies combined with GWAS and RNA profiling would further confirm these findings.

#### OA34-471-16 Combination of five small, non-coding RNAs as a biomarker for pulmonary TB diagnosis

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**Background:** The timely diagnosis of tuberculosis remains critical in the management of the disease, as it remains one of the leading causes of morbidity and mortality worldwide. Identifying biomarkers that can predict *Mycobacterium tuberculosis* (Mtb) infection is a pressing need that is yet to be fulfilled.

The objective of our study has been to identify circulating, small non-coding RNAs (sncRNAs) as a molecular tool for the diagnosis of Active-TB (ATB).

**Design/Methods:** We recruited over 30 confirmed cases of pulmonary tuberculosis (PTB) at the onset of treatment initiation and followed them up over a period of 6 months. Additionally, we also recruited 25 uninfected controls for the study. Baseline resistance to Rifampicin was ascertained using GeneXpert. Clinical data, sera and sputum samples were collected from all the subjects, and the sera samples were processed for preparing small

RNA libraries. These libraries were then sequenced using Illumina HiSeq, while sputum samples were used for bacterial culture and drug-sensitivity assays. Validation studies were performed for shortlisted sncRNAs using qRT-PCR in a separate cohort.

The study was performed as per Institutional Ethics Approvals, and Informed consent of study participants were obtained.

**Results:** Bioinformatics analysis of small RNA sequencing data identified 684 miRNAs, 120 piRNAs and 212 tRFs in sera samples. Quantitative analysis of sncRNAs using the DeSeq method identified differentially expressed sncRNAs between ATB and healthy subjects. qRT-PCR based analysis validated significant differential levels of a selected set of sncRNAs [fold change  $\geq/\leq 2$  and p value  $<0.05$ ] between healthy and ATB cohorts.

**Conclusions:** Based upon detailed ROC analysis of the data, we identified a quantitative signature of five sncRNAs for diagnosis of ATB cohort, with high sensitivity, having an AUC of 0.96. This signature included 3 upregulated miRNAs, one downregulated miRNA and one downregulated tRF.

#### OA34-472-16 Evaluation of single-nucleotide polymorphisms in *M. tuberculosis* virulence genes as markers of lineages and sub-lineages

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**Background:** Understanding the genetic diversity of *Mycobacterium tuberculosis* (*M. tuberculosis*) is very crucial for rapid diagnosis and reduction of tuberculosis transmission. This study determines lineage-specific SNPs within *M. tuberculosis* virulence genes and lineage distribution amongst *M. tuberculosis* obtained in the Tshwane region.

**Design/Methods:** One hundred and fifty *M. tuberculosis* cultures were collected and sub-cultured on a MGIT 960 machine. DNA was extracted using CTAB method and spoligotyping was done to screen for *M. tuberculosis* lineages. Beijing and Latin American and Mediterranean (LAM) lineages were sequenced for further genotyping and detection of lineage-specific SNPs on the virulence genes. Whole Genome Sequences (WGS) were aligned using the Pathosystem Resource Integration Center (PATRIC). Alignments with an identity  $>98\%$  and coverage  $>95\%$  were retained for SNP-calling.

**Results:** *Tuberculosis* isolates showed that 86.7% (n = 130) of the isolates were previously shared type (ST) and 13.3% (n = 20) orphans. Lineages detected were Beijing family (26.7%), T family (16%), LAM (13.3%), East Africa Indian (EAI) (8.7%), S (6%), Manu (4.7%), H



(4.7%), CAS (4.0%) and X3 (2.7%). A total of 41 *M. tuberculosis* virulence genes were used to detect SNPs specific to Beijing (26 genes) and LAM (15 genes) lineages. Of the 41 virulence genes, 65.9% (27/41) virulence genes were shown to have SNPs that are specific to Beijing (29) and LAM (6) lineages. Four SNPs were found to be specific for F15/LAM4/KZN strain [*cyp125* (T1076C), *mce3B* (T44 C), *vapC25* (A221C), *vapB34* (C140A)].

**Conclusions:** A significant distribution of Beijing lineage was reported in this study. Bioinformatics analysis for SNPs specific lineages reveals that the study successfully identified 29 Beijing and 6 LAM signature SNPs that can be used to classify clinical *M. tuberculosis* isolates. This study also identified lineages specific for F15/LAM4/KZN, which is highly virulent and more transmissible in Kwazulu Natal Province.

### OA34-473-16 *De novo* development of isoniazid resistance in *M. tuberculosis* strains isolated from the same patient during the course of standard anti-TB therapy

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**Background:** The incidence of isoniazid (INH) resistant *Mycobacterium tuberculosis* is rising globally. In this study, we aimed to identify the molecular mechanisms of stepwise development of drug resistance in *M. tuberculosis* strains collected from the same patients during the course treatment.

**Design/Methods:** Three *M. tuberculosis* strains were collected from the same patient before and after 4 months of standardized antituberculosis therapy. Phenotypic drug susceptibility test, MIRU-VNTR, and whole-genome sequencing (WGS) were conducted for strain characterization and identification of mutations associated with INH resistance.

The mutated *katG* were transformed into a *katG*-deleted *M. tuberculosis* strain (GA03) to validate the role of novel mutations in INH resistance. Three-dimensional (3D) structures of mutated *katG* were modeled to predict the impact on INH binding.

**Results:** The pre-treatment isolate (M\_11806) was INH susceptible where the two post-treatment strains were resistant. MIRU-VNTR and WGS revealed that all three strains were clonally identical. Genomic analysis identified a missense *katG* mutation, P232L, and a nonsense *katG* mutation, Q461Stop, in D1\_12327 and D2\_12328 strains, respectively.

Transformation experiment showed that *katG* from pre-treatment strain restored the catalase activity in GA03 while *katG* genes from the post-treatment strains remained catalase-negative and had elevated MIC. 3D

protein structure indicated P232L reduce INH-KatG binding affinity and Q461Stop truncate gene transcription.

**Conclusions:** Our results showed that the two *katG* mutations, P232L and Q461Stop, accounted for the stepwise development of INH resistant clones during standard course of anti-TB therapy. Inclusion of these mutations in the design of molecular assays could increase the diagnostic performance.

### OA34-474-16 A pilot study of managing TB treatment with a breath test using mass spectrometry in three prospective cohorts

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**Background:** Monitoring tuberculosis (TB) treatment has been challenging, with current methods such as sputum culture conversion being limited by the low sensitivity and potential biohazard risks. The breath test holds promise to solve this problem.

**Design/Methods:** The study enrolled participants in three TB treatment cohorts, and breath samples were collected along with sputum samples and other tests. Participants were categorized into positive and negative groups using three standards of treatment endpoints.

When building models, participants were randomly split into three groups: 50% of them for model construction, 20% for internal validation, and 30% for model-blinded testing.

The mass spectrum data produced by high-pressure photon ionization time-of-flight mass spectrometry (HPPI-TOFMS) was processed to select the top ten volatile organic compounds (VOCs) ions for model building.

**Results:** Finally, 411 participants provided 1027 breath samples. The culture model achieved an accuracy of 61.2%, a sensitivity of 70.0%, a specificity of 59.7%, and an AUC of 0.704 in the test set (n=290).

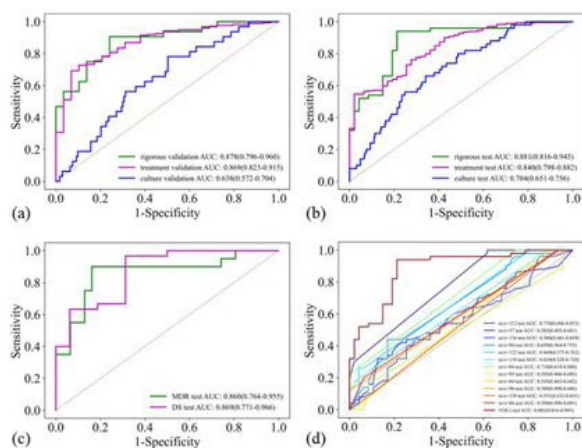
The treatment model achieved an accuracy of 65.0%, a sensitivity of 62.1%, a specificity of 83.0%, and an AUC of 0.840 in the test set (n=290).

The rigorous model achieved an accuracy of 82.5%, a sensitivity of 86.0%, a specificity of 78.7%, and an AUC of 0.881 in the test set (n=97).

For DS-TB and MDR-TB, the rigorous model achieved the AUC of 0.869 and 0.860, respectively. Twelve VOC ions were selected as a panel for TB treatment effect evaluation, with a single VOC ion having limited power in this task.

**Conclusions:** The study provides promising proof-of-concept results. The use of HPPI-TOFMS to detect VOCs in exhaled breath has the potential to offer a valu-

able tool in TB treatment monitoring. However, further studies with larger sample sizes are needed before clinical application.



**Figure 1.** The ROCs of the model built based on TB culture results, treatment periods, and our designed rigorous standard in validation (a) and test (b) datasets. The performances of rigorous standard-based anti-TB model in MDR and DS datasets (c). The discrimination power of the founded twelve VOCs in the test dataset (d). We enrolled participants in three tuberculosis treatment cohorts, a multidrug-resistant tuberculosis (MDR-TB) cohort of the MDR-Chin study ( $n=42$ ), an MDR-TB cohort of the SEAL-MDR study ( $n=173$ ), and a drug-susceptible TB (DS-TB) cohort of the ORDER TB-DM study ( $n=196$ ). After informed consent, participants provided sputum samples for MTB culture, breath samples for the breath test, and accomplished chest CT and other tests at each visit as planned till up to two years after the treatment completion. We used three standards to categorize participants into positive and negative groups for model building: (a) The time point of culture conversion without reversion, which would mostly be 2-3 months after treatment initiation; (b) The time point of treatment completion decided by clinicians or researchers, which would be six months for DS-TB and 6-12 months for MDR-TB; (c) A rigorous standard, which only included treatment-active culture-positive breath samples as the positive group and treatment-completed culture-negative breath samples as the negative group. All the enrolled participants were randomly split into three groups by participant: 50% of them for model construction, 20% for internal validation, and 30% for model-blinded testing.

## SHORT ORAL ABSTRACT SESSION (OA)

### SOA10 INTEGRATED SERVICES FOR TB CASE FINDING

#### SOA10-880-16 Integrated doorstep service delivery: Systematic screening for TB and leprosy in India

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**Background and challenges to implementation:** India intends to achieve TB related SDG targets by 2025. Early & complete diagnosis of TB plays crucial role in interrupting transmission.

**Intervention or response:** National health mission, India envisages integrated planning & service delivery of all health programmes. Maharashtra, a western Indian province with population of 120 million undertook innovative active case finding for TB & Leprosy to improve detection of TB & leprosy.

Cross sectional study was implemented for fortnight in September 22 with objective of assessing feasibility of deployment of ACF activity in entire population for screening of TB & Leprosy simultaneously. House to house screening was undertaken by trained health volunteers and presumptive cases were evaluated appropriately. Individual level data was collected in manual forms and cumulative numbers were fed in respective National digital portal.

Training & M&E support was extended by State health officials and WHO Medical consultants and incentives were extended to volunteers.

#### Results/Impact:

Population Screened	Presumptive cases identified	No. Smear done	No. NAAT done	No. X ray done	Sm pos	NAAT pos	Total TB cases diagnosed	Total Leprosy cases diagnosed
78938079	388798 (0.04%)	376253 (97%)	21858 (6%)	330261 (85%)	3317 (1%)	637 (3%)	8109 (2%)	6731

**Conclusions:** In view of > 70 million people could get screened in a fortnight yielding >15K TB & Leprosy cases indicates that whole population screening is feasible for TB in programmatic setting. Positivity on NAAT was significantly higher than on smear. Programme in line with WHO guidance may need to prioritise molecular diagnostic test for all presumptive TB patients.

Programme may consider newer modalities of community-based X ray like handheld X ray devices so that X ray can be conducted in community settings to improve access to X ray.

Incentive amount spent to identify one TB or leprosy from ACF significantly decreased to 10817 Rs from incentive amount spent to identify only TB cases (19930 Rs) or only leprosy case (Rs 22794).

Integration of case finding efforts with more than one programme brings cost effectiveness and ensures rational deployment of resources.

#### SOA10-881-16 Integration of TB into nutrition: a case study of TB screening at food distribution points in the Karamoja subregion of North-Eastern Uganda

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**Background and challenges to implementation:** The Karamoja subregion is a food and water stressed region with high rates of malnutrition. In 2022, 3.2 % and 13.9% of children aged 6-59 months screened for malnutrition in Karamoja sub region had severe acute malnutrition (SAM) and moderate acute malnutrition (MAM). In addition, 15% of pregnant/lactating women had MAM. Malnutrition increases the likelihood of activation of latent TB into active TB.

Integration of TB screening into a nutrition service is therefore a key intervention to improve TB case detection rates in this region.

**Intervention or response:** The USAID PACT Karamoja project supported trained healthcare workers to screen for TB among recipients of food aid at monthly food distribution points run by Andre Foods International (AFI). Healthcare workers screened patients for TB, and collected sputum samples from patients with presumptive TB and transported them for TB testing at nearby public health facilities.

Results were returned to the health care workers by hub riders. Participants who were diagnosed with TB were then followed up and started on treatment using available community health tracking systems like community owned resource persons.

**Results/Impact:** From October to December, 2022, TB screening was carried out at 20 food distribution points in seven districts in Karamoja sub-region. At these distribution points, 1756 people were screened for TB.

Of these, 279(15.9%) were diagnosed with presumptive TB and 257(92.1%) had their sputum samples collected & tested using GeneXpert testing. Eighteen (7%) of patients were diagnosed with TB, 10 of whom were male.

**Conclusions:** Integrating TB screening into malnutrition services among the nomadic communities in Karamoja sub region, North Eastern Uganda resulted in identification of cases of TB which would have been missed by routine TB care programs.

### SOA10-882-16 Community-level services ensure continuity of TB health service delivery during public health emergencies

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**Background and challenges to implementation:** Uganda remains one of the high tuberculosis (TB) burdened countries with an estimated annual incidence of 199/100,000. Until 2022, more than 25% of the incident TB patients were not identified, diagnosed or treated.

The Ministry of Health as part of mitigation to COVID 19 disruption launched an accelerated six monthly, country-wide community awareness screening testing and treatment (CAST) approach to find treat and prevent TB. We aimed at describing the CAST-TB and use of this surveillance data to estimate the sub national TB disease burden, establish district and regional variations in TB burden and to document lessons for improved TB surveillance and response.

**Intervention or response:** The CAST activity included targeting hot spot, contact investigation for all PBC's, door to door covering all villages Data was captured in DHIS2, analyzed and presented as notification rates per 100,000 population for each district, regional, and at national level. Notification rates >50/100,000 qualified a district as high burden (Figure 1), estimates were compared for each district based on annual notification of 2022 to identify newer districts with TB high burden districts. Data was disaggregated by sex and age.

**Results/Impact:** Through a five-day CAST, a total of 5,134,056 people were reached with a message of TB awareness. A total of 12,042 patients were diagnosed with bacteriologically confirmed TB resulting and a notification rate of 27.2 per 100,000 (95% CI: 26.8–27.8) Figure 1.

Of these 7,044 (58.5%) Males, 1.7% were children below 15 years. The TB high burden districts were 21% (n=31/146) range (50.3-159.7) per 100,000 with Obongi being the highest (160/100,000) contributing 27.6% to the annual notification in 2022 and Buikwe district the lowest.

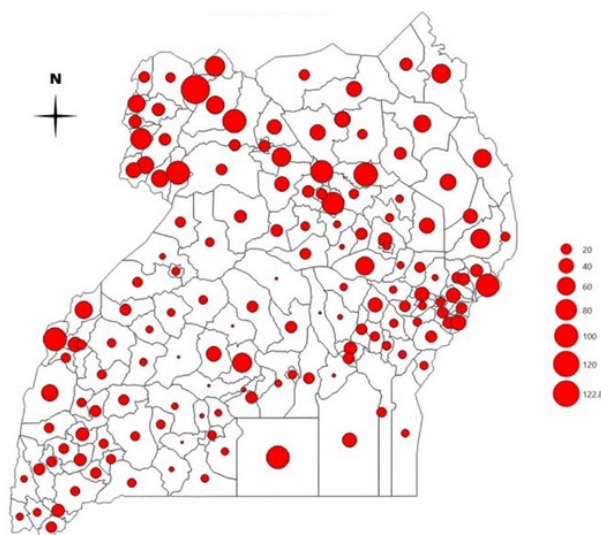


Figure 1. CAST cases per 100,000, September 2022.

**Conclusions:** In absence of National TB survey, CAST surveillance data provided an alternative estimate for TB high burden at districts and subnational level.

### SOA10-883-16 Active case-finding for TB among Afghan populations living in the refugee villages of Khyber Pakhtunkhwa and Balochistan Provinces, Pakistan

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**Background:** Afghanistan has one of the highest numbers of refugees living in Pakistan. Around 2.4 million registered and some 2.3 to 3 million undocumented Afghans are living in Pakistan- (estimated 800,000 to 1 million Afghans). It is assumed that the estimated tuberculosis incidence in this population, is same as in the country, 264/100,000 and National TB Program Pakistan is detecting only 50% of the estimated cases through passive case finding. This low detection and missing cases are the means of transmitting TB and sustain the global TB epidemic.

**Design/Methods:** This study evaluated a community based active case finding (ACF) strategy for the detection of tuberculosis cases among Afghan population living in the refugee villages (RVS) in Khyber Pakhtunkhwa and Balochistan Provinces, Pakistan from November 2019 to December 2022. ACF implemented in the 45 selected RVs by trained Field staff, through symptom screening of TB.

Presumptive TB cases identified were referred to nearest TB health facility for diagnosis and those found confirmed, registered them for treatment and then regularly followed-up.

**Results:** Total 266,285 individuals screened for tuberculosis, 30,189 (11%) were presumptive TB cases of them 2,455 (8%) found confirmed TB cases. Of the 2,455 TB cases, 53% were males and 63% were bacteriologically-confirmed.

All confirmed TB cases are registered for treatment at nearest TB health facilities. The treatment outcomes among the cases detected through ACF are better than the cases detected through routine TB Program (96% vs 94%).

**Conclusions:** Community based screening for tuberculosis is useful and have additional benefits such as contribution to early case finding and detection of additional TB patients from the refugee villages who are missing by the routine TB Program, with an extended benefit for reducing secondary cases in the community.

### SOA10-884-16 Childhood TB detection through supported decision-making in community settings in Bangladesh

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**Background:** Diagnosis of childhood tuberculosis (TB) is not straight-forward and rather challenging. The disease is paucibacillary, often presents with atypical symptoms and diagnostic tests are not sensitive enough. Multidisciplinary team of clinicians can facilitate diagnosis of complex child TB cases. Technology has impacted healthcare globally however there lacks evidence in Bangladesh on use of technology in TB diagnosis.

This study was conducted to evaluate the community-based implementation of supported decision making through multidisciplinary board (MDB) and videoconferencing in diagnosis of complex child TB cases.

**Design/Methods:** Between June 2020 and June 2021, children visiting paediatric outpatient departments of 35 public facilities in Mymensingh were verbally screened for TB symptoms by health workers. Possible child TB cases were clinically evaluated, and went through diagnostic evaluation process. Children meeting clinical criterias but without conclusive test results were referred to MDBs (comprised of paediatricians, internists, otolaryngologist and radiologists) and videoconferencing platform at designated facilities for diagnosis. Videoconferencing involved connecting cases with Child Pulmonologists at a specialized child TB Hospital through online technology. Children diagnosed with TB were linked to TB treatment.

**Results:** 21,102 possible child TB cases were identified. Of these 513 (2.4%) difficult-to-diagnose cases were invited at MDBs. 466 (91%) arrived. Of these 204 (44%)

children were diagnosed with TB. 200 (98%) children started TB treatment. On the other hand, 1,207 (5.7%) difficult-to-diagnose cases were invited for videoconferencing and 92% showed-up. Of these 521(47%) children were found to have TB of which 99% initiated TB treatment. All children from both strategies completed treatment.

**Conclusions:** Cases reviewed by MDBs and child TB experts through technology resulted in significant proportion of child TB detection among difficult-to-diagnose child TB cases in the community.

These strategies can be integrated into routine programmatic settings to increase child TB detection and contribute to achieving the UNHLM and End TB targets for TB

### SOA10-885-16 TB recovery strategies in response to the COVID-19 pandemic: screening in high-yield communities to find missing people with TB

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**Background and challenges to implementation:** In 2021, the COVID-19 pandemic resulted in a decline in TB notifications of about 25% in Vietnam; estimates of treatment coverage dropped below 50%, calling for efforts to accelerate case finding.

**Intervention or response:** In 2021, the National Tuberculosis Program (NTP) and USAID adapted the high-yield “Double X” (chest X-ray [CXR], GeneXpert) model to improve access to case finding without large community gatherings.

Key adaptations were implemented in 2022:

1. Expansion of intensified case finding (ICF) at facilities to screen all patients receiving CXR for any reason,
2. Hybrid ACF/ICF to routinely reach household contacts of people with TB and refer them for facility-based screening,
3. Community-level screening enabled commune health staff to triage people with productive cough for GeneXpert (Single X), and;
4. TB self-screening tool accessed online via QR code with referral to facilities.

**Results/Impact:** From January to December 2022, total case notifications in 24 districts of five provinces was 4,143, a 143% increase over 2021.

In 2022, expanded ICF increased facility-based notifications by 91% over 2021 and increased yield (2,626/100,000 CXR compared with 2,559/100,000 CXR); 20% of total case notifications were from adaptive approaches: online screening, Single X, and Hybrid ACF/ICF.

All adaptations were high-yield for TB detection. Hybrid ACF/ICF screened an additional 5,518 household contacts independent of ACF campaigns.

Single X and online screening reached people in communities with higher GeneXpert positivity than ACF campaigns (10.1% and 19.4% versus 9.4% for ACF).

**Conclusions:** Double X adaptations designed to mitigate service disruptions during the pandemic increased facility-based case finding and extended TB services into communities. These models continue to find TB cases using existing staff and resources, resulting in a more comprehensive approach to TB case finding. Hybrid ACF/ICF builds contact investigation capacity in facilities and Single X builds the capacity of local level health-care workers to screen people for TB.

	2021			2022					
	Active Case Finding (8 districts)	Intensified Case Finding (ICF)	Total case finding 2021	Active Case Finding (8 districts)	Expanded ICF	Hybrid Active Case Finding	Single X	Online screening	Total case finding 2022
No. evaluated with CXR	12,750	58,069	70,819	28,423	107,475	5,518	-	1,791	143,207
No. (%) TB-presumptive CXR	3,151 (24.7%)	5,977 (10.3%)	9,128 (12.9%)	4,202 (14.8%)	11,257 (10.5%)	1,165 (21.1%)	-	888 (49.6%)	17,512 (12.2%)
No. (%) with TB-presumptive CXR tested with Xpert	3,090 (98.1%)	5,460 (91.2%)	8,550 (93.7%)	4,381 (104.3%)	10,671 (93.7%)	1,163 (99.8%)	5,618	891 (100.3%)	22,724
No. (%) Xpert confirmed TB	211 (6.8%)	1,488 (27.3%)	1,699 (19.9%)	410 (9.4%)	2,791 (26.2%)	74 (6.4%)	568 (10.1%)	173 (19.4%)	4,016 (17.7%)
Total TB diagnosed	211	1,488	1,699	465	2,851	78	571	178	4,143
No. (%) initiated treatment	193 (91.5%)	1,349 (90.7%)	1,542 (90.8%)	432 (92.9%)	2,631 (92.3%)	67 (85.9%)	508 (89%)	166 (93.3%)	3,804 (91.8%)
TB case Yield/100,000 CXR	1,655	2,559	2,399	1,636	2,646	1,414	-	9,939	2,893
% of overall case finding	12.4%	87.6%	100%	11.2%	68.8%	1.9%	13.8%	4.3%	100%

Table. TB case finding by approach in 24 districts of 5 provinces of Vietnam, 2021 - 2022

### SOA10-886-16 Improving TB case-finding through community interventions using the Wellness-on-Keke Model in Nigeria

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**Background and challenges to implementation:** In Nigeria, improving TB case finding has always been prioritized due to the significant gap of about 70% in TB case notification. KNCV Nigeria with support from USAID

introduced the use of PDX with artificial intelligence (AI) in pre-diagnostic TB screening during community based active TB case finding.

To strategize and make this new tool work efficiently, the PDX machine was coupled into a one stop health-care mechanism called WOK.

**Intervention or response:** KNCV Nigeria with funding from USAID procured 4 wellness on Keke's (WOKS) which are mobile diagnostic units coupled to an Ultra-Portable Digital X-ray (UPDX) and either a TB LAMP or Truenat testing platform. The teams were deployed across 3 TB LON region 1 & 2 states of Anambra, Cross Rivers, and Kano state, with Kano having 2 WOKs. The teams provided integrated services that included TB screening and testing services, Covid-19 vaccination, screening for diabetes and hypertension.

Prior to deployment of the WOK, the teams only provided TB screening and testing. We analyzed data from the 4 WOKs comparing achievements of 3 months prior to deployment of the WOK and 3 months after deployment to assess additionality attributable to the intervention.

**Results/Impact:** The table above shows a 6% increase in the number of clients screened and an 8% increase in TB cases diagnosed with the introduction of the WOKs. Prior to commencement of the WOK integrated outreaches only 285 TB cases were diagnosed, this increased to 329 with the introduction of WOK platforms.

Intervention	Timelines	#Person screened	#person presumed to have TB	#evaluated for TB	#TB patients detected	# Put on treatment.
With WOK	Oct - Dec 2022	15769	1270	1270	329	325
Without WOK	July - Sept 2022	14267	1237	1237	285	285
What Changed	-	1502 (6%)	33 (2%)	33 (2%)	44 (8%)	42 (8%)

Table 1.

**Conclusions:** The WOK model which uses an integrated approach of providing multiple health services to the clients is a key innovation that has shown significant additionality to the traditional ways of doing community outreaches and recommended for scale up nationally to help in finding the missing TB cases in hard-to-reach communities.

## SOA11 How can we strengthen TB detection?

### SOA11-887-16 Cluster randomised controlled trial of active case-finding and linkage in Haryana, India

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**Background and challenges to implementation:** India has 1:4 cases and 1:3 deaths from TB globally. ACF is essential to accelerate TB control efforts but robust evaluation to inform, optimise and scale ACF interventions and linkage to care is lacking. This research is supported through local Public Private Partnership.

**Intervention or response:** Cluster randomised controlled trial (CRCT) among high TB burden rural populations in Haryana. Primary Care Sub-centres were the unit of randomisation - 80 intervention and 160 control – each serving 5,000-10,000 population.

Intervention sites received door-to-door ACF to identify symptomatic individuals, unscreened household contacts of recent active cases and treatment defaulters. Diagnostic camps were positioned at Sub-centres providing digital Xray and QURE.AI to triage into CBNAAT (Xpert) for all eligible patients.

Newly diagnosed cases were notified and commenced on treatment same day, where possible, and their contacts were also actively screened.

**Results/Impact:** Between Sep 2022 and Jan 2023, 40,164 households (196,369 individuals) were reached by the door-to-door teams representing 94% of the total catchment population. 3,766 individuals (2%) were invited to the diagnostic camp of whom 3,457 (92%) attended and underwent X-ray with AI reporting. 1,117 (32%) had radiologically presumptive TB and underwent CBNAAT, of whom 129 (12%) were confirmed positive (6% Rifampicin resistant).

25 additional clinico-radiologic TB diagnoses were made. All 154 new diagnoses commenced treatment. QURE.AI performance was comparable to or better than doctors reading CXRs.

**Conclusions:** Initial ACF round generated a three-fold increase in case detection and reporting. The intervention achieved very high community coverage for door-to-door identification of persons eligible for screening and high attendance rates for radiology.

The model increases access to diagnostic services for the most vulnerable and marginalised. Two further rounds of ACF will be undertaken over the next 24 months. This innovative Public Private Partnership aims to build operational research capacity and rapidly scale ACF to vulnerable populations.

### SOA11-888-16 Comparing yield of household and social contacts investigation models for bacteriologically confirmed and children under 5 years: The Global Fund Tuberculosis Project in Kenya

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**Background and challenges to implementation:** Through Global Fund support, Amref in collaboration with the National Tuberculosis (TB) Program have been implementing tracing and screening of household contacts (HHC) of bacteriologically confirmed TB patients and children under 5 years with TB countrywide since 2011.

The objective of this intervention is to enhance early diagnosis of TB and prompt initiation to treatment. However, the patients also spend time in other areas beyond the household that necessitated the project to screen social contacts (SC) of TB patients who are barely reached because of inadequate resources.

**Intervention or response:** Community Health Volunteers (CHVs) were sensitized to trace and screen contacts of index TB patients. During treatment initiation, Health Care Workers (HCW) documented contacts of TB patient in the contact management register (CMR). CHVs were allocated index patients to conduct physical tracing of their contacts.

All presumptive contacts were referred to the facility for further evaluation. Data was analyzed using R software.

**Results/Impact:** From July 2021 to December 2022, 43,954 index TB patients were visited for contact tracing and 153,352 contact persons screened for TB. Out of these, 152,163 were HHC and 1,189 were SC. From the HHC screened, 1,407 (1%) were diagnosed with TB (651(46%) males and 756(54%) females). From the SC screened, 194(16%) were diagnosed with TB (159(82%) males and 35(18%) females).

The Mean age for HHC and SC was 20yrs and 30yrs respectively. Logistics regression showed that age and type of contact person (HHC or SC) were strong predictors of TB ( $P < 0.005$ ) and gender was not. SC were 3 times more likely to be diagnosed with TB compared to HHC.

**Conclusions:** Tracing Social Contacts yielded more people with TB especially men and persons aged 25-34yrs. It is therefore crucial for programs to invest significant resources in investigating social contacts of people with TB to alleviate TB disease burden.

### SOA11-889-16 Aashwasan: a 100-day, active case-finding campaign in the tribal districts of India

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**Background and challenges to implementation:** India accounts for significant global TB burden with estimated incidence of 196 per 100,000 population in 2022. The pooled estimated prevalence of TB among the tribal population was 703 per 100,000 population as against the national average of 256 per 100,000 in 2013. A quarter of total self-reported TB cases and 10.4% of all TB-notified persons are from tribal communities.

Active Case Finding (ACF) is a key strategy to identify and to initiate treatment among those group(s) that remains undiagnosed and unreachable by the program due to various reasons.

**Intervention or response:** Aashwasan was implemented across 68,413 hard to reach villages of 174 tribal districts in 21 States/UTs of India between January and August 2022.

It aimed at actively identifying persons with presumptive pulmonary TB, including contact persons, supporting in sample collection and transport and linking for testing and treatment initiation within the National TB Elimination Program while increasing awareness of TB disease, symptoms, treatment, and prevention among the tribal communities.

**Results/Impact:** Through 1121 IEC-enabled vehicles, Aashwasan staff along with ASHA screened 1,03,84,538 persons for TB (66% of 16,677,804 reached) of whom 3,82,251 (3.6%) persons with presumptive TB were

identified. Of which, 2,80,259 (73.3%) tested for TB. Of those who were tested, 10,249 (3.6%) were detected to have TB disease, of whom 9,588 (93.5%) were initiated on treatment. At country level, Aashwasan contributed to about 13% of the overall public-sector notification.

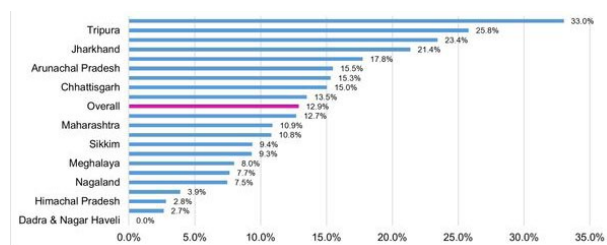


Figure. Contribution to public sector notification - January to August 2022.

**Conclusions:** First-of-its-kind, nation-wide campaign, Aashwasan, deployed field staff from within the tribal communities and leveraged community influencers for mobilizing people for screening. Mechanism for sample collection and transport, in-built in the meticulously designed micro-plans in consultation with the district NTEP were key enablers that made this 100 day per district ACF drive a success.

### SOA11-890-16 Assessing TB prevalence among school children in Kampala, Mukono and Wakiso Districts of Uganda

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**Background and challenges to implementation:** There is growing concern about the spread of TB in schools in Uganda. Among priority actions to address the disease, the Multi-Sectoral Accountability Framework to Accelerate Progress to End TB by 2030 (MAF-TB) recommends educating the masses and screening of students. During community outreach activities, the USAID Local Partner Health Services TB Activity (USAID LPHS-TB) Project, implemented by the Infectious Diseases Institute, also observed rising cases of TB in schools.

In response, the Project carried out TB screening in schools within the districts of Kampala, Mukono and Wakiso.

**Intervention or response:** Students from 33 selected primary and secondary schools in Kampala, Wakiso and Mukono districts where a TB case had been reported and those located in high burden communities were



screened for TB between February and December 2022. Those screened were both male and female, aged 6-18 years and represented both day and boarding schools. Students who were presumed with TB provided sputum samples for testing at the nearest health facility using GeneXpert. Those unable to produce sputum underwent clinical evaluation. Results were communicated through the school heads and primary caregivers notified.

**Results/Impact:** A total of 5,728 students were screened for TB, 643 were presumed and 12 were confirmed (0.2% yield). Of the confirmed, nine were from primary schools and three from secondary schools.

Kampala had the highest ratio of presumptive and confirmed persons with TB, with 6 confirmed out of 166 presumed; Mukono had 6 confirmed out of 390 presumed, while Wakiso had 78 presumed, but none confirmed.

	Kampala	Mukono	Wakiso	TOTAL
Number of primary schools visited	4	15	3	22
Number of secondary schools visited	4	2	5	11
Number screened	1,345	3,453	930	5,728
Number presumed with TB	166	390	87	643
Number diagnosed with TB	6	6	0	12

Table. Summary of TB screening in schools in Kampala, Wakiso and Mukono.

**Conclusions:** TB is a significant problem among school children and calls for increased efforts to improve prevention and treatment. Emphasis should be placed on educating the masses and screening of school children as recommended by MAF-TB. Further research is also needed to better understand TB prevalence in schools across the country and risk factors.

### SOA11-891-16 Computer-aided detection is a feasible and acceptable component of active case-finding for TB

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**Background:** Active case finding using computer-aided detection (CAD) has shown promising results for improving tuberculosis (TB) detection rates in resource-limited settings. This study aimed to assess the feasibility and acceptability of implementing CAD for active TB case finding in Manila, Philippines, from the perspectives of community members, health care workers, and key stakeholders.

**Design/Methods:** Using qualitative design this study explored perceptions around the active TB case finding being implemented using a truck installed with digital X-ray and CAD. Participants with CAD score above

threshold provided sputum for bacteriological diagnosis of TB. Participants identified with TB were referred to local health centres for treatment initiation.

In-depth interviews and focus group discussions were conducted with a total of 35 community members, 8 health care workers, and 5 key stakeholders. The data was analyzed using thematic analysis.

**Results:** The study found that the implementation of CAD for active TB case finding in Tondo, Manila, Philippines is feasible and acceptable. Participants expressed overall positive attitudes towards the project and highlighted key considerations for scaling and replicating the program in other settings.

The findings include the importance of proper preparation and the need for human resources with sufficient technical capacity to operate and troubleshoot the truck, X-ray, CAD, and data storage systems.

Participants also stressed the need to consider policy context, X-ray machine and truck specifications, referral chain and availability/accessibility of healthcare centers and medicines, community mobilization, and accurate expectation setting to ensure project success.

**Conclusions:** The study findings provide valuable insights into the feasibility and acceptability of implementing CAD for active TB case finding in Manila, Philippines.

The results can inform the design and implementation of similar programs in other resource-limited settings and highlight the importance of proper planning and community engagement to ensure the success of such programs.

### SOA11-892-16 A practical method of threshold calibration for computer-aided detection of TB

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**Background and challenges to implementation:** Threshold for computer-aided detection (CAD) software for tuberculosis (TB) detection determines who is referred for confirmatory testing. Because CAD results can vary widely across different populations, software technologies, and CAD versions, the choice of threshold can greatly affect CAD performance. We describe a practical approach to threshold determination.

**Intervention or response:** CAD4TB version 7 was implemented with digital chest X-ray (CXR) for TB active case finding (ACF) in Manila, Philippines. Participants ≥

15 years with CAD scores above threshold or with symptoms regardless of CAD score had sputum collected for GeneXpert testing. CAD threshold was determined based on:

1. Communication with experts before implementation, particularly regarding differences between CAD4TB versions 6 and 7
2. Choosing an initial threshold as low as possible with subsequent upward adjustment as needed
3. Prevalence of confirmed TB in screened population
4. GeneXpert testing capacity
5. Matching CAD to local radiologists' sensitivity for TB screening

**Results/Impact:** Retrospective analysis of CAD scores for CXR performed before CAD implementation suggested that a threshold of 25 would refer 35% of individuals for GeneXpert testing, matching local radiologists' sensitivity for TB screening and still within testing capacity. 25 was selected as the initial and lower limit of threshold. Using an adaptive method to adjust the threshold based on periodic evaluation of data, threshold was adjusted once from 25 to 28.

Data from four months of CAD are shown in Table 1. Of note, 34% ACF participants were above threshold, only two individuals positive on GeneXpert had CAD scores below threshold (i.e., false negatives) and GeneXpert positivity rates were high. As results are acceptable, the current threshold will be maintained.

CAD score	Sputum Xpert positive (n)	Total sputum done (N)	Xpert positivity rate % (n/N)
≥ 90	23	35	65.7%
80-89	18	28	64.3%
70-79	34	99	34.3%
60-69	33	124	26.6%
50-59	23	96	23.9%
40-49	14	226	6.2%
30-39	6	349	1.7%
28-29	2	114	1.8%
< 28	2	193	1.0%

Table 1.

**Conclusions:** Pre-implementation preparation, consideration of programmatic goals, and strong data collection were key requirements for threshold calibration. Matching CAD to local radiologists' sensitivity for TB screening was also important for threshold selection and acceptability of this novel technology.

## SOA11-893-16 Low concordance between QIAreach-QFT and QFT-Plus in a community IGRA survey in Blantyre, Malawi

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**Background:** Interferon-gamma release assays (IGRAs) may be used for monitoring tuberculosis epidemiology and stratifying individual tuberculosis risk. Conventional IGRAs, such as the QFT-Plus, can be challenging to deploy in low-resource settings.

The QIAReach-QFT aims to overcome these operational challenges, using a 1mL blood sample, and a battery-powered self-contained lateral flow immunofluorescence device to quantify interferon-gamma.

Previous studies found high concordance with the QFT-Plus, but with no published data from population-based surveys, high-burden settings, or young children. We therefore evaluated QIAReach-QFT against QFT-Plus in a population-based IGRA survey in Blantyre, Malawi.

**Design/Methods:** Children aged 1-5 years were recruited via convenience sampling in three primary health clinics, targeting healthy children attending for vaccinations or accompanying relatives on routine visits.

Additional participants aged 1-5 and 10-40 years were randomly sampled from a community household survey. Participants or their guardians were interviewed, and blood samples taken for QIAReach-QFT and QFT-Plus testing, following the manufacturer's instructions.

**Results:** To date, 450 participants have been recruited: 387 aged 1-5, and 63 aged 10-40.

Overall, 128/450 (28.4%) had a positive QIAReach-QFT, including 99/387 (25.6%) children aged 1-5; 59/450 (13.1%) had a positive QFT-Plus, including 38/387 (9.8%) children aged 1-5.

There was minimal concordance between QIAReach-QFT and QFT-Plus (Cohen's kappa 0.22, QIAReach sensitivity vs QFT-Plus: 54.2%, specificity 74.7%) (Table 1).

There was no agreement between the tests in young children aged 1-5 (kappa 0.067, sensitivity 34.2%, specificity 75.3%). Concordance was higher – but still suboptimal – in adults and adolescents (kappa 0.56, sensitivity 90.4%, specificity 70.3%).

		All ages (N=450)		Aged 1-5 years (N=387)		Aged 10-40 years (N=63)	
		QIAReach-QFT					
		Positive (n=131)	Negative (n=319)	Positive (n=99)	Negative (n=288)	Positive (N=32)	Negative (N=31)
QFT-Plus	Positive	32 (24.4%)	27 (8.5%)	13 (13.1%)	25 (8.7%)	19 (59.4%)	2 (6.5%)
	Negative	74 (56.5%)	218 (68.3%)	63 (63.6%)	192 (66.7%)	11 (34.4%)	26 (83.9%)
	Indeterminate	25 (19.1%)	74 (23.2%)	23 (23.2%)	71 (24.7%)	2 (6.3%)	3 (9.7%)
Cohen's kappa <sup>1</sup> (95% CI) <sup>2</sup>		0.22 (0.11-0.33)		0.067 (0-0.18)		0.56 (0.35-0.76)	
QIAReach sensitivity <sup>3</sup> (95% CI)		54.2% (40.8-67.3%)		34.2% (19.6-51.4%)		90.5% (69.6-98.8%)	
QIAReach specificity <sup>3</sup> (95% CI)		74.7% (69.3-79.5%)		75.3% (69.5-80.5%)		70.3% (53.0-84.1%)	

<sup>1</sup> Excluding QFT-Plus indeterminate results <sup>2</sup>95% confidence intervals using Fleiss et al <sup>3</sup>Against "gold standard" of QFT-Plus

Table 1 – comparison of QIAReach-QFT and QFT-Plus results, stratified by age group.

**Conclusions:** Concordance between QIAReach-QFT and QFT-Plus was low, particularly in young children. Quantitative data and additional analyses to explore possible contributing factors will be presented. IGRA surveillance was feasible, provided informative epidemiological data, and identified individuals who might benefit from preventive therapy, but QIAReach-QFT did not appear to be an appropriate alternative to QFT-Plus in this setting.

### SOA11-894-16 Applicability of artificial intelligence-based computer-aided detection for community-based, active case-finding of pulmonary TB

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**Background:** Several studies have been conducted to evaluate the performance of artificial intelligence-based computer-aided detection (CAD) for pulmonary tuberculosis (TB) in clinical settings. However, little is known about its applicability to community-based active case finding (ACF).

**Design/Methods:** We retrospectively analysed an anonymized dataset obtained from a community-based ACF in Cambodia. All of the participants in the ACF

were screened by chest radiography (CXR), followed by Xpert for sputum. A newly developed CAD by FUJIFILM Corporation was evaluated for its performance by using bacteriological and radiological references by an experienced chest physician, and its applicability to community-based ACF in Cambodia was examined.

**Results:** TB scores of the CAD were significantly associated with the CXR classifications as indicated by the TB severity, and its area under the receiver operating characteristic curve (AUC) as the bacteriological reference was 0.86 (95% confidence interval (CI): 0.83-0.89).

The AUC with the reference of "abnormality suggest of TB" by human reading as triage purpose, and with the reference of "any abnormality in the lung fields" by human reading as screening purpose was 0.93 (95% CI: 0.92-0.94) and 0.92 (95% CI: 0.91-0.93), respectively.

Using a threshold of 0.5340 for triage purposes, the human reading and bacteriological examination needed fell to 21% and 15%, respectively, detecting 95% of Xpert-positive TB in ACF. Similarly, using a threshold of 0.2835 for screening purpose, 98% of Xpert-positive TB were detected.

Purpose	TB score as threshold	N of CXR selected by CAD (% of 8,386)	N of sputum examined* (% of 8,386)	N of Xpert-positive TB (% of 130)	N of CXR with "abnormality suggestive of TB" (% of 615)	N of CXR with "any abnormality in the lung fields" (% of 1,551)
Triage	0.5340	1,770 (21.1)	1,246 (14.9)	125 (96.2)	554 (90.1)	1,246 (80.3)
Screening	0.2835	3,107 (37.0)	1,396 (16.6)	127 (97.7)	594 (96.6)	1,396 (90.0)

\* N of sputum examined = N of CXR selected by CAD - N of normal CXR by human reading

Table: Performance in triage and screening purposes at sensitivity of 90%.

**Conclusions:** The CAD is applicable to community-based ACF in high TB burden settings. The use of CAD in developing countries has the potential to expand CXR screening in community-based ACF, with a substantial decrease in the workload on human readers and laboratory labour.

Further studies are required to generalize the results to other settings by increasing the sample size and comparing the CAD performance with that of more human readers.

## SOA12 TB, gender and stigma

### SOA12-890-16 The impact of gender-sensitive interventions on improved access to TB services among women

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**Background and challenges to implementation:** Tuberculosis (TB) remains a significant global public health problem with known gender-related (male versus female) disparities. Females often face barriers to accessing quality health care because of financial and physical dependence, discrimination, stigma, and limited resources.

To best tailor its TB interventions using a gender-responsive approach, the USAID Eliminating TB in Central Asia Activity assessed gender, stigma, and other social barriers to accessing TB services in Uzbekistan.

According to the assessment, 26% of respondents among TB patients consulted a doctor within 14-30 days upon the onset of symptoms. Women seek medical care later than men (32.7% vs 17.7%, respectively) due to lack of funds (23.6%), stigma (24%), fear of diagnosis to be confirmed (10.2%) and limited information about TB (10%).

**Intervention or response:** Following gender assessment, we developed gender-responsive interventions to remove barriers and delays limiting women's access to TB diagnostic and treatment services at the individual and provider/system levels. Multidisciplinary teams were tasked to implement the interventions including:

- Identifying gender barriers during TB outreach and screening and addressing them through psychosocial counseling including with family members;
- Providing escorts to medical facilities;
- Engaging religious and community leaders as needed to influence the head of the family and providing social support to those in need;
- Gender sensitization training among service providers;
- Incorporating gender equality messages in service delivery into information materials.

**Results/Impact:** Before project interventions in 2020, the TB case detections in the Fergana region, were higher among men (819) than women (684).

After the start of implementation of project interventions in 2020, TB cases detected among women increased by 11% from 45.5% of all cases in 2019 to 50.5% in 2022 (Chart 1).

**Conclusions:** Evidence-based gender-responsive strategies are needed to overcome the unique barriers women in Uzbekistan face in accessing TB care, both on an individual basis and within the health care system.

### SOA12-891-16 Designing TB case-finding interventions for men using participatory health-seeking pathway analysis

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**Background:** The 2018 United Nations High-Level Meeting on Tuberculosis (TB) highlighted the need for gender-specific TB programmes that reach men with undiagnosed TB who account for two out of three people who are missed by TB services. We aimed to identify gender-specific TB case-finding interventions targeting men in peri-urban settings in Uganda.

**Design/Methods:** We conducted health-seeking pathway analyses among 87 stakeholders (i.e., healthcare workers, TB survivors, policymakers and researchers) through participatory workshops across four Ugandan general hospitals (Kawolo, Gombe, Mityana and Nakaseke). In separate workshops at each facility, participants identified the ideal and actual step-by-step TB health-seeking processes among men and then compared the pathways to identify barriers to TB care. The stepping stones method where a 'river' represents barriers and each stepping stone a solution was used to codesign interventions needed to link men with symptoms suggestive of TB to care. We synthesised learnings across the facilities in a further participatory workshop.

**Results:** Across locations, the actual TB care pathway (Figure 1) diverted from the ideal pathway due to health system, community, health worker and individual level barriers such as long waiting times, stigma, TB misconceptions, and delayed healthcare seeking. Based on the barriers faced by men, stakeholders suggested a male-specific TB care package involving the introduction of male-friendly spaces; integrated TB services that include screening with chest X-rays; healthcare worker training modules on integrated male-friendly services; training and supporting TB champions to deliver health education to people seeking care; and engagement of private practitioners to screen for TB.

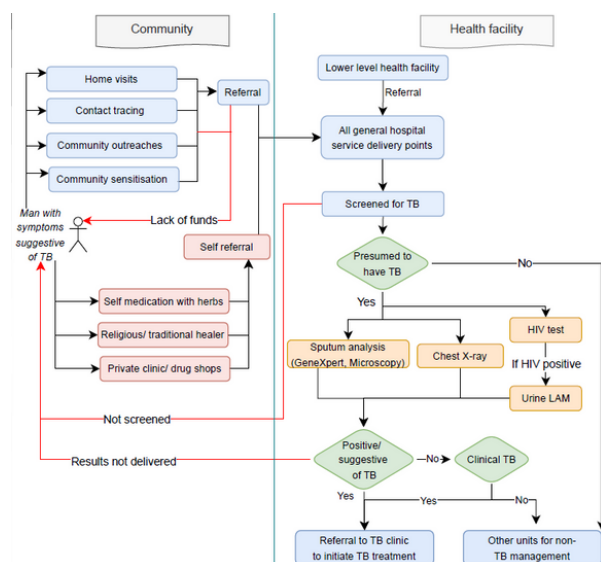


Figure 1. Actual TB healthcare seeking pathway depicting patient's health seeking activities (red), health system case finding processes (blue), TB diagnostics (orange) and decision nodes (green).

**Conclusions:** Our participatory pathway analysis approach enabled us to codesign context-specific, person-centred TB interventions for men. Simultaneously, the pathway facilitated dialogue and learning between different health actors and enhanced their support for the implementation of the intervention package. The acceptability, effectiveness and cost-effectiveness of the package will now be evaluated in a quasi-experimental study.

## SOA12-892-16 Vulnerability assessment among persons with TB in tribal and urban settings in India

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**Background and challenges to implementation:** TB is a disease with intersecting clinical, social, cultural and economic dimensions. People with TB (PwTB) are vulnerable to multiple comorbidities including malnutrition, HIV and diabetes. The TB programme in India offers routines screening and linkages to support services for HIV and Diabetes. However, there are other clinical

and social vulnerabilities like alcohol and tobacco use, malnutrition etc. Those who live alone, and those who migrate are also currently not screened or provided with any supportive services.

**Intervention or response:** As part of USAID supported Accountability Leadership by Local communities for Inclusive, Enabling Services (ALLIES) Project by REACH, an intervention was designed to assess and address vulnerabilities among PwTB.

The project trained and engaged 18 TB Champions and health care workers from the local communities who screened 656 PwTB (380 Male and 276 Female) of 18+ years in Mayurbhanj, a tribal district in Odisha and private setting in Chennai, Tamil Nādu.

The assessment tool was administered to record the vulnerabilities, ensuring confidentiality and privacy. The assessment was carried out at the health facilities or the households of the PwTB.

For malnutrition BMI was calculated and both, overweight and underweight were included as vulnerability. WHO definitions were used to define malnutrition. This abstract focuses on reporting the results of the vulnerability assessment which is the first step towards providing holistic care.

**Results/Impact:** 72% (470) of 656 PwTB screened reported having vulnerability. Of the PwTB reporting vulnerability, 45% (210) had two or more vulnerabilities. The gender-wise distribution of different vulnerabilities among PwTB is given below:

Indicator	Male	%	Female	%	Total
Number of PwTB screened for vulnerabilities	380	58	276	42	656
Number of PwTB reporting any vulnerability	302	64	168	36	470
Number of PwTB reporting alcohol as vulnerability	149	93	11	7	160
Number of PwTB reporting smoking as vulnerability	61	97	2	3	63
Number of PwTB reporting malnutrition as vulnerability	211	61	135	39	346
Number of PwTB reporting migration as vulnerability	43	51	41	49	84
Number of PwTB reporting living alone as vulnerability	7	50	7	50	14

**Conclusions:** The results indicate that there is an urgent need to expand vulnerability screening beyond HIV and diabetes and strengthen linkages with supportive services at the sub-district level. This can potentially help substantially improve treatment outcomes, critical to achieving TB elimination in India

### SOA12-893-16 On the road to ending TB: targeted intervention of truckers and allied professions in trans-shipment locations, India

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**Background and challenges to implementation:** WHO estimates 210 new TB (tuberculosis) patients/100,000 Indian population[1]. ~ 10,000-12,000 TB patients may occur annually among 5-6 million Indian truck drivers. Delay in diagnosis, treatment initiation & management remain a significant barrier for mobile workforces such as truck drivers. If infectious diseases like tuberculosis are not controlled, industries with mobile workers would face issues like absenteeism & productivity loss which will result in revenue loss.

In May 2019, NAI DISHA (New Distinctive Integrated & Sustainable Health Action) initiated “On the road to end TB” targeting truckers & allied populations in three trans-shipment locations (TSLs) of Lucknow, Agra, & Jaipur in North India. Locations’ choice was based on main transport axes in India.

[1]WHO Global TB Report 2022

**Intervention or response:** Objectives were to improve awareness about TB & general hygiene in targeted TSLs, promote early diagnosis & initiation of TB treatment, enhance mechanisms for follow up for diagnosis & to ensure treatment adherence even when truckers are mobile. Activities such as inter-personal communication (IPC), group meetings, and canopy exhibitions raised awareness through information relating to TB symptoms, treatment, WASH & COVID.

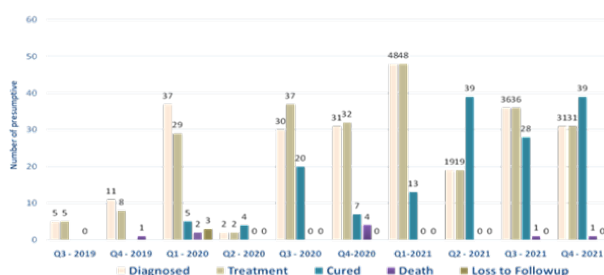


Figure. Quarterwise treatment cascade of diagnosed (cumulative) July 2019 - December 2021.

**Results/Impact:** During July 2019 – Dec 2021, 3012 presumptive identified from 109720 outreach; 1966(65%) tested, 261(9%) relived by symptomatic treatment & 785(26%) Pre-diagnosis loss to follow-up. 250 TB patients diagnosed, 247(98%) on DOTS treatment.

Outcome of 167(67%) declared; 155(93%) cured/completed treatment, 9(5%) deaths & 3(2%) Pre-treatment loss to follow-up. 83(33%) were still on treatment. Challenges faced by truck drivers are leaving truck when seeking diagnosis & treatment, owing to stigma & fear of being discovered amongst peers.

**Conclusions:** Through IPC, continuous counselling & IEC activities in TSLs, identification of presumptive is improved. It is vital to add screening of diseases prevalent among truckers & allied. ‘On the road to end TB’ encourages population on the road to have easy access to TB services.

### SOA12-895-16 Implications of TB-induced stigma and discrimination on patients accessing TB care in Ghana

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**Background:** Tuberculosis (TB) remains a significant public health challenge in Low-and-Middle Income Countries, and stigma and discrimination associated with the disease can result in delayed diagnosis and poor medication adherence among sufferers. However, evidence on the extent and drivers of TB-induced stigma at health facilities is limited.

The aim of this study was to determine the extent and drivers of TB-induced stigma among TB patients accessing healthcare at health facilities in Ghana and its implications on healthcare.

**Design/Methods:** A facility-based cross-sectional survey was conducted from November to December 2022 in purposively selected health facilities in Ghana. A total of 1103 consenting TB patients were interviewed after receiving care, and multiple logistic regression analysis was conducted to identify key drivers of TB-induced stigma at the health facility.

**Results:** The mean age of the TB patients was 41.56 years ( $\pm 13.01$ ), with an age range of 18 to 84 years. Less than 10% (6.17%, n=68) of the patients experienced stigma at the facility, with 1.36% (n=15) at the Directly Observed Treatment Short course (DOTs) centers, 1.00% each (n=11) at the outpatient department and laboratory.

The stigma experienced by these patients inhibited 14 (1.27%) from seeking care at the DOTs centers, 1.18% (n=13) from receiving an accurate diagnosis, and 0.63% (n=7) from adhering to treatment. Residential status, specifically living in an urban area (adjusted odds ratio,

aOR=2.16, CI=1.56-4.05,  $p<0.05$ ), and being anxious (aOR=8.78, CI=2.11-36.60,  $p<0.01$ ) increased the odds of a TB patient experiencing stigma at the health facility.

**Conclusions:** The study found a relatively low prevalence of TB-induced stigma experienced by patients at health facilities, but this still had significant implications for access to healthcare among vulnerable populations in resource-limited settings. Interventions to reduce TB-induced stigma at health facilities are required to improve healthcare access for TB patients.

### SOA12-896-16 A new country, life and disease: Psychosocial implications of resistant TB in a low-endemic country

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**Background and challenges to implementation:** Norway is a low endemic country of tuberculosis (TB) with an incidence of three per 100 000, and in 2021, 128 of the 154 registered patients were born abroad. Patients with drug-resistant TB (DR-TB) have a long-term and demanding treatment, and many have recently arrived. Goal: To explore patients' challenges when diagnosed with DR-TB in Norway.

**Intervention or response:** Methods: The qualitative study had a phenomenological focus to explore how the participants experienced the situation. We performed 16 semi-structured interviews with DR-TB patients (14 immigrants and 2 Norwegian).

**Results/Impact:** The participants got DR-TB-treatment from nine months to almost two years in the period from 2009-2020. Arrival screening diagnosed two participants, 14 contacted the health care (HC) because of TB-symptoms.

The immigrants had stayed in Norway from a few months to several years before getting symptoms. Several experienced a delay from seeking help from a general practitioner (GP) until final diagnosis. They described both psychosocial and physical serious side effects and persistent sequelae many years after completed treatment.

Getting a DR-TB diagnosis, forced or self-imposed isolation and felt - or self-enacted stigma reinforced psychosocial influences. Several said that if their GP had referred them to hospital earlier, maybe they had avoided great problems and sequelae. The participants had to manage daily living through a challenging illness, iso-

lation and required medical follow-up by HC, usually every day nine to twenty-four months as direct observed treatment.

**Conclusions:** The sixteen participants cured of DR-TB described a demanding period during diagnosis and treatment, and several had still psychosocial and physical sequelae. The participants expressed gratitude to family, friends, HC and government.

However, they also told about HC challenges before diagnosed, a serious illness and broken plans in a new country. It is important that HC do not forget the TB-disease in low endemic countries.

### SOA12-897-16 Self-stigma among people with TB in India: A mixed-methods study from five Indian states

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**Background:** Stigma and discrimination affect care-seeking for symptoms of Tuberculosis and treatment adherence. Stigma leads to feelings of low self-worth and deters people from disclosing their Tuberculosis diagnosis and treatment status.

**Design/Methods:** A mixed-method study was conducted in 15 districts across 5 states in India where the level of self-stigma in PwTB was measured on a 5-point scale by using a set of 12 statements. Qualitative interviews were carried out with a subset of the respondents of the questionnaire.

**Results:** Out of 2054 participants, 97% reported experiencing self-stigma, and 16% reported High Self-Stigma. It was observed to be significantly lower among people who had a primary or high school education (14%-15%) when compared to people who had never been to school (20%). High Self-Stigma was also high among people who had extrapulmonary TB (20.7%) as compared to those with pulmonary TB (15.1%), and was lower among people with drug-sensitive TB (3.8%) when compared to people with MDR-TB (11.8%).

97 participants were enrolled for in-depth qualitative interviews based on their responses to the survey tool. The majority of the PwTB practiced self-isolation and kept themselves away from their family members by living in separate rooms. "I stopped attending any kind of social event," said a 30-year-old male from West Bengal.

88% of the respondents mentioned that they distance themselves from others to prevent the spread of TB. This is corroborated by the qualitative interviews where PwTB mentioned that they confined themselves to a separate room and avoided stepping out.

Variables	Categories	Number of respondents reporting HSS	Total number of respondents	% of responders reporting HSS
Gender	Female	107	677	15.80%
	Male	228	1375	16.58%
Age	18-35	186	1129	16.47%
	37-55	93	618	15.04%
	56+	56	307	18.24%
Current Marital Status	Currently Married	245	1500	16.33%
	Unmarried / Divorced / Separated / Widow	90	554	16.24%
Currently employed	No	194	1087	17.84%
	Yes	141	967	14.58%

**Background and challenges to implementation:** Stigma and discrimination affect care-seeking for symptoms of Tuberculosis and treatment adherence. Stigma leads to feelings of low self-worth and deters people from disclosing their Tuberculosis diagnosis and treatment status.

**Conclusions:** Awareness not only improves health-seeking behaviour but also positively influences the attitude toward an illness. The role of social support and doctor-patient communication in reducing TB-related stigma should not be ignored, and treatment literacy should be made to include lesser educated people as well.

### SOA12-898-16 Assessing vulnerabilities, barriers and facilitating factors to drug-resistant TB care in Karakalpakstan, Uzbekistan

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**Background:** Uzbekistan is among the top 30 countries with a high burden of drug-resistant tuberculosis (DR-TB). Although the success rate of DR-TB treatment has improved over time, the autonomous region of Karakalpakstan experience disproportionately high rate of DR-TB compared to the rest of the country. The emergence

of resistance to newer TB-drugs, along with pre-existing disease burdens and high rate of migration, call for extension of the TB care beyond provision of medication. In Karakalpakstan there are no palliative care services available for patients with terminal forms of TB, and access to TB care remains restricted for marginalized groups, including migrants.

This study aims to identify gaps in comprehensive TB care and investigate the factors that impact disease outcomes for DR-TB patients.

**Design/Methods:** Ethnographic study with a qualitative research design, using participatory elements and visual anthropology approaches was conducted, during the first quarter of 2023 in Karakalpakstan. The data was collected by using in-depth interviews, focus groups discussions, non-participant observation and photo elicitation methods.

Purposive, snowball and convenience sampling were used to recruit study participants. Health workers (15), caregivers (15), migrants (10), decision-makers (6), lost-to-follow-up and cured patients (15) participated.

The data was analyzed using thematic analysis.

**Results:** Preliminary results show that the main factors that influence access to care and treatment outcomes are: fixed gender roles, experienced despair for TB-recurrence, lack of holistic approach to comorbidities, stigma around TB and substance abuse, insufficient social protection, scarcity of health-care options for migrants and absence of post-treatment care.

**Conclusions:** The study identified relevant social, healthcare, and individual factors influencing access to TB care that are often overlooked and might contribute to negative health and social outcomes. The study findings indicate a direction on how to consider these factors when designing a TB program and managing patients in a more holistic way.



## SOA12-899-16 Gender differences in the TB care cascade and contributing factors: A mixed-methods assessment in Uganda

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**Background:** The TB prevalence survey established geographical and gender disparities but not responsible factors. Makerere University and the National TB and Leprosy Program (NTLP) supported by The Global Fund, the Global and the Uganda STOP TB Partnership assessed the gendered factors influencing access to TB care.

**Design/Methods:** This was a mixed methods assessment. We used descriptive statistics to review program data from 2019 to 2021 and 3-month data abstracted from TB registers in 3 high-volume facilities in 12 districts across six nationally representative regions in 2022 to demonstrate gender differences in the TB care cascade. Thematic analysis of transcripts from 4 focus group discussions and 97 key informant interviews explored the reasons behind these differences.

**Results:** Men were underrepresented in the TB care cascade but had a higher TB burden across the years reviewed. In 2022, 45% of people presumed to have TB were men and a higher proportion didn't submit test samples (male 7%, female 2%) or access GeneXpert (male 24%, female 18%). The diagnostic yield was higher among males (male 12%, female 6%) who accounted for 61% of the 652 people with TB. The TB/HIV co-infection rate was higher among females in all regions except one.

In 2020/21, 46% of the 558 people notified with multi-drug resistant TB were female, whose initial loss to follow-up rate was higher (male 8%, 19% female). Men cited cultural norms and fear of losing jobs/ income as key barriers while women reported a fear of separation/divorce and dependency on men for finances.

The involvement of community resource persons and spousal support was beneficial to men while socially ascribed gender roles influenced women.

**Conclusions:** The findings highlight the need for the NTLP to design gender-responsive policies, guidelines, and services to enhance male uptake of TB services and address the high primary loss to follow-up among females.

## SOA13 Miscellaneous: from impact of vaccines to quality improvement

### SOA13-894-16 Is neglect of self-clearance biasing TB vaccine impact estimates?

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**Background:** Mathematical modelling has been used to estimate the potential impact of new tuberculosis vaccines, with most existing models assuming that individuals with *Mycobacterium tuberculosis* (Mtb) infection remain at lifelong risk of progression to tuberculosis disease. Recent research has suggested that self-clearance of infection may occur, which may affect the estimated impact of new vaccines. We explored how inclusion of self-clearance in models of tuberculosis affects estimated vaccine impact in China and India.

**Design/Methods:** We calibrated a tuberculosis model to a scenario without self-clearance and to various scenarios with self-clearance. To account for uncertainty in self-clearance properties, we varied the self-clearance rate, and the level of protection against reinfection in self-cleared individuals. We simulated new vaccine introduction in 2025, exploring vaccines that work in uninfected or infected individuals only, or that are effective regardless of infection status, and modelled scenarios with different levels of vaccine efficacy in self-cleared individuals. We estimated the relative incidence reduction in 2050 for each vaccine compared to the no vaccination scenario.

**Results:** For vaccines effective only in uninfected individuals, the inclusion of self-clearance increased the estimated relative incidence reductions by up to 12% in China and 8% in India. For vaccines effective only in infected individuals, self-clearance increased the estimated relative incidence reduction in some scenarios and decreased it in others, by a maximum of 14% in China and 15% in India. The inclusion of self-clearance had minimal impact on estimated reductions in incidence for vaccines that work regardless of infection status.

**Conclusions:** Our work suggests that the neglect of self-clearance in mathematical models of tuberculosis vaccines does not result in substantially biased estimates

of vaccine impact. It may, however, mean that we are slightly underestimating the relative advantages of vaccines that work in uninfected individuals only compared to those that work in infected individuals.

### SOA13-895-16 Evaluating the optimal duration of treatment for rifampicin-resistant TB: designing the DRAMATIC trial

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**Background:** Determining effective treatment duration is important in treating tuberculosis but is often neglected as a factor for exploration in clinical trials. A duration that is too short results in ineffective treatment, whereas a duration that is too long incurs excess cost and toxicity.

The DRAMATIC Trial will describe the relationship between the proportion of participants with durable cure and duration of an all-oral five-drug (including bedaquiline and delamanid) regimen. Participants are randomized to 16, 24, 32, or 40 weeks of treatment.

The objective of this work was to estimate the sample size and describe appropriate analytical methods for a trial to identify the optimal safe and effective duration of a tuberculosis treatment regimen.

**Design/Methods:** We created simulated clinical trial data sets with hypothetical participants allocated to one of the four durations. We adapted MCPMod from dose-finding trials, an established statistical approach that combines hypothesis testing and modeling of a dose-response curve, to analyze the duration-response relationship.

The probability of durable cure for each participant depends on treatment duration and was based on some common dose-response models: linear, Emax, sigmoid Emax, and beta.

**Results:** We found a sample size of 220 adequate to describe a range of duration-response relationships, accounting for 10% loss to follow-up. If a relationship between treatment duration and response exists, we have >80% power to detect its presence. In addition, the MCPMod approach does not require pre-specifica-

tion of the exact true model, but allows flexibility given pre-trial uncertainty; MCPMod is robust to model misspecification.

**Conclusions:** The MCPMod approach, while established in dose-finding studies, can be efficiently adapted to identify the optimal treatment duration and duration-response relationship in DRAMATIC trial. We have shown that the DRAMATIC trial design is an efficient design for evaluating the optimal duration of tuberculosis treatment and can be used in other settings.

### SOA13-896-16 Screening and initiating household contacts of TB patients on TB preventive treatment using telemedicine through E-Sanjivani platform in Uttarakhand, India

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**Background and challenges to implementation:** Joint Effort in Elimination of Tuberculosis (JEET 2.0) supported by National TB Elimination Program is implementing TB preventive Treatment (TPT) for household contacts of pulmonary TB patients, in 6 districts across Uttarakhand. Since a large part of the Uttarakhand province has tough geographical terrain, mobilizing 'healthy' household contacts to visit health facilities for medical consultation is challenging. The team has undertaken an innovative approach of using telemedicine. E-Sanjivani hub of National Health Mission was used as a platform for hosting an online TB clinic and is being actively used for screening of household contacts of Drug Sensitive TB patients.

**Intervention or response:** Medical officers were selected and trained on preliminary usage of E-Sanjivani. In the process of implementing Telemedicine for TPT, JEET staff are primary contact with household contacts of index patients. JEET staff visit household of index patients and connect the family with the online doctor. The doctors counsel the index TB patient about adherence and perform symptomatic screening for all household contacts. Based on discussion with family members relevant prescriptions are generated without any user charges. JEET staff based on prescription mobilize family members for either diagnostics or initiation of preventive treatment. This process also helps in early identification of TB presumptive family members who are further mobilized for TB diagnostics.

**Results/Impact:** The intervention initiated from 10th of January 2023 and as per preliminary results till March 2023, 40 teleconsultations have been done with the household contacts of index patients.

**Conclusions:** At household contact level, acceptance and behavior change towards TPT is yet to be ascertained. Though Teleconsultation has been a good success, it has been taken up well by families being cost effective, convenient, and provided good access to care, the preliminary results also emphasize the need for scaling up this model to every location and linking more specialists on the panel.

**SOA13-897-16 Impact of Surveillance Outbreak Response Management and Analysis System in improving TB surveillance in Nigeria: a pilot study**

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**Background and challenges to implementation:** Nigeria has a high burden of Tuberculosis that is exacerbated by under-reporting and underdiagnosis. In this study, USAID in collaboration with government stakeholders assessed the impact of SORMAS as a surveillance tool for improving Tuberculosis reporting.

**Intervention or response:** A TB module was designed in SORMAS and pre-tested after a stakeholder engagement process. Ten non-DOTS facilities were identified in each of six states across the six geopolitical zones of the country as pilot sites. Selected facilities in 39 LGAs had no records related to screening for tuberculosis before the study. For each pilot site, a Disease Surveillance Notification Officer & TB local supervisor per LGA and a healthcare worker per facility were trained on the use of SORMAS for reporting of TB cases. The pilot ran from December 2021 to December 2022. In each pilot facility, SORMAS was used to document the number of clients screened for TB, presumptive identified, presumptive evaluated and diagnosed with TB.

**Results/Impact:** Of the 50,415 clients who presented at SORMAS facilities, 24,052 (47.7%) were screened; 3910 (16.3%) were presumptive, while the TB yield was 157 (4.4%). GeneXpert accounted for 57.3% of the diagnosed cases. Children under five accounted for 3.2% of diagnosed cases, while those aged 55 and over (22.3%). A significantly higher proportion of males (0.8%) than females (0.5%) were diagnosed with tuberculosis

(p=0.001). The Number Needed to Screen for tuberculosis was significantly higher for females (202) than for males (118) (p<0.001).

Similarly, a significantly higher proportion of clients who utilized public health facilities (0.8%) were diagnosed with TB than those who utilized private facilities (0.6%) (p=0.049).

There was no significant difference between urban and rural areas (p=0.532).

**Conclusions:** The use of SORMAS enhanced TB surveillance reporting of patients who would have been missed and linked to care in selected non-DOTS sites. Scale-up is recommended to improve TB surveillance.

**SOA13-898-16 Score card, a tool to improve data use in TB programme: Lessons learnt from Malawi**

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**Background and challenges to implementation:** Data use for decision making is one of the notable challenges in TB program. Score card helps to measure performance against goals, thereby providing a better platform for implementors to make informed decisions.

**Intervention or response:** In 2020, the National TB Program developed a scorecard to help in data use at both levels. The scorecard includes all key areas related to TB care and treatment, TB preventive treatment, key population, community TB and uninterrupted supply of Anti-TB medicines. Nineteen keys indicators from the performance framework in the national strategic plan were included in the scorecard.

For each indicator, performance was categorized into high, medium and low levels-based on target or median/mean values. The intervention employed a participatory approach. Monitoring & evaluation team generated national and subnational scorecard every quarter.

Picture 1: Score Card

**Results/Impact:** Action plan was developed using the scorecard during zonal review meetings. Case finding improved in 2022 by 25% compared to performance

of the previous year. Six districts achieved target for cases finding. Treatment success rate was 90% during the latest reporting period. More than 43% of districts achieved TSR of 90% by end of the 2022. Districts with low Drug sensitivity testing DST were identified and action plan developed.

**Conclusions:** The balanced scorecard helped the national program and subnational team to focus on key outcomes in a balanced way. Use of score card has the potential to improve data driven decision making in the TB program.

It has also a potential to guide in the process of resource allocation by focusing on the low performing areas that may need more resources and effort.

### SOA13-899-16 Health system and environmental factors affecting global progress towards achieving End TB targets between 2015 and 2020

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**Background:** While health system and environmental factors may play a significant role in achieving World Health Organization (WHO) End Tuberculosis (TB) milestones, quantitative measures are scarce or non-existent at a global level.

This study aimed to measure global progress towards meeting the End TB milestones from 2015 to 2020 and identify health system and environmental factors contributing to the success.

**Design/Methods:** We obtained data from ten online data repositories. Principal Component Analysis was used to create domain specific health system performance measures. Radar charts and dumbbell plots were used to show the country's progress in Ending TB with their health systems.

A linear regression model was used to identify key health systems and environmental predictors of percent reduction in TB incidence and mortality.

**Results:** Of 191 countries, 77 (40.3%) achieved more than a 20% reduction in TB incidence between 2015 and 2020. However, only 33 (17.3%) countries reach a 35% percent reduction in TB mortality. The WHO European Region which has the strongest health system showed highest achievement with 22.8% incidence reduction.

The African Region has made relatively good progress with 18.4% mortality reduction despite its poor health system. Health system factors such as TB financing, TB-specific health service delivery, access to medicine and governance showed significant association with TB mortality reduction.

Among the environmental factors, average annual temperature, and concentration of particulate matter in the air showed significant effect on TB incidence and mortality reduction.

**Conclusions:** Weak health systems were identified as major barriers to achieving the End TB millstones in high TB burden countries. Hence, health system strengthening with special focus on TB financing, service delivery and access to medicine in these countries can be an effective strategy to achieve global End TB targets.

Considering the impact of environmental factors in TB research and prevention and care programs is also important.

### SOA13-900-16 Capacity-building of community health volunteers to strengthen the TB care ecosystem using a modernised training system

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**Background and challenges to implementation:** Community Health Volunteers (CHVs) are often the first point of contact for patients with TB, particularly in low-income countries where healthcare resources are limited.

India has a large workforce of CHVs who have a key role in TB care activities like patient finding, specimen collection and transportation, TB treatment initiation, treatment adherence, Adverse Drug Reactions (ADR) recognition, public health actions, TB prevention, and community outreach.

Training this diverse group to suit the program's needs is a challenging task considering the existing knowledge gap, differences in education level, varied geographies, cultural practices, and understanding.

**Intervention or response:** An assessment of the training needs of CHVs based on their job description in the National TB Control program conducted. The four-hour long-multilingual, multimedia-based training content was prepared to suit their training needs. Based on the principles of adult training, the training operations were designed and implemented.

The intervention used various technologies and platforms to reach out to the CHVs at distant locations to train them and build their capacity to acquire the necessary skills and knowledge to optimally perform their tasks.

They also imparted hands-on training to use the information systems employed for TB patient management. A robust system to monitor the training and assess the impact has been developed and is being implemented.

**Results/Impact:** The multilingual course content has been prepared. The capacity of states has been built to further cascade this training.

More than 3500 CHVs have been trained using the modernized approach and states are quickly ramping up their capacity to train all the CHVs in their states.

Formal assessments revealed that beneficiaries feel empowered to perform their tasks better.

**Conclusions:** Systems have been established to ensure that CHVs are adequately trained, supported, and empowered to deliver high-quality TB services at the community level. This could be contextually adapted to similar settings.

### SOA13-901-16 A Project ECHO-enabled molecular TB proficiency testing: expanding and strengthening quality assurance programmes worldwide

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**Background and challenges to implementation:** Since 2016, 14 African and Asian countries began establishing Dried Tube Specimen (DTS)-based molecular TB proficiency testing (mTB-PT) programs with Centers for Disease Control and Prevention and/ or the Ugandan Supranational TB Reference Laboratory mentorship. Phased program establishment is complex, with countries progressing at different rates. Project ECHO (Extension for Community Healthcare Outcomes) is a proven, Community of Practice (COOP)-building approach that strengthens participant capacity through remote mentorship and role-agnostic experience sharing. To meet expanding demand for mTB-PT establishment and mentorship, facilitate knowledge sharing, and understand cross-program reach and impact, a Project ECHO-based PT-COOP was established with support from the African Field Epidemiology Network.

**Intervention or response:** In 2022, 10 mTB-PT-establishing countries joined the inaugural PT-COOP and were surveyed on knowledge gaps, implementation challenges, and strengths.

Findings informed PT-COOP structure, agendas, and expert host selection. Participating teams submitted standardized program metrics prior to sessions for discussion, followed by didactic learning sessions.

Session participation data and PT program metrics were analyzed for collective PT program scope, progress, and performance-impacting factors.

**Results/Impact:** From September 2022 to February 2023, four PT-COOP sessions were held, with 5-9 countries participating, and five submitting 2022 summary metrics. In 2022, the COOP collectively enrolled 2,239

Xpert MTB/RIF or Ultra testing sites and distributed 4,413 PT panels. Results were submitted for 80% of the panels (n=3,572), with 93% (3,329/3,572) achieving satisfactory performance ( $\geq 80\%$  score).

The most frequent challenge was low participation among enrolled sites. Highlights included successful program implementation, roll-out of online mTB-PT data management tools, and ISO 17043 accreditation.

**Conclusions:** Sustainable, peer-to-peer support across country-led PT programs is needed to monitor and address shared successes and challenges quickly. As more molecular WHO-recommended diagnostics are scaled, PT-COOPs can facilitate cross-country experience sharing, monitor collective impact, and disseminate expertise as programs adapt to provide PT for all TB laboratory diagnostics.

### SOA13-902-16 Clinic-laboratory interface in the continuous quality improvement programme: Improving patient access to TB services in Uganda

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**Background and challenges to implementation:** In 2021, Uganda had an estimated 91,000 new tuberculosis (TB) cases, with only 74,800 notified, of which <70% received molecular WHO-recommended rapid diagnostic (mWRD) testing. Comprehensive patient care requires collaboration between clinics and laboratories, often across disease programs, for adequate specimen collection, testing, and treatment. Each step in the diagnostic cascade challenges patient retention. Multidisciplinary facility staff are rarely capacitated to collaboratively identify and target cascade gaps, contributing to missed and untreated TB.

**Intervention or response:** In 2021, a 4-month program, Clinic-Laboratory Interface Continuous Quality Improvement - Extension for Community Healthcare Outcomes (CLICQ!-ECHO), was implemented in Uganda for six TB/HIV clinic-laboratory pairs (CLPs).

TB and HIV testing staff assessed and measured patient retention by abstracting TB register and lab data using a Diagnostic Cascade Evaluation (DiCE) Toolkit. Additionally, staff attended two CQI Learning Sessions, conducted patient pathway analyses, developed improvement projects (IPs) with site-tracked weekly met-

rics, and attended Project ECHO-based mentorship and experience-sharing sessions. DiCE baseline and 12-week follow-up data were compared to measure CLICQ! – ECHO impact.

**Results/Impact:** Within five weeks, all six CLPs reported  $\geq 98\%$  achievement of IP metric targets. CLPs documented increases in presumptive TB patient volumes (44%), specimen collection (44%), mWRD testing (4%), mWRD-positive result availability (63%), and treatment initiation (37%) (Table 1). Despite increased patient volumes, specimen collection and testing were sustained at 100% and  $>90\%$ , respectively, while mWRD result reporting increased by 36%. Concurrently, specimen transport and result reporting turnaround times were maintained, while the time to clinic receipt of mWRD results and treatment initiation decreased by (-2.3 and -20.3 days, respectively).

TB SERVICE DELIVERY POINTS	PATIENT AND SPECIMEN VOLUMES		% CHANGE
	Pre-CLICQ! - ECHO Implementation Period (12 weeks)	CLICQ! - ECHO Implementation Period (12 weeks)	
1. Clinic-identified Presumptive TB	1732	2494	44%
2. Clinic-Collected Specimens	1730	2494	44%
Specimen Collection Coverage	100%	100%	0%
2. Clinic-Collected Specimens	1730	2494	44%
3. Lab Specimens Received	2178	2186	0%
Specimen Retention	126%	88%	-36%
3. Lab Specimens Received	2178	2186	0%
4. Lab Specimens mWRD Tested	1953	2032	4%
mWRD Testing Coverage	90%	93%	3%
5. Lab mWRD (+) Results	187	172	-8%
6. Clinic mWRD (+) Results	87	142	63%
mWRD (+) Result Retention	47%	83%	36%
6. Clinic mWRD (+) Results	87	142	63%
7. TB Treatment Initiation	324	443	37%
mWRD (+) Patient Retention	372%	312%	-60%

**Abbreviations:** TB (Tuberculosis), CLICQ! (Clinic Laboratory Interface Continuous Quality Improvement), mWRD (molecular WHO-recommended diagnostic)

*Table 1. A comparison of Diagnostic Cascade Evaluation (DiCE) Toolkit assessment data, totaled across six clinic-lab pairs (CLPs) before and after CLICQ! -ECHO implementation. Data were aggregated collaboratively by site-specific CLP staff using routine TB program registers at HIV clinics, TB clinics, and TB laboratories to enumerate patient and specimen volumes at each step in the diagnostic cascade. Percent change between pre-implementation (baseline) and implementation (follow-up) periods are calculated, as are coverage and retention of services between cascade steps.*

**Conclusions:** CLICQ! – ECHO is an effective peer-mentorship program that strengthens the capacity of multi-disciplinary staff to review, prioritize, and target site-specific gaps within their TB diagnostic cascades,

leading to improved program documentation, patient identification, mWRD testing coverage, mWRD result reporting, and timely treatment initiation.

## SOA14 MPower and tobacco control: tool, guideline, and practice

### SOA14-903-16 Smoke-free policy compliance: an observational study from nine Indian states

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**Background and challenges to implementation:** India enacted a comprehensive tobacco control law known as Cigarettes and other tobacco products act 2003. However, enforcement of the provisions under the law is still a matter of concern. Compliance survey is an effective tool to measure the status of implementation of the law at various public places. Smoke-free Jurisdiction from 9 states demonstrates commitment to good health and acceleration of tobacco programme in India.

**Intervention or response:** From 2018 and 2022, a cross-sectional observational study was carried out in 39 jurisdictions. There were 11,133 different public places chosen in all, including eateries, shops, government structures, hospitals, workplaces, and other hospitality venues.

These locations were examined for specific assessment criteria using a standardised checklist, which included evidence of active smoking, evidence of recent smoking, display of signages, presence of smoking aids, cigarette butts and bidi ends.

**Results/Impact:** Across these jurisdictions, overall compliance rate for Section 4 of COTPA ranged from 80% to 98%.

Average compliance was reported for the following indicators: No-smoking Signages (82%), No Active Smoking (91%), Absence of Smoking Smell (93%), Absence of Smoking Aid (93%), and No Cigarettes/Bidi Butts (92%).

The smokefree compliance assessment conducted using a protocol jointly developed by Johns Hopkins, Campaign for Tobacco Free Kids and The Union to assess the compliance to smokefree laws in these jurisdictions. More than 80 million people are protected from harms of Second-hand smoking.

**Conclusions:** Compliance in various indicators looks promising. Despite India having enacted an anti-tobacco legislation, enforcement of various provisions of this law including Smokefree remains a challenge across the country. These standardized work plan with clear time-

lines helped them immensely to achieve smokefree status of their jurisdictions in a short time and was easy to implement, cost effective, replicable and sustainable. The Union is using this framework to expand smoke-free up to sub-district and village level in India.

### SOA14-904-16 Local government guidelines for tobacco control, Ministry of Local Government, Bangladesh: a unique tool for tobacco control

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**Background and challenges to implementation:** Ministry of Local Government, Bangladesh has passed a comprehensive guideline for LGIs focused on TC law. This guideline is an advanced document. It has introduced more issues those are yet to be included in the current law.

The real challenge is the implementation of this guideline. In this guideline, TVL introducing, POS removal within 100 meters of Educational Institutions and Health Care Facilities and Central and local Monitoring Committee headed by government people has mentioned. All these issues are against tobacco industries and they are aggressive to stop this.

**Intervention or response:** To implement LG Guideline, Mayors and their officials were oriented through different meetings, workshops. To support in implementation, comprehensive tobacco vendor lists with all related information, were handed over to the Mayors', Taskforce Committees, District Administrations and Civil Surgeons. Worked with Municipal Association of Bangladesh and Mayor Alliance for Healthy Cities to ensure implementation.

**Results/Impact:** A complete digital database on tobacco vendor's was created to support guideline implementation.

This data is now using for;

1. TVL introduce,
  2. Remove TAPS ban violations through mobile courts,
  3. Remove POS near to educational institutions and health care facilities and monitoring the TC situation.
- We oriented 515 LG personnels through 406 meetings on TCLG Guideline. With our technical support *Cox's Bazar* Municipality was removed POS near to the schools and hospitals. *Monohordi* and *Dhamrai* Municipality arranged mass gathering to make anti-tobacco awareness as per guideline. In each gathering 3000-4000 people including students, teachers, government officials, political leaders, Member of Parliament and key persons were present.

# Municipalities/ City Corporations	Guideline implementation status
100	Communicated through mail and one-on-one advocacy
35	Uploaded guideline in their web-site
20	Allocated separate budget for TC activities
15	515 Officials of these LGIs received orientation on guideline implementation
7	Started TVL and generated BDT 491,590.00 in this FY
5	Started removing point of sells within 100 meters of educational institutions and health care facilities
3	Started TC activities by their own to inform mass people; the harm of tobacco use

**Conclusions:** Proper implementation of this guideline will take one step ahead to our TC initiatives. The implementation of the guideline will be helpful in proper monitoring of TAPS ban violations and will ensure proper reporting system. This will help to restrict tobacco products selling in everywhere, to everyone.

### SOA14-905-16 Compliance with smoke-free laws in the East and South Districts of Karachi, Pakistan – 2019 vs. 2022

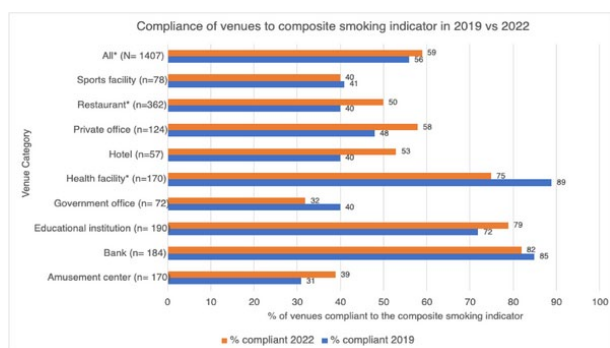
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**Background:** Smoking tobacco in public spaces is banned and no-smoking signage is required to be displayed in public venues in Pakistan as per the Prohibition of Smoking and Protection of Non-smokers Health Ordinance 2002. We assessed compliance with these laws in Karachi, Pakistan's most populous city, before and following smoke-free enforcement activities.

**Design/Methods:** An observational study of compliance with the smoke-free laws was conducted across 1,600 venues (i.e., sports facilities, restaurants, private offices, hotels, health facilities, government offices, educational institutions, banks, amusement centers) in the East and South districts of Karachi during 2019. This was followed by enforcement activities including implementation of smoke-free policies and an anti-tobacco awareness campaign. Venues were re-assessed for compliance in 2022. Venues were considered non-compliant if any of the following was observed: active smoking, ashtrays, or cigarette butts. Change in compliance overall and by venue type was assessed using the Wilcoxon rank sum test.

**Results:** Overall, there was a significant increase in compliance with the smoking ban from 2019 to 2022 (55.8% vs 59.2%,  $p=0.03$ ). By venue type, restaurants showed a significant increase in compliance while health facilities

ties showed a significant decrease in compliance. Compliance with display of no-smoking signage at the main entrance increased significantly overall (6.6% vs 14.0%,  $p < 0.001$ ) along with significant increase in compliance at restaurants, health facilities, government offices, educational institutions, and banks. Sports facilities, educational institutions and amusement centers showed significant increases in compliance to display of no-smoking signs inside the venue.



**Conclusions:** Overall compliance with smoke-free laws in Karachi, Pakistan improved from 2019 to 2022. However, compliance remains low in some venues. Routine enforcement efforts are needed to ensure continued compliance with smoke-free laws through stricter implementation of provisions and awareness campaigns.

### SOA14-906-16 Strengthening National Tobacco Control Programme in the state of Uttar Pradesh, India, through collaboration and coordination

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**Background and challenges to implementation:** Government of India launched National Tobacco Control Programme (NTCP) in 2007-08 to create awareness about harmful effects of tobacco, enforcement of Cigarette and other Tobacco Product Act (COTPA) and reduce tobacco consumption.

The State Tobacco Control Cell (STCC) is responsible for overall planning, implementation, reporting and monitoring of activities and achievement of tangible targets under the State Programme.

Voluntary Health Association of India (VHAI) worked in close association with STCC to remove bottlenecks faced, namely -

- Poor review and reporting mechanism.
- Low priority of Tobacco Control (TC).
- Lack of COTPA awareness amongst bureaucrats of key departments.
- Inactive multi sectoral enforcement mechanism.

#### Intervention or response:

- Training of stakeholders and district staff of NTCP.

- Comprehensive order from Principal Secretary- Home for enforcement, reporting and review of COTPA.
- Training of Master Trainers of Police on COTPA Module included in Police trainings with STCC.
- Developing sustainable reporting mechanisms for tobacco free educational institutions.
- Mass media strategy designed for National Health Mission for NTCP. IEC developed by VHAI for NTCP of Uttar Pradesh.

#### Results/Impact:

- Recognition of VHAI as Technical Partner and letter of appreciation from Director Health, Govt. of UP for strengthening NTCP via valuable technical contribution.
- Sensitization of policy makers and bureaucrats of key departments like Education, Police, Food & Drugs Administration & Health and subsequently order was issued for COTPA compliance and reporting.
- Trained Nodal Officer and staff of District Tobacco Control Cell of 45 Districts in coordination with STCC.
- 15 districts declared tobacco free health facilities, COTPA compliance in educational institutions, police stations, transport, courts & other public places and making tobacco free in coordination with STCC and concerned departments with reference to the orders issued by the department concerned.

**Conclusions:** Providing technical assistance to strengthen NTCP and address gap areas of STCC has improved effectiveness of TC initiatives of key departments and made it sustainable.

### SOA14-907-16 Legal procedural training and skills transfer make enforcers confident and ensures proper enforcement of the Tobacco Control Act in India

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**Background and challenges to implementation:** A series of orientations and workshops conducted in the past for implementation of Indian Tobacco Control Act in Madhya Pradesh, India. It created movement for awareness but failed to enforce different sections of tobacco control act in terms of penalty and filing cases against violations. MPVHA along with State Tobacco Control Cell decided to organize skill and procedural training for enforcement squads. This was needed as any act has defined rules and rules are effective, if the enforcers have knowledge and skills on enforcement procedures.

**Intervention or response:** 1: MP Voluntary Health Association (MPVHA) and State-Tobacco-Control-Cell decided to hold skill training for field level enforcers of various departments and form a team in each district. 2: State-Tobacco-Control-Cell persuaded to issue orders and allocate budget to districts.



- 3: MPVHA team invited to provide such training's.
- 4: 50 enforcement squad members from various departments invited for training in one batch.
- 5: Series of training's conducted at government Academy of Administration, and around 300 law enforcers trained.
- 6: Trained enforcers were provided with enforcement manuals, government orders and budget for their movement and field enforcement.
- 7: Online reporting format developed, handed over, monthly targets and reporting deadlines given to all nodal officers.

**Results/Impact:** 1: Enforcement of section 4-6 gone up. Fines against violation increased lead to sustainability of smoke-free declaration.

2: Field enforcers gained confidence and reporting streamlined.

3: Trained enforcers started doing enforcement against section 5-7, which was negligible/poor before procedural training.

4: State tobacco cell started receiving feedback from field enforcers about some legal limitations of section 5-7, expressed the needs for bringing amendments on Indian-Tobacco-Control-Act.

**Conclusions:** Skill training on procedures of laws has great importance, this should be regularly organized, as every year the new recruits are joining and many officials are being transferred. Skill training brings confidence within the law enforcers to enforce the law and improve legal compliance.

### SOA14-908-16 Identifying predictors of smokers' positive quit intention in India: A decision-tree approach

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**Background:** Quit intention is a precursor of tobacco cessation and hence predictors of quit intention play a vital role in tobacco control. This study explores predictors of Quit Intention among Indian current smokers aged 15 and above years using the Global Adult Tobacco Survey (GATS-2016) data.

**Design/Methods:** The nationally representative GATS (2016) data used a multistage geographically clustered sample survey and interviewed 74,037 individuals aged 15 years and above across all the states and two of the Union Territories of India. Current exclusive smokers' positive quit intention (thinking to quit within one year) was analysed. Significant predictors among gender, residence, age group, education, asset index, tobacco dependence (time to first smoke), healthcare providers' (HCP) advice to quit smoking, awareness about the harm

caused by tobacco, past quit attempt, smoking exposure at home, and exposure to anti-tobacco message in media were considered in decision tree (CRT - Classification and Regression Trees) analysis. Considering individual behaviour analysis, an unweighted analysis was carried out.

**Results:** Of the 6406 current exclusive smokers, 19.4% had positive quit intention. In the bivariate model using the Chi-square test, education ( $p=0.047$ ), awareness about tobacco harm ( $p=0.042$ ), past quit attempt ( $p<0.001$ ), smoking inside home ( $p<0.001$ ), exposure to anti-tobacco message in media ( $p<0.001$ ), asset index ( $p<0.001$ ) found to be significant predictors.

In the CRT decision tree model, exposure to anti-tobacco message ( $X^2=48.25$ ,  $p<0.001$ ) followed by smoking inside home ( $X^2=22.42$ ,  $p<0.001$ ) and asset index ( $X^2=16.44$ ,  $p<0.001$ ) were found to be important and significant predictors of positive quit intention.

**Conclusions:** Continued and enhanced anti-tobacco messages and making home smoke-free may help smokers to quit. A differential approach for low, middle and high-income groups is essential to increase the number of people with positive quit intention.

### SOA14-909-16 Mortality and morbidity estimates due to cigarette, bidi and smokeless tobacco in India: A meta-analysis

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**Background:** A quarter of Indian population use tobacco. Existing literature only provides odds related to tobacco consumption and disease occurrence. The present study estimates mortality (deaths and premature life years lost (YLLs)) and morbidity (disability adjusted life years (DALYs)) due to consumption of different forms of tobacco, namely cigarettes, bidis and smokeless tobacco (SLT).

**Design/Methods:** Meta-analysis was conducted on a sample of case-control studies, based on eligibility criteria. Population attributable fraction (PAF) due to specific products was calculated from pooled odds ratio and then applied to the total state disease burden to estimate the deaths, DALYs and YLLs attributable to cigarettes, bidis and SLT consumption in India. Further, a region-wise landscape analysis for Indian states/ Union Territories (UTs) was carried out.

		India	North	North West	East	North East	West	South
Cigarettes	Death	344,975.84	36,595.58	81,874.95	54,870.07	6,902.78	60,397.82	104,334.65
	DALYs	8,490,585.43	918,895.96	2,139,851.81	1,302,444.06	178,230.52	1,470,273.77	2,480,889.30
	YLLs	8,360,119.37	906,080.80	2,109,202.78	1,276,810.13	174,599.43	1,447,438.13	2,445,988.10
Bidis	Death	483,605.20	45,660.16	149,553.44	75,631.42	11,905.90	77,828.58	123,025.69
	DALYs	11,838,161.02	1,136,498.46	3,689,519.11	1,843,227.70	307,124.86	1,911,301.66	2,950,489.23
	YLLs	10,802,112.98	1,047,077.54	3,386,364.41	1,640,725.06	273,959.38	1,741,896.25	2,712,090.35
Smokeless Tobacco	Death	163,614.66	15,979.33	42,967.29	25,191.74	3,965.38	28,189.71	47,321.21
	DALYs	4,200,646.46	411,320.62	1,178,348.58	623,321.91	109,649.99	719,638.89	1,158,366.48
	YLLs	4,133,952.55	405,289.21	1,161,185.28	611,269.71	107,567.03	707,674.09	1,140,967.24
Total	Death	992,195.69	98,235.07	274,395.68	155,693.23	22,774.06	166,416.10	274,681.55
	DALYs	24,529,392.91	2,466,715.04	7,007,719.50	3,768,993.68	595,005.36	4,101,214.32	6,589,745.01
	YLLs	23,296,184.90	2,358,447.55	6,656,752.46	3,528,804.90	556,125.83	3,897,008.46	6,299,045.69

SOA14-909-16 Table.

**Results:** A total of 33 cross sectional studies were included for calculation of the PAF, comprising of data related to oral cancer, lung cancer and ischemic heart diseases (IHD) due to cigarettes; oral cancer, lung cancer, IHD and chronic obstructive pulmonary disease due to bidi; and oral cancer, stomach cancer and IHD due to SLTs. Finally, disease burden was obtained after application of the PAF to the disease burden of individual states. Maximum annual deaths were observed from Southern India (274,681.55), while maximum annual DALYs and YLLs were observed from Northwestern India (DALYs: 7,007,719.50; YLLs: 6,656,752.46). Uttar Pradesh was seen as the state with maximum disability burden (3,867,270.26 annual DALYs).

**Conclusions:** A novel methodology has been utilised to generate evidence on measurable health burden from tobacco product consumption in India. The alarming evidence generated builds a strong case for policy recommendations in the country and lays foundation for other countries to follow.

## SOA15 Molecular test and future game changers

### SOA15-910-16 Retrospective review of TB drug resistance in the Republic of Kazakhstan, 2018-2021

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**Background:** The aim of this study was to assess the dynamics of drug resistance in patients with tuberculosis in the Republic of Kazakhstan over 4 years.

**Design/Methods:** A retrospective analysis of DR-TB prevalence in the Republic of Kazakhstan for the period 2018-21 was carried out.

**Results:** 26,661 patients were analyzed, of which 14,749 were newly diagnosed and 11,912 were previously treated for TB.

Among patients, the rate of MDR-TB among new patients was 26% in 2018, 30% in 2019, 27% in 2020, and 30% in 2021; among previously treated patients: 44% in 2018, 49% in 2019-20 and 50% in 2021.

Isoniazid monoresistance was low in 2018 (6%), then stagnated at 9% in 2019-21 among new cases, 4% in 2018, and 6% in 2019-21 among previously treated cases. In new cases, poly-(H+ESZ)-resistance in absolute numbers was significantly lower in 2020-21 (16% and 14% respectively) compared to 2018-19 (18% and 19% respectively). In previously treated cases, resistance to poly (H+ESZ) was also lower in absolute numbers in 2020-21 compared to 2018-19.

In the structure of any drug resistance (except MDR), the number of monoresistant isolates increased from 31% in 2018 to 44% in 2021, the number of multidrug-

resistant ones fell from 40% in 2018 to 26% in 2021, while the number of pre- XDR increased slightly (30% in 2018 and 34% in 2020).

**Conclusions:** In the past four years, there has been a relative stabilization of DR-TB level, likely explanations are a decrease in the incidence of tuberculosis and improvement in the diagnosis and treatment and, accordingly, a lower level of transmission.

### SOA15-911-16 Utilising GeneXpert for diagnosis of childhood TB while maintaining optimal yield of TB: Programme implementation experience in Ethiopia

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**Background and challenges to implementation:** Diagnosis of TB in children remains to be challenging mainly due to the difficulty in TB diagnosis related to difficulty in getting specimens. Rollout of GeneXpert nationally and globally created good opportunity for maximizing access to rapid TB diagnostics in children and beyond.

We analyzed the experience of using GeneXpert for diagnosis of TB among under 15 years presumptive TBs.

**Intervention or response:** USAID Eliminate TB project supported Ministry of Health of Ethiopia in developing guidelines and training manuals with regard to childhood TB. The development of childhood TB road map was finalized to create uniform guidance on diagnosis and management of TB in children. Trainings and orientations were given to health workers to enable them obtain samples from children and conduct test using GeneXpert. Recording and reporting materials were availed to ensure standardized monitoring and evaluation. We evaluated the performance of 35 GeneXpert sites in Oromia region of Ethiopia.

Indicators	Age of Presumptive TBs tested		
	<15 years	>15 years	Total
Number tested by GeneXpert	5234	41978	47212
Number of Drug Susceptible TB cases identified	360	4665	5025
Number of Rifampicin Resistant TB cases identified	6	135	141
Percentage of all TB cases identified	7.0	11.4	10.9

Table: Performance of GeneXpert by age of presumptive TBs tested, October 2021-September 2022

**Results/Impact:** During October 2021-September 2021, a total of 47, 212 GeneXpert tests were conducted of whom 5234 (11.1%) were under 15 years old children presumptive TBs. The yield of all TB cases is significantly higher (p-value<0.00) in adults (11.4%) while there

is optimal yield of TB (7%) in children. One hundred forty one (2.8%) of all TB cases detected were Rifampicin Resistant TB cases

**Conclusions:** Through comprehensive support, improved access to diagnostic services have been achieved with optimal TB yield for presumptive TB children in Ethiopia. Enhancing focus on childhood TB program is recommended to further increased TB diagnosis.

### SOA15-912-16 Improved diagnosis of bacteriologically confirmed TB cases using Xpert testing in the private health sector in Pakistan

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**Background and challenges to implementation:** TB presumptive patients identified in the private sector are tested through sputum smear microscopy (SSM). The limited availability of WHO rapid diagnostic tools is causing the detection of a smaller number of bacteriologically confirmed cases, contributing to the number of undiagnosed TB cases. Pakistan faces the challenge of missing over 270,000 TB cases annually. A large proportion of these cases are either not diagnosed at all or are not notified by healthcare providers not associated with the National TB Control Program.

**Intervention or response:** Mercy Corps is implementing TB control interventions in the private health sector across 120 districts of Pakistan and has engaged 10,377 general practitioners, 341 large private hospitals, and 696 private laboratories for the diagnosis of TB presumptive cases. Laboratories have been linked with a cluster of general practitioners and hospitals. Mercy Corps has also equipped 28 health facilities with Xpert machines.

**Results/Impact:** The overall proportion of bacteriologically confirmed cases is 34%. While in health facilities where Xpert testing facilities are available the proportion of bacteriological cases is 60% (109,019 Xpert tests were conducted at 28 Xpert sites, resulting in the detection of 21,503 MTB cases and 737 RR cases). The diagnosis of TB patients through Xpert testing is therefore crucial, as bacteriologically confirmed patients are more likely to spread the disease. It has also been observed that the detection of rifampicin-resistant TB cases is high among bacteriologically confirmed cases.

**Conclusions:** The provision of WHO-recommended rapid diagnostic (WRD) tools in the private sector increases the proportion of bacteriologically confirmed cases, contributing to better rifampicin-resistant tuberculosis (RR) and tuberculosis (TB) detection, prevention, and care.

### SOA15-914-16 Diagnostic proteomic signature for distinguishing TB from other diseases in African children

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**Background:** The number of children diagnosed with tuberculosis (TB) is estimated to be one million annually, with half of those occurring in children less than 5 years of age. However, this is thought to be underestimated due to the symptoms of TB having overlapping clinical features of other common childhood diseases, such as pneumonia and malnutrition, and the difficulty in obtaining microbiological confirmation.

The risk of developing TB is 5-fold higher in children with HIV. TB detection and control requires improved diagnostic tests that are rapid, accurate and can be used at point-of-care.

**Design/Methods:** To identify a diagnostic signature of TB from other diseases (OD) we analysed serum from children recruited for suspected TB in South Africa (n=157) and Malawi (n=189) and Kenya (n=127) with and without HIV infection. Sera were analysed on cationic, anionic and IMAC arrays using SELDI-TOF mass spectrometry. LC-MS/MS and immunoprecipitation were used for protein identification and antibody-based methods for validation.

**Results:** We identified 311 proteins with significantly different levels ( $p < 0.01$ ) between TB and OD, irrespective of HIV status, in South African and Malawian children (discovery cohort). To identify the smallest number of proteins to distinguish TB from OD, patients were randomly assigned to training (80%) and test (20%) sets and logistic regression variable selection performed. A four-protein signature showed a combined AUC of 0.836 (HIV-) and 0.810 (HIV+). In Kenyan children (validation cohort), the combined AUC was 0.805 (HIV-) and 0.896 (HIV+). Antibody-based assays were further used to validate that each protein level was significant ( $p < 0.05$ ).

**Conclusions:** Proteomic analysis of serum can derive host signatures of TB infection useful for diagnostic development. Our findings demonstrate that proteins identified by mass spectrometry are translatable to antibody-based methods for POC test development.

### SOA15-915-16 The value of an optimised integrated sample referral system in early TB diagnosis and prevention in arid and semi-arid counties of Kenya

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**Background and challenges to implementation:** Developing functional, well equipped laboratories across all levels of health care system in developing countries remains a challenge. A robust, well-functioning and efficient Integrated Sample Referral System (ISRS) is critical to address this challenge.

About 80% of Kenya is arid and semi-arid lands (ASAL) inhabited mainly by pastoralists. Access to TB diagnosis and care is a challenge due to vast distances between health facilities, few diagnostic sites, migration of pastoralists among others.

Initially, Kenyan specimen referral system was a vertical model serving specific disease programs. An optimized ISRS in ASAL is key to increase uptake, coverage and timely access to quality diagnostic services.

**Intervention or response:** With Global Fund support, Amref Health Africa in collaboration with Ministry of Health, Division of Laboratory Services engaged 9 counties for ISRS to complement existing sample referral mechanisms. Health facilities (236) were mapped and appropriate sample routing determined based on location of GeneXpert machine and other laboratory services. Frequency and specific days for sample collection, transportation and results transmission were determined.

A total of 241 Health Care Workers (HCWs) and 143 riders were trained on principles of sample referral management and safety. HCWS were supported with monthly airtime for coordination of ISRS. Samples transported were for hematology, clinical Chemistry, biopsies, EID, Viral load among others.

**Results/Impact:** Between April 2022 and Jan 2023, 17,546 samples were transported across all diseases. Most of the samples were for Viral load 7,317(42%), and GeneXpert 5,970 (34%) and microscopy 2,619(14%). A total of 8,589(49.0%) TB samples tested and 1,053(12.3%) individuals diagnosed with TB.

**Conclusions:** It is possible to set up ISRS in ASAL regions. This demonstrated ability to detect diseases early and prompt management of TB patients and others. Ultimately this helps reduce transmission in the community.

### SOA15-916-16 Clinical evaluation of the Xpert MTB/XDR assay: A diagnostic accuracy study in Tajikistan

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**Background:** In late 2021, the World Health Organization endorsed the GeneXpert® MTB/XDR which allows for rapid detection of resistance to isoniazid (INH), fluoroquinolones (LFX), ethionamide and second-line injectables.

With Global Fund support, Tajikistan procured three new GeneXpert® 10-colour instruments and 500 GeneXpert® MTB/XDR cartridges in 2022.

**Design/Methods:** To support National Tuberculosis Program of Tajikistan (NTP) in implementation, the United States Agency for International Development's Eliminating TB in Central Asia (ETICA) activity supported validation of the GeneXpert® MTB/XDR assay with regard to diagnostic accuracy under Tajikistan conditions.

The study was conducted in three independent sites (Kulob Region, Bokhtar Region (Khatlon Oblast) and Republican TB Center) to assess the sensitivity of GeneXpert® MTB/XDR for rapid detection of isoniazid and fluoroquinolone resistance compared to pDST (when using MGIT) as a reference method, determine the positive and negative predictive power of the test, and assess the level of errors and uninterpretable results.

**Results:** For the validation, 471 GeneXpert® MTB/RIF-positive sputum specimens were tested with GeneXpert® MTB/XDR assay. All specimens were cultured and subsequently tested with pDST for first- and second-line drugs.

For INH, GeneXpert® MTB/XDR demonstrated 82.1% sensitivity and 98.5% specificity compared to pDST; the positive predictive value and negative predictive values were 96.5% and 91.8%, respectively. For LFX, GeneXpert® MTB/XDR demonstrated 93.7% sensitivity and 94.1% specificity compared to pDST; the positive predictive value and negative predictive values were 88.2% and 96.9%, respectively.

**Conclusions:** The diagnostic accuracy values obtained through validation of the GeneXpert® MTB/XDR assay in Tajikistan align with WHO data and enable this assay to be integrated into Tajikistan's national TB diagnostic spectrum.

### SOA15-917-16 Impact of placing TB screeners at large private hospitals on TB case notification in Pakistan

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**Background and challenges to implementation:** Pakistan is facing the challenge of missing an estimated 270,000 TB cases annually. A large proportion of these cases are either not diagnosed or not notified by health-care providers who are not associated with Pakistan's National TB Control Program.

**Intervention or response:** As a part of the public-private mix, large private hospitals have been engaged to improve the notification of TB cases. The lack of effective linkages between different departments and no centralized reporting systems for TB cases results in a lack of reporting of TB cases. This is despite the availability of TB care services in the respective hospitals.

Mercy Corps Pakistan is implementing TB Control activities in the private health sector across 111 districts, with 341 large private hospitals. Since 2010, the overall contribution in national TB case notification from private health networks engaged with Mercy Corps has been estimated at 25%. Mercy Corps has placed project staff designated for TB screeners at selected private hospitals. The main role of these TB screeners is to coordinate with all departments, sensitize them, screen TB symptomatic patients in OPD, and facilitate them in the examination, diagnosis, treatment initiation, and follow-up for adherence.

**Results/Impact:** The Mercy Corps has taken on board 341 private hospitals, from July 2021 until January 2023. These hospitals have notified 32,000 TB cases, which is an estimated 16% contribution to the total cases notified throughout the grant from all interventions. A total of 129 screeners are placed in 201 private hospitals. The hospitals with screeners have notified an average of 18 TB patients per quarter (compared with 9 patients per quarter for hospitals without a screener).

**Conclusions:** The provision of dedicated staff at large private hospitals can help increase case notifications for TB and contribute to quality diagnosis, treatment, and adherence of the registered TB patients.

### SOA15-918-16 Prevalence and patterns of drug resistance in patients at high risk for drug-resistant TB in Lusaka Province, Zambia

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**Background and challenges to implementation:** The prevalence of any resistance, rifampicin-resistance, and isoniazid-resistance among TB cases was estimated at 5.9%, 2.0%, and 4.4% respectively when using drug susceptibility testing (DST) during the TB drug-resistance (DR) survey conducted in Zambia in 2019-2020. Access to culture and DST is suboptimal among high-risk DR-TB patients.

The purpose of the study was to determine the prevalence and resistance patterns of DR-TB among patients with high-risk for DR-TB in Lusaka province.

**Intervention or response:** We analyzed data collected from the UTH TB culture laboratory between 1 January to 31 December 2022 to determine the prevalence and type of drug resistance among the samples submitted for culture and drug susceptibility testing (DST).

**Results/Impact:** The laboratory cultured 1918 samples (corresponding patients had a median age of 41(IQR 21-50) and 1,273(66%) were male) of which 313(16%) were culture positive. A total of 298 (95%) were Mycobacterium tuberculosis complex (MTBC) and 15 (5%) were non-tuberculous mycobacteria (NTMs). DST was performed successfully on 156 (52%) of the MTBC isolates of which 37 (24%) had any resistance to first-line drugs. The prevalence of any resistance to rifampicin, isoniazid, and ethambutol (E) was 8%, 19%, and 4% respectively. The prevalence of isoniazid monoresistance and multi-drug resistance were 10% and 8% respectively. There were 3 (2%) patients with resistance to all the first-line drugs. All forms of resistance were more prevalent among males at 70% (26/37).

**Conclusions:** Isoniazid resistance was detected in at least one in ten high-risk DR-TB patients. Challenges of access to culture/pDST can be addressed through the use of Xpert MTB/XDR which is currently not widely available in Zambia. Factors associated with a higher prevalence of resistance among male need to be investigated and targeted interventions put in place.

Resistance against No. DST conducted for High-Risk for DR-TB patients

	No	%
DST	156	
Any resistance to H	30	19%
Any resistance to R	12	8%
Any resistance to E	6	4%
H only	16	10%
MDR	12	8%
RR only	0	0%
RHSE	3	2%

## E-POSTER SESSION (EP)

### EP09 How could we improve TB detection

#### EP09-1075-16 Impact of contact investigation on childhood TB case-finding in tertiary health facilities in Oyo State, Nigeria

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**Background and challenges to implementation:** Children who are in contact with index Pulmonary TB patients are at high risk of TB infection and progression to active TB disease. The National Tuberculosis Program in the last few years has made consistent efforts to increase Childhood TB case finding in the country. Recent efforts are on TB screening of contacts of index patients through contact investigation (CI).

In 2021, there was an increase in the childhood TB proportion of cases notified from 6% in the previous year to 7%. However, Oyo State recorded a 5% childhood TB proportion in 2021.

**Intervention or response:** To strengthen childhood TB case detection through CI, two contact tracers were engaged, trained on TB (with emphasis on childhood TB) and CI, and stationed in two tertiary facilities for three months in Oyo State. The staff remuneration was based on performance in terms of index-patient coverage, contact-index ratio, presumptive TB yield, and childhood TB cases identified. Stool sample collection was emphasized for testing for children who cannot produce sputa, coupled with free chest X-ray services based on the physicians' recommendation after reviewing children and Xpert results.

**Results/Impact:** A total of 148 index-PTB patients were contact traced, with 570 contacts identified and screened for TB (contact index ratio of 4:1). Children presumed to have TB accounted for 49% of the total presumptive TB (220). All presumptive TB were evaluated using GeneXpert, with stool Xpert evaluation accounting for 27%. Childhood TB cases accounted for 67% of the total TB cases. 50% of the children diagnosed with TB were stool Xpert positive. Childhood TB case detection from CI accounted for 42% of cases from all other interventions in the two facilities. All diagnosed cases were enrolled for treatment.

**Conclusions:** Missing childhood TB cases can be identified by engaging individuals saddled with the responsibility of CI against using facility staff.

### EP09-1076-16 Serial mass screening for TB among incarcerated persons in Brazil

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**Background:** The implementation of systematic mass screening in prisons can be an effective strategy for identifying and containing outbreaks of tuberculosis in incarcerated populations. However, successful implementation requires careful planning, adequate resources, and collaboration between correctional and public health authorities.

In addition, the effectiveness of serial mass tuberculosis screening in high-risk populations, such as incarcerated persons, is still debated.

**Design/Methods:** Three rounds of mass screening were carried out in three prisons in Brazil between 2017 and 2021. Health and social questionnaires, chest x-rays, and sputum testing with Xpert MTB/RIF were performed. A tuberculosis case was defined as any individual with a positive Xpert sputum test, or medical diagnosis based on clinical-epidemiological criteria, according to Brazilian national guidelines.

We assessed the prevalence of tuberculosis per 100,000 people, among incarcerated people with tuberculosis-related symptoms. The study were approved by the Brazilian National Research Ethics Committee and by the Institutional Review Board of Stanford University.

**Results:** Over 80% of each prison population was screened. Overall, 684 cases of pulmonary tuberculosis were diagnosed, and the prevalence of tuberculosis per 100,000 persons was 8,497 (95% CI, 7,346–9,811), 11,115 (95% CI, 9,471–13,082), and 7,957 (95% CI, 6,380–9,882) in screening rounds one, two and three, respectively.

Similar to our overall results, there were no statistical differences between screening rounds and within individual prisons. We found no statistical differences on CAD4TB (Computer Aided Detection for Tuberculosis) scores across screening rounds among people with tuberculosis – the median scores in rounds 1, 2, and 3 were 82 (IQR, 63–97), 77 (IQR, 60–94), and 81 (IQR, 67–92), respectively.

**Conclusions:** In this prison setting with hyperendemic rates of tuberculosis, three rounds of mass screening did not reduce the overall tuberculosis burden.

Additional interventions or more frequent screening may be necessary to address the substantial amount of undiagnosed tuberculosis in prisons.

### EP09-1077-16 Spot to tent - using a systematic approach to contact investigation in Kano State, Nigeria

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**Background and challenges to implementation:** Contact Investigation is a critical public health strategy used to identify and control spread of infectious disease. KNCV Nigeria through the USAID funded TB LON 1 & 2 project introduced a systematic approach to contact investigation.

We share findings of comparison of yield from contact investigation when implemented as a passive standard of care activity limited to bacteriologically positive index cases and their household contacts versus when implemented as an active-case-finding (ACF) strategy to facilitate early identification of individuals at high risk of tuberculosis (TB) infection.

**Intervention or response:** KNCV TB LON in 2020 introduced the spot to tent intervention in which Community TB workers were engaged to systematically contact investigate household contacts of index cases through home visits to index residence (Spot) and simultaneously conduct active case finding activities within 2km radius of index residence (Tent) Samples from identified presumptive TB were logged to nearby diagnostic sites for processing, TB cases diagnosed linked to DOTS unit for enrollment on treatment and those found eligible for TPT also linked to care. Presumptive TB yield and TB case yield for 2019 (pre-intervention) was compared with that of 2021 (post intervention)

**Results/Impact:** In 2019, 4571 presumptive were evaluated with 276 TB cases diagnosed. 2021 post intervention, 4209 households were visited with 100% index patient coverage. 32793 clients were screened for TB with an average household contact size of 5 persons, 8611 presumptive evaluated (88% increase compared

to 2019), 419 bacteriologically diagnosed (52% increase compared to 2019). 3032 eligible clients were enrolled on TPT (100% increase compared to 2019).

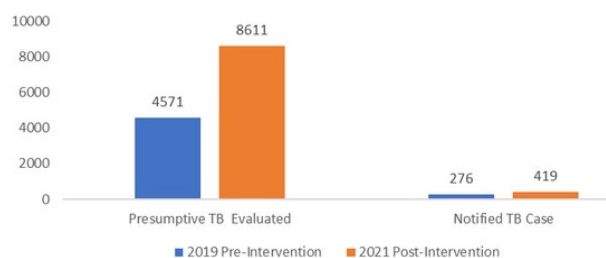


Figure. Contact investigation TB yield before and after spot to tent intervention.

**Conclusions:** The spot to tent method demonstrated significant increase in index case coverage and case detection. It has also proven useful in identifying eligible persons for TB preventive therapy. We recommend scale up of the model across other states to improve CI yield and TPT enrollment countrywide.

### EP09-1078-16 Nationwide systematic screening of TB for older adults and homeless people in a high-income country

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**Background:** South Korea is one of intermediate tuberculosis (TB) burden country. TB incidence was gradually decreased, but more action would be required to meet the global and national target for the elimination of TB.

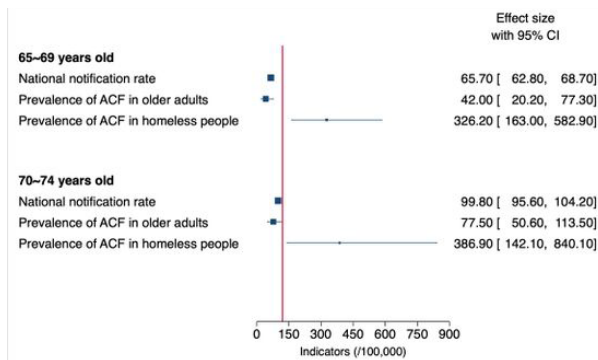
**Design/Methods:** Korean National Tuberculosis Association conducted community-based screening as an outreach setting collaborated with health centers and civil society supporting homeless people. There were two main group including older adults ( $\geq 65$  years old) and homeless people.

All participants invited chest X-ray (CXR) screening and referred to microbiologic evaluations if there was any abnormality on CXR or TB-related symptoms. Pulmonary TB prevalence per 100,000 people were calculated with 95% confidence intervals (CI).

Generalized linear models constructed to identify predictors associated with active TB. Active TB cases were matched with national TB registry using the propensity score method to identify the impact of the active case finding (ACF) on treatment outcome and the fatality compared with passive case finding (PCF).



**Results:** Totally 300,254 and 15,455 participants were included in the older adults and homeless group, respectively. The prevalence of pulmonary tuberculosis was 130.9 (95% CI: 118.0-144.8) and 438.2 (95% CI: 239.8-734.1) among the older adults and rough sleeper, respectively. Old age, male and coughing symptoms were associated with active tuberculosis. Among the older adults, the treatment success rates were not differed between ACF and PCF group, while the fatality was slightly higher in ACF group than PCF group (hazard ratio: 1.37, 95% CI: 0.96-1.96).



**Conclusions:** Community-based screening for the hard-to reach group in high income country was a feasible and yielded project. However, the ACF strategy may not outweigh the other vulnerability that participants already had and was unable to reduce the fatality. Therefore, social supports would combine with ongoing ACF projects.

## EP09-1079-16 Impact of decentralisation and strengthening paediatric TB diagnosis and use of short TB preventive treatment on childhood TB management in Cameroon and Uganda

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**Background:** The CaP-TB project strengthened paediatric tuberculosis (TB) diagnosis at peripheral health care levels using symptom-based screening, child-adapted specimen collection and Xpert testing and supported household contact management (HCM) using 3-months rifampicin-isoniazid (3RH) tuberculosis preventive treatment (TPT).

In Cameroon and Uganda, community-based HCM was added as part of the CONTACT cluster randomized trial. We assessed the effect of the CaP-TB intervention on paediatric TB case finding and TPT management, and the value of adding community-based HCM.

**Design/Methods:** Sub-study of the CONTACT trial using a pre-post design to compare the proportion of children among all TB cases and the TPT completion rate among contacts <5 years before (March 2018 to March 2019) and during CaP-TB intervention (September 2020 to September 2021) using facility registers data.

During CaP-TB, 12 facilities received the CaP-TB intervention alone and 12 combined with community-based HCM, equally distributed between countries. Comparisons used a General Linear Mixed Model to account for clustering.

**Results:** The proportion of children among all TB cases increased from 113/2373 (4.8%) before to 276/2512 (11.0%) during CaP-TB intervention ( $p < 0.001$ ): 59/1413 (4.2%) to 74/1225 (6.0%) in Cameroon and 54/960 (5.6%) to 202/1287 (15.7%) in Uganda. CaP-TB intervention had a prominent effect in children <5 years, while community-based HCM had major effect in children 5-14 years. All contacts <5 years received 6 months isoniazid TPT during pre-intervention and 84.2% (708/841) 3RH during CaP-TB intervention. TPT com-

Clusters	All sites			Sites receiving CaP-TB intervention alone			Sites receiving Cap-TB + community HCM interventions		
	Pre n/N (%)	Post n/N (%)	OR [95% CI], P value	Pre n/N (%)	Post n/N (%)	OR [95% CI], P value	Pre n/N (%)	Post n/N (%)	OR [95% CI], P value
	19 clusters including 24 facilities			10 clusters including 12 facilities			9 clusters including 12 facilities		
Period									
Proportion of children among all registered TB cases									
< 15 years	113/2373 (4.8%)	276/2512 (11.0%)	2.27 [1.80 - 2.86] <0.001	68/1288 (5.3%)	104/1179 (8.8%)	1.75 [1.27 - 2.40] 0.001	45/1085 (4.1%)	172/1333 (12.9%)	2.96 [2.10 - 4.18] <0.001
< 5 years	41/2373 (1.7%)	143/2512 (5.7%)	3.35 [2.36 - 4.77] <0.001	19/1288 (1.5%)	64/1179 (5.4%)	3.99 [2.38 - 6.68] <0.001	22/1085 (2.0%)	79/1333 (5.9%)	2.81 [1.74 - 4.56] <0.001
5 - 14 years	72/2373 (3.0%)	133/2512 (5.3%)	1.59 [1.18 - 2.13] 0.002	49/1288 (3.8%)	40/1179 (3.4%)	0.89 [0.58 - 1.36] 0.584	23/1085 (4.1%)	93/1333 (7.0%)	2.89 [1.81 - 4.62] <0.001
TPT completion among contacts initiated on TPT with an available outcome									
< 5 years	58/77 (75.3%)	798/841 (94.9%)	10.80 [4.84 - 24.12] <0.001	27/35 (77.1%)	272/295 (92.2%)	6.62 [1.84 - 23.82] 0.004	31/42 (73.8%)	526/546 (96.3%)	14.26 [5.35 - 38.04] <0.001

EP09-1079-16 Table. Paediatric TB case finding and TPT completion before and after intervention.

pletion rate increased from 58/77 (75.3%) to 798/841 (94.9%) between the two periods: 29/38 (76.3%) to 342/382 (89.5%) in Cameroon and 29/39 (74.4%) to 456/459 (99.3%) in Uganda. The effect increased in sites with community-based HCM. (Table)

**Conclusions:** Decentralizing and strengthening TB diagnosis and using short TPT improved childhood TB case finding and TPT completion. Both effects increased when combined with community-based HCM.

### EP09-1080-16 TB screening among contacts of bacteriologically confirmed TB patients in Rwanda, July 2016 to June 2019

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**Background:** Although Rwanda has made substantial progress in TB control, it remains a major public health challenge. From July 2016 to June 2019, the TB surveillance system reported 17,535 all-forms TB cases with 13,132 (75%) bacteriologically confirmed. Since 2016, Rwanda has conducted active case finding through symptoms' screening among contacts of bacteriologically confirmed TB patients at the beginning and at the end of TB treatment.

We analysed the data of TB screening among contacts of bacteriologically confirmed TB patients to determine TB positivity trends among the contacts

**Design/Methods:** A retrospective review of surveillance data from Rwanda National TB Program from June 2016 to July 2019 was conducted. Contact screening data are collected and reported electronically to the HMIS by each health facility. We extracted the contact screening data from HMIS and analysed the aggregated data. Proportions of contacts of bacteriologically confirmed TB patients screened for TB both at the beginning and at the end of TB treatment were calculated

**Results:** From June 2016 to July 2019, the proportion of contacts screened for TB at the beginning and at the end of treatment was 96% (40735/42392) and 87% (38973/44606) respectively. The presumptive TB positivity rate at the beginning and at the end of treatment was 21% (8650/40735) and 11% (4342/38973) respectively. Among presumptive TB cases, 4.4% (376/8650) and 3.2% (140/4342) were confirmed TB respectively. TB positivity yield among contacts at treatment initiation were 0.7% (93/13338), 1.0% (132/13477) and 1.1% (151/13920) in 2016/2017, 2017/2019 and 2018/2019 respectively.

**Conclusions:** Contact screening contributed to identifying a significant number of TB patients in Rwanda, with an increasing yield from 2016 to 2019. Contact screening notification rate was  $\geq 18$  folds higher compared to the general population. This calls for the continuity and reinforcement of this strategy.

## EP09-1081-16 Pulmonary TB and HIV screening in Ethiopian prisons

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**Background:** The elevated prevalence of tuberculosis (TB) in prison settings is attributed to overcrowding, poor nutrition, unsanitary conditions, inadequate health care provision, and high turnover of prisoners. The ubiquity of the disease in such settings poses a significant problem for inmates, staff, and the population at large. We conducted TB and HIV screening in inmates and staff of 14 prisons across Ethiopia.

We also assessed the utility of symptom screening against Xpert®/MTB/RIF Ultra (Xpert) analysis of pooled sputum samples.

**Design/Methods:** Inmates and prison staff were invited for TB and HIV screening. TB was screened using the standard signs and symptoms (cough for  $\geq 2$  weeks, fever, night sweating, weight loss, chest pain, and loss of appetite) and spot sputum samples were collected from all regardless of the signs and symptoms. Samples were pooled (5:1) and analyzed by Xpert assay. HIV testing was conducted onsite using finger prick blood tests as per the national guideline.

**Results:** Among 24,175 invited 21,785 (90%) were enrolled and screened for TB. The screening yielded 89 bacteriologically confirmed pulmonary TB cases.

Thirty-two (36%) of the cases had either cough and/or at least two of the other signs and symptoms while 57 (64%) were without any signs or symptoms. The prevalence of newly diagnosed pulmonary TB was 409/100,000 (95% CI: 324-494 per 100,000).

Seventy six percent (18,423/24,175) of the participants were screened for HIV screening and 87 were positive. The prevalence of newly diagnosed HIV was 0.47% (95% CI: 0.46-0.48%).

**Conclusions:** Our finding indicated higher prevalence of TB in prison settings than the general population. We demonstrated collecting sputum samples from all

participants, including asymptomatic, in a congregate setting is technically feasible and increase case findings compared to restricting sputum-based diagnostics to presumptive TB patients.

Furthermore, pooling sputum samples prior to Xpert analysis saves huge resources compared to individual sample testing.

## EP09-1082-16 Implementation of sputum pooling for TB active case-finding in four Brazilian prisons: Yield, efficiency and resource savings

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**Background:** Active case finding (ACF) is recommended in populations with high burden of tuberculosis (TB) to reduce transmission and avert morbidity. However, testing each individual by molecular rapid diagnostic tests (mRDTs) is costly, posing a barrier to scale-up in resource-constrained settings. Pooling multiple sputum samples and testing by mRDTs, followed by individual testing of positive pools, can conserve resources while maintaining high sensitivity. We aimed to evaluate the implementation of sputum pooling in an ACF program.

**Design/Methods:** We performed ACF using sputum pooling in four prisons in Mato Grosso do Sul, Brazil between November 2021-May 2022. All consented participants provided a spot sputum sample regardless of the presence of TB symptoms. We tested pools of 8 sputa by Xpert MTB/RIF Ultra (Xpert), followed by individual testing of positive pools. Our primary study outcome was screening yield expressed as TB prevalence (%) and 95% confidence interval (CI).

**Results:** We screened >95% of incarcerated residents of four prisons (n=4564) in 61 days. Of screened individuals, 121 had a positive Xpert result after confirming with individual testing of positive pools, yielding an overall TB prevalence of 2.7% (95% CI 2.2-3.1). The highest TB prevalence was reported from the largest prison (prison D) with a total of 2,134 individuals screened in 24 days; yielding a TB prevalence of 3.8% (95% CI 3.0-4.7) (Table 1).

By implementing sputum pooling method in our screening program, we used >60% fewer Xpert cartridges compared to individually testing all participants.

	Prisons				TOTAL
	A	B	C	D	
Total individuals screened	1467	472	491	2134	4564
Individual test positive (TB cases)	30	5	5	88	121
TB prevalence (%; 95%CI)	2.0 (1.4-2.9)	1.1 (0.4-2.3)	1.0 (0.4-2.2)	3.8 (3.0-4.7)	2.7 (2.2-3.1)
Screening duration (days)	22	8	7	24	61

Table 1. Results from sputum pooling in a tuberculosis active case finding program in four prisons in Mato Grosso do Sul, Brazil (N=4564).

**Conclusions:** Pooled sputum testing enabled us to screen >4500 individuals in four prisons in just 61 days, yielding an overall high TB prevalence (2700 per 100,000), while conserving mRDT costs. In settings with a high prevalence of TB like prisons, sputum pooling can be an efficient strategy for active case finding, enabling screening to be performed more rapidly and with fewer resources than individual testing.

### EP09-1083-16 Implementation of population-wide active case-finding and prevention in Kiribati: Findings from the PEARL study pilot

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**Background:** Tuberculosis and leprosy remain major public health problems in Kiribati, with estimated incidence of tuberculosis of 424 per 100,000 in 2021 and the case notification rate of leprosy being the highest in the world. Transmission and new case detection within the country is focused in the main urban area, South Tarawa. Despite implementation of high quality case management and an ongoing program of contact investigation and community outreach active case finding, rates have trended slightly upward in the period 2000-2022. In response, the Kiribati Ministry of Health and Medical Services has formed a partnership with University of Sydney to deliver systematic, population-wide screening, treatment and prevention for TB and leprosy in South Tarawa – the PEARL project. A pilot of this intervention was completed in Nanikai village in South Tarawa from October to December 2022.

**Design/Methods:** The pilot activities included intensive community mobilisation efforts, household enumeration, screening with CXR/CAD, symptoms, TST, and skin check for leprosy, facilitated referral for cases, and risk assessment for TPT followed by community supported treatment for those eligible. We also offered a single dose of rifampicin as leprosy prevention for participants not eligible for any other rifampicin-based treatment.

**Results:** We enumerated 1252 residents of Nanikai village, residing in 179 households. Of the 977 people who registered for screening, 553 (56.6%) were female, and 212 (21.7%) were aged <10 years. Results are summarised in table 1.

Number completed screening	934 (95.6%)	
TB cases	8 (0.86%)	2 micro confirmed, the rest clinically diagnosed inc EPTB
LEProsy cases	9 (0.96%)	All confirmed by NLP, none micro confirmed
TST result recorded	847 (86.7%)	
TST positive	126 (14.9%)	
Started TPT	112	14 not started – pregnancy, high risk or refused
Completed TPT	108	4 people discontinued due to side effects

**Conclusions:** We conducted community-wide screening, treatment and prevention for TB and leprosy using best practices in a high-burden transmission setting, reaching >80% of the eligible population, one of the first examples of this approach in the Pacific region.

Case detection of TB and leprosy was high, and we hope will be the ‘high water mark’ for these diseases in Nanikai. Lessons learned will be applied to the scale-up phase for this intervention.

### EP09-1084-16 TB household contacts in Zimbabwe, Mozambique and Tanzania

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**Background:** Household *M.tuberculosis* (Mtb) transmission contributes significantly to tuberculosis (TB) burden. Understanding TB prevalence and prevalence of Mtb infection in TB-affected households may help design case finding and targeted prevention strategies.

**Design/Methods:** 2101 household contacts (HHC) (≥10 years of age) of adults with microbiologically confirmed pulmonary TB were recruited into a prospective cohort study (ERASE-TB) across three sites (Mozambique, Tanzania, and Zimbabwe) between 2021 and 2023. Symptom screening and chest X-rays were performed, followed by Xpert MTB/Rif Ultra if either suggested

TB. Testing for Mtb infection was with interferon gamma release assays (IGRA; SD Biosensor). Here we present the baseline data.

**Results:** An average of 2.4 contacts per household were recruited. One-quarter of HHC were adolescents aged 10–18 years. The table presents detailed characteristics stratified by country.

A total of 321 (15.3%) HHC were living with HIV, most (85.4%) of them knew their status and were taking antiretroviral therapy. The proportion of HHC who drank alcohol, had ever smoked, worked in a mine, or travelled to South Africa was 33%, 8%, 3%, and 12% respectively.

On screening, 355 (17%) had symptoms TB-related symptoms and 114 (5%) had chest X-ray findings suggestive of TB. Prevalence of pulmonary TB at baseline was 0.7% (6 cases, 2 cases, and 6 cases from Zimbabwe, Mozambique, and Tanzania respectively) while prevalence of *M.tb* infection was 49%, 64% and 48% for Zimbabwe, Mozambique and Tanzania respectively.

Characteristics of household contacts	Total n=2101 n (%)	Tanzania n=690 n (%)	Mozambique n=711 n (%)	Zimbabwe n=700 n (%)
Men	795 (37.8%)	249 (36.1%)	282 (39.7%)	264 (37.7%)
Median age (IQR)	26.6 (16.7 – 41.8)	29.4 (16.4 – 43.8)	23.9 (16.4 – 39.2)	27.2 (17.0 – 41.1)
Education				
None or primary	955 (45.5%)	503 (72.9%)	266 (37.4%)	186 (26.6%)
Secondary or tertiary	1146 (54.5%)	187 (27.1%)	445 (62.6%)	514 (73.4%)
Sleeping arrangement with an adult with TB				
Different room	1482 (71%)	519 (76%)	515 (74%)	448 (64%)
Same room / different bed	168 (8.1%)	60 (8.8%)	56 (8.0%)	52 (7.4%)
Same room / same bed	430 (21%)	105 (15%)	127 (18%)	198 (28%)
TB Preventive therapy				
Ever received	139 (6.6%)	46 (6.6%)	38 (5.4%)	55 (7.8%)
HIV				
Positive	321 (15.3%)	92 (13.3%)	119 (16.7%)	110 (15.7%)

**Conclusions:** While a considerable proportion of HHC had symptoms and/or chest X-ray findings suggestive of TB, less than 1% were found to have TB at baseline. This is despite a relatively high HIV prevalence, albeit mostly known and on treatment. Other modifiable risk factors for TB such as smoking and alcohol use were also highly prevalent.

## EP10 TB Management from diagnosis to treatment

### EP10-1085-16 Assessing the burden of TB and readiness of healthcare facilities to provide TB care in NEPal: A comprehensive analysis

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**Background:** Tuberculosis (TB) is a significant public health problem in Nepal. Evaluating the burden of TB and the effectiveness of the healthcare system in addressing this disease is essential for implementing effective control and prevention measures.

This study aimed to analyze the data from three different national sources to assess the burden of TB in Nepal and the readiness of the healthcare system in addressing this disease.

**Design/Methods:** This study analyzed data from the National TB Prevalence Survey conducted in 2018-2019, the Nepal Health Facility Survey conducted in 2020, and the Integrated Health Management System (2017-2020). Appropriate statistical methods were used to evaluate the status of TB in Nepal.

**Results:** The National TB Prevalence Survey revealed that the prevalence of TB in Nepal was 301 cases per 100,000 population. Older age groups, male gender, lower education status, and low wealth quintile were identified as risk factors for TB.

Social Determinants associated with TB in Nepal in multivariate logistic regression (N=53,576)					Factors associated with readiness of health facilities in multivariate logistic regression (N=1,250)								
Characteristic	OR	Unadjusted 95% CI	p-value	Adjusted 95% CI	p-value	Characteristic	OR	Unadjusted 95% CI	p-value	Adjusted 95% CI	p-value		
<b>Age</b>						<b>Residence</b>							
15-24	1			1		Urban	1						
25-34	1.02	0.51, 2.01	0.94	0.97	0.45, 2.11	0.93	Rural	0.97	0.62, 1.50	0.88			
35-44	1.99	1.10, 3.66	0.02	1.83	0.81, 3.38	0.19	<b>Ecological Region</b>						
45-54	3.33	1.93, 5.96	<0.001	2.2	1.13, 4.27	0.025	Mountain	1			1		
55-64	6.16	3.46, 10.75	<0.001	3.38	1.77, 6.94	<0.001	Terai	0.54	0.24, 1.20	0.13	0.49	0.22, 1.09	0.08
65+	13.49	7.53, 19.51	<0.001	5.15	2.74, 10.48	<0.001	Hill	1.17	0.74, 1.85	0.49	1.09	0.58, 3.84	0.006
<b>Sex</b>						<b>Ownership</b>							
Male	1			1		Private	1			1			
Female	2.8	2.12, 3.72	<0.001	2.28	1.62, 3.28	<0.001	Public	1.02	0.84, 1.24	0.17	1.00	0.88, 1.25	0.11
<b>State</b>						<b>Provinces</b>							
Hilly rural	1			1		Abhi	1			1			
Hilly urban	1.01	0.65, 1.56	0.97	1.21	0.78, 1.88	0.4	Madhesh	1.48	0.59, 3.71	0.4	1.02	0.35, 2.97	0.97
Kathmandu rural	1.66	0.50, 4.12	0.33	1.35	0.40, 3.30	0.57	Bagmati	2.31	1.03, 5.17	0.04	2.87	1.25, 6.64	0.013
Kathmandu urban	0.89	0.38, 2.01	0.89	1.31	0.57, 2.51	0.58	Chandri	2.03	0.86, 4.77	0.11	2.41	0.95, 6.11	0.062
Mountain rural	0.78	0.34, 1.84	0.4	0.61	0.28, 1.19	0.18	Lumbini	2.21	0.97, 5.04	0.06	1.87	0.88, 4.22	0.28
Mountain urban	0.74	0.30, 1.54	0.46	0.8	0.33, 1.68	0.6	Karnali	0.74	0.28, 2.07	0.56	0.91	0.33, 2.50	0.88
Terai rural	0.89	0.55, 1.41	0.62	1.07	0.66, 1.72	0.78	Sudurpashchim	4.45	2.00, 9.90	<0.001	5.24	2.31, 11.92	<0.001
Terai urban	0.91	0.63, 1.33	0.63	1.21	0.83, 1.80	0.33	<b>Type of facility</b>						
<b>Education</b>						Private	1			1			
None	1			1		Hospital	0.08	3.71, 9.99	<0.001	5.93	3.27, 10.76	<0.001	
Primary	0.32	0.22, 0.43	<0.001	0.40	0.34, 0.49	<0.001	<b>External Supervision</b>						
Secondary and above	0.22	0.14, 0.31	<0.001	0.33	0.32, 0.87	0.015	No	1			1		
<b>Occupation</b>						Yes	1.43	0.88, 2.33	0.15	1.27	0.75, 2.14	0.38	
Professional	1			1		<b>Quality Assurance</b>							
Clerical	0.84	0.11, 5.08	0.85	0.79	0.10, 4.83	0.8	Not Performed	1			1		
Sales and Services	1.27	0.25, 5.91	0.73	1.12	0.31, 3.28	0.87	Performed	1.5	0.95, 2.37	0.08	1.33	0.83, 2.13	0.23
Skilled manual	1.71	0.49, 7.81	0.43	1.32	0.37, 4.19	0.69	<b>Client Opinion</b>						
Unskilled manual	1.05	0.19, 5.66	0.96	0.85	0.12, 5.62	0.6	No	1			1		
Agriculture	2.84	1.45, 15.63	0.02	1.59	0.50, 4.76	0.45	Yes	2.09	1.01, 4.32	0.05	1.7	0.77, 3.75	0.19
Students	0.6	0.17, 2.75	0.45	1.05	0.27, 2.28	0.95	<b>Meaning of Health Facility</b>						
Housewife	0.98	0.25, 4.07	0.97	0.89	0.30, 4.11	0.91	None	1			1		
Others	5.13	1.89, 21.10	0.01	1.9	0.65, 5.14	0.3	Sometimes	1.61	0.70, 3.68	0.26			
<b>Wealth Quintile</b>						Monthly	1.55	0.78, 3.15	0.23				
Rich	1			1									
Middle	1.78	1.20, 2.61	<0.001	1.54	1.02, 2.32	0.04							
Poor	2.25	1.65, 3.11	<0.001	1.75	1.18, 2.50	0.005							

The analysis of routine data found that the higher notification rate and lower treatment success rate for TB were found in older age groups and male gender. The Nepal Health Facility Survey identified gaps in TB standards and guidelines (25.16), medicine (31.9), and diagnostics (36.03), with an overall readiness score of 32.41. Bagmati and Sudurpashchim provinces had higher odds of

readiness score compared to the Koshi province. Hospitals had higher odds of readiness score than peripheral health facilities.

**Conclusions:** This study highlights the significant burden of TB in Nepal and identifies key risk factors and gaps in the healthcare system's readiness to address this disease. The study emphasizes the need for continued efforts to improve TB diagnosis, treatment, and prevention in Nepal, particularly among vulnerable populations. Using multiple data sources and appropriate statistical methods is essential for evaluating the burden of TB and assessing the effectiveness of healthcare systems in addressing this disease.

### EP10-1086-16 Introducing new screening tools in TB programming: Mobile TB clinic implementation experiences from Uganda

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**Background:** World Health Organization(WHO) recommends the use of highly sensitive screening and diagnostic approaches such as digital X-ray and Xpert MTB/RIF-Ultra to rule out Tuberculosis (TB) among the most at-risk populations for TB.

With Global Fund support, Uganda acquired 2 mobile TB clinics which are trucks mounted with digital X-ray and computer aided diagnostic software for TB (CAD4TB), Genexpert machines and a consultation room to aid in same day TB screening, diagnosis and treatment initiation.

**Design/Methods:** From March 2022 to March 2023, we conducted screening of people from hot spots and high risk communities using mobile TB clinic as determined by the burden of TB disease and high risk population categories. A total of 160 hotspots and risk group communities from 42 districts were selected based on programmatic notification data.

We performed genexpert testing on all presumptive TB patients irrespective of the chest x-ray (CXR) results and provided same day treatment initiation for people with TB disease from the nearest health facility.

**Results:** A total of 18,471 people were screened using digital X-ray, 6% (1,124) had abnormal CXR (CAD4TB score  $\geq 50\%$  or radiological features suggestive of TB). Among people screened with X-ray, 28% (5,182) were able to provide an appropriate sample for Xpert MTB/RIF-Ultra testing and 77% (3,986/5,182) were tested with Xpert. The overall TB yield among general-popu-

lation was 2% (397/18,471). High TB yield was observed among fisher-folks (5%) and prison-inmates (4%) respectively. Of the diagnosed TB cases, 53% (211/397) had bacteriological confirmation by genexpert, 84% (334) had same day TB treatment initiation.

Community setting	No. Screened with digital X-ray	No. abnormal CXR	No. sample referred to the Laboratory	No. samples tested with genexpert	No. diagnosed with TB (P-CD + P-BC)	No. Bacteriologically confirmed (P-BC)	No. started on TB treatment same day	TB yield in general population
Fisher folks	662	40	364	319	34	31	15	5%
Uniformed people	5,268	186	735	210	83	24	79	2%
Prisons	229	20	99	57	9	6	9	4%
Market Places	1,049	77	453	317	24	15	11	2%
Health Camps	1,473	244	648	410	41	28	38	3%
Schools	913	44	290	290	17	14	15	2%
Other	8,877	513	2,593	2,593	189	93	167	2%
<b>Total</b>	<b>18,471</b>	<b>1,124</b>	<b>5,182</b>	<b>3,986</b>	<b>397</b>	<b>211</b>	<b>334</b>	<b>2%</b>

**Conclusions:** The mobile TB clinics are effective tools for same day TB screening, diagnosis and treatment initiation. We recommend National TB programs to adopt this innovative strategy for active TB case finding in the most at-risk populations to archive the global target of ending TB by 2030.

### EP10-1087-16 Methodologies for care pathway analysis for TB and related diseases: A methodological review

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**Background:** The World Health Organization estimates over 4 million people with tuberculosis (TB) went undiagnosed or unreported to national TB programs in both 2020 and 2021. People with TB experience significant challenges in accessing testing and diagnostic services, particularly in high-burden low- and middle-income countries. Researchers have used several methodologies to describe care-seeking pathways from the perspectives of people affected by TB and their care providers, and each approach has strengths and limitations.

At their core, these methodologies seek to answer these questions: why, how, and where in their care trajectories do patients miss or find standard care?

**Design/Methods:** We conducted a methodological review of the literature to identify and analyze relevant research methods used to describe care-seeking pathways,

including symptom recognition, diagnosis, and treatment. Guided by expert consultations, we extracted and organized key concepts, variables, and relationships to form a comprehensive framework aimed to aid future research.

**Results:** 21,222 articles were identified, 254 underwent full-text review and 61 studies were included. Most studies (56.3%) took place in central and southeast Asia and were on TB care pathways (76.6%). More than half of studies were quantitative (67.2%) and used in-depth, semi-structured or structured questionnaires (73.4%) for data collection. Most TB studies included information on number of provider encounters and type and sector of the providers visited. Alignment of services was less commonly explored in the included papers. Few studies included information on pathways to treatment.

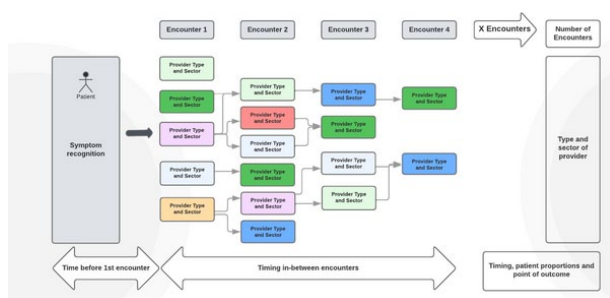


Figure. Pathway to care - conceptual framework.

**Conclusions:** The wide range of methodologies used to determine and describe care-seeking pathways results in difficulty comparing across settings and time points. Our review presents a conceptual model that comprehensively encompasses and defines the distinct terms related to care-seeking pathways.

This model can be useful for researchers and intervention developers in identifying bottlenecks along the care pathway and designing appropriate measures and programs to optimize healthcare for patients.

## EP10-1088-16 Using care cascade analysis to identify gaps in drug-resistant TB case-finding in Anambra State, south-east Nigeria

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**Background and challenges to implementation:** Nigeria is estimated to have about 15,000 multi-drug resistant/ri-fampicin-resistant tuberculosis (MDR/RR-TB) in 2021 with only about 20% notified same year leaving a gap of 80%. Anambra state has been implementing interven-

tions aimed at contributing to closing the notification gap in the country. The aim of this study is to demonstrate how cascade of care can be used to identify gaps in drug resistant TB (DRTB) case finding.

**Intervention or response:** This study is a retrospective analysis of routine surveillance data covering the period of 2020 to 2022. The routine data are aggregated from the national TB programme recording tools used in the health facilities. The data was extracted into Excel which was used for the analysis.

**Results/Impact:** Figure 1 below shows a summary of the three years DRTB cascade analysis. All 359 presumed DRTB cases were tested, 140 (39%) were confirmed positive, and 66% started on 2<sup>nd</sup> line anti-TB medicine. 73% of the patients who started treatment were initiated in the community and 27% in the treatment center. The treatment success rate among the 2020 cohort was 88%.

The analysis shows that there are no gaps in identifying presumptive DRTB cases, testing or case holding. The gap is in enrollment of confirmed cases. Interventions geared towards ensuring all diagnosed DRTB cases are placed on treatment should be the priority of the state TB programme.

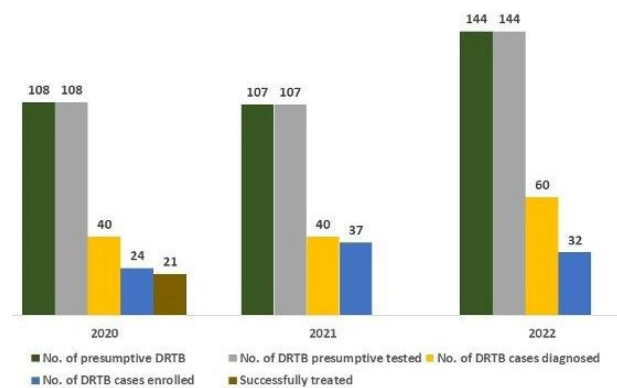


Figure 1. Anambra state DRTB cascade analysis 2020 to 2022.

**Conclusions:** The cascade of care analysis is a model that should be adopted in the TB programme. It has been proven to assist in identifying bottlenecks along the cascade of care. Further research is however needed to identify reasons for the observed enrolment gaps in the state.

### EP10-1089-16 Improving documentation and rEPorting of TB screening at a tertiary facility in Uganda

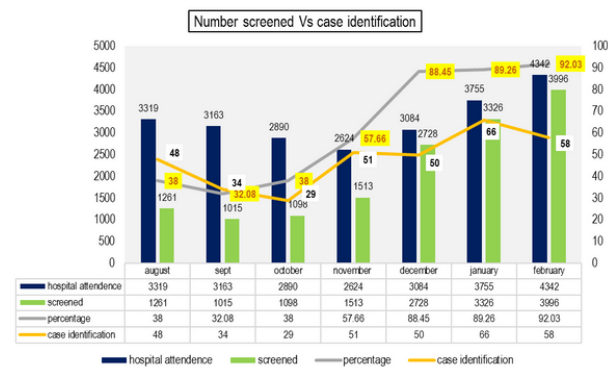
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**Background and challenges to implementation:** Screening patients who present at outpatient clinics for signs and symptoms of TB is critical in early TB diagnosis and attainment of the WHO’s End TB target which aims to diagnose 90% of incident TB cases in all high TB burden countries.

In Uganda, screening for TB at outpatient clinic remains suboptimal at below 70%. At Kiruddu National Referral Hospital, located in Uganda’s capital city (Kampala) only 38% of all patients attending the outpatient clinic were screened for TB in August 2023. This was partly attributed to poor usage of national reporting tools by the assigned community volunteers.

**Intervention or response:** The community volunteers were oriented on the use of national reporting tools (registers and forms) used to record and report the TB screening process. A team lead was selected and assigned to supervise and monitor TB screening and recording at different hospital entry points daily and periodically compile and submit TB screening reports to the data officer for verification and reporting.

**Results/Impact:** The proportion of persons screened for TB in the outpatient clinics improved from 38% in August 2022 to 92% in February 2023 (Graph 1). Further, the number of TB cases identified and registered within the same period also improved.



**Conclusions:** Task shifting helps to address human resource gaps and promotes achievement of good outputs, but enhancing knowledge and skills of community volunteers on the tasks assigned is very important.

### EP10-1090-16 India’s differentiated TB care guidance: Is it feasible to implement and act upon?

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**Background:** In January 2021, India’s national tuberculosis(TB) elimination programme recommended severity assessment using 16 indicators (comprehensive assessment using history, general condition including anthropometry, vitals, testing for HIV and Diabetes, complete blood count and chest radiograph) for all TB patients at diagnosis.

Patients with a total composite score more than one or emergency criteria were eligible for referral and inpatient care (admission in facility with high dependency or intensive care unit if total score more than three). This guidance is yet to be implemented statewide anywhere in India. Even in ideal settings, we wanted to know how many would be assessed and eligible for inpatient care?

**Design/Methods:** In this cross-sectional study, for a period of one month (June 5 and July 5, 2022), we intended to comprehensively assess all adults (≥ 15 y) with TB (drug-sensitive) notified from eight select public teaching hospitals (tertiary care facilities) in Tamil Nadu, a southern Indian state.

Criteria	Considered to be emergency	Scoring criteria	Score assigned
1 Pulse rate (per minute)		<60 >100 (persistent after 30 minutes)	2
2 BMI (kg/m <sup>2</sup> )	Yes (<14)	<14 <16 with pedal oedema	1
3 MUAC (cm)		<16 >41	1
4 Temperature (Celsius)	Yes (<35, >41)	<35 >41	2
5 Blood pressure (mm Hg)	Yes	Hypertension (≥140/90) Hypotension (diastolic below 60)	3
6 Respiratory rate (per minute)	Yes (>24)	18-24 25-30 >30	2 1 2
7 Oxygen saturation (%)	Yes (<94)	90-93 85-90 <85	1 2 3
8 Haemoglobin (g%)	Yes (<7)	<7	2
9 Icterus		Present	1
10 Pedal oedema		Present	1
11 General condition	Yes (if unable to walk, drowsy, unconscious)	Inability to walk but conscious and oriented Conscious, not oriented Drowsy	1 2 3
12 HIV		Positive and on ART Positive and not on ART	2 2
13 Random blood sugar		<70 >128	2
14 Total white blood cell count		TC > 11000 TC < 4000	1
15 Chest radiograph	Yes (massive pneumothorax, hydropneumothorax)	Hydropneumothorax Bilateral consolidation	3 2
16 Haemoptysis	Yes	Present	3

TB - tuberculosis, BMI - body mass index, MUAC - mid upper arm circumference, HIV - human immunodeficiency virus, ART - antiretroviral treatment, \*Total score >1 - to be referred for inpatient care, total score >3 - to be referred for inpatient care in a facility with intensive care unit. If there is an indicator suggesting emergency, the person with TB should be referred for inpatient care.

Figure. Scoring system for referral for inpatient care\* for people with TB based on January 2021 technical guidance on differentiated TB care in India.



**Results:** Among 557 notified, 399 (71.6%) were comprehensively assessed. Among 399, a total of 246 (61.7%) were eligible for inpatient care: i) 114 (28.6%) had a total score of two or three ii) 114 (28.6%) more than three and iii) 18 (10.5%) had a total score of zero or one with presence of emergency criteria.

**Conclusions:** Even in facilities with clinical and diagnostic capacity and in study settings (not routine operational settings), only seven in ten adults were comprehensively assessed.

This appears impractical to implement for all TB patients, many of them are diagnosed in primary and secondary level facilities. Among those assessed, seven in ten were eligible for inpatient care.

Therefore, this is also impractical to act upon. This supports Tamil Nadu's differentiated TB care strategy to introduce an 'easy to use and interpret' triage tool followed by referral, comprehensive assessment, and inpatient care of eligible patients.

### EP10-1091-16 Improving enrolment of diagnosed drug-resistant TB patients through social media and networking platform in Osun State, Nigeria

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**Background and challenges to implementation:** Drug resistant tuberculosis (DR-TB) is undoubtedly a huge challenge in the control of tuberculosis. In 2021, there was an estimated multidrug resistant/rifampicin resistant tuberculosis (MDR/RR-TB) case burden of 450,000 worldwide. Nigeria is one of the countries with high estimated DR-TB burden where estimated proportion of MDR/RR-TB among new TB cases is 2.5% and 19% among previously treated TB cases. Osun state is one of the states with high burden of DR-TB cases in Nigeria with over 100 cases diagnosed in a quarter.

The proportion of diagnosed DR-TB patients that start treatment each quarter is low (as low as 23%) posing great danger of disease transmission within the community and increasing risk of death for the patient.

**Intervention or response:** The USAID TB LON 3 project implemented through the Institute of Human Virology Nigeria (IHVN) and other partners in collaboration with the state tuberculosis control programme put in place the following strategies to close the DR-TB enrollment gap:

1. Line listing, sorting and mapping of diagnosed DR-TB patients per quarter.

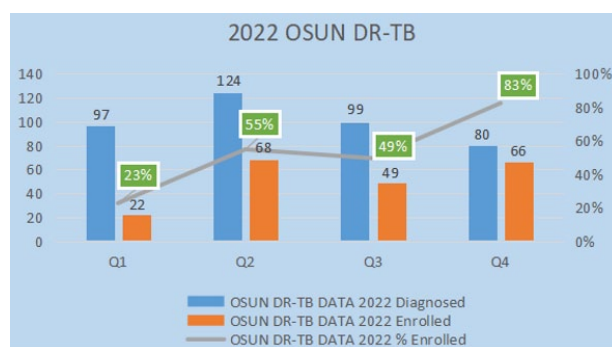
2. Creation of social media/networking platform via mobile phone devices to include all health workers where these DR-TB patients were diagnosed.

3. Early retrieval and dissemination of positive DR-TB results to the health workers via the social media platform.

4. Prompt, intense tracking and close follow-up of all diagnosed DR-TB cases by the state DR-TB focal person, local government tuberculosis supervisors (LGTBLS), facility directly observed treatment (DOT) officers, community volunteers (CVs).

5. Provision of technical support in DR-TB care and provision of transportation and nutritional support to patients to motivate their willingness to access treatment.

**Results/Impact:** The enrollment rate increased from 23% in first quarter of 2022 to 83% in fourth quarter of 2022.



**Conclusions:** Use of social media and networking platform for prompt result dissemination and tracking can improve enrollment of diagnosed DR-TB patients.

### EP10-1092-16 Determinants of initial loss to follow-up among notified persons with TB in India

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**Background:** India's National TB Elimination Programme (NTEP) achieved highest ever TB-notification (2.4 million) in 2022. Digital tracking and tracing of notified persons-with-TB are possible almost on real-time in Ni-kshay (India's case-based web-based TB surveillance system). We conducted this study on determinants of initial loss-to-follow-up (LTFU) – among persons-with-TB notified but not initiated on TB treatment.

**Design/Methods:** This is a retrospective data analysis of TB-notification cohort of 2021 available in Ni-kshay.

**Results:** Out of 2.07 million person-with-TB notified in

2021, 96.2% (1.99 million) were initiated on treatment and 3.8% (78,329) were initial LTFU. Male (63.9%), Age group 15-44 years (53.4%), public sector (81.4%) and new-TB type (88.1%) were the major demographic indicators for initial LTFU. The reasons for initial LTFU were refusal for treatment (9.5%), untraceable due to incorrect address (16.9%) or migration (5.8%), died before treatment initiation (14%) and not evaluation (53%).

#	Indicator	Person-with-TB notified to health system	%
1	Drug-suscEPTible TB (DSTB) notified at diagnosis	2,071,818	
2	Initial lost-to-follow-up (LTFU) - person-with-TB diagnosed and notified but could not initiated on treatment	78329	3.8%
3	Of 2, Males	50040	63.9%
4	Of 2, Age group 15-44 years	41864	53.4%
5	Of 2, Notified from public sector	63783	81.4%
6	Of 2, New-TB type	68986	88.1%
Reasons for Initial LTFU			
7	7a. Treatment refusal; 7b. Untraceable due to incorrect address; 7c. Untraceable due to migration; 7d. Died; 7e. Could not be evaluated	7434 (9.5%); 13234 (16.9%); 4572 (5.8%); 10976 (14%); 42113 (53.8%)	

Table: Determinants of initial lost-to-follow-up.

**Conclusions:** Most reasons for initial LTFU are modifiable. Post-notification counselling is critical intervention for addressing the challenges such as refusal, incorrect address, and migration. High death rate even before initiation of treatment could be averted by early detection and introduction of innovative differentiated TB care at notification. The 'not evaluated' is a data entry issue and could be resolved with monitoring and feedback for updating Ni-kshay.

### EP10-1093-16 STAMP: leveraging technology to monitor treatment adherence and empowering people affected with TB

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**Background and challenges to implementation:** India's TB incidence is 210/100,000 population (2021), compared to baseline 256 (2015); it is vital to strengthen treatment adherence. Support for Treatment Adherence

to Medication protocol (STAMP) is an integrated system of smart hardware dispenser & server backend that addresses privacy, cost & capacity issues of program. It uses both dispenser (on-time alert) & patient's mobile phone (SMS & automated voice calls) to remind taking medicine, draws in social support network to assist in adherence to treatment, alerts healthcare worker (HCW) to potential issues & automatically assures health system of medication treatment adherence. STAMP has an escalation protocol that sends reminders to patient in the event medication is not dispensed. If patient has not dispensed their medications despite reminders, HCW is notified to ensure timely follow-up.

**Intervention or response:** In February 5 2023, pilot of STAMP started with people with TB in trucker & allied population in three locations – Jaipur, Lucknow & Gurugram in India. Training session for HCWs on STAMP was conducted & HCWs in turn created awareness amongst patients and educated them on use of STAMP. This played critical role in overcoming initial reluctance in adopting new technology that was expressed by some patients.

**Results/Impact:** Medication adherence within pilot population was observed 97% - 99% (includes on-time and delayed medications) in first two months. In addition to reducing time spent on daily checks & follow-up via phone calls by HCWs. STAMP has allowed HCWs to quickly identify patients who required additional support.

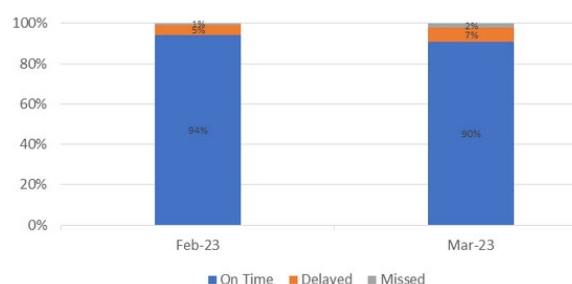


Figure. Medication adherence amongst STAMP users monitored by GLRA.

**Conclusions:** STAMP provides an accurate and detailed data set of medication adherence amongst patients, and allows TB program to identify and assist patients who are unable to adhere to medication more effectively. STAMP has potential to help health programs improve effectiveness of patient treatment across disease modalities, specifically in those requiring patients to take medications consistently for an extended period.

## EP10-1094-16 Patient and provider acceptability of digital adherence technologies for TB treatment in Ethiopia

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**Background:** Among TB patients, digital adherence technologies (DATs) have the potential to increase medication adherence by overcoming the challenges of directly observed therapy: allowing patients greater freedom to self-manage and participate in their own care, reduce financial burdens and restore autonomy and dignity. Our aim was to understand the acceptability of DATs from patient and provider perspectives, within an ongoing cluster-randomized trial of the *Adherence Support Coalition to End TB* study in Ethiopia.

**Design/Methods:** In-depth qualitative interviews were conducted with TB patients (n=33) and TB care providers (n=20) between March 2022-February 2023. Participants were purposively selected from 10 health facilities implementing DAT interventions (smart pillboxes and SMS labels). Data-driven thematic analysis was conducted using NVivo software to identify themes, conceptual categories, commonalities and differences in responses.

**Results:** DATs were highly acceptable to both patients and TB care providers. Three themes were identified capturing the reasons for DATs acceptance. First, DATs were seen to improve TB treatment adherence by reducing patients' burden of daily health facility visits and allowing more flexibility in terms 'when and where' to take medications.

Providers reported DATs reduced workload and the chance of work-related TB exposure. Second, patients and providers considered DATs improving patient-provider relationships, creating a means for better bi-directional communication opportunity.

Finally, while both patients and providers were concerned about the technical complexity of DATs use (before the intervention was started), practically they found them simple and user-friendly across the implementation phase. Patients reported few negative issues which included reminder delays due to network and electricity interruptions.

**Conclusions:** Our study highlights that DATs are highly acceptable to both patients and providers. The findings will have important implications for future policy and

practice by contributing evidence to support the adoption of DATs in TB care, which have a potential to overcome the challenges of DOT.

## EP11 Effectiveness of TB screening

### EP11-1095-16 Spectrum of TB disease and treatment outcomes in a mobile community-based, active case-finding programme in Yogyakarta Province, Indonesia

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**Background:** The World Health Organization recommends using chest X-ray (CXR) in Active case finding (ACF) to improve case detection.

The aim of this study was to describe the spectrum of TB disease diagnosed through a mobile community based ACF program in Yogyakarta and compare outcomes between groups of active TB disease defined by bacteriological and symptom status.

**Design/Methods:** This was a prospective cohort study. We included people who attended TB screening in an ACF screening program in Yogyakarta between January 1<sup>st</sup>, 2021 to June 30<sup>th</sup>, 2022. All eligible participants above 10 years old underwent CXR and symptom screening.

We defined 4 groups representing the active TB spectrum based on clinical and bacteriological findings as follows: Group 1: symptomatic, bacteriologically confirmed TB; Group 2: symptomatic, not bacteriologically confirmed; Group 3: asymptomatic, bacteriologically confirmed TB;

Group 4: asymptomatic, not bacteriologically confirmed.

Subclinical TB was defined as group 3 and group 4, asymptomatic whether bacteriologically confirmed or not. Treatment outcomes data were obtained from the national program TB database.

**Results:** 47,735 people attended the ACF program in two districts. The yield of TB disease was 0.86 % (393/45,938). There were 217 symptomatic cases, of whom 72 (33.2%) were bacteriologically confirmed (Group 1) and 145 (66.8%) were not bacteriologically confirmed (Group 2).

There were 176 asymptomatic cases, of whom 52 (29.5%) bacteriologically confirmed (Group 3) and 124 (70.5%) were not bacteriologically confirmed (Group 4). Overall treatment success was 70.7% with high loss to follow up 10.9% and not evaluated 17.1%. In multivariate analysis there was no difference on treatment outcomes between groups.

**Conclusions:** CXR use in TB ACF programs is important, since it may increase TB notifications rates, with a high proportion of subclinical TB. Linkage to care in ACF program is also important to increase successful treatment outcomes.

### EP11-1096-16 Quality of active case-finding for TB in India: How we are faring at the district, state and national levels

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**Background:** Since 2017, India is implementing active case finding (ACF) for TB among marginalised and vulnerable (high-risk) populations. Its impact will depend on the scale, frequency, and choice of high-risk populations. ACF will be effective if two ACF cycles are implemented in a year (high-risk populations screened twice) with acceptable ACF quality indicators.

**Design/Methods:** In this descriptive study using aggregate programme data from each ACF activity in 2021, we calculated three TB ACF quality indicators at national, state and district level: percentage population screened (at least 10%), percentage tested among screened (at least 4.8%) and percentage diagnosed among tested (at least 5%). We also calculated the number needed to screen (NNS  $\leq 1538$ , total screened divided by total diagnosed).

**Results:** Most of the states and districts implemented one ACF cycle (aimed to cover the high-risk populations once). When aggregated at the national level, for one ACF cycle, 9.3% population was screened, 1% of the screened were tested and 3.7% of the tested were diagnosed as TB. The NNS was 2824. None of the 36 states or 768 districts met all the three TB ACF quality indicators' cut-offs. Two states, namely Arunachal Pradesh and Tripura and 36 districts met the NNS cut-off with percentage population screened 5.0-9.9%. By high-risk populations at national level, the NNS was consistently good ( $\leq 1538$ , even lower than 770 in some instances) for ACF in institutional facilities and

poor (far higher than the cut-off) for population-based groups. Data was not consistently available to calculate the extent of high-risk populations covered, percentage of presumptive TB among screened and percentage tested among presumptive.

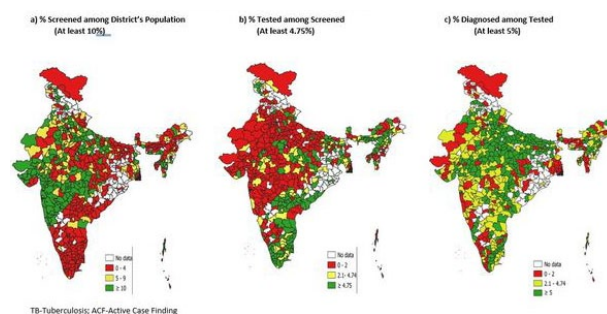


Figure. District map of India depicting the various TB ACF quality indicators (first cycle), 2021.

**Conclusions:** In 2021, India did not implement one ACF cycle with acceptable ACF quality indicators. As we gear up to achieve the SDG 2030 TB targets, these ACF quality indicators will act as baseline for future analyses.

### EP11-1097-16 Comparing effectiveness of TB screening methods for diagnosing TB disease among household contacts in Karachi, Pakistan

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**Background:** Household contacts of TB patients are considered a high-risk group for developing TB disease. The preferred screening method for contact screening in LMICs is verbal symptoms screening as it is cheaper and quicker.

We compared the effectiveness of verbal symptoms screening and chest X-ray screening in diagnosing TB in household contacts.

**Design/Methods:** We implemented programmatic management of household contacts of TB patients in Karachi, Pakistan from January-2018 to December-2019. Household contacts underwent chest x-ray, TB-PCR testing (if able to produce sputum) and medical assessment by clinician including symptoms screening, physical exam, and medical history.

We report the results of sensitivity/specificity analysis when using chest x-ray or verbal symptoms screen or combination of both as TB screening method.

**Results:** We evaluated 7,422 household contacts for TB disease, of which 365(4.9%) were diagnosed with TB. When used alone, verbal symptoms screening was able to identify 304 patients while chest X-ray identified 283 patients with the disease each respectively missing 61(16.7%) and 82(22.4%) patients with the disease. However, using a combination of verbal symptoms

screening and chest x-ray identified 342 patients with a sensitivity of 93.7% (95% CI:90.6-95.9) missing only 23(6.3%) patients with the disease.

Screening Method	Disease Prevalence n (%)	Sensitivity	Specificity	Negative Predictive Value		Positive Predictive Value		Likelihood Ratio	
				% (95% Confidence Interval)	% (95% Confidence Interval)	Negative	Positive	Negative	Positive
Verbal Symptoms Screen	342 (91.36 - 86.97)	79.23 (76.26 - 82.21)	98.92 (98.42 - 99.42)	17.18 (15.45 - 18.91)	0.21	4.02			
Chest X-ray	342 (91.36 - 86.97)	77.53 (72.90 - 81.71)	74.79 (73.76 - 75.80)	98.47 (98.10 - 98.78)	13.72 (12.27 - 15.29)	0.3	3.08		
Combination of Verbal Symptoms Screen & Chest X-ray	342 (91.36 - 86.97)	93.70 (90.69 - 95.96)	67.31 (66.21 - 68.40)	99.52 (99.28 - 99.69)	12.91 (11.66 - 14.25)	0.09	2.87		

Table. Performance characteristics of TB screening methods for household contact screening.

**Conclusions:** TB household contact screening is an important strategy in finding missing TB patients. Using the conventional verbal symptoms screening method is likely to miss TB disease in contacts while combining it with a chest x-ray improves the disease yield in household contacts. Programs should incorporate chest X-rays as part of TB contact screening practice as ruling out TB disease is the first step in the TB prevention treatment cascade which has a monumental role in the EndTB strategy.

### EP11-1098-16 Population-level assessment of transmissibility of drug-resistant TB in southern Taiwan

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**Background:** Previous studies have suggested that the acquisition of drug resistance in tuberculosis (TB) may be associated with reduced virulence and transmissibility. However, the evidence on the transmissibility associated with specific mutations has been diverse.

**Design/Methods:** We used whole genome sequencing to analyze a total of 3,097 TB cases, accounting for 82% of all notified cases between January 2019 and September 2022 in Kaohsiung City, Taiwan. After defining clustered cases based on SNP distance from any other strains, we estimated clustering rate by resistance status to assess the fitness cost. The resistance status for the four main TB drugs (Isoniazid, Rifampicin, Ethambutol, Streptomycin) was identified using known resistant-conferring mutations.

**Results:** Applying the threshold of 5 SNP, we found that 487 cases (15.7%) were clustered. Cases with genotypic resistance to any of the four drugs had a lower clustering rate with susceptible cases (11.1% vs 16.6%, p-value=0.003). When stratified by mono-resistance to each drug, the clustering rates were all lower than those of

susceptible ones but were not significant. However, Hr-TB (isoniazid resistant and rifampicin susceptible) had a significantly lower clustering rate (9.5%) compared to drug-susceptible strains. On the other hand, MDR-TB showed a similar rate of clustering (16.7%) with susceptible cases.

Moreover, among the clustered MDR-TB cases, five out of six (83.3%) harbored known compensatory mutations on rpoC gene, which was significantly higher than non-clustered MDR-TB cases (30.8%).

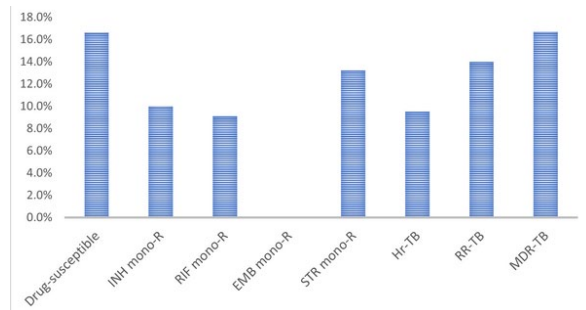


Figure. Clustering rate by resistance status.

**Conclusions:** This study was the first to explore the transmissibility of drug-resistant TB using whole genome data within a population-based design in Taiwan.

The findings revealed potential fitness costs associated with drug resistance in TB. To gain a comprehensive understanding of fitness costs as a crucial determinant of drug resistance transmission and future trends in tuberculosis burden, further analysis is needed, particularly in relation to diverse gene mutations and strain lineages.

### EP11-1099-16 Estimated reductions in TB prevalence following population-wide screening

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**Background:** Population-wide x-ray screening for tuberculosis disease was used until the 1970s when symptom screening was recommended as more cost-effective.

With the development of new screening tests and the understanding of the spectrum of disease, we investigated if symptom screening was still the most effective method for detecting disease, infectious or non-infectious.

**Design/Methods:** We created a transmission model of tuberculosis with progression from infection to the spectrum of disease and constant background symptom screening. We simulated three rounds of population-wide screening, with either Xpert MTB/RIF alone or screening tests (one of symptoms, C-reactive protein (CRP), blood-biomarkers, or X-ray) followed by Xpert confirmation, and compared outcomes to the same

population with no additional interventions. We measured the reduction in prevalence of infectious (subclinical and clinical) disease from a baseline of 500/100,000, and numbers of false-positive and false-negative diagnoses.

**Results:** Xpert-only screening, with treatment for all people who test positive, was the most effective method to reduce prevalence (44.7% reduction after three years [95% confidence interval, 35.8-54.4]).

Screening with digital x-ray followed by a confirmatory Xpert reduced prevalence by less (by 39.6% [31.3-49.6]) but reduced the number of people without infectious disease who received treatment by 83%.

Xpert-only screening missed 5.8% [1.9-10.5] of opportunities to detect infectious disease compared to the range of other screening tests from x-ray (9.7% [4.9-14.8] missed) to CRP (69.4% [65.6-73.2] missed).

For individuals with non-infectious disease (between initial infection and subclinical disease), 95% [91-100] were excluded from treatment following Xpert confirmation.

**Conclusions:** Population level screening paired with a confirmatory Xpert can detect more people with infectious disease than passive symptom screening alone which could enable more people to be treated earlier.

This will not only reduce prevalence and transmission, but likely also post-TB sequelae. Consideration needs to be given to the diagnostic and treatment pathways for individuals with non-infectious disease.

### EP11-1100-16 Using a grid model approach and active case-finding data to predict risk of TB at the community level in Pakistan: Experience and challenges

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**Background and challenges to implementation:** Commonly used modelling approaches that identify TB hotspots remain restricted only to large administrative units.

However in high burden and more populous countries there is a need for a more granular view of the geographical distribution of disease.

We used TB active case finding (ACF) data and several other variables known to be associated with TB to train a predictive Bayesian TB risk model at the level of 2kmx2km units.

We aimed to improve the model performance and maximize the resolution of predictions of TB positivity rates to identify high case-finding efficiency areas.

**Intervention or response:** We overlaid the population distribution of Pakistan with a grid of 2kmx2km and then removed unpopulated areas where no population settlements exist.

Community level ACF data were then distributed using a gaussian distribution within a 6 KM diameter around the ACF site's geographical location, assumption being that ACF events attract people from the neighboring localities as well, apart from only those who live in the immediate vicinity.

This methodology was compared to our previously developed Voronoi representation model based on sub-national units of 10000 persons generated by weighted K-means clustering of population raster data.

**Results/Impact:** The output was a 2x2 Km resolution bacteriological TB positivity rate predictive model that outperformed a voronoi representation model (Mean squared error being 38.10 and 61.29 respectively). It allowed better standardization of contextual variables and improved handling of ACF data.

Small pockets of high TB risk surrounded by relatively low risk areas could be identified, which would have gone unnoticed in a low resolution model. However the model query volume increased significantly leading to longer processing time.

**Conclusions:** Predictive performance of the model was improved using this grid model approach. This predictive model may help to prioritize case finding in communities with a high risk of TB and low access to care.

### EP11-1101-16 Spatial characteristics and prediction model of recent transmission of TB in Kaohsiung, Taiwan: An integrated analysis of EPidemiological and genomic data

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**Background:** Recent transmission (RT) is a major cause of new tuberculosis (TB) cases. The aims of this study are to identify spatial patterns of recent TB transmission in Kaohsiung, Taiwan, to explore the relationship

between individual risk factors and the occurrence of the recent transmission event, and to develop the prediction model for RT of TB.

**Design/Methods:** From Jan 2019 to Jul 2021, the *Mycobacterium tuberculosis* isolates from TB patients in Kaohsiung, Taiwan were genotyped by WGS. Global and Local Moran's I were applied for spatial analysis to assess TB cases' spatial patterns. Multivariable logistic regression analysis was applied to estimate the odds ratios (OR) and 95% confidence interval (CIs) for epidemiological and spatial factors associated with the RT of tuberculosis. For the development of prediction models, backward elimination based on AIC was used to improve prediction efficiency. The prediction model's performance was evaluated by Area Under the Receiver operating characteristic (AUROC). Furthermore, we performed time-split validation to conduct internal validation.

**Results:** From Jan 1, 2019, to Jul 31, 2021, 1323 cases of culture-positive tuberculosis were included. The spatial autocorrelation analysis revealed that there was a significant positive spatial autocorrelation of RT (Moran I statistic: 0.063,  $P < 0.01$ ). Results of multivariable logistic regression analysis showed that factors such as age under 25 (*vs.* age over 65, OR: 4.79, 95% CI: 2.17-10.68), the need for social support (OR: 2.34, 95% CI: 1.06-5.14), positive sputum smear result (*vs.* negative result, OR: 1.49, 95% CI: 1.07-2.05) were the most influencing factors on recent TB transmission. The AUROC obtained from time-split validation was 0.626 (H-L test:  $p < 0.01$ ). **Conclusions:** Our study identified that the distribution of recent TB transmission is spatially dependent. The analysis combining epidemiological, spatial, and genomic information provided valuable information and could be further implemented in future studies for infectious diseases.

### EP11-1102-16 Infectiousness decay of *M. tuberculosis* droplets exposed to ultraviolet germicidal irradiance combined with evaporation

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**Background:** Several studies have reported environmental interventions that minimize TB transmission using ultraviolet germicidal irradiance (UVGI), passive and active ventilation, relative humidity (RH) to enhance

evaporation. These have been used to either reduce the concentration of, or increase the rate of deactivation of respiratory droplet-borne pathogens. However, data describing measures and estimates of the decay of infectiousness when these interventions are implemented are sparse. We aimed to model the decay of infectiousness of *Mycobacterium tuberculosis* (Mtb) when expelled through the nose or mouth, and exposed to UVGI coupled with evaporation at specific RH.

**Design/Methods:** Computational fluid dynamics were used to simulate droplets propagating Mtb. ANSYS@2020R2 was used to model a discrete phase setting, which considers the droplets dynamics expelled by coughing, sneezing and speaking, while they propagate in a closed environment with initial conditions of 25% relative humidity at 25°C. Killing of Mtb was defined when the infectiousness reduced below a certain threshold. External scalar quantities based on user defined function were implemented to determine the survival rate of infectious Mtb.

**Results:** The infectiousness of Mtb as observed for different exhalation events was significantly reduced due to evaporation (see Figure).

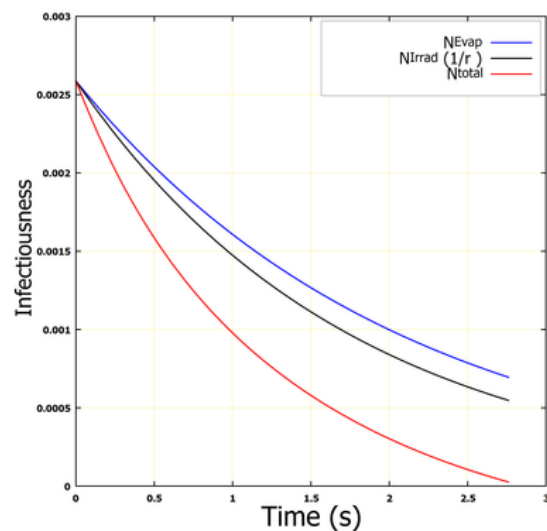


Figure: Infectiousness of Mtb when exposed to evaporation ( $N^{Evap}$ ), irradiance ( $1/r$ ), and irradiance coupled with evaporation ( $N^{total}$ ).

However, when evaporation was coupled with UVGI, the infectiousness of Mtb decreased faster with a reduction rate of more than 93%. Irrespective of the exhalation events, the infectiousness of Mtb significantly reduced when exposed to UVGI combined with evaporation. The proposed model can track the infectiousness of Mtb more rapidly during coughing and sneezing. The fractional survival rate of the Mtb linearly decreases as the UV dose increases.

**Conclusions:** This study provides insights of an engineering intervention to mitigate the spread of Mtb that might reduce TB transmission in confined spaces such as clinics, and transport systems.

## EP11-1103-16 Community health workers as gamechangers in improving TB case notification: Experience from Pwani Region in Tanzania

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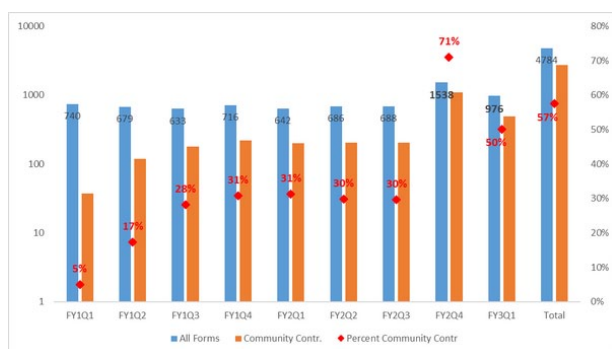
**Background and challenges to implementation:** Tanzania is among the 30 countries in the World with high TB burden with an estimation of 132,000 TB cases in 2021 (WHO TB Report 2021). In the past 15 years, Tanzania in collaboration with development partners have invested efforts to increase case notification to reach 30% target as community contribution.

**Intervention or response:** During July -December 2021, CHWs were engaged to conduct active TB case finding (ACF) and index contact tracing including TB screening and linkage to facilities. CHWs worked hard to educate, sensitize and vigilantly screened clients for TB. Not only that but door to door campaigns were conducted, Screened and sample collection were done. Those who could not afford to go for Xrays, CHWs reported them to Ward Executive Officer for waiver.

Furthermore, CHWs facilitated sensitization to the community for TB diagnostic mobile van conducted at Chalinze, Kibaha DC, Kisarawe and Bagamoyo where Confirmed TB cases were initiated treatment.

Also, Contact Tracing and defaulter tracing were done by CHWs. Recording and reporting of results were done using national standard registers. Data extracted from ETL were disaggregated by quarterly in order to compare performance with previous periods.

**Results/Impact:** Majority of clients were referred by CHWs. Data extracted from ETL for the past six quarters (2021-2022) shows four quarters with 30-31% community contribution while in quarter four 2022 and quarter one 2023 cases jumped to 71% and 51% respectively. The sharp was attributed by robust community sensitization, and presence of TB diagnostic mobile in the affected community.



**Conclusions:** Community health workers are of paramount importance in TB case finding in communities affected when combined with diagnostic TB mobile

van outreach. CHWs are potential to our programs and should be included in council health plans for sustainability.

## EP11-1104-16 Travel and tuberculosis in migrants

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**Background:** Tuberculosis (TB) rate among migrants remains poorly understood. It is usually assumed to be due to the progression of *Mycobacterium tuberculosis* infection acquired before arrival.

An alternative hypothesis is that incidence follows rapid progression after re-exposure during return travel to the country of origin.

**Design/Methods:** We assessed TB sputum smear-positive notifications in foreign-born adult patients over a 20-year period in the London Borough of Hackney, UK. We recorded information on most recent travel to a high TB burden country (usually, country of origin of individual or spouse) and time of entry to the UK.

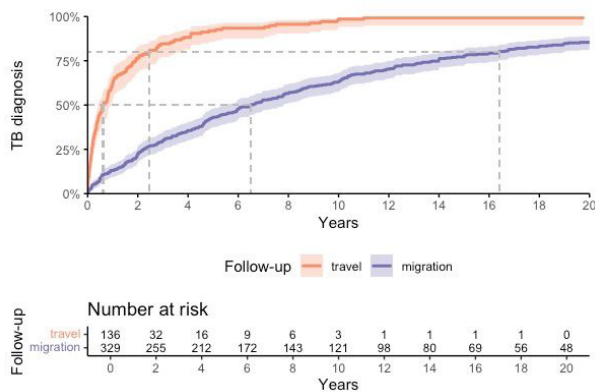
A survival curve for time to first contact with the health-care system leading to a TB diagnosis was constructed to compare time since migration and most recent travel. These were compared to reported rates of rapid progression after exposure from literature.

**Results:** We assessed 329 individuals, of whom 136 (41%) reported travelling to a high-burden country between their first arrival and their TB episode. For individuals who travelled, 50% of TB diagnoses occurred within the first year (0.62; 95% CI:0.42-0.93) and 80% before the fourth year (2.46; 95% CI:1.80-3.72) after their return (Figure – orange line).

Conversely, when considering time from entry into the UK as the time since last TB exposure (Figure – purple line), 50% and 80% of TB cases were diagnosed after five years (6.49; 95% CI:5.50-7.80; and 14 years (16.42; 95% CI:14.00-18.97). Using time since last travel closely matched reported progression rates of TB disease following infection.

Restricting the times of entry to the UK to only those who reported travel did not qualitatively change the curve.





**Conclusions:** High TB incidence in migrants is often due to rapid progression after *Mycobacterium tuberculosis* exposure during travel.

### EP11-1105-16 A new, versatile and open-source mathematical modelling framework applied to estimating the impact of novel TB vaccines

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**Background:** The impact of TB interventions can be estimated with transmission models. We developed a new transmission modelling framework to project the health benefits and costs of TB vaccine strategies.

**Design/Methods:** A modelling framework that simulates the dynamics of Mtb transmission and TB disease progression was developed in R. A system of ordinary differential equations represents the model population which is structured by the following core dimensions: age, vaccination status, risk status, socioeconomic status, HIV stage, and TB stage. The user specifies the number of classes in each dimension (e.g. the stages of TB natural history) and the interdependencies between model parameters.

Transmission is determined by the transmission probability per contact and the number of contacts per day between 5-year age groups specified by contact matrices. The R package deSolve was used for numerically solving the differential equations. Model calibration is quick and efficient using the new R package hmer (*D Scarponi et al. Epidemics 2023; 43, 100678*).

**Results:** Our model estimates that in 105 low- and middle-income countries (LMICs) accounting for 93% of global incidence, routine vaccination of those aged 9 years and one-off vaccination for those aged 10 years and older would prevent 44 million tuberculosis cases and 5 million tuberculosis deaths before 2050 compared

to no new vaccine introduction (*RA Clark et al. Lancet Global Health 2023; 11: e546–55*). Costs and cost-effectiveness of introducing novel TB vaccines in LMICs were reported in (*A Portnoy et al. Plos Medicine 20 (1), e1004155*).

**Conclusions:** We developed a new transmission model that was successfully applied to estimate the health impact, costs, and cost-effectiveness of novel TB vaccines. The model can be used to compare the impact of additional interventions, e.g. enhanced case finding vs. preventive treatment, and to estimate the optimal mix of interventions for a given budget (i.e. allocative efficiency).

### EP12 TB information system - Management of TB

#### EP12-1106-16 Uptake of TB preventive therapy (3HR): experiences from Akwa Ibom, Cross River and River States, Nigeria

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**Background and challenges to implementation:** Tuberculosis (TB) preventive therapy (TPT), including isoniazid preventive therapy (IPT), has been implemented within the Nigerian human immunodeficiency virus (HIV) programme since 2014. Tuberculosis preventive treatment (TPT) is a critical intervention to reduce tuberculosis mortality. To facilitate scale-up of TPT in Nigeria, the United State Agency for International Development (USAID) supported the National TB Programme through implementing partners to roll out the 3HR regimen.

**Intervention or response:** In March 2022, 100 health workers from 56 public and private health facilities across the 3 states were trained on contact management using 3HR regime. The training also included the use of data recording and reporting tools as stipulated by the National TB programme. The 3HR regimen and weighting scales were distributed to all trained health facilities and 3HR stock levels were closely monitored for prompt stock requisition. Contact management fund allocation was increased to ensure 100% index patient coverage across the implementing sites.

**Results/Impact:** Data review from July – December 2022 revealed the following: Number of contacts eligible for TPT 18847 (paediatric 20.4%), number of eli-

gible contacts enrolled on 3HR 4640 (paediatric 33.1%), number of eligible contacts enrolled on 6H 1228 (paediatric 20.4%). Despite an enrolment rate of 31%, TPT enrolment increased from 173 to 5868 when compared to the same period in 2021.

**Conclusions:** Increased funding and logistic management will drive TPT implementation. A major bottleneck within the period was the stock out of 3HR regimen. Also, funding capacity to scale up 3HR implementation to other health facilities has been a challenge. There is need for the National TB programme and implementing partners to invest more as the shorter regimen continuously gains more acceptability.

### EP12-1107-16 Leveraging a web-based electronic case-based surveillance system to track the management of persons with multidrug-resistant TB in Uganda

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**Background and challenges to implementation:** The use of electronic medical records platforms to support the management of multidrug-resistant (MDR) TB is recommended by WHO and the Ugandan Ministry of Health. Accurate patient-level data remains a key requirement in the programmatic management of MDR TB given the observed complexities of linkage, drug regimens assignment, monitoring side effects, and assigning final treatment outcomes for each person under management.

**Intervention or response:** The National Tuberculosis and Leprosy Programme (NTLP) and Division of Health Information (DHI) together with implementing partners set to roll out the TB Electronic Case Based Surveillance System (eCBSS) across all Diagnostic and Treatment Units (DTUs) with particular emphasis on MDR TB treatment centres across the country. The USAID LPHS TB Activity, as a national TB flagship project supporting NTLP, supports 17 MDR TB treatment centres to implement the use of eCBSS through capacity building, onsite data use, and sharing of analytics with the national coordination teams and facility teams. The weekly status of MDR TB case detection versus enrolment is routinely shared with all stakeholders.

**Results/Impact:** Routine use of data from eCBSS for monitoring of real-time data on treatment initiation versus case detection has contributed to an increase

from 76% linkage in Oct-Dec 2021 to 110% in Oct-Dec 2022 (previously missed cases were also enrolled). 100% of persons with MDR TB registered at treatment sites in the DR-TB Register were updated in the eCBSS by March 2023. The update of eCBSS has further eased hot spot mapping, national projections for anti-MDR TB drug ordering, and is invaluable in the centralized assignment of treatment outcomes.

**Conclusions:** Strengthening the use of patient-level electronic medical records systems is critical in the programmatic management of MDR TB and provides a robust channel for information systems for TB, program monitoring, and TB surveillance in the roadmap to ending TB.

### EP12-1108-16 The Automated Partners Progress REPort: Strengthening data-driven approach to TB case notification in Nigeria

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**Background and challenges to implementation:** With over 262,000 missing cases in 2021, Nigeria ranks sixth in global TB burden. Among other factors, deficient surveillance and data management systems, limits data use capacity to identify gaps in TB services, implement effective interventions, and track progress toward finding the missing TB cases.

This study examined whether onboarding TB program data sets and indicators on Automated Partners Progress Report (APPR), a DHIS2-based data management system, facilitated TB case notification by providing a comprehensive and accurate TB cases record.

**Intervention or response:** In April 2022, the APPR for managing aggregate TB program data went live. The APPR had several important features including well-structured data collection system, clearly defined reporting timelines and responsibilities, validation rules, and customized analytics to support data-driven decision-making. Within 10 months we examined data on TB case notifications before and after the implementation of the APPR in 18 USAID-funded TB local organization network (TB LON) project states. Descriptive statistics and a Wilcoxon signed rank test were used to compare monthly TB cases before (April 2021–Jan. 2022) and after (April 2022–Jan. 2023) APPR deployment.

**Results/Impact:** The project used APPR to collate and report TB cases more accurately. TB Case-finding increased by 26.6% from 61,101 cases before APPR de-

ployment (April 2021 – Jan 2022) to 78,101 after APPR rollout (April 2022 – Jan 2023). Wilcoxon signed ranks test revealed that median number of monthly TB cases notified was significantly higher after intervention (Median = 335.0, n=180) than before intervention (Median = 278.50, n = 180),  $Z = -8.20$ ,  $p < 0.01$ , with a small effect size,  $r = 0.01$ , indicating that the intervention had a significant effect on TB case notification.

Wilcoxon Signed Ranks Test

		N	Mean Rank	Sum of Ranks
After APPR Rollout - Before APPR Rollout	Negative Ranks	39 <sup>a</sup>	60.59	2363.00
	Positive Ranks	140 <sup>b</sup>	98.19	13747.00
	Ties	1 <sup>c</sup>		
	Total	180		

a. After APPR Rollout < Before APPR Rollout

b. After APPR Rollout > Before APPR Rollout

c. After APPR Rollout = Before APPR Rollout

**Conclusions:** The APPR provides a single point for data integration and synthesis, enhancing data use and allowing implementing partners to better focus their resources and interventions to improve TB case notifications.

### EP12-1109-16 Real-time monitoring of the performance of GeneXpert machines through a locally developed web-based application

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**Background and challenges to implementation:** National TB Program in Nepal has considered GeneXpert MTB/RIF testing as primary tool for diagnosis of Tuberculosis among presumptive TB cases since 2019. The program has installed 124 GeneXpert machines across 109 sites. There were challenges in monitoring functionality of these machines on real-time basis leading to delay in maintenance/calibration and low utilization.

**Intervention or response:** GXMIS, web-based connectivity application, was developed by national IT experts following HL7 protocol: international standards

for transfer of clinical and administrative data between software applications used by various healthcare providers. GeneXpert machines were configured through onsite/remote desktop support and networked to the GXMIS system. Through this application, functionality of each module of a machine is monitored. This feature monitored and analyzed errors, positivity rate, Rifampicin Resistance rate and utilization at the central and provincial level.

The GeneXpert sites were able to report any issues related to functionality of the machines and modules by raising tickets in the system. GeneXpert service engineers responded to the issues visiting to the sites or through remote assistance at the earliest possible. A total of USD 8000 was spent to develop the system.

**Results/Impact:** Out of 109 GeneXpert sites under the NTP, 100 are enrolled in the GXMIS system. In 2022, 147548 tests, 8248 errors, 716 invalid tests, MTB positivity rate of 14%, RR rate of 4% and the utilization rate 32.31% were reported in the system nationally.

88 issues were reported by raising tickets and service engineers responded to 88 of them by physical and virtual means. The functionality of the GeneXpert machine was higher in 2022 (avg. 88%) compared to that in 2021 (avg 85%).

**Conclusions:** GXMIS is low-cost web-based application for real-time monitoring of the performance of the GeneXpert machines. The application helps to improve utilization of the machines through real-time reporting of functionality issues and immediate response from service engineers.

### EP12-1110-16 Live monitoring and maintenance of an artificial intelligence solution for nationwide TB risk stratification

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**Background:** We develop a Machine Learning (ML) approach for predicting propensities of adverse treatment outcomes for tuberculosis (TB): Loss-to-follow-up (LFU - treatment interruption for a month), and death, with the aim of deploying in all 784 districts in India, which has ~2.6 Mn TB patients annually.

We describe solution development, consider deployment concerns, and describe the impact on the public health system. We share retrospective performance results on

2021 Ni-kshay (India's central line-list) data for patients from two regions in India, where we plan to pilot the solution as the official AI partner of India's Central TB Division.

**Design/Methods:** Our ML model, to be used at the time of treatment initiation, outputs combined LFU and mortality risk scores from 0-1, thresholded at the district level to "High"/"Low" risk. It is trained on Ni-kshay records of ~1.7Mn pan-India patients initiated on treatment in 2020-2021. The model is evaluated on sensitivity while targeting 35% of patients, showing 40% improvement above a 10-variable rule. Our solution consists of a portal to display patient risk, linked to an application displaying high-risk patients for health workers to intervene through phone calls. Working with local authorities, we design quasi-experimental evaluation studies. Some highlights:

Machine learning:

1. Live data-and-model monitoring, with threshold up-dation to manage varying loads.
2. Evaluation across important cohorts e.g. location, month-of-initiation, gender, PHI-type, etc.
3. Interpretability, fairness, and robustness methods

Public health system:

1. Adverse outcome reduction.
2. Improved worker-bandwidth utilization through targeted interventions.
3. Better data/technology practices like validation checks.
4. Responsible practices ensuring no patient is denied care.

**Results:**

Cohort (2021 Q4)	# Patients	# Adverse	Prevalence	Sensitivity @ 35 (Rules-based baseline)	Sensitivity @ 35 (Model)
Overall	26658	1978	7.42%	0.53	0.75
Mumbai	11585	906	7.82%	0.570	0.809
Haryana	15073	1072	7.11%	0.499	0.702

**Conclusions:** We design an ML-powered solution for enabling targeted interventions to reduce adverse outcomes for India's TB program. We find that the ML solution has a significant increase in sensitivity above rule-based prioritization. Experiments with interventions are planned for impact evaluation, which will be used to inform a future pan-India deployment.

## EP12-1111-16 Learnings from the implementation of TB infection management in the Union Territory of Dadra Nagar Haveli, Daman & Diu, India, 2020-2022

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**Background and challenges to implementation:** Prevention is the key strategy under the National Strategic Plan (2017-25) for eliminating TB in India. Providing TB Preventive Treatment (TPT) to already TB infected persons is one of the preventive strategies under endogenous re-activation prevention. TPT prevents breakdown of TB disease from TB infection by up to 60% among non-HIV individuals and up to 90% among PLHIV.<sup>2</sup> But, as the beneficiaries are asymptomatic, its uptake was major challenge.

The study was done to evaluate the acceptance of TB infection testing, its positivity rate and comparison of compliance for TPT regimens in household contacts (HHC) of Index TB patients from 2020-2022.

**Intervention or response:** Union Territory of Dadra Nagar Haveli, Daman & Diu, India has started implementation of TB Infection management in 2019 on pilot basis but its actual implementation started from December 2020. Interferon Gamma Release Assay (IGRA) was offered to all consented household contacts (HHC) of TB patients (both pulmonary and extrapulmonary TB).

Those with IGRA positive result were offered 3RH regimen in 2021 and 3HP regimen in 2022. TPT Card were maintained. Rigorous monitoring of treatment was done by involving general health staff. The acceptance for TBI testing, its positivity rate and TPT compliance was evaluated by MIS and Ni-kshay data.

**Results/Impact:** Out of the total 4350 HHCs of public sector who were offered IGRA, 3019 (69%) HHCs were tested with IGRA with positivity of 35% (1043/3019). Among those who were IGRA positive, 94% (978/1043) were initiated on TPT, of which 636 (65%) and 342 (35%) were initiated on 3RH and 3HP regimens respectively.

The treatment completion rate was 99% (339/342) and 97% (615/636) in 3HP & 3RH regimens respectively.

**Conclusions:** Rigorous monitoring and involvement of general health staff ensured effective implementation and further scale up of TB Infection management in the UT.

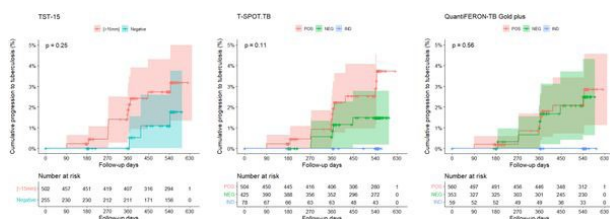
## EP12-1112-16 Prognostic value of interferon- $\gamma$ release assays and the tuberculin skin test in predicting the development of active TB: A prospective cohort study in Madagascar

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**Background:** Defining a cost-effective policy for screening and management of TB infection in Madagascar remains elusive. Here, the predictive values of the tuberculin skin test and two interferon- $\gamma$  release assays for the development of active TB were estimated in household contacts (HHC) of active TB cases through a community-based approach.

**Design/Methods:** Active TB index cases (ICs) were recruited from TB screening centers in Antananarivo, Madagascar. Clinical field research assistants ensured household contact visits for each IC and performed TBI screening using TST and two IGRAs (T-SPOT.TB and QuantiFERON-TB Gold plus; QFT-P). All-HIV negative HHCs were followed up over an 18-month period, with interim visits at months 6, 12, and 18 for assessment of TBI status.

**Results:** Between December 2020, and April 2023, a total of 390 ICs and 1030 HHCs were recruited. HHCs were followed for a median of 1.5 years (range 364 days to 547 days). At baseline, TST-15, T. SPOT-TB, and QFT-P positivity rates among HHCs were 49.2%, 50.0%, and 57.6%, respectively. During the 18-month follow-up period, 19 (1.8%) of 1030 HHCs developed active TB. The annual incidence among participants with a positive result was highest for T-SPOT.TB (23.9 per 1000 person-years, 95% CI 13.7 - 40.1), TST-15 (21.8 per 1000 person-years, 95% CI 11.6 - 37.3) and QFT-P (18.5 per 1000 person-years, 95% CI 9.5 - 32.2). Positive T-SPOT.TB results and TST-15 were significantly better predictors of progression than TST-5; TST-10 and QFT-P.



**Conclusions:** In Madagascar, a screening strategy combining TST-15 and T-SPOT.TB seems to be the most suitable to identify, among household contacts, those

who will progress to active TB. These results underscore the importance of a field-based approach to defining a cost-effective strategy for improving management of high-risk populations by targeting beneficiaries of TB preventive treatment.

## EP12-1113-16 Maximising TB preventive therapy intervention coverage through context-adapted innovative strategies - lessons from India

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**Background and challenges to implementation:** Under the guidance of the National TB Program, FIND, through the Joint Effort for Elimination of TB (JEET), has been supporting 22 district across 4 states of India for TB preventive therapy (TPT) among household contacts (HHCs) of pulmonary TB patients since September'21.

Challenges during the implementation included non-availability of all HHCs of a family at households during screening visits, HHCs not willing to travel to health facilities for undergoing medical evaluation, difficulty in monitoring daily intake of TPT (6H regimen for 6 months) by HHCs, and inability to cover hard to reach geographies to provide TPT services.

**Intervention or response:** From April 2022, the project introduced tele/video consultation through which field staff were able to conduct screening for TB and Medical Evaluation of HHCs by medical officers for TPT initiation was strengthened through tele/video consultation.

To improve coverage of TPT services in hard-to-reach areas, the project team liaised with the general health system and utilized special ambulance service named "104 mobile medical unit" equipped with a medical officer, drugs, and basic diagnostics.

To improve monitoring of treatment adherence, drugs for a period of one month were segregated and provided in separate zip-lock pouches for each HHC with proper identification.



**Results/Impact:** From April'22-Dec'22, the project identified 147,856 HHCs of 48,405 notified index pulmonary TB cases. Of the 115,928 (78%) HHCs screened, 92,260 underwent medical evaluation and were provided TPT. During treatment, 611 HHCs underwent consultation for adverse events of which 393 completed the treatment after medical evaluation. Among HHCs who initiated their treatment between Apr-Jun'22, more than 90% completed their 6 month treatment successfully while this was 81% for April'22.

**Conclusions:** Innovative context adapted strategies helped in mitigating the challenges faced in the initial stage of the project and expanded the coverage and completion of TB preventive treatment (TPT).

### EP12-1114-16 TB treatment outcomes in migrants: preliminary results from a European multicentric, retrospective cohort study

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**Background:** More than two-thirds of tuberculosis (TB) cases in low-incidence countries are comprised of migrants, yet evidence indicates they have poorer treatment outcomes.

**Design/Methods:** Using a retrospective cohort study design, we investigate TB presentation, assess management strategies and evaluate patient outcomes. This multicentric, European wide study spearheaded by TBNet collected both patient and centre data from 2013-2018 utilising two data collection tools. STATA software was used to perform descriptive statistics and logistic regressions.

**Results:** Nine centres across Europe including 1764 patients participated. The majority of centres offered outpatient facilities with an affiliated ward.

Overall, 70.9% of patients were migrants, 80.3% (n=1417) had active TB, and 19.7% (n=347) had latent tuberculosis infection (LTBI). The median age was 34 years (range 0–92), and 63.6% were male. The mean days seen in the centre were higher among non-migrants (t-test mean difference 95.2, 95% CI 34.6–155.7).

Migrants and non-migrants were treated for a similar length of time in months, mean 8.0 (95% CI 7.7–8.3) and 7.9 (95% CI 7.5–8.4). For LTBI, treatment completion was lower for migrants, 64.5% compared with 79.0%. For active TB, treatment outcomes tended to be higher amongst non-migrants, with migrants recording a higher loss to follow-up; 4.4% compared to 0.7% for microbiologically confirmed pulmonary TB.

Multivariable analyses found duration in country to have an influence on odds for loss to follow-up (OR 3.7 for duration in country <1 year, baseline >3 years, 95% CI 1.3–10.3).

**Conclusions:** Migrant patients made up the majority of TB cases in this study. Although the mean number of days seen in the centre was higher for non-migrants, treatment time was similar.

Nevertheless, migrants showed lower rates of treatment completion and higher rates of loss to follow-up. These findings echo existing evidence and indicate an increasing need to implement migrant sensitive strategies to improve patient outcomes.

### EP12-1115-16 Pretomanid Resistance Surveillance Program, 2020 to 2025 – an interim rEPort

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**Background:** The Pretomanid Resistance Surveillance Program (PAEGIS) was initiated to fulfill a post-marketing requirement established by the United States (US) Food and Drug Administration following the approval of pretomanid.

PAEGIS aims to monitor changes in *Mycobacterium tuberculosis* (MTB) susceptibility to pretomanid over a period of 5 years (01 July 2020 to 30 June 2025) in 7 countries – US, South Africa, Tajikistan, Ukraine, India, France, and Vietnam.

The abstract presents the interim results for Year 1 (01 July 2020 to 30 June 2021) and Year 2 (01 July 2021 to 30 June 2022).

**Design/Methods:** MTB isolates from Tajikistan and Ukraine were tested in the German National Reference Laboratory (NRL), Gauting. Isolates from other countries were tested in the respective NRLs. Isolates had to be resistant to, at least, rifampicin and isoniazid (i.e., multidrug-resistant, MDR) to be included in the study. Pretomanid minimum inhibitory concentrations (MIC) were determined in the BACTECT™ MIGHT 960, and MIC values >2 µg/mL were indicative of resistance (based on previous studies).

**Results:** As of June 2022, all countries had started pretomanid susceptibility testing, except France and Vietnam, and pretomanid MICs were available for 741 isolates, including 8 (from different countries) with MIC >2 µg/mL.

MIC data was available for both years from US, India, and South Africa. The pretomanid MIC distributions appeared very similar, suggesting that there had been no shift to higher MICs or increased resistance rates from Year 1 to Year 2. (Table 1.)

Additionally, there was no notable difference between MIC distributions stratified by overall resistance profile, i.e., MDR, pre-extensively drug-resistant (pre-XDR), or extensively drug-resistant (XDR).

Country	Year	n	MIC <sub>50</sub> (µg/ml)	MIC <sub>75</sub> (µg/ml)	MIC <sub>90</sub> (µg/ml)	MIC <sub>95</sub> (µg/ml)	Min (µg/ml)	Max (µg/ml)
India	1	122	0.125	0.25	0.5	0.5	0.06	1
	2	123	0.125	0.25	0.25	0.5	0.03	0.5
South Africa	1	98	0.25	1	1	2	0.06	2
	2	59	0.125	0.25	0.5	0.5	0.03	0.5
United States	1	59	0.25	1	2	2	0.06	2
	2	70	0.25	1	1	4	0.06	4
Tajikistan	1	102	0.125	0.25	0.25	0.25	0.06	0.25
Ukraine	1	100	0.25	0.25	0.5	0.5	0.06	0.5
Total	Year 1	481	0.25	0.5	1	2	0.06	2
	Year 2	252	0.125	0.25	0.5	1	0.03	4

Abbreviation: Pa MIC, Pretomanid Minimum Inhibitory Concentration  
n=number of isolates; Year 1=01 July 2020 to 30 June 2021; Year 2=01 July 2021 to 30 June 2022

Table 1. Summary statistics of Pretomanid minimum inhibitory concentration (Pa MIC) data sets.

**Conclusions:** A pretomanid resistance surveillance program has been set up, involving 7 countries where BPAL has been/is being introduced. The interim results reported here suggest pre-existing pretomanid resistance rates/MIC levels remained similar from Year 1 to Year 2.

## EP12-1116-16 The impact of active contact screening in Afghanistan, 2013-2022

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**Background:** National TB Program (NTP) in Afghanistan introduced household contact screening of all bacteriologically confirmed index TB cases in 2013 with the support of partners and mostly the approach was a passive method.

In 2015 an active contact screening method was implemented by the USAID-funded Challenge TB project and Global Fund till 2018, that active screening approach covered continued till 2022 with the support of GF in 34 provinces.

**Design/Methods:** An active contact investigating approach was piloted in Kabul in 2014 with the support of partners in 2025 the approach expanded to 5 big provinces and in 20218 expanded to all 34 provinces with the support of the Global fund. Health care staff conducted active household visits and screened family members and identify children of INH preventive therapy.

**Results:** In 2013, 31622 all TB cases were identified (14277 were bacteriologic confirmed TB cases) and 48122 (56%) households were registered (the estimated household for screening was 85662). 8274 households were found as presumptive TB cases (17% of HH registered), 788 (9.5%) all from of TB cases identified and started the treatment.

In 2013, 10620 children under the age of five registered and IPT started for 7690 (72%) 4924 children completed IPT which was 46%.

In 2022, the NPT notified 51668 of all form TB cases and 26225 were bacteriologically confirmed TB cases. 216462 households registered in 873 reporting health facilities of Afghanistan. 41754 (19%) were presumptive TB cases of then 7299 (11%) all from of TB cases identified, 36241 children under the age 5 registered and IPT started for 32250 (89%) and 24092 (75%) completed IPT. The yield of TB case notifications is 3372 in 100,000 household contacts.

**Conclusions:** Active household contact screening had a remarkable contribution to TB case detection and the provision of IPT for children in Afghanistan.

## EP13 Access to quality TB care

### EP13-1117-16 Continuous quality improvement: Applying the Institute for Healthcare Improvement model to increase TB screening in a rural health unit outpatient dEPartment in Nueva Ecija, the Philippines

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**Background and challenges to implementation:** In 2021, the Philippines had an estimated TB incidence of 741,000 cases, of whom only 43% were notified. Ongoing policy actions to curtail the transmission of COVID-19 had widespread economic, societal, and health system impacts.

A 37% drop in notifications in 2020 (263,300 cases versus 419,102 cases in 2019) reflects the effect of the COVID-19 pandemic on the continuity of TB services.

**Intervention or response:** In collaboration with the Philippines Department of Health's National TB Program and the Pantabangan, Nueva Ecija Municipal Health Office, USAID's Platforms for Sustainable Detection, Care and Treatment Activity applied the Institute for Healthcare Improvement (IHI) Model to accelerate TB screening among outpatient visitors in the Pantabangan Rural Health Unit (RHU).

**Results/Impact:** Implemented from October to December 2022, the IHI model standardized the screen-all approach to find more TB cases using the TB Self-assessment Form (SAF) and continuous staff mentoring on using data to drive improvement. Program staff conducted leadership engagement, capacity-building, and onsite mentoring visits.

Additionally, TB Platforms established a Standard Evaluation System (SES) to monitor performance indicator accomplishments, track monthly and weekly progress, and guide process adjustments as needed. The intervention led to a 90% increase in the number of OPD patients screened for TB using SAF (1,134 vs. 11; 91% from a 0-1% baseline). The number of notified TB cases also increased by 31% (16 vs 12).

**Conclusions:** Applying the IHI model as a CQI approach has led to progressive, incremental improvements in TB service processes and intensified efforts to find missing TB cases. Increased funding is essential for sustainable TB services.

With continued implementation, CQI can sustain the increasing trend in TB screening among outpatient visitors and help healthcare facilities become more efficient and patient-centered.

### EP13-1118-16 House-to-house screening and community outreach approaches for TB active case-finding in Southwest, Nigeria: A systematic assessment of the USAID TB LON 3 project

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**Background and challenges to implementation:** Nigeria's National Tuberculosis and Leprosy Control Program heavily relies on passive case finding. This method only detects patients with tuberculosis (TB) who present with symptoms at health institutions. Nevertheless, community active case finding (ACF) programs like house-to-house screenings are crucial for locating undiagnosed people who have not visited health facilities. The USAID TB Local Organizations Network, Region 3 (USAID TB-LON 3) project implements community ACF interventions utilizing house-to-house screening and outreaches in Southwest Nigeria.

**Intervention or response:** Predictive geo-spatial hotspot mapping analytics using the Epidemic Control Platform (EPCON) platform was deployed to predict TB hotspots in >8,000 population clusters across 1,214 wards in 103 local government areas. Portable digital X-ray devices in Oyo and Osun States are being used optimally to conduct mass radiological screening for TB in hotspots during outreaches and the optimized collaboration with Lagos State Global Fund-supported X-rays, both fixed and mobile vans, which consistently add value to screening in community outreaches.

**Results/Impact:** In all the community ACF activities conducted between October 2021, to September 2022, 1,026,765 out of 1,036,473 eligible clients were screened, giving a screening rate of 99.0% with 127,714 (12.0%) people presumed to have TB. Among these, 124,978 (98.0%) were tested, and 8,534 (7.05%) active TB cases were diagnosed. Out of these 8,534 active TB cases diagnosed, 7,864 (92.0%) were placed on treatment. The number needed to screen (NNS) was 121, and the number needed to test (NNT) was 14. The monthly TB case-finding target of 540 for the community ACF intervention was surpassed across all reporting months.



**Conclusions:** Targeted active case-finding programs are effective in identifying active TB disease within the community. More efforts will be put into this in the next project year.

### EP13-1119-16 Increased facility TB screening coverage and TB case notification in Kisumu County, Kenya

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**Background and challenges to implementation:** Program Quality and Efficiency (PQE) Active Case Finding is a crucial aspect of healthcare delivery, especially in Kenya, where tuberculosis (TB) is prevalent. Despite concerted efforts to combat TB, the country still struggles to diagnose all cases, with 40% of TB cases being missed. In Kisumu County, efforts have been made to address challenges of diagnosing and treating TB, which has led to the implementation of several PQE strategies in 14 high volume facilities.

**Intervention or response:** Our Lady of Perpetual Support (OLPS) partnered with AMREF GF TB grant to implement PQE interventions in 14 health facilities in Kisumu County. The main objective of the program was to diagnose all clients visiting the health facilities with TB through enhanced TB screening and evaluation coverage.

PQE interventions were initiated in Kisumu in October 2022. Healthcare workers (HCWs) were trained on PQE by the National Leprosy and Tuberculosis Program. Tools were also provided by the Ministry of Health and OLPS to support the interventions. Monthly PQE data review, mentorship, and on-the-job training meetings were conducted by OLPS and the MOH.

**Results/Impact:** The results of the interventions were encouraging, in Katito and Nyakach Hospitals, a total of 5071 clients were screened for TB, representing a 59% increase from the previous quarter. Additionally, 174 patients were identified with presumptive TB, an increase from the 34 patients identified in the previous period representing 81% increment. However, the index of suspicion remained at 2%. Furthermore, 14 patients were diagnosed with bacteriologically confirmed TB, a significant increase from the previous quarter, where case detection was at zero.

**Conclusions:** PQE strategies are essential in improving healthcare delivery, especially in resource-limited settings. The success of the interventions in Katito and Nyakach sub county hospitals provides a blueprint for other healthcare facilities in Kenya to adopt similar approaches in addressing challenges of TB diagnosis and treatment.

### EP13-1120-16 Decentralizing tuberculosis services to improve tuberculosis case notification at lower health facilities in Uganda: an experience of the Uganda Protestant Medical Bureau

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**Background and challenges to implementation:** The USAID Local Services Delivery for HIV/AIDS Activity (USAID/LSDA) project supports delivery of TB and HIV services in the 188 private not for profit health facilities in Uganda. In October-December 2020 quarter, majority of Tuberculosis (TB) patients were notified by Hospitals which are tertiary health facilities of care and only 14% notified by Health Centre II's (HC IIs). A review of gaps to TB case notification identified missed opportunities for TB diagnosis at the lower health facilities (HC IIs). This was mainly due to capacity gaps in active case finding activities for TB. The LSDA project set to build capacity of health workers in TB management across the 6-supported USAID regions in the subsequent quarter.

**Intervention or response:** Training in TB case management using TB desk job aides was done at all 160 Health facilities, followed by quarterly mentorships for trained facilities. Quarterly regional performance reviews meetings were conducted to review performance and address performance gaps.

**Results/Impact:** The proportion of TB notification at lower Health facilities (HC II) significantly increased from 14% (155/1071) in October-December 2020 to 37% (650/1716) in October-December 2021 with an observed gradual proportionate decrease in TB cases notified at Hospitals from 38% (410/1071) to 26% (561/2116) in respective periods. The proportion of TB cases at HC IIs remained above baseline 14% raising to 28% (479/1713) in October-December 2022 with similar reduction in notification at Hospital level to 34% (557/1713) in October-December 2022.



Figure. TB case notification per Health Facility Level.

**Conclusions:** Decentralizing TB services to lower-level health facilities presents a meticulous approach for addressing missed opportunities for TB case finding in high burden TB countries such as Uganda.

### EP13-1121-16 Expanding TB screening to truck drivers as an entry point to their at-risk social contacts through a peer-led model in Mombasa, Kenya

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**Background and challenges to implementation:** The 2016 Kenya Prevalence Survey showed that 67% of people with Tuberculosis (TB) signs and symptoms in the community did not seek care. This underscored the need to identify and reach underserved at risk populations through tailored interventions.

Long-distance truck drivers are at increased risk of acquiring HIV and potentially TB due to long periods away from home and social norms associated with truck-stop settings. However, they and their social contacts along transport corridors had not been prioritized for targeted community TB screening initiatives.

**Intervention or response:** Through Global Fund support, Amref in collaboration with the National TB Program, supported NorthStar Alliance to implement an intervention to find people with TB in Mombasa, where the Northern Corridor begins, from August 2019 to date. It targeted truck drivers, People Who Inject Drugs (PWID), Men who have Sex with Men (MSM), Female Sex Workers (FSW), and other corridor communities such as traders and public transport operators.

Peers identified among the populations were sensitized on TB and conducted health education and TB screening for respective populations. Periodic day and night-time outreaches were conducted to truck companies and key population hotspots.

Linkage to diagnosis was through spot sample referral or direct referrals.

**Results/Impact:** By February 2023, a total of 145,669 people had been screened for TB and 30,972(21%) found symptomatic. Of the 15,210(49%) referred after further inquiry, 10,636(70%) were investigated, 957(9%) diagnosed with TB (95% bacteriologically), and 946(99%) initiated on treatment.

Other corridor communities contributed 553(58%) of people diagnosed, truck drivers 143(15%), PWID 130(14%), FSW 93(10%) and MSM 38(4%). Escorted referrals improved proportion of presumptive investigated from 1% (May 2021) to current 29%.

**Conclusions:** The innovation was effective in finding people with TB among key and vulnerable populations for HIV. Sample and escorted referrals significantly in-

creased the presumptive investigated. Plans to mainstream the intervention into regular programming are underway.

### EP13-1122-16 Pre-treatment loss to follow-up in adults with pulmonary TB in Western Kenya: Prevalence and patient-associated factors

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**Background:** In high tuberculosis (TB)-burden countries, pre-treatment loss to follow-up (PTLFU) contributes to patient losses in the TB care cascade. PTLFU rates vary from 4% to 38% worldwide, with the highest rates observed in Africa. Data on PTLFU in Kenya are limited.

We aimed to ascertain the prevalence of PTLFU and associated patient factors in adults with pulmonary TB in Western Kenya.

**Design/Methods:** From the laboratory register of the county referral hospital in Western Kenya, we retrospectively reviewed data for all patients who were bacteriologically confirmed with pulmonary TB from January 2018 to December 2021.

We then traced patients at the treatment register for at least three months from the date of diagnosis to establish the date of treatment initiation.

We defined PTLFU as failure to initiate treatment within 14 days of diagnosis. We used multivariable logistic regression modeling to identify patient factors associated with PTLFU

**Results:** Preliminary results: Of 501 with bacteriologically confirmed TB, 166 (33.1%) were initiated on treatment, 133 (26.5%) were referred for treatment in other health facilities outside the study site and 202 (40.3%) were not initiated on treatment within 14 days (PTLFU).

Not having the address recorded was associated with PTLFU compared to having the address recorded (aOR 15.05 (95% CI 1.28-176.67), p=0.031).

Having only the address recorded (aOR 30.83(95% CI 17.15-55.42), p=<0.001, and only the telephone number recorded (aOR 19.74 (95%CI 3.44-113.35), p=0.001, were associated with PTLFU compared to having both the address and telephone number recorded.

Age, sex, human immunodeficiency virus status, history of TB treatment, and category of residence (urban versus rural) were other factors investigated but were not associated with PTLFU.

**Conclusions:** PTLTFU contributes markedly to patient losses in TB in Western Kenya. To follow up with patients and reduce attrition before treatment begins, proper documentation of the patients' contact information will be essential.

### EP13-1123-16 Improving treatment initiation among people with drug-resistant TB in Bihar, India – a peer-led, guided and personalised support model

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**Background and challenges to implementation:** Bihar accounts for 6% of the total DR-TB burden in India. For people with DRTB (PwDRTB), the pathway between diagnosis and treatment initiation is complex. They must undergo comprehensive pre-treatment evaluation (PTE), a multistep process over several days, involving multiple investigations at different facilities. This pathway is rarely explained to PwDRTB and difficulties are compounded by use of multiple treatment regimens, leading to higher pre-treatment lost to follow-up (PTLTFU). In Bihar, PTLTFU was 14% among people with MDR/RR-TB and 10% among people with INH-mono-resistant TB in 2022.

**Intervention or response:** A peer-led, guided, and personalised support model was designed and implemented in 8 districts which contribute 50% of all people with DR-TB in Bihar. 25 TB survivors were trained as TB Champions (TBCs) and involved to provide comprehensive care and support for all PwDRTB. TBCs supported PwDRTB through PTE process after diagnosis, accompanying PwDRTB through different tests and procedures to ensure timely treatment initiation. Based on needs assessment and to reduce out-of-pocket expenditure, eligible PwDRTB were supported with travel costs, costs of PTE tests and additional nutritional support. TBCs provided treatment literacy, peer counselling, and psychosocial support.

**Results/Impact:** Between January and December 2022, the intervention supported 1,625 (42% females) people diagnosed with RR-TB. Overall, 91% (n=1483) were initiated on DR-TB treatment. When compared with Bihar based on India TB Report 2023, the implementation districts have performed better with regards to treatment initiation.

**Conclusions:** TB Champions play a crucial role in providing comprehensive DR-TB care. They help in navigating the health system thereby reducing the PTLTFU and reducing the delay in treatment initiation among PwDRTB. The greatest problem plaguing TB treatment is treatment compliance, which is due to ignorance, feeling cured halfway, or in many cases due to labyrinth of tests, consultations and admissions. There could be no influencers better than the TB survivors for PwDRTB.

### EP13-1124-16 Critical route to improve diagnosis of possible TB cases in a rural area of the highlands, Chiapas, Mexico

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**Background and challenges to implementation:** Compañeros en Salud (CES) works in Chiapas, the Mexican state with the highest TB burden in (2). In an area with 77,943 inhabitants (1), between 2014 to 2019, 89 patients were diagnosed with TB, mostly through passive case finding and smear microscopy. Contacts were not screened.

The COVID-19 pandemic further hampered TB control efforts. To address this gap, in collaboration with the Ministry of Health (MOH) and rural health clinics, CES assessed knowledge about TB guidance and developed an intervention.

**Intervention or response:** Teams in 10 clinics were interviewed about their knowledge of current guidance for screening, diagnosis, treatment, follow-up, and about barriers to quality care.

We developed context-specific strategies for case detection and identification of contacts eligible for preventive therapy. In accordance with guidance from WHO and the Zero-TB Initiative, CES established mechanisms that simplified data entry and sharing of required information to expedite screening for TB and trained health-care workers.

The strategy included: organizing notification and sample transport, scheduling xray, and distribution of medicines. Contact screening and prophylaxis were performed in the community.

For patients who were discharged from the local hospital with TB symptoms or confirmed diagnosis, CES established follow-up and facilitated initiation of treatment. Nutritional support and PPE were provided.

**Results/Impact:** From 2021 to 2022, 122 patients started TB treatment: 87 were diagnosed by X-ray and the remainder by smear microscopy. 20 were initiated on treatment upon discharge from the hospital. Through contact screening, we identified 24 pediatric cases of active TB and 59 contacts requiring preventive therapy.

Diagnosis of active disease increased from an average of 14.8 /year before the intervention to 61 /year afterwards.

**Conclusions:** In a vulnerable area, detection of active TB and TB infection can be increased through active case finding, increased communication, and accompaniment of health care workers and patients.

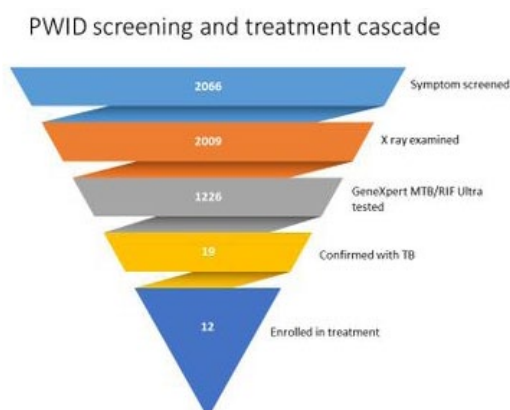
### EP13-1125-16 Active TB case-finding among people who inject drugs in the country of Georgia

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**Background and challenges to implementation:** Georgia had an estimated Tuberculosis (TB) incidence of ~64 per 100,000 population, and the case notification rate was 42 per 100,000 population in 2021. To bridge the gap between TB incidence and notification, the country made effort to expand the systematic screening among high-risk population sub-groups.

**Intervention or response:** ScreenTB tool was used to prioritize high-risk groups and identify the optimal screening algorithms. Household contacts, People Living with HIV (PLHIV) and People who Inject Drugs (PWID) were given the top priority. There is well established process for systematic screening of contacts and PLHIV, an innovative approach was used to cover PWID.

Mobile unit (van) equipped with Computer Aided detection (CAD)-enhanced X-Ray device and GeneXpert system was used for active case finding among beneficiaries of the selected Harm Reduction Network and Opioid Substitution Therapy (OST) sites in Tbilisi, Georgia. The algorithm included symptom screening and Chest X-Ray (CXR) of all beneficiaries. CAD4TB thresholds of  $\geq 60$  scores were used. Xpert MTB/RIF Ultra testing was provided for those with productive cough.



**Results/Impact:** In total, 2066 beneficiaries were symptom screened, 2009 had CXR and 1226 were tested with Xpert MTB/RIF Ultra. Active TB was bacteriologically confirmed in 19 cases, including 3 with Rifampicin resistant forms.

This yield significantly exceeded the national estimated incidence and outcomes of similar screening among other risk groups such as miners, Internally Displace People (IDP) or those living in neighborhoods with higher TB prevalence rates.

All presumptive and/or confirmed TB cases were referred to specialized TB service for further diagnostics and treatment.

**Conclusions:** Using a mobile unit to reach OST and Harm Reduction Network beneficiaries and combination of TB symptoms, CXR and GeneXpert testing as the initial screening tests represent an effective approach for detecting missing cases among PWID.

### EP13-1126-16 Improved systematic TB screening among health facility attendees, the role of TB volunteers in Global Fund-supported 56 district councils of Tanzania

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**Background and challenges to implementation:** Tanzania is still among the countries with high Tuberculosis (TB) burden with a 208/100,000 incident rate. About 46,000 new patients with TB are missed in a year causing continuous infection in the community. Underlying barriers include a sub-optimal screening of TB symptoms, and human resources in the Health Service delivery facilities shortage is at 53% (2020/2021).

The peripheral regions still face a critical shortage of Human Resources among the major barriers to case detection in facilities and communities.

MDH assesses and evaluates the engagement of health facility TB volunteers (HFTBV) in improving TB case detection across facilities departments.

**Intervention or response:** From July to December 2022 innovatively MDH introduced facility-based intervention whereby 283 TB volunteers identified, trained, and deployed in 192 TB Quality Improved health facilities in 56 district councils. HFTBVs were tasked to reach out to persons attending clinics at the facilities for outpatient services and administer health education and systematic TB screening with five questions to ascertain the presence of symptoms suggestive of TB disease.

Persons found to have suggestive TB symptoms were linked to clinicians for further TB screening and laboratory/radiological testing and TB investigations.

**Results/Impact:** Baseline, quarter January-March 2022, In 192 health facilities, were unable to capture persons who were screened for TB but manage to be documented 10,472 presumptive TB cases were identified and documented of which 10,093 were investigated for TB, and 1,552 TB cases were diagnosed, By the end of the implementation period July - December 2022 there were 742,731 received health education and screened for TB, 73,174 presumptive TB were identified and investigated resulted to 3,194 TB cases diagnosed, Systematic TB screening cascade Table 1.

56 Councils	# HFTBV	# QI Health facilities	# Screened clients documented	# Pre-sumptive TB	# Investigated presumptive TB	# Notified TB cases	# bacteriological confirmed (%)	# Started TB medication (%)
Baseline April - June 2022	NA	NA	NA	28,944	25,546	927	362 (39%)	925 (99%)
July - Sept 2022	283	192	308,059	37,210	23,030	1,723	1,245 (72%)	1,723 (100%)
Oct-Dec 2022	283	192	434,672	35,964	22,984	1,471	1,438 (98%)	1,471 (100%)

Table 1.

**Conclusions:** Engagement of HFTBV improved systematic TB screening, intensified TB case finding and detection among health facility attendees.

## EP14 TB Infection and TPT

### EP14-1127-16 Non-inferior completion rate and safety of the 1HP regimen compared to the 3HP regimen for the treatment of latent TB infection in a non-HIV population

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**Background:** Effective treatment for latent tuberculosis (LTBI) is an important element for the elimination of tuberculosis (TB). The 3HP regimen—weekly rifampentine plus isoniazid for 12 doses—improves the completion rate of LTBI treatment, but unpredictable systemic drug reactions, particularly flu-like syndrome is the major cause for early treatment termination. The new 1HP regimen—daily rifampentine plus isoniazid for 28 days—first introduced in Brief TB trial demonstrated low toxicity and high completion rate in HIV-infected populations. However, its safety in non-HIV population remains unclear.

**Design/Methods:** This randomised, multicentre trial compared the completion rate, clinical manifestations of systemic drug reactions (SDRs), and discussed the association of SDRs with the offending plasma drug with their metabolites levels of 1HP and 3HP regimens in  $\geq 13$ -year-old non-HIV subjects with LTBI between September 2019 and December 2022 ([ClinicalTrials.gov: NCT04094012](https://clinicaltrials.gov/ct2/show/study/NCT04094012)).

**Results:** Up to December 30<sup>th</sup>, 2022, a total of 481 eligible LTBI cases were screened, and 206 and 197 individuals were randomised into 1HP and 3HP groups for final analysis, respectively. In overall, 155 (82.4%) and 133 (85.0%) subjects, respectively, completed their preventive therapy ( $p = 0.507$ ). A total of 37 (9.2%) participants experienced SDRs, including 19 in 1HP group and 18 in 3HP group ( $p = 0.976$ ), with manifested predominant of urticaria in 1HP group (68.4%) and flu-like syndrome in 3HP group (83.3%). In 1HP group, the 14<sup>th</sup> doses of 2 hour post treatment (C2) RPT level was associated with the development of urticaria (median: 30.09 vs. 21.19  $\mu\text{g/mL}$ ;  $p = 0.032$ ).

**Conclusions:** We herein reported the similar high completion rate and SDR risk in 1HP and 3HP groups, while the predominant manifestation of SDR under 1HP was urticaria rather than flu-like symptoms and most were tolerable to complete treatment. The occurrence of SDRs under 1HP is likely to be associated with the C2 RPT level in blood.

### EP14-1128-16 Lessons learnt from 3HP pilot facilities supported by PEPFAR South Africa

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**Background and challenges to implementation:** Tuberculosis (TB) preventive treatment (TPT) is essential to reducing TB morbidity and mortality in people living with human immunodeficiency virus (PLHIV). In May 2021, PLHIV in South Africa were introduced to 3-month weekly isoniazid-rifampentine (3HP) for TB prevention. We aimed to review 3HP uptake in selected pilot facilities supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) to identify practices that will inform 3HP country scale-up.

**Intervention or response:** We used a cross-sectional study design to analyze 3HP initiations and completions in PLHIV, reported through routine program data from

May 2021 to December 2022 in 69 pilot facilities in OR Tambo, eThekweni and Ekurhuleni districts in South Africa. The selected pilot facilities receive intensive quality-improvement support on HIV prevention, care and treatment.

**Results/Impact:** A total of 13,622 (42%) of 32,569 potentially eligible patients initiated 3HP; of whom 13,391/13,622 (98%, 95% Confidence Interval (CI):97%–98%) were already on antiretroviral therapy (ART), virally suppressed, and had already been switched from Tenofovir-Emtricitabine-Efavirenz (TEE) to Tenofovir-Lamivudine-Dolutegravir (TLD), 9,272/13,622 (68%, CI:67%–69%) were female, and 5,776/13,622 (42%, CI:41%–43%) were in Differentiated Service Delivery models.

Overall 3HP completion rate was 78% (7,259/9,293; CI:77%–79%).

Completion was significantly lower in females 4,898/6,458 (75%) than males 2,361/2,835 (83%) (odds ratio (OR) 0.63, CI:0.56–0.71, p-value=0.00).

Completion was also significantly lower in PLHIV already on ART 7,082/9,095 (78%) than in PLHIV new on ART who were started on TEE 177/198 (89%) (OR 0.42, CI:0.25–0.66, p-value<0.001).

**Conclusions:** 3HP scale-up mainly occurred among PLHIV already switched to TLD, which suggests that sustained TLD transition efforts will increase 3HP uptake. 3HP completion differed between males and females, and between PLHIV already on ART and those new on ART.

### EP14-1129-16 Using differentiated service delivery models to increase uptake of TB preventive therapy among 5 years+ contacts of pulmonary TB patients in Eastern Central Region, Uganda

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**Background and challenges to implementation:** About one fourth of the world's population is estimated to be infected with *M. tuberculosis*. The risk of TB disease after infection depends on several factors. Household contacts of patients with pulmonary TB (PTB) are at risk of TB infection and subsequent active disease. TPT decreases progression to active TB diseases.

While TPT access is gradually expanding globally, access among persons at risk remains low. In the EC region, TPT uptake among 5+years contacts of PTB patients was as low as 4% following the WHO TPT guidelines to be expanded to all contacts regardless of HIV

status or age. Some factors attributed to the low uptake in this age group include; poor/no contact tracing, slow adaptation of the national guidelines, stock outs of TPT and prolonged duration of TPT among others.

**Intervention or response:** The USAID Local Partner Health Services (LPHS-EC) project implemented by Makerere Joint AIDS Program, supported health facilities in the region to implement TPT among 5 years + contacts using different service delivery models, where some facilities used community service delivery to conduct contact tracing and distribution of TPT, and some facilities maintained the facility-based contact tracing and distribution of TPT.

We analyzed programmatic data from 2020 to track progress in scaling up TPT among 5 years+ contacts using differentiated service delivery models in EC region.

**Results/Impact:** In 2020, 6.4% 5 years + contacts accessed TPT through community DSD model with 2.9% accessing through facility-based DSD model, average of 3082/65190 (4.7%). In 2021, 8.6% accessed TPT through community DSD model, 5.5% through facility-based, average 8739/125138 (7%). In 2022, 71% 5 years + contacts received TPT through community DSD, 22% were covered through facility-based model with average of 104480/227205 (46%).

**Conclusions:** There is better coverage of TPT among 5 years + contacts using the community-based DSD models compared to facility-based delivery models.

### EP14-1130-16 Leveraging short-course regimen to improve TB preventive therapy uptake at Nsambya Hospital, Uganda

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**Background and challenges to implementation:** Tuberculosis (TB) preventive treatment (TPT) reduces TB morbidity and mortality among people living with HIV (PLHIV). Despite its proven efficacy, TPT uptake was low through April 2022 across facilities supported by the Uganda Episcopal Conference (UEC) through funding from the President's Emergency Plan for AIDS Relief (PEPFAR).

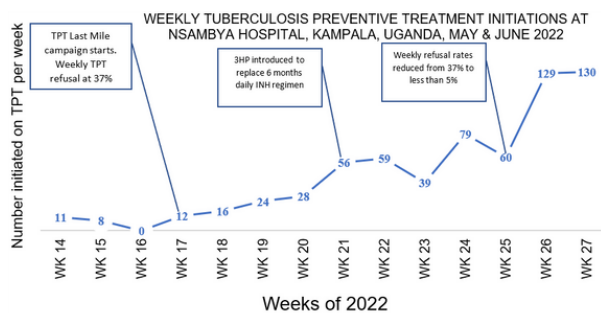
We share experiences of improved TPT uptake at Nsambya Hospital, the largest supported facility, after introduction of the short-course TPT regimen.

**Intervention or response:** UEC, in collaboration with health workers at Nsambya Hospital, implemented the national Ministry of Health "TPT Last Mile" campaign during May and June 2022 to close TPT enrolment gaps among PLHIV. From Week 17 of 2022, the TPT Last Mile package included continuing medical education,

client health education, noting charts of TPT-eligible clients each morning, direct TPT dispensation from clinicians, community delivery, and daily review of initiation and refusal data. From Week 21, a shorter TPT regimen, three months of weekly doses of isoniazid and rifampentine (3HP), was introduced to substitute the six-month isoniazid regimen. We used routine facility registers to determine weekly TPT initiations and refusal rate.

**Results/Impact:** Chart reviews identified 1,560 (19%) TPT-eligible of 8,204 total clients. Weekly TPT uptake increased 2.3 times in the first three weeks of the TPT Last Mile campaign from 12 (Week 17) to 28 (Week 20) initiations, and an additional 4.6 times after introduction of the 3HP regimen (130 in Week 27).

TPT refusal decreased from 36% (40 of 110 eligible; Week 17) to 4.4% (3/68; Week 25). Some weeks had few eligible clients due to multi-month antiretroviral therapy dispensation; this was addressed through community TPT delivery or by calling clients to the facility.



**Conclusions:** Client willingness to initiate TPT increased after introduction of the shorter 3HP regimen. This might improve TPT uptake and reduce TB morbidity and mortality among PLHIV.

## EP14-1131-16 Shorter TB preventive therapy among children living with HIV and child household contacts of pulmonary TB patients: a 3HP demonstration project in Pune, India

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**Background:** WHO guidelines recommend Isoniazid (H) and Rifampentine (P) once weekly for three months (3HP) as tuberculosis (TB) preventive therapy (TPT) among children (>2years). As India's national TB elimination program plans to roll out this TPT regimen, understanding feasibility and describing the adverse drug events among children in programmatic settings is critical for its widespread implementation.

Here, we aim to present the findings of a targeted scale up of 3HP among children living with HIV (CLHIV), and child household contacts (>2 to < 6 years) of pulmonary TB patients (CHHC).

**Design/Methods:** Weekly dosages of 3HP were given for three months to eligible CLHIV and CHHC participants at antiretroviral therapy (ART) and TB clinics of a public tertiary care hospital in Pune, India, between December 2021 and July 2022. All participants were followed monthly for 3 months, at 6 and 12 months.

**Results:** Of 99 children (35 CLHIV and 64 CHHC) screened, 92 children were initiated on 3HP (32 CLHIV and 60 CHHC) after ruling out active TB disease, five were not willing to participate and two were ineligible. The median age of CLHIV was 14 (IQR 10.5-15.5) years, 21 (65.6%) were males, all were ART stable. Forty (67%) CHHC were >2 and <5 years and 28 (47%) males. Of 32 CLHIV, 31 (97%) completed 3HP, none were discontinued 3HP due to adverse events (AE). Of 60 CHHC, 56 (93%) completed full course, and none discontinued due to AEs.

None of the child participants developed TB during initial six months of 3HP and 31(34%) who completed 12 month follow up were also TB free. High adherence (95.6%) to 3HP TPT regimen was observed among Children.

**Conclusions:** Our study provides evidence on its acceptability and feasibility for the planned nationwide roll-out of 3HP with high adherence and no adverse events among children.

## EP14-1132-16 Improved TB preventive treatment outcome using short regimens in a person-centred approach among TB household contacts in Yogyakarta, Indonesia

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**Background and challenges to implementation:** The end TB strategy highlights the importance of tuberculosis preventive treatment (TPT) in high-risk groups. Coverage of TPT in Indonesia is inadequate, and persons who start TPT often don't complete treatment. World Health Organization-recommended shorter TPT regimens are effective in reducing risk of active TB with higher completion rates than longer regimens. In 2020, Zero TB Yogyakarta (ZTBY) implemented person-centered contact investigation and shorter TPT regimen provision in collaboration with primary health care centers.

**Intervention or response:** Household contacts of persons with bacteriologically confirmed TB (index case) from January 2020 to August 2022 were assessed for eligibility for TPT and given a 3-month TPT regimen (3RH or 3HP). A dedicated nurse monitored contacts on TPT for treatment adherence and side effects every week in the first month and every two weeks in the next months. Contacts were also able to contact the ZTBY nurse by phone or ask for home visits at any point if they had any concerns.

Side effects were managed by referring people to the nearest health facility. Completion of TPT was defined as 80% intake of their regimen within 120 days since treatment was started.

**Results/Impact:** A total of 1016 contacts were eligible for TPT: 772 (78.8%) started short regimen TPT with 706 (91.5%) completing their TPT. Reporting any side effect was associated with non-completion of TPT in univariate analysis (OR 1.89 CI 1.17-3.16) and in multivariate analysis (aOR 3.59 C 1.80-7.29).

**Conclusions:** High rates of TPT uptake and completion can be achieved among household contacts through person-centered care and use of shorter regimens. Develop-

ment of any side effect is a risk for not completing TPT. Side effect monitoring and management while on TPT is vital for improving TPT completion.

## EP14-1133-16 Nationwide surveillance of emerging rifampicin resistance after implementation of short-course regimens for TB preventive therapy

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**Background and challenges to implementation:** The monitoring of rifampin resistance at both population and individual levels is crucial for implementation of short-course regimens for TB preventive therapy (SR-TPT) program.

**Intervention or response:** The results of drug susceptibility test (DST) testing on isolates were presented for both SR-TPT and control groups and the estimated rifampin resistance at population levels was calculated in reverse by confirming levels of rifampin resistance proportional to bacteriological confirmation. For contacts who developed TB after SR-TPT, M. tuberculosis isolates of paired index patients and contacts were compared with 10-loci MIRU-VNTR typing.

		IGRA(+) or TST(+)		Incidence Rate	MTBC	DST	RMP Resistance	The Estimated Persons of RMP Resistance <sup>a</sup>	
		n	n(%)					n	per 1000 <sup>a</sup>
Total	no LTBI treatment	31,545	107(63.4)	664(21.0)	653(20.7)	11(0.3)	11	0.35	0.134
	Enter LTBI treatment (3HP/HP FDC/4R)	21,289	92(0.4)	723(4)	713(3)	3(0.1)	3	0.14	
Controlling for age 0-12	no LTBI treatment	3,197	6(11.9)	21(6.6)	21(6.6)	3(0.9)	3	0.94	0.623 1.000
	Enter LTBI treatment (3HP/HP FDC/4R)	705	1(0.1)	1(1.4)	1(1.4)	0(0)	0	0.00	
13-17	no LTBI treatment	1,937	73(3.8)	38(19.6)	37(19.1)	0(0)	0	0.00	1.000
	Enter LTBI treatment (3HP/HP FDC/4R)	698	6(0.9)	5(7.2)	5(7.2)	0(0)	0	0.00	
18-29	no LTBI treatment	5,578	208(3.7)	97(17.2)	96(17.2)	3(0.5)	3	0.54	1.000
	Enter LTBI treatment (3HP/HP FDC/4R)	3,017	13(0.4)	7(2.3)	6(2.0)	0(0)	0	0.00	
30-64	no LTBI treatment	15,450	438(2.8)	283(18.3)	279(18.1)	2(0.1)	2	0.13	1.000
	Enter LTBI treatment (3HP/HP FDC/4R)	13,815	44(0.3)	34(2.5)	34(2.5)	3(0.2)	3	0.22	
65-79	no LTBI treatment	3,279	177(5.4)	120(36.6)	118(36.0)	1(0.3)	1	0.30	1.000
	Enter LTBI treatment (3HP/HP FDC/4R)	2,198	15(0.7)	13(5.9)	13(5.9)	0(0)	0	0.00	
>=80	no LTBI treatment	2,104	119(5.7)	105(49.9)	102(48.5)	2(1.0)	2	0.95	1.000
	Enter LTBI treatment (3HP/HP FDC/4R)	856	13(1.5)	12(1.4)	12(1.4)	0(0)	0	0.00	

LTBI: latent TB infection; IGRA: interferon gamma release assay; TST: tuberculin skin test; MTBC: M.tuberculosis; DST: drug susceptibility test; RMP: rifampin

Footnote:

\*: MTBC/TB

\*\* : DST/MTBC

\*\*\*: RMP resistance/DST

<sup>a</sup>: The Estimated Persons of RMP resistance = number of persons with positive culture for MTBC × proportion of DST results available for those with culture positive for MTBC × proportion of RMP resistance among those with DST result

\*\*\*\*: p-value for Fisher Exact Test and Cochran-Mantel-Haenszel statistic for stratification analysis

#: "per 1000" means the estimated persons of RMP resistance × 1000/ persons with LTBI (IGRA positive or TST positive)

**Results/Impact:** From April 2008 to December 2021, a total of 52,834 latent tuberculosis infected (LTBI) contacts whose index patients identified as no rifampin resistance were enrolled in our study and were followed until July 2022. Among them, 21,289 received SR-TPT



with a total of 44,706.9 person-year observation and the others did not receive any treatment (37,854 person-year). The estimated rate of rifampin resistance was 0.14 vs 0.35/1,000 ( $p=0.134$ ) at population levels for the SR-TPT group and the control group (Figure).

For 21,289 who received SR-TPT, 85 LTBI contacts developed TB during the study period and three out of 85 contacts (3.5%) developed new rifampin resistance clinically. One of the strains of resistance had the disputed mutation of H526N, matched with his index patient, implied not newly developed resistance. The other two strains were not matched with their index patients' strains and the two contacts developed diseases before commencement of TPT. The newly emerging rifampin resistance was 2.4% (2/85).

**Conclusions:** No significant difference in rifampin resistance was detected at population level after long-term observation. Since the background rifampin resistance rate among newly diagnosed TB patients was 0.6%, the emerging of rifampin resistance among SR-TPT is warranted to be monitored and evaluated periodically.

#### EP14-1134-16 Characteristics of TB preventive therapy uptake and completion among self-reported HIV-positive persons, the Malawi PHIA survey, 2020-2021

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**Background:** Despite the successful scale-up of tuberculosis preventive treatment (TPT) for people living with HIV in Malawi from 2017, monitoring and evaluation has been suboptimal. We utilized the Malawi Population-based HIV Impact Assessment (MPHIA) 2020-2021 survey data to understand TPT uptake and completion among self-reported HIV-positive (srHIV+) persons.

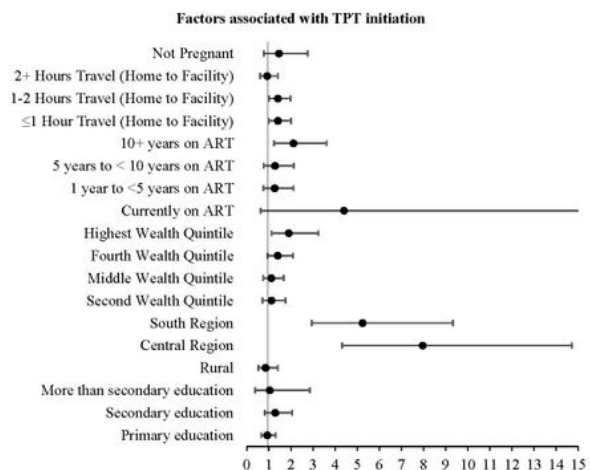
**Design/Methods:** We estimated the percentage of srHIV+ persons ever taken TPT, and among those who were currently on TPT, what percentage had completed >6 months of TPT. This cutoff was used because continuous isoniazid remained widely used at the time of the survey.

Bivariate and multivariable logistic regression were conducted to calculate odds ratios and 95% confidence intervals for factors associated with ever taken TPT. HIV

status, antiretroviral treatment (ART) and TPT history were self-reported. This analysis was weighted and accounted for survey design.

**Results:** Of the 26,519 MPHIA respondents, 7.5% (2,320) were srHIV+ and 98.5% (2,264) were on ART. Of those who reported HIV-positive, 38.8% (36.4-41.3) had ever taken TPT. TPT uptake was higher among those on ART, at 39.5% (37.0-41.9), compared to 19.1% (8.1-38.9) among those not on ART. Region, wealth quintile, and years on ART were significantly associated with TPT uptake.

The adjusted odds of ever taking TPT were 8.0 and 5.2 times as high in the Central and Southern regions, respectively, compared to the Northern region, 1.9 times higher among those in highest wealth quintile and 2.1 times higher for those on ART >10 years. Among srHIV+ persons who had ever taken TPT, 29.1% (25.4-33.2) were currently taking TPT. Of those currently taking TPT, 56.2% completed >6 months of TPT.



Note: The upper limit of "Currently on ART" exceeds the scale of the diagram

Figure 1. Forest plot of adjusted odds ratios with corresponding upper and lower 95% confidence limits of factors associated with ever taken TPT, Malawi Population-based HIV Impact Assessment (MPHIA) 2020 - 2021.

**Conclusions:** These results suggest low TPT uptake and >6 months completion rates among srHIV+ persons. Initiatives to create demand, strengthen adherence, and mitigate catastrophic costs, especially among those in the lower wealth quintiles and the Northern region would improve TPT uptake.

### EP14-1135-16 Incidence of *M. tuberculosis* infection among healthcare workers in HIV clinics in North Central Nigeria

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**Background:** Healthcare workers (HWs) in Low-Middle Income Countries (LMIC) are at increased risk of *Mycobacterium tuberculosis* infection considering the huge burden of TB, HIV, and the inadequate infection control practices in these settings. Nigeria, a LMIC has a 44.8% prevalence of IGRA positivity among HWs. However, the incidence of M tuberculosis infection is still uncertain.

We measure the incidence of M tuberculosis infection using serial testing with IGRA among HWs as a surrogate for assessing effectiveness of TB infection control and document the cumulative risk and incidence rate of M. tuberculosis infection among HWs in Nigeria.

**Design/Methods:** A prospective cohort study was conducted among HWs in facilities with dedicated HIV clinics in north-central Nigeria. HWs of varying cadre who voluntarily consented were enrolled over a period of 4 months, and TB exposure assessed using an interviewer-based questionnaire. All were screened with IGRA at baseline and only those with negative IGRA results at baseline were followed up with serial IGRA testing at month 6, 12 and 24.

**Results:** 641 HWs with negative IGRA results at baseline were followed up. The mean age of participants was 38.4years (SD9) with majority being women (65%). The cumulative risk of M. tuberculosis infection at 6, 12 and 24 months were 22%, 13% and 14% respectively.

However, the incidence rate at month 6, 12 and 24 time points were 44.4/100 person years (py), 39.6/100 py and 31.2/100 py respectively. When stratified by type of clinic (i.e. HIV clinic vs non HIV clinic), we found no statistical difference in the cumulative risk and incidence rate ( $p>0.05$ ).

**Conclusions:** There is a high incidence of M tuberculosis infection in HWs in Nigeria which remains fairly stable after 1 year. Working in HIV clinics is not associated with increased risk. There is urgent need for implementation of effective TB infection control in Nigeria.

### EP15 TB Treatment: Monitoring and evaluation of adverse events and outcome

#### EP15-1136-16 Emergence of extensively drug-resistant TB in an urban setting in Brazil

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**Background:** Brazil has a high tuberculosis (TB) and TB/HIV burden and is among the priority countries for TB prevention and care. Multidrug-resistant TB (MDR-TB) makes ending TB more challenging. WHO has recommended bedaquiline, delamanid, linezolid, and clofazimine to treat MDR-TB.

In Brazil, linezolid and clofazimine are in use since 2018 for treatment of pre-extensively drug-resistant (XDR) and XDR-TB, while bedaquiline and delamanid were only introduced in September 2021.

However, there is limited data on the emerging resistance to these drugs.

**Design/Methods:** A prospective study is being carried out at Adolfo Lutz Institute, the reference laboratory for the São Paulo state, Brazil, to determine *Mycobacterium tuberculosis* (MTB) phenotypic and genotypic resistance to medicines of the groups A, B, and C used for the treatment of MDR-TB, as recommended by WHO.

Since 2022, all MDR MTB isolates detected by the GenoType MTBDR<sub>plus</sub> in the diagnostic routine are being submitted to drug susceptibility testing (DST) by MGIT960 and to whole-genome sequencing (WGS) using the Illumina platform. FastQ sequences are being evaluated by TBProfiler and PhyResSE pipelines.

**Results:** In 2022, 78 MDR isolates (one per person) were identified, all of them underwent MGIT960, and 68 WGS. MGIT detected 12 (15.4%) pre-XDR (fluoroquinolone-resistant) and 4 (5.1%) XDR isolates: two were resistant to bedaquiline and clofazimine, one to delamanid and linezolid, and one to linezolid. All four isolates were recovered from persons under TB treatment and three underwent WGS.

Both TBProfiler and PhyResSE identified the rplC Cys154Arg mutation in the two linezolid-resistant isolates. No known mutations associated with delamanid, bedaquiline or clofazimine resistance were found.

**Conclusions:** This study highlights the importance of scaling up DST in order to identify MTB resistance early to ensure the prescription of adequate treatment, as well as to control the transmission of drug-resistant strains.

### EP15-1137-16 Cutaneous lesions of patients treated with BPaL in the Philippines under operational research

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**Background:** In 2020, WHO-recommended 6 months BPaL consisting of bedaquiline, pretomanid and linezolid under operational research (OR) for fluoroquinolone-resistant, intolerant and non-responsive rifampicin-resistant TB patients. Adverse events (AE) of special interest of BPaL are focused on neuropathies and myelosuppression which are associated with Linezolid. Other AEs may occur in the clinical setting noted during active drug safety monitoring and management (aDSM).

**Design/Methods:** This is a descriptive study of patients on BPaL in the Philippines that manifested with cutaneous lesions.

**Results:** The BPaL OR in the Philippines enrolled 103 patients from June 2021-December 2022 of whom at least 24 (23%) were observed to have cutaneous lesions: 63% female; 54% aged 20-29 years (range: 20-52 years). While 58% did not have any comorbidity, 25% had diabetes, 13% had prior hypersensitivity, and 13% were PLHIV. Lesions were mostly acne-like, 72% occurring on the face, 17% on the chest, 13% in the underarms; few under the breasts, abdomen, lower extremities, scalp and neck.

Others manifested as finer raised lesions; others as flat areas of erythema or hyperpigmentation, or as scaly lesions. Two patients had hair loss and psoriasis.

The onset occurred within the first month of BPaL initiation in 92%, and 8% within the second month. No interventions were done in 46%; Cetirizine was taken in 46%; two patients consulted with specialists.

Partial or complete disappearance of the lesions was observed in 96% during the treatment course; 4% were undocumented.

**Conclusions:** aDSM remains crucial as new drugs and regimens are being introduced more widely. Although non-life-threatening, cutaneous manifestations occurred in a quarter of patients and, if left unaddressed, can cause unnecessary anxiety, possibly leading to loss to follow-up. It was, however, observed that these AEs tend to be mild and reversible, reassuring both patients and health providers of the safety of the regimen on the skin.

### EP15-1138-16 Inclusion of children in a novel 6-month rifampicin-resistant TB treatment regimen in the pragmatic BEAT-Tuberculosis trial in South Africa

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**Background:** Although the WHO has recently endorsed 6-month RR-TB treatment guidelines for children, there remain limited paediatric data for newer drugs and shorter regimens. Further, children are routinely excluded from adult efficacy trials.

**Design/Methods:** The BEAT-Tuberculosis trial is a phase III, open-label, pragmatic, randomized controlled trial evaluating the efficacy and safety of an all oral 6-month regimen (Study strategy; bedaquiline, delamanid, linezolid, levofloxacin and/or clofazimine) or the current South African standard of care (Control strategy). The primary efficacy outcome is a successful outcome (cure or treatment completion) defined as success at both end of treatment and after 76 weeks of follow-up. Participants aged <18 years at randomization underwent an age-appropriate assent process after the informed consent of their parent or guardian. The trial included children of at least 6 years and 16 kilograms weight. Participants ≥12 years required bacteriologically confirmed RR-TB for inclusion, whereas younger participants could be included with probable RR-TB.

**Results:** Thirty child participants (8–17 years) with bacteriologically confirmed RR-TB were enrolled, 17 to the Control and 13 to the Study strategy. Seven (24%) had TB resistant to fluoroquinolones. At the time of data review, 22 had completed their assigned RR-TB treatment. Culture conversion by week eight was achieved in 77% and 100% on the Control and Study strategies, respectively. One 17-year-old participant with baseline bedaquiline- and clofazimine-resistant RR-TB was switched to a salvage regimen. There were five linezolid related grade 3 or 4 adverse events (two each of anaemia and optic neuritis, one peripheral neuropathy). Delamanid was discontinued for neuropsychiatric side effects in one participant on the Control strategy.

N (%) unless otherwise specified	Control Strategy	Study Strategy	Total
Total randomized	17	13	30
Baseline:			
Age at screening (median, range)	16 (8-17)	16 (10-17)	16 (8-17)
Mean BMI (median, IQR)	18.3 (16.0-19.9)	16.7 (16.4-18.1)	17.5 (16.0-19.9)
Fluoroquinolone suscEPtibility (where available)			
SuscEPtible	8 (47%)	8 (62%)	16 (53%)
Resistant	4 (24%)	3 (23%)	7 (24%)
Culture conversion by 8;12 weeks	77%; 88%	100%; 100%	86%; 93%
End of treatment status			
Still on treatment	5 (29%)	2 (15%)	7 (23%)
Cured	11 (65%)	11 (87%)	22 (73%)
Treatment failed (lack of sputum culture conversion)	1 (6%)	0 (0%)	1 (3%)
76-week outcome (among those with at least 76 weeks in the study)			
Total	7	4	11
Cured at end of follow-up (76 weeks)	6 (86%)	4 (100%)	10 (91%)
Unsuccessful outcome	1 (14%)	0 (0%)	1 (9%)
Adverse events			
Grade 3-5 AE	6 (35.3%)	3 (23.1%)	9 (30.0%)
SAE	3 (17.6%)	1 (7.7%)	4 (13.3%)
NE: Permanent stop of TB medication	1 (5.9%)	3 (23.1%)	4 (13.3%)
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total duration of Linezolid median (range) in weeks* (*3 of 30 participants still on linezolid and not included in this calculation)			
	8.9 (6.0, 78.3)	26.0 (22.3, 31.0)	22.3 (6, 78.3)
Number received DLM			
	5 (30%)	13 (100%)	18 (60%)
Total duration of Delamanid median (range) in weeks** (**1 of 18 participants still on delamanid and not included in this calculation)			
	9.9 (4.1, 70.1)	24.1 (8.0, 28.4)	24.0 (4.1, 70.1)

**Conclusions:** BEAT-Tuberculosis demonstrated that children can and should be included in trials for regimens with improved duration and/or tolerability. Linezolid toxicity continues to require close monitoring and clinical management.

### EP15-1139-16 Anaemia in patients on the all-oral shorter regimen for drug-resistant pulmonary TB

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**Background:** Anemia develops with a chronic inflammatory state and is seen early in tuberculosis. Linezolid (LZD), a key drug in the treatment of drug-resistant tuberculosis (DR-TB), is also known to cause myelosuppression thus making it difficult to differentiate the cause of anemia in patients on treatment for DR-TB.

**Design/Methods:** We conducted a multi-centric prospective cohort study in India on 209 pulmonary DR-TB patients with pre-treatment hemoglobin (Hb) of 8gm% or above. Patients were initiated on an all-oral shorter LZD (600mg daily)-containing regimen and followed. Occurrence of anemia during treatment was assessed. A 10% reduction of Hb from baseline was considered as a criterion for anemia.

**Results:** Of the 209 patients, 112 (54%) were males, and the mean age and body mass index were 30.1 years (SD: 10), and 18.3 kg/m<sup>2</sup> (SD: 4) respectively with 35% having extensive lung involvement on the chest x-ray. At treatment initiation, 64 (31%) had grade I or II anemia (<10.4gm%: females and <10.9gm%: males). Of them, 48 showed improvement in Hb levels during treatment and completed treatment without any interruption. Forty-four (21%) patients (16 from baseline and 28 during treatment) developed a 10% reduction of Hb levels from baseline (grade I- 7, grade II- 15, grade III- 19, and grade IV- 3). Of these, 33 (grades: I, II, and a few III) continued on the same dose of LZD. Anemia resolved in 23 without LZD interruption while 10 had persistent anemia after 12 weeks, requiring LZD interruption later. Of the remaining 11/44 patients, anemia persisted even after 12 weeks of treatment, requiring LZD dose reduction to 300mg.

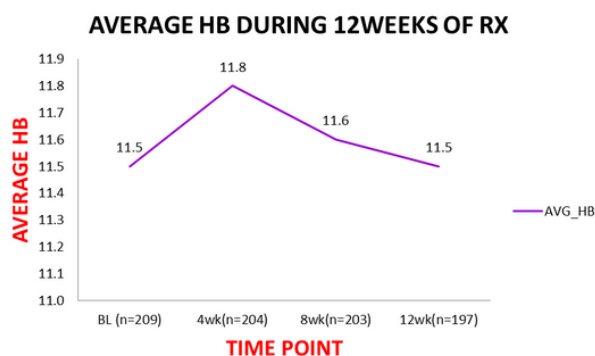


Figure: Mean increase in Hb levels during the first 12 weeks of treatment.

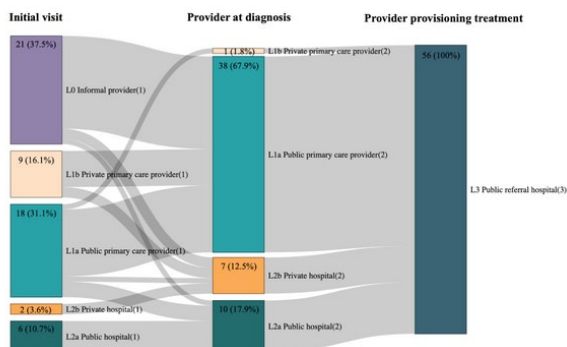
**Conclusions:** Anemia seen early DR-TB is due to the chronic inflammatory state of TB, resolves with the continuation of anti-TB treatment, and may not require LZD dose interruption/reduction.

## EP15-1141-16 Patient pathway and delays in rifampicin-resistant TB management in Bandung, Indonesia

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**Background:** Rifampicin-resistant tuberculosis (RR-TB) patients often experience long delays and complex journeys across multiple healthcare facilities before receiving treatment. In Indonesia, which is among the seven countries with the highest RR-TB burden globally in 2021, research on this topic remains limited. We investigated patient pathways among RR-TB patients in West Java province, which accounts for the highest prevalence of RR-TB cases in Indonesia.

**Design/Methods:** This cross-sectional study is ongoing. We recruited patients from public referral hospitals designated as programmatic management of RR-TB (PMDT) hospitals in Bandung, Indonesia since February 2023. Consenting participants were interviewed with a validated, structured questionnaire regarding their general characteristics, symptoms, and patient pathways. Descriptive analyses were conducted to describe the patient pathway and to identify delays. By December 2023, we anticipate to have reached our target of recruiting 300 participants. Risk factors will be identified using multivariable logistics regression.



**Results:** Complex pathways were observed among the 56 recruited DR-TB patients in their attempts to receive appropriate TB management. Over half of these patients initially visited an informal or private provider (57%) before transitioning to the public sector to receive RR-TB diagnosis (81%) and treatment (100%). Less than

half of the patients were diagnosed at the provider they initially visited (32%). From the onset of symptoms, it took a median of 14 days (IQR 2-38.3) to the initial visit to provider, 59.5 days (IQR 27.5-114.8) to diagnosis, and 87 days (53-135.3) to the start of treatment. The median number of visits before treatment was 6 (IQR 4-8).

**Conclusions:** RR-TB patient pathways in Indonesia are complex, with substantial delays and multiple encounters required before a diagnosis can be reached. Strengthening diagnostic network for early detection of RR-TB is crucial to enable timely DR-TB management.

## EP15-1142-16 The effectiveness and safety of an all-oral ultra-short regimen in China: preliminary results of a randomised controlled trial (TB-TRUST study)

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**Background:** Researches on all-oral shorter regimens for rifampicin-resistant tuberculosis (RR-TB) were urgently needed. Refining MDR-TB Treatment Regimens for Ultra Short Therapy (TB-TRUST) was a multicenter non-inferiority randomized controlled trial to evaluate the efficacy and safety of an all-oral shorter regimen in China.

**Design/Methods:** RR-TB patients susceptible to fluoroquinolones and aminoglycosides were recruited and randomly assigned 1:1 to the ultra-short regimen and the WHO injectable-containing shorter regimen.

In the ultra-short regimen, pyrazinamide-susceptible patients received levofloxacin, linezolid, cycloserine and pyrazinamide for 24 weeks, and pyrazinamide-resistant patients replaced pyrazinamide with clofazimine for 36 weeks. The favorable status was defined as participants with consecutive negative cultures for *Mycobacterium tuberculosis* without previous unfavorable outcomes.

Bacteriological failure, major regimen change, death and lost to follow-up were considered unfavorable outcomes. Data in this preliminary analysis was updated in January 2023.

**Results:** Between June 2, 2020, and December 1, 2021, 354 participants were randomly assigned. Treatment has been completed and post-treatment follow-up is ongoing. Of 312 participants in the modified intention-to-treat population, 128 of 156 (82.1%) in the ultra-short regimen group and 101 of 156 (64.7%) in the WHO shorter regimen group attained favorable status (difference: 17.3%, 95% CI 0.07–27.1).

Of 270 participants in the per-protocol population, 120 of 135 (88.9%) in the ultra-short regimen group and 100 of 135 (74.1%) in the WHO shorter regimen group attained favorable status (difference: 14.8%, 95% CI 0.05–24.3). Common adverse event of grade 3–5 was QTc prolongation (21.3%), liver toxicity (18.3%), ner-

vous system disorders (3.4%) in the ultra-short regimen group, and QTc prolongation (12.1%), anemia (9.2%), liver toxicity (6.4%) in the WHO shorter regimen group.

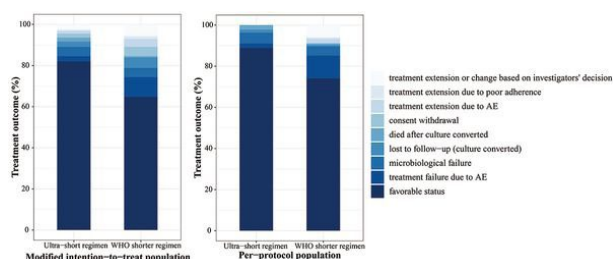


Figure 1 Treatment outcomes in TB-TRUST study.

**Conclusions:** The preliminary results showed the ultra-short regimen had superior efficacy compared to the WHO injectable-containing shorter regimen, with fewer cases of liver toxicity and QTc prolongation. (ClinicalTrials.gov number, NCT03867136).

### EP15-1143-16 TB-HIV co-infection and drug-resistant-TB mortality in KwaZulu-Natal, South Africa, 2020

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**Background:** South Africa has been ranked among the countries with the highest burden of TB/HIV co-infection and DR-TB globally. In 2021, 53% of TB patients with known HIV status were HIV positive, with 89% of these on ART. While shortened regimens for DR-TB using new and re-purposed drugs such as bedaquiline, linezolid and clofazimine have improved treatment success rates, high mortality rates are still observed.

**Design/Methods:** Through the USAID TB-LON programme, THINK conducted a retrospective mortality cohort review in four districts in KZN, South Africa. Files of patients who started treatment between January and June 2020, and died while taking DR-TB treatment, were examined. A univariate analysis of patient characteristics, risk factors for mortality, HIV and ART status, CD4 counts and viral loads was performed.

**Results:** Of 30 folders reviewed, 50% were male patients and the overall median age was 40 years (IQR; 31-52). There was no statistically significant difference in age by gender ( $p=0.79$ ). High rates of HIV co-infection were observed; 90% (27/30) were HIV positive, with 93% (25/27) having an already known HIV-positive status. Viral load suppression was present in 24% (6/25).

Furthermore, there was evidence of advanced immunological suppression with 81% (22/27) having CD4 < 200 cells/mm<sup>3</sup> and 37% (10/27) with CD4 < 50 cells/mm<sup>3</sup>. Median time to death was 50 days (IQR 6-94) for HIV negative and 5 days (IQR 3-11) for HIV positive patients respectively. There was no statistically significant difference in time to death by HIV status ( $p=0.24$ ).

**Background and challenges to implementation:** South Africa has been ranked among countries with the highest burden of TB/HIV co-infection and DR-TB globally. In 2021, 53% of people diagnosed with TB, with known HIV status, were people living with HIV (PLHIV), with 89% of these on ART.

While shortened regimens for DR-TB using new and re-purposed drugs such as bedaquiline, linezolid and clofazimine have improved treatment success rates, high mortality rates are still observed.

**Intervention or response:** Through the USAID TB-LON programme, THINK conducted a retrospective mortality cohort review in four districts in KZN, South Africa. Files of people who started treatment between January and June 2020, and died while taking DR-TB treatment, were examined. A univariate analysis of individual characteristics, risk factors for mortality, HIV and ART status, CD4 counts and viral loads was performed.

**Results/Impact:** Records of 30 people were reviewed. Of these, 50% were male, and the overall median age was 40 years (IQR; 31-52). There was no statistically significant difference in age by gender ( $p=0.79$ ).

High rates of HIV co-infection were observed; 90% (27/30) were HIV positive, with 93% (25/27) already known to be PLHIV. Viral load suppression was present in 24% (6/25).

There was evidence of advanced immunological suppression with 81% (22/27) having CD4 < 200 cells/mm<sup>3</sup> and 37% (10/27) with CD4 < 50 cells/mm<sup>3</sup>. Median time to death was 50 days (IQR 6-94) for those who tested HIV negative and 5 days (IQR 3-11) for PLHIV respectively.

There was no statistically significant difference in time to death by HIV status ( $p=0.24$ ).

**Conclusions:** There was a high prevalence of advanced, poorly controlled HIV co-infection within this mortality cohort, despite a high proportion of people with previously known HIV status.

Identification of high-risk individuals for targeted interventions, intensified TB/HIV co-infection management and integrated TB/HIV care is critical to improving treatment outcomes in people with DR-TB.

## EP16 TB focal support and TB management

### EP16-1144-16 Factors associated with post-TB lung disease in Kenya

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**Background:** Post-tuberculosis (TB) lung disease (PTLD) is an increasingly recognized cause of morbidity after TB treatment. Risk factors predisposing to the subsequent development of PTLD after treatment remain unclear. We evaluated risks factors for PTLD.

**Design/Methods:** We implemented a prospective, observational, cohort study enrolling adults ( $\geq 18$  years) at the time of TB diagnosis through 24 months in Nairobi, Kenya. All consenting participants undergo questionnaires, chest x-rays (CXR) and C-reactive protein (CRP) testing at baseline, then spirometry at 6 months (treatment completion) and 12 months.

We defined PTLD as abnormal spirometry (obstruction, restrictive pattern, or both) at most recent study visit. Wilcoxon rank sum, Chi square, and logistic regression were used to compare outcomes by sex.

Variable	Univariate regression		Multivariable <sup>a</sup> regression	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Female sex	0.70 (0.20, 2.2)	0.55	0.75 (0.18, 2.9)	0.68
Age	1.0 (0.96, 1.0)	0.96	1.0 (0.96, 1.0)	0.99
CRP	1.0 (0.99, 1.0)	0.34	1.0 (0.99, 1.0)	0.75
Cavitary disease	2.4 (0.88, 6.8)	0.10	2.4 (0.78, 8.6)	0.14
HIV	1.2 (0.28, 4.9)	0.79	2.0 (0.39, 11)	0.40

a defined by abnormal spirometry (obstruction, restrictive pattern, or both), b adjusted for all listed covariates

Planned to adjust for smoking *a priori* however given low percentage of participants

rEPorting smoking, this was not included in the model

CI confidence interval

*Table. Logistic regression analyses: factors associated with PTLD <sup>a</sup> in Kenya (N=82)*

**Results:** We enrolled 82 participants with acceptable spirometry (55% at 6 months), including 67 (82%) men. Thirty-three (40%) participants had abnormal spirometry, with 21 (26%) having a restrictive pattern, 8 (9.8%) having obstruction, and 4 (4.9%) having both.

Women and men had similar age (median 28 [IQR 22, 39] vs. 36 [28, 44] respectively,  $p=0.13$ ) and similar rates of abnormal spirometry (33% and 42% respectively,  $p=0.75$ ). Thirty-three percent of women and 27% of

men reported ongoing respiratory symptoms (cough, phlegm production, or dyspnea) after treatment completion ( $p=0.89$ ). Median (IQR) CRP at baseline was similar among women 31mg/dL (6.5, 111) and men 78mg/dL (28, 102,  $p=0.29$ ).

At baseline, 67% of participants had cavitary lung disease on CXR and 11% HIV. In regression analyses (table) the assessed factors were not associated with PTLD. **Conclusions:** In this cohort of Kenyan adults, PTLD (defined by abnormal spirometry) was common even 6 months after treatment completion. Women had similar prevalence of PTLD to men.

Traditional risk factors, such as cavitary disease, do not fully explain risk for PTLD, thus we are retrospectively evaluating host immunological risk factors for PTLD.

### EP16-1145-16 Trends in TB notifications in the pre-COVID and the COVID era in Suriname

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**Background and challenges to implementation:** The *Sars-CoV-2* virus reached Suriname by March 2020. The government implemented several measures aiming to contain the spread of the virus, such as lockdowns and limiting public transport.

These measurements resulted in diminished access to care for the population. Also fear of contracting the *Sars-CoV-2* virus has resulted in delayed health seeking behavior. It is therefore assumed that the COVID-19 pandemic might have an effect on the notification of TB patients.

**Intervention or response:** This is a descriptive analysis comparing data from 2015-2019 (pre-COVID era) and 2020-2022 (COVID era). We assessed the TB notification of the aforementioned periods.

**Results/Impact:** On average 144 TB patients were notified in the period 2015-2019. The notification of TB patients decreased in 2020 with 21% compared to 2019 and in 2021 with 16% compared to 2020. Altogether a decrease of 34% in 2021 since the start of the pandemic. In 2022, the notification increased again to 127 (9% less than the patients notified in 2019).

The number of diagnostic tests conducted in 2020 and 2021 were almost half of the number in 2019, with a higher GXP-positivity rates (up to 30%) than in the pre-COVID era (<20%).

		2015	2016	2017	2018	2019	2020	2021	2022
People with presumptive TB tested	N	666	503	578	652	491	256	256	526
	%	11.7	15.9	14.4	16.3	18.3	29.3	30.1	19.6
GXP-MTB detected	N	78	80	83	106	90	75	77	103
	%	11.7	15.9	14.4	16.3	18.3	29.3	30.1	19.6
RIF-resistance	N	8	4	8	14	11	11	10	7
	%	10.3	5.0	9.6	13.2	12.2	14.7	13.0	6.8
Total number of TB notifications	N	150	116	136	179	139	110	93	127
	%	11.7	15.9	14.4	16.3	18.3	29.3	30.1	19.6

*Table 1. Notification of TB patients in Suriname, rifampicin resistance and people with presumptive TB examined 2015-2022*

**Conclusions:** This study shows that during the COVID-19 era both the number of persons with presumptive TB examined for TB as well as the TB notifications decreased considerably compared to the pre-COVID era. The National TB program should develop a preparedness plan to guarantee access to care for persons with presumptive TB during challenging periods such as the COVID-19 era.

### EP16-1146-16 Transforming challenges into opportunities: improving access to TB care and services during COVID-19 and the profound political crisis in Myanmar

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**Background and challenges to implementation:** COVID-19 pandemic hardly hit Myanmar and disrupted TB care and services. This is further exacerbated by the profound political crisis causing the near collapse of the country's public health system. Prolonged conflicts and COVID-19 restrictive measures increased barriers to access TB care and services. This is more difficult in people who use/inject drugs (PWUD/PWID) who have a natural reluctance to access healthcare.

**Intervention or response:** Asian Harm Reduction Network (AHRN) and sister organization Best Shelter implement TB-HIV integrated harm reduction programmes in northern Myanmar where a geographical and epidemiological rationale is present.

In 2021, AHRN started collaboration with Best Shelter, strengthened community-based TB care activities through capacity building of local communities, peers and enhancing TB screening through innovative community-based interventions in remote-rural areas during COVID-19 lockdowns and conflicts.

While national TB active case finding (ACF) activities were suspended because of travel restrictions, AHRN mobilized portable digital X-rays from ACF teams to

key population service centers (KPSC) and engaged with private sectors to prioritize chest X ray (CXR) as first TB screening tool.

**Results/Impact:** While during COVID-19 pandemic presumptive TB screening dropped from 28,399 in 2019 to 15,259 in 2020, due to program interventions screening bounced back to 18,603 in 2021 and 42,613 in 2022. Overall TB notifications also increased under program operations from 1,255 in 2019 and 906 in 2020 to 1,649 and 2,508 in following years. Based on lessons learned, AHRN adopted screen for all approach to all KPSC attendants and enhanced TB-COVID-19 bidirectional diagnosis.

**Conclusions:** Despite profound COVID-19 and political challenges, AHRN and Best Shelter developed and integrated efficient strategies to turn challenges into opportunities, convert evidence into practice in improving access to TB care and services among vulnerable populations. CXR screening followed by smear microscopy and/or Xpert can reduce the cost/workload and achieved double TB case notification.

### EP16-1147-16 Ensuring access to quality-assured TB diagnostics through the implementation of a quality management system in selected TB laboratories in the Philippines

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**Background and challenges to implementation:** The National TB Control Program's Laboratory Network Strategic Plan's priority objectives include the development and maintenance of QMS for TB laboratories. However, as of 2023, National TB Reference Laboratory—Research Institute for Tropical Medicine (NTRL-RITM) remains the only International Organization for Standardization (ISO)-15189-accredited TB laboratory in the Philippines. To strengthen QMS implementation in other TB laboratories and assist towards accreditation, USAID's TB Innovations and Health Systems Strengthening (TBIHSS) and NTRL-RITM, provided technical assistance to the University of the Philippines-Medical Research Laboratory (UP-MRL) and Batangas Medical Center (BatMC) to improve their QMS based on ISO-15189:2012.

**Intervention or response:** TBIHSS and NTRL-RITM assisted and coached the laboratories to develop quality manuals, standard operating procedures, and forms



based on ISO-15189 management and technical requirements and provided QMS training complemented by workshops and mentoring activities.

NTRL-RITM and TBIHSS evaluated QMS implementation through baseline assessment and post-intervention mock audit. Baseline scores were attained using WHO-FIND Harmonized Checklist, a tool based on the Step-wise Laboratory Quality Improvement Process Towards Accreditation (SLIPTA) v.2:2015 and Global Laboratory Initiative (GLI) v1.0 checklists. The mock audit utilized the Philippine Accreditation Bureau's ISO-15189:2012 checklist, with sections correlating to the baseline tool.

**Results/Impact:** UP-MRL showed improvement in all sections, whereas BatMC's scores declined in Equipment and Purchasing sections. However, assessment of overall scores showed statistically significant change in both laboratories, with a 7.7% ( $p=0.021$ ) and 9.2% ( $p=0.031$ ) increase, respectively, which reflects improved compliance to ISO-15189 requirements and readiness for accreditation.

Section	Total points per section	UP-PGH-MRL		Batangas Medical Center	
		% Change	p-value	% Change	p-value
1. Documents and Records	28	18.2%	0.252	0%	1.000
2. Management Reviews	14	0%	1.000	0%	1.000
3. Organization & Personnel	22	9.1%	0.664	22.7%	0.122
4. Client Management & Customer Service	10	10.0%	1.000	10.0%	1.000
5. Equipment	33	0%	1.000	-12.1%	0.325
6. Internal Audit	15	6.7%	0.100	13.3%	0.483
7. Purchasing & Inventory	24	0%	1.000	-4.2%	0.771
8. Process Control and Internal & External Quality Assessment	30	13.3%	0.284	6.7%	0.606
9. Information Management	21	4.8%	1.000	33.3%	0.024
10. Corrective Action	19	0%	1.000	26.3%	0.097
11. Occurrence/Incident Management & Process Improvement	12	0%	1.000	8.3%	0.682
12. Facilities and Safety	43	11.6%	0.194	16.3%	0.121
<b>Total Points</b>	271	7.7%	0.021*	9.2%	0.031*

\*Significant using Pearson chi-square test

**Conclusions:** TB laboratories play a crucial role in TB elimination efforts. Strengthening QMS in the TB diagnostic network will improve the capacity of laboratories and enhance delivery of effective and efficient services.

## EP16-1148-16 Applying a behavioural lens to the role of TB counselling in treatment journeys

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**Background and challenges to implementation:** Tuberculosis (TB) counseling is widely used by TB programs as an intervention to address treatment gaps. However, counseling content is often focused solely on didactic medical information and does not examine the behavioral aspects conditioned by emotional, cultural, and social factors surrounding people's experiences. Despite the attention to treatment literacy, information asymmetry remains, with limited impact on people's ability to cope with illness.

**Intervention or response:** Interviews were conducted in the form of story-telling narratives that described how people took care of their health and well-being. A total of 356 individual micro-stories documented the daily activities of people affected by TB and healthcare providers in the Indian districts of Surat, Gujarat and Ranchi, Jharkhand. Data was analyzed with a behavioral design framework that examined the strength and directionality of connections between variables in order to identify conditional patterns.

**Results/Impact:** Three conditions affecting treatment journeys were identified:

**Emotional state:** Anxiety and guilt had significant connections within the treatment journey, associated with the perception of disease as a punishment for past actions; being a burden to the family; and a mismatch between what is an expected recovery vs. the actual experience of adverse drug reactions that seemingly worsen symptoms.

**Cognitive function:** Confusion and an inability to make decisions was identified throughout the treatment journey, attributed to unexpected changes in physical condition; as well as the inability to reconcile TB with prior illnesses that required short-term antibiotics. Resulting behavior was the substitution or supplementation of TB medication.

**Aesthetic presentation:** The experience of specific aesthetic changes such as darkening of the skin and loss of weight resulted in behavioral patterns contributing to treatment experimentation.

**Conclusions:** Findings indicate that TB counseling should be transformed from solely treatment literacy into a delivery of behavioral communication services designed to empower people affected by TB and cope with circumstances of illness.

### EP16-1149-16 Assessment of dietary intake and nutritional status of people with pulmonary TB in Morang District, NEPAL

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**Background:** Severe malnutrition increases risk of mortality from tuberculosis (TB). In 2020, a quarter of the 10.8 million people who developed TB were undernourished. In Nepal, there is limited evidence on dietary patterns and nutritional status among TB patients to inform treatment support strategies. This study measured nutritional status in a cohort of TB patients, evaluated gap between recommended energy value and dietary intake during treatment and explored barriers and facilitators to consumption of nutritious food

**Design/Methods:** From February to December 2022, we consecutively recruited 50 TB patients and conducted mixed-methods study employing parallel study design in Morang district. We assessed dietary patterns using validated 24-hour dietary-recall questionnaire and photographic atlas. We measured body mass index (BMI). Individuals with BMI  $\leq 18.5$  kg/m<sup>2</sup> were considered underweight. Focus group discussions (FGD) with purposively selected people with TB and TB care providers explored barriers and facilitators to consuming nutritious food during TB treatment

**Results:** Seventy percent of people with TB were underweight. Mean age was 47.3 $\pm$ 17.9 years. Three-fourths of participants were male (72%, 36/50) and married (74%, 37/50). Average daily energy intake was lower than the recommended value (2361 $\pm$ 956kcal vs. 2480kcal). 56%, 22%, and 19% did not meet energy, proteins, and fats requirements respectively.

S.N.	Nutrient/ Energy	Recommen- ded Dietary Allowance (RDA) for all participants	% of total participants below RDA	Recommen- ded Dietary Allowance (RDA) for male	% Male participants below RDA	Recommen- ded Dietary Allowance (RDA) for female	% Female participants below RDA
1	Protein (g)	58.0	22%	60.00	22%	55	21%
2	Fat (g)	27.5	19%	30.00	19%	25	0
3	Energy (Kcal)	2480.0	56%	2730.00	67%	2230	36%
4	Calcium (mg)	600.0	22%	600	28%	600	21%
5	Iron (mg)	19	53%	17	47%	21	43%
6	Zinc (mg)	11	50%	12	58%	10	29%
7	Carotene (mcg)	4800	83%	4800	86%	4800	71%
8	Vitamin C (mg)	40	28%	40	31%	40	21%

A higher percentage of males did not consume recommended calories of energy compared to females (67% vs 33%).

FGDs identified poor purchasing capacity, inadequate knowledge and practice on balanced diet, and infertile land as major barriers to good nutrition. To overcome these barriers, participants suggested supporting people with very low socioeconomic conditions with education on food habits and hygiene, and monthly food packages.

**Conclusions:** The majority of people with TB were underweight and had inadequate calorie intake. The study highlights the need to provide locally-appropriate food support along with integrated nutrition education programs to support recovery and improve outcomes in the most vulnerable TB patients in Nepal.

### EP16-1150-16 Health-related quality of life among persons with pulmonary TB: A cross-sectional study in Bangladesh

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**Background:** Stigma is reported to negatively influence the mental and physical well-being of individuals with tuberculosis (TB). Evidence shows that even after persons were microbiologically cured of TB following a recommended treatment, their mental well-being remained low. Understanding the quality of life of persons with TB during the cascade of care is important to ensure a better prognosis and to prevent future morbidity.

This study aimed to generate baseline evidence about HRQoL and its associated factors among persons with pulmonary TB (PTB) in Bangladesh – a high TB burden country.

**Design/Methods:** In this cross-sectional, exploratory study, persons with PTB visiting icddr,b TB Screening and Treatment Centres (TBSTCs) located in Dhaka were recruited between February-August'22. Data were collected through face-to-face interviews within 7-10 days of testing positive for PTB. The semi-structured questionnaire included socio-demographic characteristics, care-seeking factors, and a validated Bangla version of the Short Form (SF)-12 scale to assess HRQoL. Multiple linear regression models were performed to determine associated factors.

**Results:** Among the 424 participants, mean age was 37( $\pm$ 15) years, majority were male (74%) and married (70%). Many (42%) reported past mental health issues. Mean physical component summary (PCS) scores and mental component summary (MCS) scores were 46.76 $\pm$ 26.76 and 59.84 $\pm$ 24.71 respectively. Linear re-

gression analysis reported that both lower PCS and MCS scores were significantly associated with a low educational level, past mental health issues, poor diet, not maintaining personal hygiene, and lack of physical exercise.

Additionally, lower mean MCS scores were significantly associated with being distressed about their recently diagnosed TB.

**Conclusions:** Compromised MCS and PCS scores indicate the deteriorated quality of life of individuals with TB. These findings provide valuable insight into the unexplored HRQoL issues in persons with TB from Bangladesh. Further systematic follow-up studies are needed to understand the course of HRQoL throughout the cascade of care.

### EP16-1151-16 Health-related quality of life among Ugandan TB survivors

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**Background:** 155 million people globally have survived tuberculosis (TB) and many report substantial on-going health issues. There is an urgent need to improve identification of individuals at risk of poor post-TB outcomes.

We characterize health-related quality of life (HRQoL) among Ugandan TB survivors a year after treatment completion and identify predictors of poor HRQoL.

**Design/Methods:** We surveyed a cohort of Ugandan TB survivors 12-25 months after treatment cessation. HRQoL was assessed with the EQ-5D 5L tool, a 6-item validated generic utility-based instrument that measures capacity in five health domains: mobility, self-care, usual activities, pain and anxiety/depression.

We calculated summary index scores using previously validated Uganda-specific weights. An index score of one indicates perfect health and zero indicates a health state equivalent to death. We fit a normal linear model to identify demographic and clinical features predictive of the index score.

**Results:** We successfully traced 2,110 (87.7%) of 2,406 TB survivors; 138 (5.7%) were deceased. Of the remaining 1,972 TB survivors, 1,923 (97.5%) completed the survey. Participants reported high rates of impairment in most domains (Table).

Degree of impairment	Health domain				
	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression
None	1422 (73.9%)	1812 (94.2%)	1334 (69.4%)	1236 (64.3%)	992 (51.6%)
Slight	334 (17.4%)	85 (4.4%)	401 (20.9%)	483 (25.1%)	648 (33.7%)
Moderate	85 (4.4%)	14 (0.7%)	103 (5.4%)	116 (6.0%)	178 (9.3%)
Severe	74 (3.8%)	10 (0.5%)	64 (3.3%)	84 (4.4%)	94 (4.9%)
Very Severe	8 (0.4%)	2 (0.1%)	21 (1.1%)	4 (0.2%)	11 (0.6%)

Table.

Over a quarter of participants experienced at least some impairment in mobility (26.1%), usual activities (30.6%), and pain/discomfort (35.7%); about half experienced anxiety/depression (48.4%). The median index score was 0.92 (interquartile range: 0.80-1.00). Female sex and older age were associated with lower summary scores (-0.03, 95% confidence interval [CI]: [-0.06, -0.01], and -0.02, 95% CI: [-0.02, -0.02], respectively). Living with HIV was associated with a higher score (0.05, 95% CI: [0.03, 0.08]).

**Conclusions:** TB survivors reported challenges in several health domains after TB treatment. Higher HRQoL among people living with HIV suggests that ongoing contact with the healthcare system could ameliorate some of these health issues. TB survivors may benefit from routine health screening and referrals to interventions like pulmonary rehabilitation to promote health post-TB.

### EP16-1152-16 Post-TB health-related quality of life: A systematic review

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**Background:** There is little information of the health related quality of life (HRQoL) in people with past-tuberculosis (TB) treatment history and of the effect of post-tuberculosis lung disease (PTLD). This systematic review assessed the HRQoL in people previously treated for TB globally and according to the presence of PTLD. **Design/Methods:** Screening of manuscripts published prior March 20, 2023 followed by data extraction was performed by two independent reviewers.

The primary outcome was the proportion of impaired HRQoL (as defined in each study) after TB treatment and secondary outcomes were the comparison (i) with healthy individuals without TB and (ii) between individuals with and without PTLD, as defined by the study. Results are presented per type of HRQoL tool.

HRQoL tools	Dimensions	Studies n	All post-TB <sup>§</sup>	Studies n	Post-TB vs healthy people without TB <sup>§</sup>	Studies n	Post-TB with PTLD <sup>§</sup>	Studies n	Post-TB without PTLD <sup>§</sup>
<b>SGRQ</b> Score from 0-100. The highest score indicates worse quality of life	Total score	8	23.7 – 42.3 <sup>‡</sup> 7.8 – 45.5 <sup>*</sup>	1	23.7 vs 10.2 <sup>‡</sup>	3	37.7 – 51.4 <sup>‡</sup> 14.2 <sup>*</sup>	3	5.4 – 17.3 <sup>‡</sup> 4.9 <sup>*</sup>
<b>SF-36 &amp; SF12v2</b> Score from 0-100. The lower score indicates worse quality of life	Physical well-being	4	37.7 – 74.0 <sup>‡</sup>	2	44.8 vs 50.0 <sup>‡</sup> 48.4 vs 46.9 <sup>‡</sup>	1	68.0 <sup>‡</sup>	1	78.0 <sup>‡</sup>
	Mental well-being	4	39.0 – 68.0 <sup>‡</sup>	2	39.0 vs 50.0 <sup>‡</sup> 44.4 vs 42.6 <sup>‡</sup>	1	55.0 <sup>‡</sup>	1	55.0 <sup>‡</sup>
<b>ED-5Q</b> Index values range between 0 (worst imaginable health state) and 1 (best imaginable health state)	Index score	3	0.89 – 0.93 <sup>‡</sup>	1	0.93 vs 0.94 <sup>‡</sup>	1	0.84 <sup>‡</sup>	1	0.93 <sup>‡</sup>
<b>SOLDQ</b> (Seattle's Obstructive Lung Diseases Questionnaire) The higher score denotes better QoL for all the components of the questionnaire	Physical function	1	66.6 <sup>‡</sup>	0	–	2	58.70 <sup>‡</sup> 82.18 <sup>‡</sup>	2	89.9 <sup>‡</sup> 98.7 <sup>‡</sup>
	Emotional factor	1	71.2 <sup>‡</sup>	0	–	2	65.0 <sup>‡</sup> 80.9 <sup>‡</sup>	2	93.9 <sup>‡</sup> 98.9 <sup>‡</sup>
<b>WHOQOL-BREF</b> (WHO Quality of Life Questionnaire) Score from 0-100 Higher scores denote higher QoL	Physical health Psychological health	1	21.0 <sup>‡</sup> 16.1 <sup>‡</sup>	1	21.0 vs 22.2 <sup>‡</sup> 16.1 vs 17.6 <sup>‡</sup>	0	–	0	–
<b>QLQ-C30</b> (Cancer core Quality of Life Questionnaire) Score from 1–7 (from very poor to excellent)	Global score	1	5.2 <sup>‡</sup>	0	–	0	–	0	–
<b>CAT</b> (COPD Assessment Test questionnaire) A score ≥ 10 indicates significant impact on quality of life	Global score	1	15.1 <sup>‡</sup>	0	–	0	–	0	–

<sup>§</sup>Individual study results or range if >2 studies; <sup>‡</sup>Mean; <sup>\*</sup>Median

EP16-1152-16 Table: HRQoL scores in people with past-TB treatment history.

**Results:** Of 17,166 articles, 66 were assessed for full text eligibility and 20 met criteria for systematic review. Sixteen studies were from low-middle income countries, 5 included a healthy reference group and 6 assessed HRQoL among individuals with and without PTLD. Most common HRQoL tools used were the St George's Respiratory Questionnaire (SGRQ), n=8; the Medical Outcomes Survey Short-Form questionnaire (SF-36 and SF12v2), n=4 and the European QoL 5-Dimension questionnaire (EQ-5D), n=3.

Out of 19 studies with primary outcome result, 17 reported impaired HRQoL, but studies having a healthy reference group without TB did not show major change between the two groups.

Studies reported a major reduction of HRQoL scores among people with PTLD as compared to those without PTLD (Table).

**Conclusions:** The impairment of HRQoL in people with past-TB treatment history is more prominent among those with PTLD. The heterogeneity in the PTLD definition, HRQoL tools used and methodology between studies is a limitation to draw conclusion and highlights the need for more standardized approaches.

**ABSTRACT PRESENTATIONS  
FRIDAY  
17 NOVEMBER 2023**

**ORAL ABSTRACT SESSION (OA)**

**OA35 Capacity building and TB prevention and care**

**OA35-475-17 Health system strengthening for TB preventive therapy: a lesson learnt from the Project Axshya Plus in Howrah District of West Bengal, India**

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**Background and challenges to implementation:** Achieving the TB elimination in India will require substantial improvements in the performance of service delivery of Peripheral Health care Institutions (PHI). Project Axshya Plus supported by the Global fund, aligned with the National Strategic Plan (NSP) of India is working in Howrah district of West Bengal, has created a sustainable intervention model by effectively engaging Public and Private sector providers for the successful implementation of Programmatic Management of TB Preventive Therapy (PMTPT).

In this study, we captured implementation experiences and lessons learned.

**Intervention or response:** The project identified the need of meaningful engagement of public and private sector providers for health system strengthening. It planned and conducted sensitisation sessions and trainings across the district for 1200 Accredited Social Health Activists (ASHA), 1400 Auxiliary Nurse and Midwives (ANMs), 900 Community Health Officers (CHOs), 11 Block Medical Officers, and it provided 7 Continuing Medical Education (CME) sessions to the Private Sector Providers on TB Preventive Therapy (TPT). 50 community awareness sessions conducted, and a joint follow up mechanism was developed for treatment adherence. Drug supply chain management systems streamlined to prevent drug stock out scenario in 350 PHIs.

**Results/Impact:** Support from health care staff improved, and TPT initiation increased in the last two consecutive periods (Table 1).

90% of House Hold Contacts (HHCs) successfully followed up, and ensured drug adherence (2,457 out of 2,730). 85% of the PHIs are now ensured with adequate drug stock (INH 100mg-25,00,000 & INH300mg-21,00,000).

	(April-Sep 22)	(Oct-March 23)
Total TB Cases Notified	1987	1638
No. of Eligible Index Patient (Pulmonary TB Cases)	1670	1274
Asymptomatic Found	4213	3528
Initiated on TPT	3355	2541
TB Detected	7	2

**Conclusions:** Sensitized and trained human resource is an important pillar for quality health care service delivery. Project Axshya Plus demonstrated a successful model in improving the healthcare services delivery mechanism, by engaging with the Private and Public Sector practitioners in Howrah District. Health care system strengthening efforts may start by sensitizing and training of existing staff of health system for better results for any new project.

**OA35-476-17 Advancing community health worker programmes to build resilient and equitable health systems that accelerate the expansion of primary healthcare for universal health coverage**

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**Background and challenges to implementation:** Uganda is one of the 30 high Tuberculosis burden countries globally with an annual Tuberculosis incidence of 199 per 100,000 population. In 2020, the COVID-19 pandemic caused disruption of Tuberculosis service delivery, resulting in a decline in the national Tuberculosis case detection rate from 78.6% to 61.6% (against a national target of 90%). To reverse this trend, the Uganda National Tuberculosis and Leprosy Program (NTLP) designed and implemented the community awareness, screening, testing, prevention and treatment to end TB in Uganda campaign (CAST-TB).

The aim of the campaign was to find persons with Tuberculosis who were not diagnosed during the COVID-19 periods.

**Intervention or response:** The CAST -TB campaign was a bi-annual event implemented in March and September 2022, for a period of 5 days. The NTLP together with Implementing Partners mobilized, built capacity and coordinated community health workers (CHWs) to conduct health education, distribution of information, education and communication materials, door to door TB screening, sputum sample collection and transportation to the nearest health facilities. Spu-

tum samples were carried by hub riders to GeneXpert sites for testing. Results were relayed back to CHWs through phone calls. The CHWs referred patients diagnosed with TB to the nearest health facility for TB treatment initiation.

In addition, CHWs screened household contacts of patients diagnosed with TB and referred those eligible for TB preventive therapy to health facilities for initiation.

**Results/Impact:** A total of 71,564 CHWs participated in the CAST-TB campaign. 2,175,792 households visited and screened 5,134,056 people for TB. 813,100 sputum samples collected and 12,042 patients were diagnosed with TB of whom 7,110 were initiated on treatment. 23,559 clients were initiated on TB Preventive Therapy.

**Conclusions:** Engagement of CHWs resulted in a significant increase in TB case detection following the COVID-19 pandemic. Continued engagement of CHWs can help find missing TB cases in high TB burden countries.

### OA35-477-17 Strengthening TB screening among recipients of HIV care through continuous quality improvement, Baringo County Referral Hospital, Kenya

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**Background and challenges to implementation:** People living with HIV are 16 times more likely to develop active TB compared to those who are HIV-negative according to WHO. Subsequently, TB screening should be done to all the recipients of HIV care to help in early detection of undiagnosed TB active cases and start them on treatment. As of Nov 2021, the TB screening rate for the recipients of care in Baringo County Referral Hospital was at 73%.

This review documents the success of the implementation of a Continuous Quality Improvement (CQI) project to improve TB screening rates among recipients of care

**Intervention or response:** The USAID Tujenge Jamii project working in collaboration with the county department of health of Baringo supported the implementation of a CQI project to improve the low TB screening among PLHIV. The root causes identified were; low TB screening for clients served in the community ART distribution groups (CAGs), high numbers of treatment supporter drug pickup, gaps in documentation of TB screening and knowledge gaps among HCWs. Integration of TB screening in the CAGs, reducing the number of treatment supporter drug pickups and building capacity in both documentation and TB screening were done to address the root causes of the problem.

**Results/Impact:** Comparing results in a six-month period before and after the implementation of the CQI, there was an improvement in the TB screening rates by 13% from a baseline of 73% in Nov 2021 to 88% in July 2022. The screening rate increased from 68% to 88% and 75% to 88% among men and women respectively. Community TB screening increased from 0% to 90% in the same period.

**Conclusions:** Implementation of CQI projects for elements that are nonperforming is central to identifying underlying causes of the gap and developing solutions based on context. Projects should consider adopting CQI to address results areas with low performance.

### OA35-478-17 Skilling TB Survivor-Champions in communications for better outreach to communities: experiences from India

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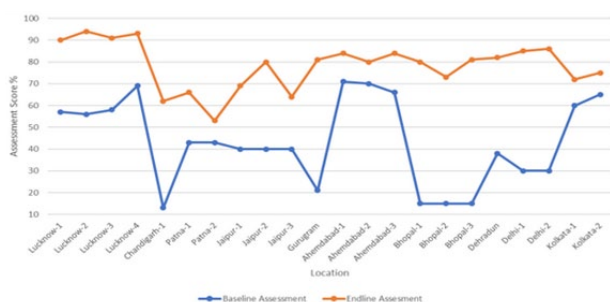
**Background and challenges to implementation:** Inadequate public understanding and awareness of tuberculosis in India remains an impediment to the country's ambitious TB elimination goals. Enhanced community participation and improved knowledge of TB among communities can help address this.

**Intervention or response:** Through the Unite to ACT project, as part of the COVID-19 Response Mechanism (C19-RM), TB survivor-Champions (TBCs) received communications skilling, through a specially designed and previously piloted curriculum. Two-day communication workshops were organised at the state-level to equip TBCs with the skills and expertise to develop creative collaterals on TB.

The content of the workshop contains the overall enhancement of different means of communications aspects of TB champions so that engaging information and communication materials can be developed for creating awareness among the populations.

**Results/Impact:** Workshops were held for 880 TB Champions in 22 batches from 80 districts of 10 states. Among those trained, 53.3% were male. Each trained TBC created multiple communication products that were reviewed and feedback provided to improve the quality of the material and the accuracy of the messages. Till December 2022, 800 TBCs have developed 3684 communication materials and organised 2180 community meetings. Materials have included slogans, flyers, posters, poems, songs, photos, nukkad-natak scripts, and others in 5 languages (English, Hindi, Bengali, Gujarati, and Punjabi).

While the communication products were all technically sound, a comparison of pre and post-test data also reveals their understanding of the subject has improved (see figure attached).



**Conclusions:** Communications skilling can help enhance the skills and ability of TB survivors and Champions to communicate effectively, through multiple mediums and in local languages, to their communities, thereby improving understanding of TB. This has the potential to improve health-seeking behaviour.

**OA35-479-17 The value-add of capacity-building and mentorship of primary healthcare nurses on gastric aspiration yields in Joe Gqabi District, Eastern Cape, South Africa**

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**Background and challenges to implementation:** Tuberculosis (TB) is a communicable disease, major cause of ill-health and leading cause of death worldwide. Tuberculosis in children is often missed due to non-specific symptoms. Each year 39 000 under 5s with TB are reported in SA. Children done Mantoux test are not always brought back timeously for reading. It is difficult for children to produce sputa.

To improve TB diagnosis by GeneXpert, the MatCH Institute NPC USAID TB LON project team facilitated trainings on gastric aspiration (theory and practical) for nurses in PHC facilities.

**Objectives:**

- To train PHC nurses on gastric aspiration
- To increase the number of under 5s diagnosed and treated for TB

**Intervention or response:** On-site gastric aspiration training was facilitated for PHC nurses, followed by supervised practical demonstration on identified TB contacts under 5s. The number of nurses trained, facilities reached, and children done gastric aspiration were recorded. Mentoring was conducted after training. Early diagnosis of under 5s, treatment initiation, parent counselling on treatment adherence, side effects and monitoring were completed at PHCs.

**Results/Impact:** Overall, 70 PHC nurses were trained between October 2021 and September 2022. From the baseline of eight under 5s diagnosed in 2020, there was 575% increase in 2022 with fifty-four children diagnosed with Drug Susceptible TB, two Drug Resistant TB and all linked to care.

**Conclusions:** Capacity building and mentorship of PHC nurses on gastric aspiration in children promotes early diagnosis, linkage to care, and treatment closer to their homes reducing catastrophic costs for the family.

**OA35-480-17 TB deep dive analysis: a methodical approach to reviewing programme implementation and enhancing operational plans for TB care and prevention**

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**Background and challenges to implementation:** Program Implementation Reviews (PIR) are essential to program improvement. PIRs allow Local Government Units (LGUs) to comprehensively examine various strategies across the TB cascade of care including governance, financing, regulation, and service delivery to identify gaps and propose evidence-based solutions to strengthen LGU operational plans. Given the COVID-19-related challenges, no TB PIRs were conducted between 2020 and 2022.

**Intervention or response:** In February 2023, USAID’s TB Platforms for Sustainable Detection, Care and Treatment Activity collaborated with the Center for Health Development (CHD) IV-A and provincial health offices, to support a series of program implementation reviews for TB service delivery points in the region, utilizing the “Deep Dive” approach. The Deep Dive is a methodical analysis of each indicator and sub-indicator in the TB care cascade to identify gaps.

Fishbone analysis was utilized to determine the root causes of major gaps identified, using the 6M classification: manpower, machine, method, materials, milieu, and money.

**Results/Impact:** Four hundred seven TB program managers and implementers from 133 (94%) LGUs received capacity-building on Deep Dive analysis, improving their TB data analysis and utilization skills to inform TB programming. A review of local epidemiological indicators assisted the teams in identifying specific communities needing priority high level support.

Local TB cascade indicators were analyzed, helping the teams identify specific service delivery gaps, such as low testing rate and high lost to follow-up, and determine

solutions to address the 6M root causes. Accordingly, the 2023 LGU TB program plans were revised to incorporate identified solutions.

**Conclusions:** Employing the deep dive approach to analysis facilitates an in-depth review of the TB care cascade and program management, identifying the root causes of major gaps. In turn, service delivery points developed evidence-based and doable action plans to improve performance and achieve targets.

## OA36 Spatial and Molecular epidemiology of TB

### OA36-481-17 An ecological study of the spatial association with loss to follow-up from tuberculosis treatment in Brazil, 2010-2021

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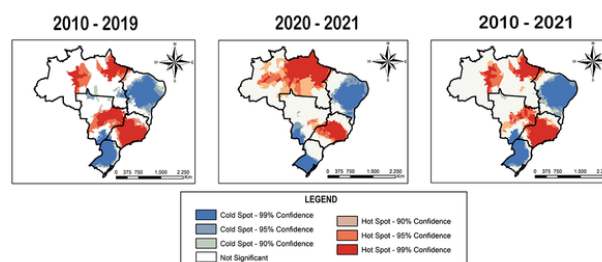
**Background:** Tuberculosis (TB) was the leading cause of death by a single infectious disease worldwide until COVID-19 onset. The pandemic disrupted programmatic actions of TB control, including the operationalization of Directly Observed Treatment (DOT), which can lead to catastrophic repercussions on treatment outcomes. Therefore, this study aimed to identify areas of spatial association of loss to follow-up from TB treatment in Brazil and verify COVID-19 impact in cluster formation.

**Design/Methods:** Ecological study held in Brazil composed of all cases of loss to follow-up in TB treatment from 2010 to 2021 extracted from DATASUS. Rates of loss to follow-up per 100 000 population were calculated for each municipality and were carried out the Getis-Ord GI\* technique, which identifies areas of spatial association for clusters of high (Hotspots) and low (Coldspots) intensity.

**Results:** A total of 1,054,772 cases were notified, of whom 134,399 were lost to follow-up from TB treatment.

For the period from 2010 to 2019 (pre-pandemic) and 2010 to 2021, there was a similar spatial pattern distribution, being that it was detected two clusters of high incidence in the North region, one in the Midwest and one in the Southeast, whereas in the Northeast and South regions were detected low incidence clusters for loss to follow-up. From 2020 to 2021 (COVID-19 pandemic

period), there was a different spatial distribution, with high incidence clusters in North and Southeast regions; and protection clusters in the Northeast and South.



**Conclusions:** It was possible to identify areas of high and low incidence of loss to follow-up from tuberculosis treatment in Brazil. The difference in the spatial pattern found during the pandemic could indicate priority areas to implement complementary actions in TB control, considering the pandemic impact in those areas.

### OA36-482-17 Geospatial overlap of undernutrition and TB in Ethiopia

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**Background:** Undernutrition is a key driver of the global tuberculosis (TB) epidemic, but little is known about the spatial co-distribution of both diseases. Understanding the geospatial overlap of the two conditions is essential for implementing cost-effective integrated control programs. This study aimed to determine the spatial co-distribution and socio-climatic drivers of undernutrition and TB in Ethiopia.

**Design/Methods:** Data on wasting, underweight, stunting, and adult undernutrition were obtained from the Ethiopian Demographic and Health Survey (EDHS). Data on TB were obtained from the Ethiopian national TB survey. Environmental and demographic variables relevant to our study were obtained from available sources.

We applied a geostatistical model using a Bayesian framework to predict a high-resolution prevalence of undernutrition and TB across the country. Predicted prevalence maps were then overlaid to determine areas of spatial overlap.

**Results:** Spatial variation in the prevalence of TB and undernutrition was observed in Ethiopia. Spatial overlap of undernutrition and TB prevalence was detected in Afar and Somali regions. Population density was associated with the spatial distribution of TB [mean regression coefficient ( $\beta$ ): 0.008; 95% CrI: 0.001, 0.014], wasting [ $\beta$ : -0.017; 95% CrI: -0.032, -0.004], underweight [ $\beta$ : -0.02; 95% CrI: -0.031, -0.011], stunting [ $\beta$ : -0.012; 95% CrI: -0.017, -0.006] and adult undernutrition [ $\beta$ : -0.007;



95% CrI: -0.01, -0.005]. Distance to a health facility was associated with the spatial distribution of stunting [ $\beta$ : 0.269; 95% CrI: 0.08, 0.46] and adult undernutrition [ $\beta$ : 0.176; 95% CrI: 0.044, 0.308].

**Conclusions:** The spatial distribution of TB and undernutrition were associated with healthcare access and demographic factors. Spatial overlap of undernutrition and TB prevalence was observed in Afar and Somali regions, suggesting that geographically targeted service integration may be more effective than nationwide service integration.

### OA36-483-17 Temporal trends in the TB burden in an ageing population in China: secondary data analysis from GBD 2019

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**Background:** With the rapid population aging in China, it has been a big challenge to achieve the goal of End the global TB epidemic.

This study aimed to describe the temporal trend of tuberculosis (TB) burden in China during 1990-2019, and to evaluate the effect of age, period and birth cohort on China's TB burden.

**Design/Methods:** The trend of incidence, mortality and disability-adjusted life years (DALYs) of TB was described using the data of Global Burden of Disease 2019 study. Join-point regression model was applied to calculate the average annual percentage change (AAPC) of TB burden for different groups. Age-period-cohort (APC) model was fitted for rate and relative risks (RR) of each age group were computed.

**Results:** In 2019, the highest TB deaths (5 232, 95% uncertainty interval [UI]: 4 375~6 171) and DALYs (155 180, 95% UI: 126 471~190 554) happened in population aged 70-74 years old in China. In patients with newly diagnosed TB, the proportion of patients aged above 65 years increased from 16.73% in 1990 to 28.92% in 2019, so as to the TB deaths, the proportion rose from 38.34% to 59.42%.

During the 30-year period, the AAPC of age-standardised rate of mortality (-7.77, confidence interval [CI]: -8.44~ -7.10) and DALY (-7.48, 95% CI: -7.98~ -6.97) of TB decreased in general, while the decrease in the 75-79 years group was much lower.

The period effect and cohort effect for TB incidence and mortality have shown a general trend of decreasing, while the age effect presented an obvious rising trend for TB mortality, especially among the age of 85-89 years (RR=4.59, 95% CI: 4.25~4.95).

**Conclusions:** The disease burden of TB remains considerable in the elderly Chinese population. TB case findings should be enhanced in this high-risk elderly population, together with innovative approaches for early detection and reactivation prevention.

### OA36-484-17 Molecular epidemiology of *M. tuberculosis* complex in Ireland over a 10-year period with a focus on whole-genome sequencing of informative clusters

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**Background:** Ireland is a low tuberculosis (TB) burden country with declining crude incidence rates. Despite this, enhanced focus on interrupting TB transmission is needed to meet WHO End TB Strategy goals. Mycobacterial interspersed repetitive unit – variable number tandem repeats (MIRU-VNTR) genotyping has recently been replaced by whole genome sequencing (WGS) genotyping as the gold standard typing method for Mycobacterium tuberculosis complex (MTBC).

This study aims to describe the molecular epidemiology of MTBC in Ireland over 10 years, and to gain further insights into informative clusters using WGS genotyping and TB surveillance data.

**Design/Methods:** MIRU-VNTR data was used to characterise the molecular epidemiology of MTBC isolates collected from 2010 – 2019 and received in the Irish Mycobacteria Reference Laboratory (IMRL). Twenty-three clusters with identical MIRU-VNTR genotype, selected to represent a range of lineages and cluster sizes, were genotyped using WGS. National TB surveillance data for clustered cases were analysed to compare genotyping performance across various subgroups.

**Results:** High lineage diversity was demonstrated within isolates collected from 2010-2019 (n=2275). Six global lineages were found, including West-African lineages. Euro-American lineage 4 predominated at 66%. 43% of isolates were clustered using MIRU-VNTR genotyping (n=972 isolates, n=231 clusters). Median cluster size was 2 (range 2-52). The largest clusters mainly involved Irish-born cases.

MIRU-VNTR and WGS matched for 52% informative clusters. WGS genotyping gave a more highly resolved view of relatedness in 48% of clusters. 13% were completely refuted, 17% had some isolates ruled out of the cluster and 17% had more than one sub-cluster found with WGS genotyping. Analysis is continuing to mine surveillance data, possibly giving further insight into these clusters.

**Conclusions:** Ireland has a heterogenous MTBC population, dominated by Lineage 4. MIRU-VNTR genotyping has over-estimated TB clusters within Ireland, confirmed by WGS genotyping now in place. Efforts to interrupt MTBC transmission can be better targeted with WGS genotyping.

### OA36-485-17 Describing direct transmission of rifampicin-resistant TB between known contacts in Khayelitsha, South Africa: a molecular epidemiology study

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**Background:** Direct tuberculosis transmission is often inferred using single nucleotide polymorphism (SNP) thresholds of 1-12 (genomic distance).

However, there is limited data to support this approach from high HIV, TB and rifampicin-resistant TB (RR-TB) burden settings.

**Design/Methods:** Khayelitsha has TB case notification >1,000/100,000/year with ~70% HIV co-infection and ~200 RR-TB patients diagnosed annually.

Whole genome sequence (WGS) data, from the earliest available isolate, were used to describe SNP differences (drug-resistance conferring mutations excluded) between epidemiologically linked RR-TB patients routinely diagnosed across 2008-2017.

**Results:** WGS data were available for 108 RR-TB patients with known close contact (63, 58% HIV-positive at RR-TB diagnosis). These patients were epidemiologically linked into 43 clusters containing 65 linked pairs, irrespective of time between diagnoses.

Overall, 42 (65%) pairs were separated by 0-1 SNPs, with a further 8 (12%) separated by 2-7 SNPs; 2 pairs had SNP differences of 13 and 19 respectively.

The remaining 13 (20%) pairs showed SNP differences between 195-1084, representing infections with different strains. RR-TB strains were isolated from patient pairs a median of 371 days apart (IQR 177-804 days), with no association between time and SNP differences (Figure). Among the 42 pairs separated by 0-1 SNPs, the median time between isolates was 342 days (IQR 158-710), with no difference by HIV status of either patient in the pair.

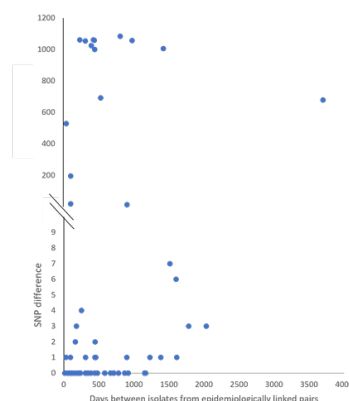


Figure. SNP and time (days) differences between RR-TB isolates from patient pairs.

**Conclusions:** The majority of transmission events showed very low genomic variation suggesting that low SNP thresholds can be used to discern direct transmission of RR-TB between individuals. There were, however, two patient pairs with known links with intermediate SNP differences, which may represent transmission of clonal populations. Significant time differences (up to years) between pairs with 0-1 SNP differences highlight the need for intensified post exposure management for RR-TB contacts and lengthy patient cohorts to fully assess transmission, even in high HIV prevalence settings.

### OA36-486-17 Mortality among people with drug-susceptible TB in South Africa

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**Background:** Mortality due to tuberculosis (TB) is a challenge globally. To reduce TB mortality, we need to document deaths and understand who are at greatest risk of death. By doing so, we will be able to prioritize resources and implement strategies that will mitigate the challenge.

We report on mortality and its risk factors amongst people with drug-sensitive TB in South Africa.

**Design/Methods:** This is sub-analysis from the ASCENT trial, a cluster-randomized trial evaluating the use of digital adherence technologies to support TB treatment adherence.

The trial took place in 60 primary health care facilities across 2 provinces in South Africa and enrolled adults ≥ 18 years who were on TB treatment. End of treatment outcomes data were abstracted from the TB register. Poisson regression with random effects (facility-level)

was used to assess individual- and time-frames of calendar period and treatment phase (using lexis expansion) factors associated with on-treatment mortality rate.

**Results:** Between November 2021 to March 2023, treatment outcomes for 4830 patients were abstracted. Majority of participants 3000 (62%) were males, 1496 (31%) were aged between 30-39 years and 2834 (59%) had bacteriologically confirmed TB. Over half were living with HIV 3006 (62%) of whom 2614/3006 (87%) were on antiretroviral therapy.

Mortality risk at end of treatment was 358/4830 (7%). Older age, those living with HIV but not on ART or unknown ART status and those clinically diagnosed with TB had an increased mortality rate while those who reached continuation phase had a decreased mortality rate (table).

Variable		Total deaths	Mortality rate (/100 person-years)	Adjusted Rate ratio (95% confidence interval)
Gender	Male	229	15.8	1
	Female	129	14.2	0.91 (0.73 - 1.14)
Age group, years	<30	29	7.8	1
	30-39	85	11.5	1.36 (0.88 - 2.10)
	40-49	93	14.5	1.64 (1.07 - 2.52)
	50-59	70	19.5	2.10 (1.34 - 3.30)
	≥60	81	32.9	3.58 (2.30 - 5.58)
HIV ART	Negative	102	12.6	1
	Positive - on ART	190	14.6	1.25 (0.96 - 1.61)
	Positive - not on ART	34	26.4	2.34 (1.55 - 3.52)
	Positive - unknown ART	13	27.3	2.29 (1.26 - 4.16)
Disease classification	Bacteriological	151	11.0	1
	Clinical	207	21.0	1.85 (1.47 - 2.32)
Calendar period	Aug 2020 - Sep 2021	63	18.2	1.05 (0.74 - 1.47)
	Oct - Dec 2021	74	17.2	1.06 (0.77 - 1.46)
	Jan - March 2022	86	15.2	1
	April - June 2022	92	16.7	1.09 (0.81 - 1.48)
	July 2022-	43	9.2	0.69 (0.47 - 1.01)
Treatment phase	Intensive	189	24.1	1
	Continuation	169	10.7	0.49 (0.39 - 0.61)

**Conclusions:** There was high mortality amongst our study population over a short period of time. Interventions targeting older generations, those living with HIV and clinically diagnosed are needed to reduce mortality

### OA36-487-17 The influence of occupation on community participation and results in a TB prevalence survey, India

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**Background:** National Tuberculosis prevalence survey was conducted in India between 2019-2021 in which 354541 eligible participants were enrolled. Several measures were taken to ensure maximum community participation. This includes meticulous planning in advance, communication and engagement of local authorities, community representatives and explaining benefits of participation in the survey.

During survey, participants were also offered refreshments at the survey sites along with basic amenities including, seating arrangements, drinking water to make them comfortable.

**Design/Methods:** All eligible survey participants who consented were enrolled (in digital data management system for survey) in prevalence survey during their home visit. They were given QR code-based identity card along with the time and place of appointment (based on their convenience) for participation in survey at respective sites.

Enrolled participants not reporting at survey sites were followed up at their home at least three times to pursue their participation in the survey.

Finally, reasons of non-participation were ascertained and entered on last day of survey cluster activity.

**Results:** Overall, 91% 3,22,480 people participated. Highest non-participation was among salaried employees (14.9%) and those having business (12.9%).

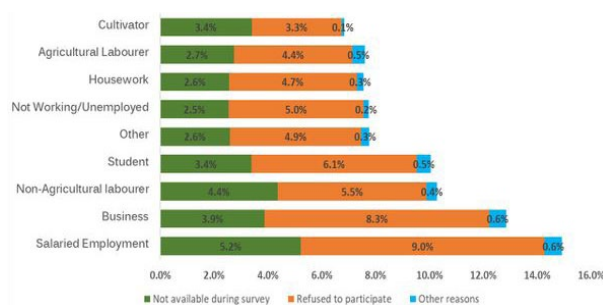


Figure: Reasons for non-participation in tuberculosis prevalence survey.

Overall proportion of ‘refusal to participate’ was higher than that of ‘non-availability’ in all types of occupations. Among non-participants, non-availability of the

participants was highest (60%) among salaried employees due to unsuitable timings. Among laborers, temporary travel & migration was 50% in non-agriculture and 47% in agricultural laborers. Unemployed had highest TB prevalence (655/1,00,000) and lowest in houseworkers (126/1,00,000).

**Conclusions:** Nominal compensation like refreshments during the survey procedures are important but not enough for participation, at least for few types of occupation. Among salaried employees and those in business, fee day-off or compensatory off as well as flexible timing of surveys may be useful. Occupation-wise statistical adjustments must be made for more accurate estimation.

## OA37 Access to quality TB care and services

### OA37-488-17 Harnessing the power of persuasive communication to find and treat missing TB cases among TB household contact persons: the COME ALIVE strategy

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**Background and challenges to implementation:** Tuberculosis (TB) household contact persons are at high-risk for TB. Although contact investigation (CI) results in earlier case identification, decreased disease severity, and reduced transmission, its practice remains sporadic in many settings. In the Philippines, the implementation and documentation of CI remain inconsistent and difficult to quantify.

**Intervention or response:** USAID's TB Platforms for Sustainable Detection, Care and Treatment project implemented the COME ALIVE (Communicate and Mentor Effectively through A-L-I-V-E) Strategy to improve the capacity of community health workers (CHWs) to deliver social behavior change campaigns. The strategy focuses on five critical communication skills: Asking questions, Listening actively, Informing dynamically, Verifying and Encouraging behaviors. These skills are used during house-to-house visits to communicate with TB contact persons, assess for TB signs and symptoms, convince them to undergo testing as needed, and enroll in treatment if diagnosed. COME ALIVE anchors on the premise that people are easily persuaded if messengers are perceived as competent, trustworthy, and appealing.

**Results/Impact:** From 2021 to 2022, the Activity trained 3,223 CHWs on COME ALIVE, who proceeded to screen 56,449 contact persons of 4,257 index TB patients during house-to-house visits. Of those screened, 4,516 (8%) were presumed to have TB; 3,568 (79%) were tested, and 2,647 TB contact persons were diagnosed with TB (Bacteriologically confirmed (BC): 54%, Clinically diagnosed: 46%); 2,619 (99%) were enrolled in treatment. Forty contact persons needed to be screened to find 1 BC TB case. The overall yield was 5% - comparable with other documented community-based case-finding activities.

**Conclusions:** CHWs make a difference in TB detection and treatment, especially if capacitated to become competent agents of case detection, trustworthy treatment partners, and dynamic referrers. Their social capital and relationships are instrumental in addressing community perceptions of TB and improving health-seeking behavior. Building CHW capacities are worth healthcare systems' investments.

### OA37-489-17 e-Referral of presumptive TB patients from private pharmacies: results of a pilot in North Sumatera, Indonesia

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**Background and challenges to implementation:** Globally, Indonesia has the second highest TB burden. A 2017 study showed that 52% of TB patients initially seek care in private pharmacies which are not engaged under TB public-private-mix (PPM). Pharmacies lack a formal mechanism to refer clients for TB diagnosis. SwipeRx is an all-in-one app for pharmacy professionals to connect, find accurate drug and health information, and access free continuing professional development (CPD) modules.

**Intervention or response:** USAID TB Private Sector utilized the SwipeRx platform to develop and pilot a digital referral tool (e-referral) within the SwipeRx application to identify presumptive TB among pharmacy clients between June 2021-May 2022 in Medan City, North Sumatera.

A total of 226 pharmacy professionals from 148 private pharmacies were engaged and trained. Pharmacies referred to engaged public health centers (41) and private clinics (8).

To promote participation, incentives were provided for successful referrals as CPD credits for pharmacists/pharmacy assistants and mobile recharge vouchers for non-professional staff from March-May 2022.

**Results/Impact:** In total 423 pharmacy clients were screened and 97 identified as presumptive TB with referral to health facilities for diagnosis. Among those referred, 39 were recorded and tested for TB at the facilities. Of those, 49% (19) were re-referred for chest X-Ray or to their appointed primary facility registered for national health insurance. Of those recorded at the referral facilities, 44% (17) were diagnosed with TB and started treatment. Mobile recharge vouchers as an incentive, increased TB screening activities in 22 selected pharmacies by 76% (63 to 111).

**Conclusions:** Having a pharmacy referral mechanism in place in Indonesia can help identify missing people with TB by identifying presumptive TB among pharmacy clients. However, structured mechanisms using digital platforms to facilitate screening and referral from private pharmacies to NTP are needed. Data sharing mechanisms enabling seamless referral and tracking are pivotal in increasing the yield of this intervention.

### OA37-490-17 Engagement of the private sector for finding missing TB cases in Nigeria: prospects and challenges

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**Background and challenges to implementation:** Nigeria is among the 30 high Tuberculosis (TB) burden countries globally with an estimated 250,000 TB cases missing annually. The engagement of the private sector is one of the Interventions deployed by the National TB Programme (NTP) in finding these missing TB cases. This paper provides an analysis of the gains and the challenges of this intervention.

**Intervention or response:** The engagement of the private sector in TB care and management has been passive since the inception of the NTP. However, there was a deliberate effort by the USAID and the Global Fund to actively engage the private sector in 2018 and 2019 respectively through Intermediary Organizations (IO). The hub-and-spoke model was adopted by the IOs. While the spokes made up of the Community Pharmacist, Patent and Proprietary Medicine Vendors, Traditional Birth Attendants mainly identified and referred presumed TB cases, the hubs made up of the private-for-profit and faith-based organization facilities offered the full range of TB care. Linkage mechanisms between the spokes and hub ensured complete referrals. Financial incentives and enablers are given to providers for screening, referral, testing, contact management, and

case-holding. Electronic applications for TB screening were deployed. The NTP tools are used for documentation, reporting is through the NTP reporting channels.

**Results/Impact:** Private facilities providing TB services increased from 977 in 2017 to 4,038 in 2022. Figure 1 shows the 10 years trend of TB notification through the private sector.

As funding for TB dwindles, there is the likelihood that this may lead to a downward trend in the significant increase in TB notification from the private sector experienced in the past five years.



Figure 1. PPM TB notification trend from 2013 to 2022 in Nigeria.

**Conclusions:** The NTP and its partners need to identify sustainable means of incentivizing private providers to ensure sustainability of the gains so far. A detailed analysis of the threats associated with this mode of engagement is recommended.

### OA37-491-17 Improving private sector TB notifications and access to quality TB services through strategic engagement and intermediary partners in Indonesia

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**Background and challenges to implementation:** Indonesia has the second highest number of unreported TB cases globally with an estimated 275,000 in 2022. Private primary providers have an important role in finding the missing TB patients, yet have limited access to GeneXpert (GX) testing, fixed dose combination (FDC) drugs, and the national TB surveillance system (SITB) which hinder their contributions. Addressing the barriers private primary providers face is critical to find the missing TB patients and improve TB treatment quality.

**Intervention or response:** Starting October 2020, USAID Tuberculosis Private Sector (TBPS) supported six districts (Medan, North Jakarta, South Jakarta, Gresik, Denpasar, Samarinda) in Indonesia to engage private primary providers in a District-based Public-Private-Mix (DPPM). This focused on i) promotion and improvement of access to GX testing, ii) improved access

to programmatic TB drugs and iii) facilitating provider access to SITB. Additionally, TBPS provided the local PPM leads - district health offices and public primary health centers - with technical assistance to conduct facility supervisory visits and sub-district PPM reviews. In four out of six districts, the TBPS intervention package was delivered by contracted local intermediary partners (IPs).

**Results/Impact:** Between October 2020 and December 2022, the number of private primary providers engaged in DPPM increased from 122 to 1,139 and the number of presumptive TB cases reported through SITB increased from 1,576 to 5,438 in six supported districts. TB case notifications increased from 689 to 1,535 and the proportion of presumptive TB patients tested with GX among private sector referrals increased from 60% (947/1,576) to 77% (4,204/5,438).

**Conclusions:** Barriers in access to GX testing, FDC, and the complicated national TB surveillance system (SITB) hinder TB notification from private primary providers. In collaborative application, TBPS delivered intervention packages often through contracted local IPs, which improved DPPM engagement and increased presumptive TB reporting and TB notifications from private primary providers.

### OA37-492-17 TB screening in traditional psychiatric homes: a strategic community active case-finding model for improving TB case-finding in a low-yielding local government area, Ogun State, Nigeria

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**Background and challenges to implementation:** Alternative Medicine Practice is gradually playing a significant role in the prevention and control of diseases of public health importance, particularly in developing countries like Nigeria, where there are limited resources for universal health coverage and tuberculosis is no exception.

However, engagement is still suboptimal and consequently creating a lot of missed opportunity in TB case finding.

**Intervention or response:** Two Traditional Psychiatric Homes were identified in Ode community, Remo North LGA of Ogun state. After due advocacy and appropriate education on Basics of TB, TB screening was carried out on all residents of the homes using the WHO symptomatic screening questions (cough of  $\geq 2$  weeks, fever, night sweat, and unexplained weight loss) to identify TB presumptive cases whose sputum samples were subsequently sent for GeneXpert testing. The home comprises of teenagers and young adults who are substance abusers and were brought by family members for unorthodox form of care. Living condition in the home is a crowded, congregate-like setting accompanied with poor feeding, all of which favor the manifestation and spread of TB disease.

**Results/Impact:** A total of 331 residents were screened in both homes with 117 TB presumptive identified, and 38 TB cases diagnosed representing 32% TB yield. The intervention was responsible for a 300% increase in TB case finding in quarter 4 2022 over the previous quarter as shown in the chart below and accounted for about 59% case contribution to the total TB case finding in the LGA.

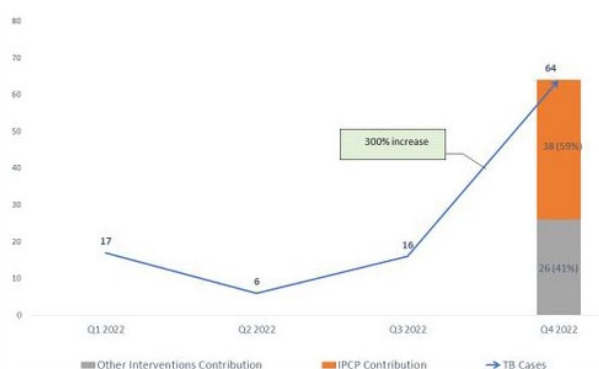


Figure. LGA case finding trend - Q1 - Q4 2022.

**Conclusions:** Active collaboration with Traditional Medicine Practitioners is an evolving and viable intervention that requires more attention and resource mobilization in TB control programs as it carries a high potential for rewarding outcomes in rapidly finding the missing TB cases and consequently reducing TB burden, and as such, a systematic scale-up of engagement with Traditional Medicine Practitioners is highly recommended.

### OA37-493-17 Continuity of TB essential health services during an outbreak of Ebola 2023: lessons from Uganda

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**Background and challenges to implementation:** On 20th September 2022, the Ministry of Health declared an outbreak of Ebola Virus (EVD) in Mubende and Kasanda districts. The government of Uganda then adapted aggressive public health interventions to mitigate the spread of Ebola including the movement restrictions and lockdown two districts.

Although these measures were successful in limiting the local spread of Ebola, it is less clear how they may have affected TB services.

**Intervention or response:** We collected information on key TB priority indicators for three specific periods, the pre-pandemic period (before September 2022), the emergency response period (Sept 2022–Jan 2023), and the mitigation period (Feb 2023 onwards).

We collected information on the proportions of outpatients screened for TB, the number of patients diagnosed with TB and the proportion of health facilities submitting the TB weekly surveillance report.

The Man-Kendal test for trend analysis was conducted for cases reported from pre-pandemic phase over the EVD response period. *P* value <0.05 was considered statistically significant.

For the mitigation phase we are implementing coordination at all levels, active case search using mobile van TB clinics mounted with, gene expert and an Artificial Intelligence enabled CAD for TB screening, utilization of patient-centered approaches and use of digital adherence technologies.

**Results/Impact:** There was an observed decline in screening and reporting rates (fig 1 & 2), case finding for TB in the epicenters by 52.8% when compared to the prior period (epi week36/2021-Week 5/2022), and Week 36/2022-Week 5/2023), and far below National Strategic Plan (NSP) targeted weekly 28 cases for the epicenters, a significant decline in numbers of TB cases reported (*P*<0.0001).

**Conclusions:** Restriction and lockdowns imposed by the government could have affected care-seeking and access, hence undermining gains in TB control.

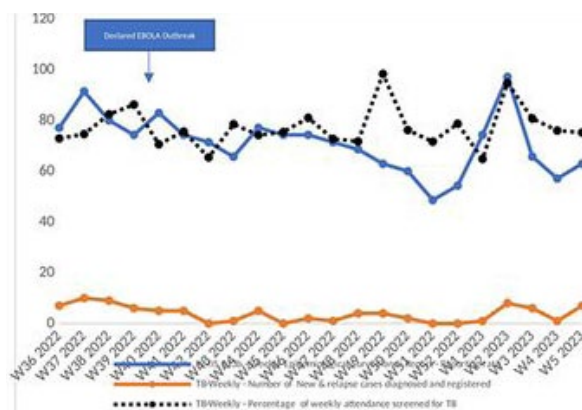


Figure 1. Showing trends in reporting rates, TB screening & notification disaggregated by epi weeks, Kasandra district.

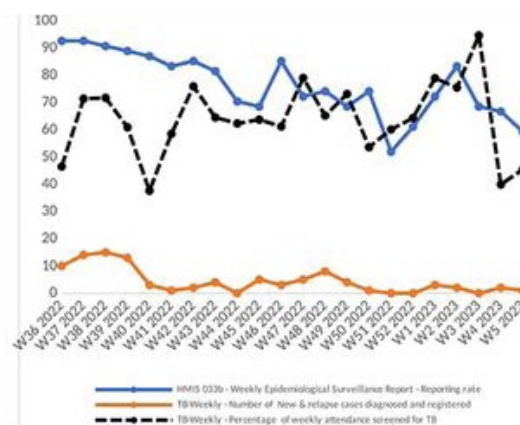


Figure 2. Showing trends in reporting rates, TB screening & notification disaggregated by epi weeks, Mubende district.

### OA37-494-17 Scaling up point-of-care TB screening and diagnostic tools for indigenous peoples: utilisation of computer-aided detection and portable rapid diagnostic test in active case-finding

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**Background and challenges to implementation:** Access to basic health services remains a problem for the 10-20% of the Philippines' Indigenous Peoples (IP) population. In Rodriguez, Rizal challenges to IPs' access to health services are aggravated by their remote community locations, particularly in San Rafael, Puray, and Macabud villages with over 40% indigenous populations.

IPs have limited TB testing and screening opportunities, given the municipality's challenging topography and the limited availability of chest x-ray (CXR) services.

**Intervention or response:** The USAID's TB Platforms for Sustainable Detection, Care and Treatment Project supported Active Case Finding (ACF) activities in the three IP communities, by deploying mobile TB CXR with CAD services to provide initial CXR reading, allowing onsite identification of IPs presumed to have TB. Onsite sputum specimens were collected from IPs presumed to have TB for TrueNAT testing, a portable, rapid TB diagnostic testing device. The strategy aims to facilitate point-of-care diagnosis reducing early lost-to-follow-up.

**Results/Impact:** The program intervention resulted in all 321 indigenous community members receiving a CXR with CAD. Of these, 95 (30%) were presumed to have TB and tested. As a result, 80 individuals were diagnosed with TB and enrolled into treatment, equivalent to 9% of total TB case notifications from the three communities. The initiative reduced the turnaround time from screening to testing from an average of seven days to less than a day.

**Conclusions:** Utilization of point-of-care screening and diagnostic platforms improves access to TB services in geographically isolated places. There was no comparison of costs between TrueNAT and Xpert MTB/Rif, or between fixed and portable CXRs. The use of point-of-care screening and diagnostic tools, significantly reduced turnaround times, minimized lost-to-follow-up, maximizing the impact among marginalized and underserved communities.

### OA37-495-17 Decentralising drug-resistant-TB care using telemedicine (*e-sanjeevani*) from health and wellness centres in Jharkhand, India

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**Background and challenges to implementation:** India contributed to 27% of the global Drug-resistant tuberculosis (DR-TB) burden in 2020. The state of Jharkhand has a death rate of 7.5% and Lost to follow-up rate of 8% in people diagnosed with MDR TB in 2022. The out-of-pocket expenses incurred for TB patients in India is 713.4 USD (direct and indirect costs).

**Intervention or response:** Jhpiego, through its JnJ grant, trained Community Health Officers (CHOs) posted at two districts on MDR TB and linked these HWCs to specialists' hubs, utilizing the *e-sanjeevani* platform for addressing adverse drug reactions, providing counseling and ensuring compliance.

Intervention was piloted between July 2022 and December 2022. The District TB Centers and CHOs were capacitated and teleconsultations were facilitated between CHOs and specialists after mapping the existing people needing DR-TB care to their catchments. The activities were monitored using NIKSHAY and *e-Sanjeevani* data (Online portal for TB program and teleconsultation program respectively).

**Results/Impact:** 95% of HWCs (N=244) in the two districts were linked in *e-sanjeevani*. All notified people needing DR-TB care during the pilot (N=35) were registered on *e-sanjeevani*. A total of 108 teleconsultations were made. 65 accounts of adverse drug reaction were timely identified and managed jointly by CHOs and MOs. An average of 84% patients in ES and 39% in Ranchi were followed-up monthly by the CHOs.

**Conclusions:** The pilot led to timely detection and redressal of ADRs, reduced travel to higher facilities, and quicker consultations. Including CHOs in the management of MDR TB can play a significant role in preventing treatment disruptions, early detection and redressal of ADRs, thus leading to favorable treatment outcomes. The unavailability of internet at the HWCs and the absence of a cadre of specialists for teleconsultation were identified as the major issues in the implementation of the program.

### OA38 Implementation of TPT in PLHIV

#### OA38-496-17 The TB preventive therapy cascade of care among people with HIV undergoing systematic TB screening in Uganda

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**Background:** Tuberculosis preventive therapy (TPT) is recommended for all people with HIV (PWH) as being highly effective in reducing TB incidence and mortality, but uptake and completion rates are suboptimal. We characterized the TPT cascade of care for PWH participating in a trial offering short-course TPT (3HP, 3-months of weekly isoniazid+rifapentine).



**Design/Methods:** TB SCRIPT is a randomized trial evaluating the impact of C-reactive protein (CRP)-based TB screening on case detection and TPT uptake among adult PWH initiating antiretroviral therapy (ART) in four HIV clinics in Uganda (ClinicalTrials.gov NCT04557176).

We characterized the TPT cascade of care for PWH who screened negative by their randomization assignment (CRP <5 mg/L or 0/4 WHO symptoms), with each step expressed as a proportion of the preceding step. 3HP eligibility was assessed using a standardized questionnaire, liver enzyme testing, and urine pregnancy testing.

Eligible PWH (liver enzymes <3x upper limit-of-normal, non-pregnant) initiating 3HP were assessed for adverse events and adherence by pill count and recall. 3HP completion was defined as taking ≥11 doses within 16 weeks.

**Results:** From November 2020 to December 2022, 826 PWH screened negative for TB (71.9% female, median age 28 years [24-35], median CD4 count 285 cells/uL [176-445]). All 826 PWH (100%) were assessed for 3HP eligibility, of whom 595 (72.0%) were eligible (Figure 1).

Most PWH ineligible for 3HP were pregnant (179/231, 77.5%) or had transaminitis (16/231, 6.9%). Of the 549 (92.3%) eligible PWH who presented for 3HP initiation, 531 (96.7%) initiated and 498 (90.7%) completed 3HP. The cumulative proportion initiating and completing 3HP was 64.3% and 60.3%, respectively.

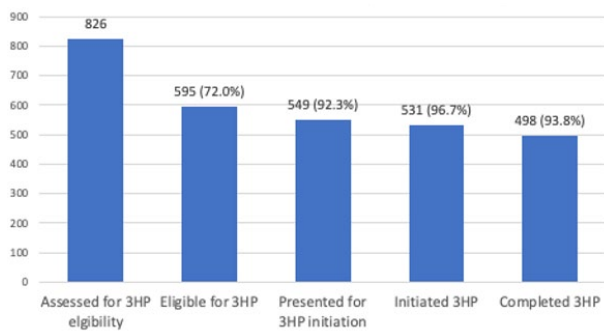


Figure 1. 3HP cascade of care for ART-naive outpatient PWH in Uganda.

**Conclusions:** 3HP completion rates were high, suggesting high tolerability. However, nearly one-quarter of all PWH were ineligible due to pregnancy. Rigorous safety data for short-course TPT regimens during pregnancy is urgently needed to optimize TPT benefit for pregnant women with HIV.

### OA38-497-17 Preferences for TB preventive treatment regimens among persons living with HIV in Uganda – a discrete choice experiment

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**Background:** Tuberculosis (TB) preventive treatment (TPT) is recommended for persons living with HIV in high TB burden settings. While 6 months of daily isoniazid (6H) is widely available, a short-course regimen consisting of 12 weekly doses of isoniazid and rifampine (3HP) is being rolled out globally.

Other regimens, including 1 month of daily isoniazid and rifampine (1HP), are considered for future roll-out. However, little is known about individuals' preferences for TPT regimens.

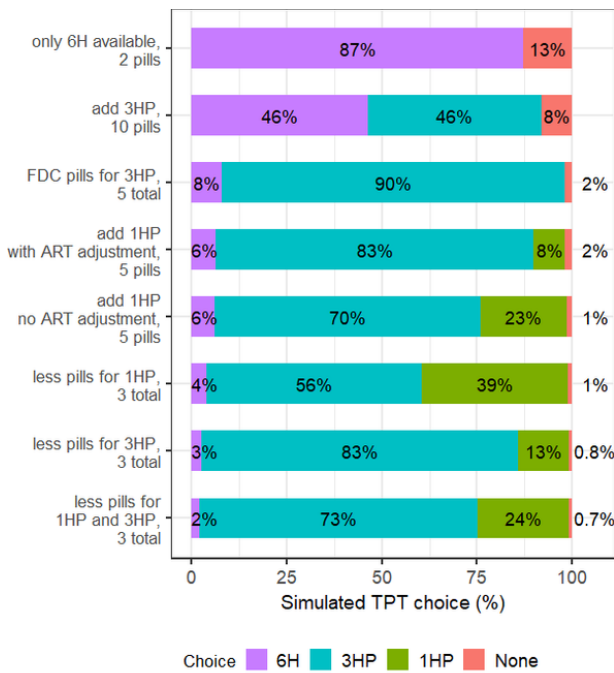
**Design/Methods:** We administered a discrete choice experiment survey among adults living with HIV engaged in care at an HIV clinic in Kampala, Uganda.

In 9 random choice tasks, participants (1) chose between two regimens based on treatment burden (number of pills, frequency, duration, adjusted HIV antiretroviral dosage) and side effects, and (2) answered if they would prefer the selected treatment if available versus no treatment. We analyzed preferences using hierarchical Bayesian estimation and simulated predicted TPT choice.

**Results:** Among 400 participants (median age 44, 72% female, 91% with previous TPT), across tasks, 60% (241/400) accepted all regimens, 39% (157/400) accepted some regimens, and 0.5% (2/400) accepted none.

Figure 1 shows predicted choices in scenarios where additional existing regimens are added as choices or have improved features. If only 6H was available, 13% would prefer no treatment. A 10-pill 3HP regimen was predicted to be equally desirable as 6H (46% vs. 46%). However, a 5-pill 3HP fixed dose combination (FDC) regimen was preferred over 6H (90% vs. 8%).

More participants preferred a 5-pill 3HP regimen over a 5-pill 1HP regimen, both in scenarios where 1HP required (83% vs. 8%) and did not require antiretroviral dosage adjustment (70% vs. 23%).



**Figure 1. Simulated choice among TPT regimens.** Scenarios follow historical availability (6H only, 3HP rollout with 10 pills, rollout of FDC for 3HP), and predictions for potential improvements. 6H: 6 months daily doses of isoniazid/rifapentine, 3HP: 3 months weekly doses of isoniazid/rifapentine, 1HP: 1 month weekly doses of isoniazid/rifapentine, ART: antiretroviral therapy, FDC: fixed dose combination, TPT: TB preventive therapy.

**Conclusions:** Predicted uptake of short-course TPT was high with FDC, and FDC 3HP was highly preferred to 1HP. Development of future, more person-centered TPT regimens should focus on reducing pill burden and non-daily dosing.

### OA38-498-17 A choice architecture-based intervention to increase prescription of TB preventive treatment to people living with HIV in southern Africa: results from a cluster-randomised trial

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**Background:** TB preventive treatment (TPT) is a highly effective but underutilized tool for reducing the risk of TB disease among people living with HIV (PLHIV). We evaluated the effectiveness of a choice-architecture-based approach to increase TPT prescribing to PLHIV in Malawi, Mozambique, and Zimbabwe. Choice-architecture structures clinical operations to make a preferred action the default choice for clinicians.

**Design/Methods:** We conducted a cluster-randomized trial within the IMPAACT4TB 3HP rollout in which clinics were randomly assigned to choice-architecture (intervention) or standard TPT prescribing (control). We sought to link TPT prescribing to antiretroviral therapy (ART) prescribing and to make TPT prescribing the default. The intervention was supported by a default prescribing module built into the point-of-care HIV electronic medical record in Malawi and by stickers placed in clients' clinical stationery in Mozambique and Zimbabwe. Data were collected in aggregate at clinic level and the primary outcome was the clinic-level proportion of new ART clients who initiated TPT, reported by study country.

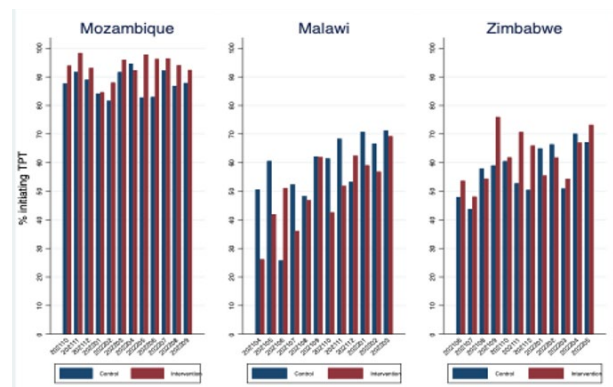


Figure.

**Results:** 57 clinics were included from Mozambique (n=20), Malawi (n=19), and Zimbabwe (N=18). There were a median of 6 and 10 new ART clients per month in intervention and control clinics, respectively, in Mozambique; 17 and 15 in Malawi; and 13 and 13 in Zimbabwe. Comparing intervention to control clinics, mean TPT prescribing to new ART clients was 86.9% vs 70.9% in Mozambique (t-test p-value=0.15), 55.5% vs 56.5% in Malawi (p=0.89), and 55.9% vs 56.2% in Zimbabwe (p=0.98).

**Conclusions:** The choice-architecture intervention did not overcome barriers to TPT prescribing. The intervention may have led to an improvement in TPT prescribing in one study country but no differences were observed in the other countries. Implementation challenges included delays due to COVID-19, similar training across intervention and control arm clinics, cross-over of the default prescribing module in Malawi, and concerns regarding the safety of default prescribing.

### OA38-499-17 Advancing toward TB preventive therapy saturation in people living with HIV and its implications on TB-HIV: a successful case in Zambia

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**Background and challenges to implementation:** Zambia is one of the high TB/HIV burden countries with a rate of 60% in 2018. The country has prioritized TB Preventive Therapy (TPT) as a key strategy of TB control toward elimination. Collaboratively, TB and HIV programs in 2018 embarked on a campaign to scale up TPT in PLHIV to attain 90% TPT saturation by 2022 from 8% in 2018.

**Intervention or response:** Preparation for this approach included consensus building, target setting, securing TPT commodities, capacity building in TPT and raising public awareness. TPT Saturation was defined as TPT coverage of at least 90% of the total clients on ART. We, therefore, targeted and offered TPT to both new ART and treatment-experienced PLHIV who had no prior exposure to TPT and were free of active TB as per the WHO and national guidelines.

**Results/Impact:** Cumulatively, by the end of 2022, TPT initiations had reached 91% (1,141,384 total initiations against 1,253,641 on anti-retroviral therapy), all age groups inclusive. Coverage of TPT varied at the sub-national level. At least 6 of the 10 provinces had cover-

age above the national average. Northwestern province had the lowest coverage of 69% and Copperbelt was the highest at 95%. By end of 2022, TB/HIV co-infection reduced to 32%.

**Conclusions:** Routine data shows that Zambia has successfully attained TPT saturation coverage in PLHIV, which may have contributed to the decline in TB/HIV co-infection rates. Strategic interventions, political will and resilient supply chain system between the two programs were catalytic in achieving the national target on TPT. Provinces with coverage below the national average require more effort and a differentiated approach. These results show that full TPT coverage is attainable. Therefore, policymakers and implementers must consider TPT saturation a national goal.

### OA38-500-17 Cost comparison of delivery strategies for the 3-month isoniazid+rifapentine (3HP) treatment regimen among people living with HIV

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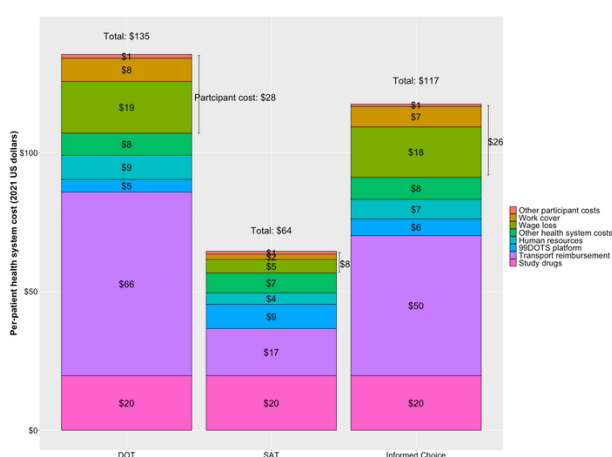
**Background:** Short-course regimens for tuberculosis (TB) prevention, such as three months of Isoniazid-Rifapentine (3HP), have shown high levels of treatment completion in a trial of facilitated directly observed therapy (DOT), facilitated self-administered therapy (SAT), and informed choice between facilitated DOT and facilitated SAT (using a shared decision-making aid) among people living with HIV (PLHIV). We aimed to compare per-patient costs for 3HP across delivery strategies.

**Design/Methods:** In a pragmatic trial (3HP Options), PLHIV at Mulago HIV/AIDS clinic in Kampala, Uganda, were randomly assigned to receive 3HP by facilitated DOT, facilitated SAT, or informed choice. At recruitment, we administered a short costing survey (e.g., time required for clinic attendance) to all participants and a more detailed costing survey at the dose-six visit to a random subset of 50 participants per arm. Study and

routine clinic staff were asked to log the time requirements for their job duties related to implementing study activities on a weekly basis; clinical activities were directly observed using time-and-motion surveys.

**Results:** Facilitated SAT was substantially less costly to the health system (\$57 vs. \$107 per participant) and to participants (\$8 vs. \$28) than facilitated DOT (total cost: \$64 vs. \$135).

This difference primarily reflects more frequent clinic visits for DOT, requiring increased payments for transport reimbursement that outweighed the higher cost of the digital adherence technology (99DOTS) platform for SAT. Participant costs reflected more frequent clinic visits which incurred lost wages and requirements for work coverage (e.g., childcare). Implementing shared decision-making added only minimally to the total cost.



**Conclusions:** For PLHIV receiving 3HP, facilitated SAT required less than half the cost of facilitated DOT. This cost differential may be reduced in clinics that are located closer to participant homes and/or workplaces. Shared decision-making is feasible to implement from the cost perspective.

## OA38-501-17 TB preventive treatment programme successfully reduces TB incidence among people living with HIV on antiretroviral therapy in Uganda

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**Background:** The Ministry of Health has scaled up TB preventive therapy (TPT) in Uganda. We aimed to determine how the TPT program has impacted TB incidence among PLHIV on ART in Uganda.

**Design/Methods:** This was a case-cohort study where data were abstracted from the HIV care database and paper-based TPT registers for PLHIV aged 15 years and above who were initiated on ART during the period from 2016 to 2019 at the six public health facilities during the test and treat era.

We used Poisson methods and Kaplan-Meier to estimate incidence and probability of TB. Log-rank test and weighted Cox proportional regression model were used to compare probabilities and hazards of TB between non-TPT group versus TPT group.

**Results:** We enrolled 1,866 participants: 67.2% (1,253) were females, with median age of 30 (IQR 25 – 36) years, 86.8% were in WHO clinical stage 1 or 2 at ART initiation, 42.0% (783) initiated on TPT whereas 58.0% (1,083) did not.

The probability of developing TB was higher among PLHIV who never initiated TPT compared to those who initiated, i.e. 0.5% versus 0.2%, 1.3% versus 0.4%, 2.0% versus 0.9%, 2.9% versus 1.3%, 3.8% versus 1.6% respectively, at months, 3, 6, 12, 24, and 36 since ART initiation (P value<0.001). The risk of developing TB among PLHIV on ART initiated on TPT was 57% lower than that among those who never initiated TPT (adjusted hazard ratio 0.43, 95% CI 0.31 – 0.60). Male sex, being underweight and advanced HIV disease at ART initiation were associated with a high risk of acquiring TB after ART initiation.

**Conclusions:** TPT successfully reduced TB incidence among PLHIV on ART in public healthcare settings in Uganda. However, male patients, the underweight, and those who start ART with advanced HIV disease need expedient TB evaluation, prevention, or treatment.

Factors	Levels	Person-time Per 1000-person years	Number of TB cases	Un adjusted		Adjusted	
				HR (95%CI)	P value	HR (95%CI)	P value
TPT status (time-varying covariate)	Non-TPT group	27997.68	423	1		1	
	TPT group	9961.74	64	0.43 (0.33 – 0.58)	<0.001	0.43 (0.31 – 0.60)	<0.001
Total duration on ART before incident TB event or censor (per month increase)		N/A	N/A	0.69 (0.61 – 0.78)	<0.001	0.62 (0.52 – 0.73)	<0.001
Total duration on TPT before incident TB event or censor (per month increase)		N/A	N/A	0.35 (0.19 – 0.63)	<0.001	0.66 (0.37 – 1.18)	0.163
Sex	Male	9956.75	239	1		1	
	Female	28002.67	248	0.38 (0.30 – 0.47)	<0.001	0.46 (0.35 – 0.61)	<0.001
Age categories <sup>a</sup>	15 – 24	8359.84	81	1		1	
	25 – 34	18814.63	219	1.23 (0.91 – 1.66)	0.172	0.86 (0.62 – 1.20)	0.366
	35 – 44	7440.31	130	1.87 (1.34 – 2.62)	<0.001	0.91 (0.61 – 1.37)	0.663
	≥45	3344.65	57	1.81 (1.20 – 2.75)	0.001	0.94 (0.58 – 1.51)	0.799
WHO stage at ART start <sup>b</sup>	Stage 1 or 2	35596.25	328	1		1	
	Stage 3 or 4	2357.55	158	7.33 (5.41 – 9.95)	<0.001	5.01 (3.63 – 6.92)	<0.001
Body mass index, kgs/m <sup>2</sup>	<18.5	4101.35	146	3.65 (2.76 – 4.81)	<0.001	2.49 (1.81 – 3.41)	<0.001
	≥18.5	33227.05	327	1		1	
Had any opportunistic infection other than TB (time-varying)	No	30628.24	371	1		1	
	Yes	7331.18	116	1.43 (1.09 – 1.87)	0.009	1.35 (0.97 – 1.87)	0.074

OA38-501-17 Table.

### OA38-502-17 Implementation gaps in tuberculosis diagnosis, treatment, and prevention for children living with HIV: an assessment survey of IeDEA sites

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**Background:** Tuberculosis (TB) is a leading cause of mortality for children living with HIV (CLHIV). We investigated TB diagnostics, screening, management, and TB preventive therapy (TPT) at sites caring for CLHIV

within the International epidemiology Databases to Evaluate AIDS (IeDEA) Consortium--a global research collaboration that collects and analyzes observational data from HIV care sites.

**Design/Methods:** A site assessment survey was implemented from September 2020 to February 2021, with questions querying pre-pandemic practices.

This analysis included only sites in low- and middle-income countries providing care for CLHIV that reported diagnosing TB in 2019. Responses were analyzed using descriptive statistics, with regional differences assessed using chi-square tests.

**Results:** Of 238 IeDEA sites, 227 (95%) responded; 135 were included in this analysis. Most sites reported screening for TB disease at enrollment in HIV care (Table).

Access to diagnostics varied significantly by region, including for GeneXpert (range 67-100%), mycobacterial culture (range 43-83%) and drug-susceptibility testing (range 30-82%) (p<0.001). On-site provision of TB treatment was high (90%).

Reported stock-outs occurred for isoniazid (23/116, 20%) and other TB medications (11/114, 9.6%, range 0-33%, p=0.008).

TPT provision ranged from 50-100% (p<0.001). At 108 clinics providing TPT (80%), eligibility criteria included children <5 years (82%; p=0.027); children 6-15 years (64%, range 20-82%, p<0.001); and/or test of TB infection (26% overall, range 0-73%, p<0.001).

TPT regimens for children included: 6H (88%), 9H (3.7%), 12H (3.7%), 36H (0.9%), 4R (1.9%), 3HP (0.9%), 3HR (2.8%), and regimens for multidrug-resistant TB exposure (4.6%).

Characteristic n (%)	All (n = 135)	Asia-Pacific (n = 17)	Caribbean, Central and South America (n = 6)	Central Africa (n = 17)	East Africa (n = 63)	Southern Africa (n = 22)	West Africa (n = 10)	P-value
Routine TB disease screening <sup>1</sup> at HIV care enrollment	121 (89.6%)	14 (82.4%)	5 (83.3%)	14 (82.4%)	59 (93.7%)	22 (100%)	7 (70.0%)	0.08
Acid fast bacillus smear	99 (73.3%)	13 (76.5%)	6 (100.0%)	8 (47.1%)	48 (76.2%)	14 (63.6%)	10 (100.0%)	<0.001
GeneXpert	110 (81.5%)	14 (82.4%)	4 (66.7%)	13 (76.5%)	55 (87.3%)	14 (63.6%)	10 (100.0%)	<0.001
Chest x-ray	105 (77.8%)	14 (82.4%)	5 (83.3%)	13 (76.5%)	46 (73.0%)	17 (77.3%)	10 (100.0%)	0.008
Mycobacterial culture	70 (51.9%)	12 (70.6%)	5 (83.3%)	8 (47.1%)	27 (42.9%)	13 (59.1%)	5 (50.0%)	<0.001
Drug susceptibility testing	63 (46.7%)	14 (82.4%)	3 (50.0%)	6 (35.3%)	24 (38.1%)	13 (59.1%)	3 (30.0%)	<0.001
Provision of TPT for persons who screened negative for TB disease	108 (80.0%)	11 (64.7%)	3 (50.0%)	7 (41.2%)	60 (95.2%)	22 (100%)	5 (50.0%)	<0.001
TPT eligibility for children <5 years (out of 108 sites that provided TPT)	88 (81.5%)	8 (72.7%)	3 (100.0%)	6 (85.7%)	55 (91.7%)	13 (59.1%)	3 (60.0%)	0.027
TPT eligibility for children 6-15 years (out of 108 sites that provided TPT)	69 (63.9%)	6 (54.5%)	1 (33.3%)	5 (71.4%)	49 (81.7%)	7 (31.8%)	1 (20.0%)	<0.001

<sup>1</sup>Symptom screening +/- additional tools.

OA38-502-17 Table.

**Conclusions:** Overall availability of GeneXpert and integrated TB/HIV treatment are encouraging, but vary by context. Heterogeneous implementation gaps remain—particularly for culture, drug susceptibility testing, TPT delivery and TPT regimens—which have implications for TB management and care outcomes for CLHIV. There is a need to improve equitable availability of critical tools for TB care and prevention for CLHIV.

### OA38-503-17 Improving TB-HIV clinical care outcomes through a National TB Quality Improvement Collaborative in Uganda, October 2021-December 2022

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**Background and challenges to implementation:** An estimated 86,000 people in Uganda develop active TB annually, however, only 75% of the incident cases were diagnosed and notified in 2020 falling short of the 90% National target. We present findings of efforts to improve TB clinical care cascade through the quality improvement collaborative. In May 2021, the Ministry of Health (MoH), with support from US President's Emergency Plan for AIDS Relief (PEPFAR) rolled out the TB treatment cascade collaborative aimed at improving clinical outcomes among TB patients co-infected with HIV.

**Intervention or response:** The collaborative was implemented purposively between October 2021 and December 2022, at outpatient departments of selected 879

sites offering TB/HIV services across the country, that contribute 80% of the TB/HIV case load at the time. Our interventions included the following: holding stakeholders' entry meetings, conducting baseline data collection, orienting health facility staff and conducting quarterly coaching and mentorship visits to identify barriers to TB service provision. To monitor site-level performance, monthly performance reviews were held with the sites teams to identify and address gaps in TB symptom-screening, GeneXpert testing for presumptive TB patients (PTPs), TB patients diagnosed, TB cure rate and PLHIV initiated on TPT. One on one learning session to facilitate sharing of best practices and lessons learnt was held.

**Results/Impact:** Overall, TB screening among outpatients improved from 73% to 96.4%; GeneXpert testing for PTPs improved from 54.9% to 80.8%, TB patients diagnosed and registered increased from 86.8% to 100%, TB cure rate increased from 58.0% to 74.0%; and PLHIV initiated on TPT increased from 24.9% to 70.2%. We learned that establishing TB clinics and involvement of community resource persons improved TB care.

**Conclusions:** The TB-QI collaborative involving key stakeholders at all levels can improve TB/HIV treatment outcomes and National programs should support adaptation and scale-up of high impact practices to optimize service delivery.

## OA39 WHO Rapid Diagnostic Tests

### OA39-504-17 Deciphering the relationship between host transcriptional markers and bacteriological markers of TB disease

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**Background:** Several host gene markers that differentiate confirmed pulmonary active tuberculosis (ATB) from other respiratory diseases (ORDs) have been reported. These markers are not yet fully evaluated. Bacterial burden in ATB has been linked to disease severity. We sought to determine whether gene expression is related to TB bacterial burden.

**Design/Methods:** Patients presenting with TB-like symptoms were enrolled at healthcare facilities in Blantyre, Malawi. ATB disease was confirmed by sputum MGIT culture, and sputum bacterial load was measured using TB-Molecular Bacterial Load Assay (TB-MBLA). Expression of Sweeney3 gene panel (GBP5, DUSP3, KLF) and/or in combination with CD64 (Sweeney3+CD64) in whole blood was evaluated using reverse transcriptase quantitative polymerase chain reaction (RT-qPCR) assay. Spearman's rho correlation was used to determine the relationship between the variables.

**Results:** A total of 118 participants were included in the baseline evaluation. Longer baseline MGIT Time-to-Positivity (TTP) was associated with downregulated gene expression; Sweeney3 score  $r(116) = .73$ ,  $p < 0.0001$  [95% C.I. = .63 to .80,] and a combination of the Sweeney3+CD64,  $r(116) = .71$ ,  $p < 0.0001$  [95% C.I. = .61 to .79]. Similarly, high baseline bacillary load was associated with an upregulation in expression; Sweeney3 score  $r(74) = -.48$ ,  $p < 0.0001$  [95% C.I. = -.64 to -.28], and Sweeney3+CD64 combination,  $r(74) = -.52$ ,  $p < 0.0001$  [95% C.I. = -.67 to -.32]. In response to therapy, median TTP increased from 7 days to 66 days while bacillary load declined from  $3.78 \pm 1.5 \log_{10} \text{CFU/mL}$  to  $0.9 \pm 0.8 \log_{10} \text{CFU/mL}$  by month-6 of treatment. Correspondingly, Sweeney3 and Sweeney3+CD64 expression scores downregulated from mean delta Cycle quantification (Cq) of 1.4 to 3.3 and 4.4 to 8.4 respectively, reaching the mean expression levels in healthy individuals.

**Conclusions:** The results reveal an association between bacteriological measures of TB severity and host-gene expression, opening the possibility of adopting these gene markers for TB clinical grading at baseline and during therapy.

### OA39-505-17 Optimisation of fluoroquinolone resistance detection using Xpert MTB/XDR and the impact on rifampicin-/multidrug-resistant TB treatment

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**Background:** Second-line LPA tests, which have been the predominant genotypic method to determine resistance to fluoroquinolones and second-line injectable drugs (SLID), were used to choose a suitable therapy for people affected by RR/MDR-TB. Unfortunately, its diagnostic power has limitations, with ambiguous results in around 50% of all specimens tested and more than 80% of negative smear sputum specimens.

The Xpert MTB/XDR assay is advertised as a rapid molecular test for the detection of fluoroquinolone, isoniazid, and SLID resistance, with a sensitivity ranging from 88% to 96% (for fluoroquinolone resistance) and a detection limit of 86 CFU/ml for sputum sediments.

This study presents a preliminary performance analysis of Xpert MTB/XDR in TB patients in Lima, Peru.

**Design/Methods:** Sputum specimens collected for diagnostic confirmation were tested in parallel with Xpert MTB/XDR and Genotype MTBDRsl v 2.0 in the Socios En Salud Sucursal Peru Lab and the performance was compared with the stratification of specimens by bacterial load to predict the potential value of the new method.

**Results:** The proportion of valid drug resistance results produced by Xpert MTB/XDR was much greater (25/25 (100%)) than that produced by Genotype MTBDRsl v 2.0 [21/25 (84%)]. The proportion of valid results using Xpert MTB/XDR was greater [6/6 (100%) vs. 2/6 (33%)] in samples with low and very-low bacterial loads.

**Conclusions:** A better fluoroquinolone resistance testing performance (and maybe INH and SLID) of Xpert MTB/XDR has been observed in comparison to Genotype MTBDRsl, being higher among specimens with low and very low bacterial loads from patients with TB. Peru, which has a high burden of MDR-TB, is going through a decentralization process of molecular testing and the Xpert MTB/XDR should be widely deployed to support timely clinical decision-making so fewer patients will be left without specific therapies, thus addressing the reduction of MDR-TB and XDR-TB burden more effectively.

### OA39-506-17 Interpretation of false-positive rifampicin resistance detected on paucibacillary clinical samples using the Xpert MTB/RIF assay

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**Background:** Although the Xpert MTB/RIF (Xpert) assay simultaneously detects *Mycobacterium tuberculosis* (MTB) and rifampicin resistance (RR) with high sensitivity and specificity, studies have reported false RR particularly in paucibacillary pulmonary samples.

To avoid highly toxic inappropriate treatment for RR/MDR-TB, a diagnostic algorithm should be included to correctly interpret the false RR results.

In this study, we aimed to investigate the discordant RR results detected by initial Xpert testing.

**Design/Methods:** From July 2022 to March 2023, 599 RR-TB patients detected by Xpert assay were enrolled from 10 DR-TB management sites across Bangladesh. Fresh sputum samples were collected for repeat Xpert assay, drug susceptibility testing (DST), line probe assay (LPA) and targeted next generation sequencing (tNGS) to ascertain the final rifampicin susceptibility status.

**Results:** After repeat Xpert testing on 599 specimens, 266(44.4%) patients were confirmed as RR, 134(22.4%) rifampicin sensitive (RS) and 195(32.6%) MTB not detected. The initial bacterial burden for 134 RS cases were: high-14.9%, medium-11.2%, low-15.7%, very low-31.3%, and 26.9% were unknown burden. Majority of discordant results were found from low and very low burden cases (47%). DST, LPA and tNGS results were available for 35/134 RS cases.

Our results demonstrated RS cases from repeat Xpert showed 97.1% (34/35) concordance with DST, 97.1% (34/35) with LPA, and 91.4% (32/35) with tNGS. tNGS assured the discordance (3/35) results as 'hetero-resistant'.

**Conclusions:** While low and very low bacillary loads are more prone to false RR results in the repeat Xpert assay, we also found discordance in high and medium MTB burden.

We recommend that Xpert testing algorithm should include repeat testing of RR detected on paucibacillary samples, as well as for patients with no previous history of TB or no contact with RR-TB patients.

Additionally, molecular tests such as LPA or tNGS should reaffirm RR before initiation of highly-toxic RR/MDR-TB treatment.

### OA39-507-17 Improving pleural TB diagnosis using the prediction model with Xpert Ultra

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**Background:** Pleural tuberculosis (TB) diagnosis remains challenging even with the use of Xpert-Ultra. The study aimed to build a prediction model using pre-specified clinical factors in combination with Xpert-Ultra to improve the diagnosis for pleural TB against other pleural effusion diseases.

**Design/Methods:** We conducted a prospective cohort study on pleural effusion patients from Cho Ray Hospital in Vietnam. Pleural TB cases were identified by microbiological testing (culture and PCR) or pleural biopsy. Other pleural effusion causes were identified by laboratory tests and clinical judgement.

In our model development, we utilized logistic regression with eight pre-specified variables. Firstly, we simplified the model by employing two variable selection methods: backward stepwise selection and the extension of the least absolute shrinkage and selection operator (group-LASSO). The selected variables were most frequently included across all bootstrap datasets. Then, we conducted internal bootstrap validation to assess each developing model's discrimination and calibration, in comparison with random-forest model.

**Results:** A total of 126 pleural effusion patients were included for analysis, comprising 29 cases of pleural TB and 97 cases of non-TB pleural effusion (64 cancer and 33 other confirmed diagnoses cases). The reduced model, based on the group-LASSO method and selected four covariates (Xpert-Ultra, age, adenosine deaminase (ADA), and lymphocyte percentage), showed the best performance with an optimism-corrected AUC of 0.98 (Table 1).

	Optimism-corrected AUC	Optimism-corrected calibration in the large	Optimism-corrected calibration slope	Variables
Full model	0.98	-0.09	0.95	Xpert Ultra, age, ADA, lymphocyte percentage, pleural fluid protein, symptoms' duration, smoking status and diabetes
Reduced model - LASSO variable selection	0.98	-0.05	1.09	Xpert Ultra, age, ADA, lymphocyte percentage
Reduced model - backward stepwise variable selection	0.98	-0.04	1.19	Xpert Ultra, ADA, lymphocyte percentage
Model with Random Forest	0.85	-0.59	0.87	Xpert Ultra, age, ADA, lymphocyte percentage, pleural effusion protein, symptoms duration, smoking and diabetes

Table 1: Performance comparison of different models.



The Youden-index identified sensitivity and specificity of 0.94. This was an improvement over the model that did not include Xpert-Ultra (AUC 0.89) or the model that only included Xpert-Ultra (AUC 0.79). We further applied this model and were able to detect 78% patients who were diagnosed with pleural TB only by clinical judgement and good treatment response.

**Conclusions:** The model of combining ADA, pleural lymphocyte percentage, age and Xpert-Ultra showed excellent performance (AUC 0.98) to differentiate pleural TB from other pleural effusion diseases.

### OA39-508-17 Impact of laboratory quality management system on *M. tuberculosis* detection rates using Xpert MTB/RIF testing: a retrospective data analysis in Cambodia

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**Background:** In Cambodia, the number of laboratories equipped with GeneXpert to detect *Mycobacterium tuberculosis* (MTB) has remarkably increased from one site in 2011 to 92 sites in 2023. However, MTB detection rates continue to decline. This review aims to compare the MTB detection rates in laboratories with and without laboratory quality management system (LQMS) implementation.

**Design/Methods:** To increase MTB detection, two laboratories have introduced a sputum rejection criterion, one of the LQMS criteria. Data from laboratories was routinely extracted from GeneXpert Dx software and entered into a standard report form before being reported to the central level via telegram in photo format. After verification, the data were entered into MS Excel for analysis. We retrospectively analyzed data from two and 29 laboratories, with and without a sputum rejection criterion, from 2020 to 2022, respectively, to compare MTB detection rates.

**Results:** A total of 122534 sputum samples were tested by Xpert, of which 9732 and 112802 were tested in two laboratories and 29 laboratories with and without a

sputum rejection criterion, respectively. Overall, MTB detection rates in laboratories without LQMS implementation in 2020, 2021, and 2022 were, respectively, 10.1%, 10.6%, and 9.7%.

However, a significantly high proportion of positivity rates were seen in laboratories with the introduction of the sputum rejection criterion, with a proportion of 25.3% in 2020, 26.8% in 2021, and 23.8% in 2022.

**Conclusions:** A sputum sample rejection criterion could be implemented as a measure to enhance MTB detection, which would increase the number of bacteriologically confirmed tuberculosis (TB) cases. This criterion might be a way to improve sputum quality and make the best use of cartridges. To intensify TB case detection across the nation and take a step toward finding missing TB cases, the national TB program should take into account this innovation in other laboratories.

### OA39-510-17 Treatment monitoring capacity of stool-based *M. tuberculosis*-specific quantitative polymerase chain reaction test

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**Background:** Tuberculosis (TB) remains the leading cause of death among people living with HIV in high-burden low- and middle-income countries (LMIC), largely due to challenges with sputum collection for diagnosis and treatment monitoring. Stool is an alternative sample that can be used to detect *Mycobacterium tuberculosis* (*Mtb*) and is endorsed as a non-invasive specimen for TB diagnosis. Current monitoring of TB patients' response to therapy relies on culture methods which are laborious, time consuming and prone to contamination.

There are no rapid molecular tests to monitor TB treatment. We evaluated the capacity of a quantitative stool-based PCR assay for TB treatment monitoring.

**Design/Methods:** To evaluate the assay's capacity for treatment monitoring, we applied a soil DNA isolation kit to stool and used the *Mtb* insertion sequence 6110 (IS6110) with an improved limit of detection (LOD) of a PCR diagnostic test for TB. We quantified the decrease in *Mtb* DNA at time of initiation, after 2 weeks and 8 weeks of antituberculosis treatment (ATT) in a cohort

of participants with TB from Tanzania, Mozambique and Eswatini between September 2020 and September 2022.

**Results:** A total of 266 participants with suspected TB were recruited. The initial median baseline bacillary burden was 107.9 fg/ $\mu$ L and after 2 weeks of therapy decreased 1 log<sub>10</sub> to 19.9 fg/ $\mu$ L ( $p = 0.0002$ ; Mann-Whitney; Figure 1A). Bacillary burden further decreased to a median of 1.2 fg/ $\mu$ L by 8 weeks of ATT ( $p = 0.008$ ; Mann-Whitney).

The quantity of *M. tuberculosis*-specific DNA in stool inversely correlated with sputum MGIT time to positivity ( $r = -0.39$ ;  $p = 0.0002$ ; Spearman correlation), Figure 1B.

Quantitative stool-based patient treatment monitoring.

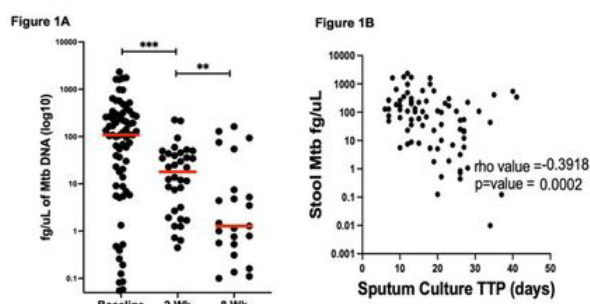


Figure 1. (A) *Mycobacterium tuberculosis* (*Mtb*) burden decreases during antituberculosis treatment (ATT). Individuals with tuberculosis provided stool samples at time of enrollment and again at 2-weeks and 2-month follow-up visit. (B) Stool-based quantified *Mtb* bacillary load by qPCR correlates with sputum culture time to positivity (TTP).

**Conclusions:** These preliminary results suggest that quantifiable *M. tb*-specific DNA from stool can aid in TB treatment monitoring. Considering sputum collection is frequently challenging, and culture is slow, this methodology may help to improve efficacy of TB treatment monitoring.

## OA39-511-17 Demonstration of an improved, automated *M. tuberculosis* rRNA extraction method from raw sputum samples using Erba Captimag™ magnetic beads

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**Background:** The high ratio of rRNA copies to genomic DNA in viable MTB complex cells makes rRNA a useful candidate target to improve the sensitivity of qualitative LAMP and PCR-based amplification tests. Further, MTB-rRNA has been utilised as a viability marker in Molecular Bacterial Load Assays (MBLAs).

More recently, measurements of the ratio between markers for precursor-rRNA as compared to mature rRNA have shown improved correlation with phenotypic measurements of drug efficacy.

However, traditional MTB rRNA-based assays are significantly hindered by time-consuming, multi-step extraction workflows. We demonstrate a low-cost, easily automatable method with room temperature stable reagents.

The Erba Captimag™ RNA capture beads are robust to detergents, chaotropes, proteases and interference from non-target RNA. The method incorporates an MS2 extraction control to indicate the presence of inhibitors.

**Design/Methods:** Twenty-four pooled sputum samples were spiked with equal copies of MTB complex rRNA and MS2 phage and heated to  $>95^{\circ}\text{C}$  with 1ml of Erba Lysis buffer. Lysates were then loaded onto a ThermoFisher Kingfisher Duo™ plate pre-loaded with Erba extraction reagents, including Captimag™ magnetic beads. Eluate from each extraction was tested using an in-house MTB-rRNA/MS2 RT-PCR mix.

**Results:** Figure 1 demonstrates that copies/ reaction for MTB rRNA and the MS2 RNA extraction control were highly comparable despite being extracted directly from raw sputum with no pre-processing (such as liquefaction or centrifugation) prior to the addition of sputa to Erba Lysis buffer.

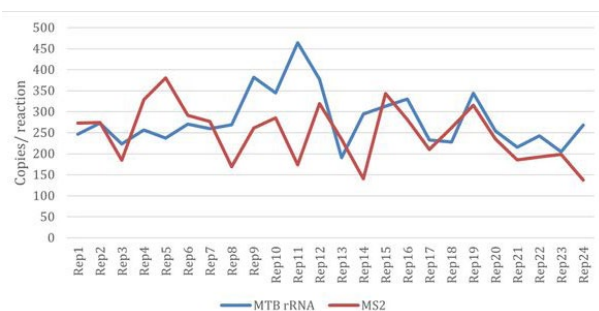


Figure 1.

**Conclusions:** The Erba Captimag™ beads allow the reliable extraction of rRNA and an RNA extraction control from raw sputum samples. The method takes <40 minutes.

## OA40 DM theme

### OA40-512-17 In patients with drug-resistant tuberculosis, prediabetes may be associated with the disease severity

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**Background:** Prediabetes based on glycemic parameters above normal but below diabetes thresholds is frequent in patients with pulmonary tuberculosis (PTB). This hyperglycemia may be caused by stress induced by tuberculosis infection. Hyperglycemia may, in turn, lead to a proinflammatory response and progression of TB disease. Unlike diabetes mellitus (DM), limited research has explored the association between prediabetes and severity of tuberculosis disease. We estimate the association between baseline prediabetes and severity of PTB in patients with multidrug/rifampin-resistant (MDR/RR-) TB.

**Design/Methods:** This was a cross-sectional analysis of baseline data from 754 consenting participants, with PTB, age ≥15 years, enrolled in the endTB trial (ClinicalTrials.gov Identifier: NCT02754765) in seven countries in Asia, Europe, South America, and Southern Africa. All participant isolates were resistant to rifampin by rapid, valid molecular tests and susceptible to fluoroquinolones by Genotype MTBDRsl. Participants met other eligibility criteria for the parent study. Participants with DM or glycosylated hemoglobin (HbA1c) ≥6.5% were excluded from the present analysis. We defined

prediabetes as HbA1c 5.7-6.4% and normoglycemia as <5.7%. Disease severity was classified as limited (cavitation absent AND ≤1+ smear, or negative smear) and extensive (cavitation present AND ≥1+ smear; or ≥2 smear).

We performed adjusted (for baseline [age, sex, BMI, hemoglobin, HIV and alcohol use]) Log-Poisson (robust regression to estimate prevalence ratio (PR).

**Results:** We excluded 122 participants with DM. 29.4% of participants had prediabetes. Extensive disease was more common in prediabetic than normoglycemic (60.8% vs. 55%; p=0.178) patients. In multivariable analysis, the risk of extensive disease was elevated in patients with prediabetes compared to that in normoglycemic patients (PR 1.16; 1.01-1.33, p=0.042).

Characteristics	Bivariate Analysis			Multivariable Analysis**			
	PR	CI 95%	p	PR	CI 95%	p	
Glycosylated hemoglobin	Normoglycemia (<5.7%)	Ref		Ref			
	Prediabetes (5.7 to <6.4%)	01. Nov	0.96 - 1.28	0.167	*1.16	1.01 - 1.33	0.042
Sex	Woman	Ref		Ref			
	Man	Jan 27	0.95 - 1.48	0.002	Jan 33	1.13 - 1.56	0
Age	15 to <18 years	Ref					
	18 to <30	Jan 14	0.75 - 1.75	0.53	Jan 26	0.85 - 1.88	0.245
	30 to <60	Jan 19	0.78 - 1.81	0.425	Jan 37	0.92 - 2.04	0.12
	>60	01. Mai	0.95 - 2.35	0.082	Jan 71	1.11 - 2.65	0.016
BMI	Low weight	Jan 24	1.08 - 1.43	0.003	Jan 19	1.03 - 1.39	0.019
	Normal weight	Ref		Ref			
	Overweight	1	0.78 - 1.30	0.982	0.95	0.75 - 1.21	0.672
	Obesity	01. Mrz	0.62 - 1.73	0.907	Jan 21	0.70 - 2.10	0.5
Hemoglobin	g/dl	1	1.00 - 1.01	0.434	0.96	0.94 - 0.99	0.005
Alcohol abuse	No	Ref		Ref			
	Yes	0.91	0.64 - 1.30	0.583	0.86	0.60 - 1.22	0.392
HIV status	Negative	Ref		Ref			
	Positive	0.84	0.31 - 2.27	0.736	0.82	0.63 - 1.06	0.124

HIV: Human Immunodeficiency Virus. \*Outcome \*\*Adjusted Model with sex, age, BMI, hemoglobin, alcohol abuse, HIV and country.

Table 1. Multivariable regression analysis of association between prediabetes and the severity of pulmonary tuberculosis in patients with multidrug/rifampin-resistant (MDR/RR-) TB.

**Conclusions:** Prediabetes is prevalent and associated with extensive disease in MDR/RR-TB patients. In this cross-sectional analysis, we cannot ascertain the direction of this relationship. However, non-DM hyperglycemia should be carefully followed as part of patient-centered care for TB.

### OA40-513-17 How glycaemic control impacts multidrug-resistant TB treatment

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**Background:** The treatment of multidrug-resistant tuberculosis (MDR-TB) remains challenging, especially for those with comorbidities (e.g. type 2 diabetes mellitus, T2DM). It remains unknown what role poor glycaemic control plays in the drug exposure and the MDR-TB treatment response.

This study aimed to investigate the relationship between poor glycemic control and drug exposure as well as the impact of poor glycemic control on MDR-TB treatment among diabetic patients.

**Design/Methods:** In this multicenter prospective cohort study, patients with combined MDR-TB and T2DM were included. Monthly follow-ups were performed to ascertain the time to sputum culture conversion and the treatment outcome. Poor glycemic control was defined by haemoglobin A1c value  $\geq 7\%$  at baseline. Drug exposures were estimated by noncompartmental analysis using the intensively sampled pharmacokinetics data. The associations of glycemic control with drug exposure and treatment outcome were evaluated by univariate and multivariate analysis. The classification and regression tree analysis were used to identify the clinically relevant thresholds.

**Results:** Of 131 patients, 43 were in poor glycemic control. Poor glycemic control was associated with reduced exposure to moxifloxacin, linezolid, bedaquiline and cycloserine compared to those with good glycemic control. Patients with poor glycemic control had higher risks of 6-month sputum culture conversion failure (adjusted OR 12.3, 95% CI 4.5-34.0) and unfavourable treatment outcomes (adjusted OR 20.3, 95% CI 4.4-92.9). The thresholds predictive of 6-month sputum culture conversion and favourable treatment outcome were bedaquiline AUC/MIC of 245 and moxifloxacin AUC/MIC of 67, which was validated in both patients with and without poor diabetic control. Patients with poor glycemic control were less likely to reach these thresholds.

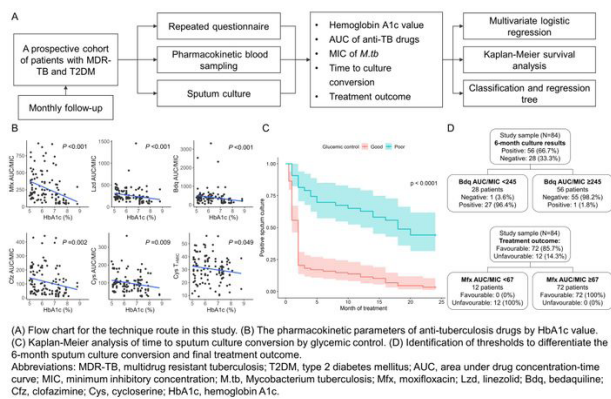


Figure 1 Drug exposure and treatment outcomes in patients with MDR-TB and T2DM.

**Conclusions:** Strict glycemic control should take priority in MDR-TB treatment to improve the drug exposure and subsequently the treatment outcome.

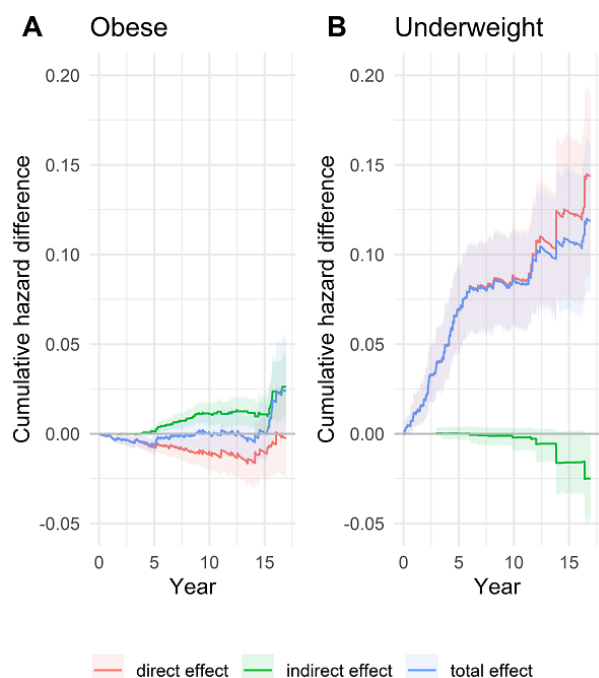
### OA40-514-17 Body mass index and lower respiratory tract infections: diabetes as a mediator

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**Background:** Body mass index (BMI) extremes (e.g. underweight or obese) are associated with higher overall infection risk, but obesity may protect against tuberculosis. To better understand the impact of BMI and diabetes on lung health beyond tuberculosis, we investigated the link between BMI and lower-respiratory tract infections (LRTIs) and the mediating role of diabetes.

**Design/Methods:** 49,179 respondents from Taiwan's National Health Interview Survey consisted the study cohort. We identified new cases of diabetes and hospital admissions for LRTIs using Taiwan's National Health Insurance Research Database (NHIRD). To determine the association between BMI and LRTIs risk, we conducted Cox regression analysis. Moreover, we utilized a causal mediation model to evaluate the indirect (mediation) effect of BMI on LRTIs mediated through diabetes across time and examine the significance of the mediation effect. Sensitivity analysis that additionally adjusted for household income and excessive alcohol drinking was also performed.



**Results:** During the median 9-year follow-up, 5,244 participants (10.66%) developed diabetes and 2,119 (4.31%) were hospitalized with LRTIs. Compared to those of normal weight, underweight individuals had a hazard ratio of 1.58 (95% CI, 1.31-1.90) and obese individuals had a hazard ratio of 1.01 (95% CI, 0.82-1.23) for LRTIs hospitalization.

The mediating effects of diabetes were significant for both underweight and obese groups, with the obese group having an increased risk and the underweight group having a decreased risk (indicated by green lines in Graphs A and B). However, the direct effects not mediated by diabetes showed lower risk for obese individuals.

**Conclusions:** Underweight individuals face a significant risk of LRTIs hospitalization, but not the obese group. The protective direct effect on LRTI in the obese group differs from that on overall infection, suggesting the need to explore factors related to lung health. Moreover, diabetes control may lower LRTIs risk in obese individuals, according to the mediation finding.

### OA40-515-17 Diabetes mellitus and drug-resistant TB treatment outcomes in Indonesia: a retrospective cohort study

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**Background:** The rise in drug-resistant tuberculosis (DR-TB) threatens global TB control, as it is associated with higher rates of treatment failure, loss to follow-up and death. Diabetes mellitus (DM) is a risk factor for unsuccessful treatment outcomes in drug sensitive TB, but this is unknown for DR-TB. We therefore determined the association between DM and DR-TB treatment outcomes in West-Java, Indonesia.

**Design/Methods:** Patients aged ≥18 years with Xpert MTB/RIF-diagnosed DR-TB and treated in the Hasan Sadikin referral hospital, Bandung, between March 2020 and December 2021 were included in this retrospective cohort study. Patient-, disease-, and treatment characteristics were retrieved from medical records and the Indonesian tuberculosis information system (SITB). DM diagnosis was based on a HbA1c ≥ 6.5% and WHO pre-2021 definitions were used for treatment outcomes.

Treatment was according to line probe assay and phenotypic drug susceptibility testing. The association between DM and treatment outcomes was analysed using multivariable logistic regression adjusting for age.

This is a preliminary analysis, data collection is still ongoing.

**Results:** Of 248 included DR-TB patients, 65 (26.2%) were diagnosed with DM. Median ages were 34 and 51 for non-DM and DM patients, respectively. 72.3% with DM and 66.7% without DM had prior TB therapy history. Median HbA1c at baseline for DM was 9.9%. Short-term regimens were more frequently prescribed than long-term regimens (69.8% vs 30.2%).

Less than 50% of patients had a microbiological cure (table 1), and unsuccessful treatment appeared more common in diabetic patients (aOR 1.85; 95% CI 0.96-3.62, p=0.067), with more and earlier deaths (median 55.5 resp. 110 days after therapy initiation, p=0.12).

Treatment outcomes	DM (n=65)	Non-DM (n=183)	Overall (n=248)
Successful	22 (33.8%)	90 (49.2%)	112 (45.2%)
Cured	22 (33.8%)	90 (49.2%)	112 (45.2%)
Completed treatment	0 (0%)	0 (0%)	0 (0%)
Unsuccessful	43 (66.2%)	93 (50.8%)	136 (54.8%)
Failed treatment	4 (6.2%)	31 (16.9%)	35 (14.1%)
Death (any cause)	22 (33.8%)	23 (12.6%)	45 (18.1%)
Lost to follow-up during intensive phase	14 (21.5%)	35 (19.1%)	49 (19.8%)
Lost to follow-up during continuous phase	3 (4.6%)	4 (2.2%)	7 (2.8%)

Table 1. DR-TB treatment outcomes in DM and non-DM patients treated in the Hasan Sadikin hospital between March 2020 and December 2021.

**Conclusions:** This interim analysis suggests that outcome of DR-TB treatment is poor in this setting, with high early loss to follow-up, and that DM is associated with more and earlier deaths during treatment. Further study is necessary to identify underlying causes and improve outcomes.

### OA40-516-17 Intensifying detection of TB among people with diabetes in health facilities in seven high TB burden provinces in Vietnam, 2020 – 2022

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**Background and challenges to implementation:** The estimated prevalence of diabetes mellitus (DM) in Vietnam is 11%. Since the risk of developing TB disease is two to four times higher for people with DM, the NTP targeted TB screening among DM using the high-yield Double-X strategy.

**Intervention or response:** From 2020-2022, the USAID Support to End TB project integrated TB screening into DM outpatient visits in public health facilities (HFs) across 7 provinces.

Over the implementation period, we revised screening criteria and mentored on-site to increase effectiveness; and applied computer-aided detection artificial intelligence in seven selected sites to improve CXR interpretation.

In 2022, CXRs were indicated for DM patients with newly diagnosed DM or DM with any of the following: TB symptoms (cough >2 weeks, fever, weight loss, night sweat), elevated HbA1c  $\geq 8\%$  or fasting blood sugar  $\geq 10$  mmol/l;  $\geq 60$  years old and no CXR within 6 months; smoking  $\geq 10$  cigarettes/day and no CXR within 6 months. GeneXpert was indicated for abnormal "TB-presumptive" CXR and/or TB symptoms; clinical consultation diagnosed non-bacteriologically confirmed TB.

**Results/Impact:** Among 71,387 CXRs obtained from TB screening in DM clinics, 7.3% CXRs were TB-presumptive, leading to 4,944 people tested with GeneXpert and 722 diagnosed with TB disease, including 6 non-bacteriologically confirmed cases.

In 2020, we only screened diabetics with TB symptoms, resulting in fewer people screened ( $n=5,755$ ) and high rates of TB-presumptive CXR (23.5%) and TB detection yield (1,825/100,000 CXRs).

After expanding criteria in 2021-2022, the number of CXR increased, the rate of TB-presumptive CXR and yield for TB detection decreased, but the yield remains higher than the national TB incidence rate (173/100,000).

Year	# of sites	Screened with CXR	##% TB-presumptive CXR	##% Tested with Xpert	##% TB Diagnosed (All forms)	##% Initiated TB treatment	Yield per 100,000 CXR
2020	20	5,755	1,355 (23.5%)	1,282 (94.6%)	105 (8.2%)	90 (85.7%)	1,825
2021	38	29,671	1,684 (5.7%)	1,522 (90.4%)	228 (15.0%)	213 (93.4%)	768
2022	39	35,961	2,189 (6.1%)	2,140 (97.8%)	389 (17.9%)	356 (91.5%)	1,082
Total	-	71,387	5,228 (7.3%)	4,944 (94.6%)	722 (14.5%)	659 (91.3%)	1,011

*Table. TB screening for people with diabetes mellitus in 7 provinces of Vietnam, 2020-2022.*

**Conclusions:** TB-DM screening based on clinical assessment and risk factors is feasible to improve TB detection in the general healthcare system. The Vietnam NTP has scaled up this model since 2022 to all public facilities providing DM services nationwide.

## OA40-517-17 Implementing latent TB infection treatment in patients with diabetes mellitus: uptake, adverse events and discontinuation

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**Background:** Adherence to preventive treatment for latent tuberculosis (TB) infection (LTBI) is crucial for its protective efficacy against active TB. We investigated the decisions to take the LTBI treatment, adverse events (AE), and treatment completion in patients with diabetes mellitus (DM).

**Design/Methods:** This prospective cohort study enrolled patients with DM aged over 45 years who had an HbA1C  $\geq 9\%$  in 2020-2021. Participants were screened for LTBI with the interferon-gamma-releasing assay (IGRA).

Treatment regimens included once-weekly isoniazid and rifapentine for 12 weeks, daily isoniazid and rifampin for 12 weeks, daily isoniazid for 9 months, and daily rifampin for 4 months. The demographic and clinical characteristics, including the anti-diabetic medications, were recorded.

**Results:** Among the 609 participants, 606 underwent IGRA, 149 (24.6%) had positive IGRA results, and two were diagnosed with active TB. The mean age was  $68.3 \pm 11.1$  years, and 53.6% of them were female. LTBI treatment was commenced in 83 (56.5%). 57 (68.7%) completed the treatment despite a high prevalence (54.4%) of AE. A lower prescription rate of dipeptidyl peptidase-4 inhibitors (64.3% vs. 22.7%,  $p < 0.001$ ), and a higher incidence of AE (90.9% vs. 55.4%,  $p = 0.003$ ), were noted in those with treatment discontinuation.

Otherwise, the prescription of anti-diabetic agents in those who completed and discontinued the treatment was similar.

The multivariate logistic regression disclosed that AE (odds ratio, OR=8.065, 95% confidence interval, CI 1.72, 37.85), administration of dipeptidyl peptidase-4 inhibitors (OR=0.163, 95% CI 0.05, 0.51), and linagliptin (OR=0.221, 95% CI 0.07, 0.68) were independent predictors for treatment discontinuation.

**Conclusions:** The uptake and completion rates for LTBI treatment among aged patients with DM were low due to a high prevalence of treatment-associated AE. A per-

sonalized holistic care program taking concurrent prescriptions for underlying diseases into consideration is required to improve the safety and completion of the treatment.

### OA40-518-17 Integrating diabetes care into TB treatment in Uganda: a parallel convergent mixed-methods study

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**Background and challenges to implementation:** The World Health Organization (WHO) recommends that all persons initiating treatment for TB be screened for diabetes mellitus. We sought to assess the fidelity and implementation of this recommendation in a high HIV-TB burden setting.

**Intervention or response:** We conducted a mixed-methods study nested within a prospective cohort study of treatment outcomes among 285 persons with TB in two TB treatment units in Kampala, Uganda.

We followed up 65 participants with high blood sugar levels through the DM care cascade steps of

1. Screened,
2. Diagnosed,
3. Initiated on treatment,
4. Retained before and after TB treatment.

We purposively selected 23 cohort participants with HbA1C $\geq$ 6.1% and 6 providers involved in their care for in-depth interviews. Interviews were recorded, transcribed verbatim, translated, and analyzed with Atlas.ti to identify barriers and facilitators using the Consolidated Framework for Implementation Research (CFIR).

**Results/Impact:** All participants (285) were screened for DM. Of 65/285(22.8%) who screened as probable DM, 27/65(41.5%) were referred to non-communicable diseases (NCD) clinic for diagnosis, 9/65(13.8%) received a diagnosis, 1/65(1.5%) received regular treatment, and 4/65(6.1%) received DM treatment after TB treatment discharge. Individual barriers included not accepting the diagnosis of diabetes, multimorbidity (HIV/TB/DM) and pill burden, inconsistent medicines, and health worker attitudes. Providers cited barriers including inconsistent availability of testing kits and diabetes medications, low workforce, lack of policies to integrate DM care, and lack of access to

specialized DM care. Health worker support, research projects in TB-DM, DM education and counseling, and continuous medical education were perceived facilitators.

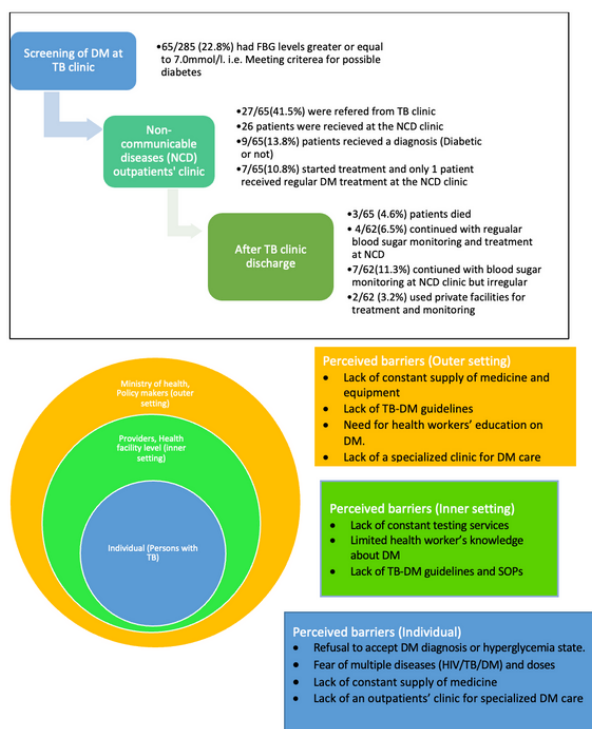


Figure 1. TB-DM care cascade and CFIR framework for barriers to DM care.

**Conclusions:** Persons initiating TB treatment in Uganda had a high prevalence of undiagnosed hyperglycemia. Most who were diagnosed with DM did not receive regular DM care due to a lack of integration of diabetes services with TB care. Better education, consistent test kits, and clearer policies are needed to improve TB-DM care.

## OA40-519-17 Community-based, integrated service delivery for TB, hypertension and diabetes screening in Viet Nam

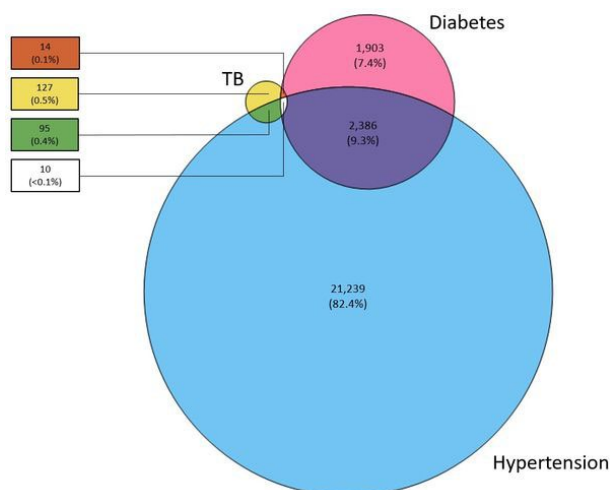
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**Background and challenges to implementation:** Integrated service delivery combines multiple interrelated healthcare services, allowing for the provision of people-centered care and the efficient use of resources.

**Intervention or response:** Between April 2019 and December 2022, 402 days of integrated disease screening were organized across five urban provinces of Viet Nam. Participants at higher risk of TB (e.g. contacts, the elderly, etc.) were mobilized for screening with chest X-ray (CXR). Individuals with an abnormal CXR result were asked to give sputum for testing with the Xpert MTB/RIF Ultra assay. Eligible participants also had their blood pressure and capillary blood glucose levels measured; eligibility for these non-TB tests varied between provinces, but they were usually prioritized for older participants (aged  $\geq 40$ ).

Participants with hypertension (systolic  $\geq 140$  mmHg or diastolic  $\geq 90$  mmHg) and suspected diabetes (if fasting  $\geq 7$  mmol/L or if random  $\geq 11.1$  mmol/L) were referred to public health facilities for confirmatory testing and treatment; people with TB were linked to appropriate treatment with the District TB Unit or the Provincial Lung Hospital.

**Results/Impact:** 138,017 community members were mobilized and screened using CXR, resulting in the diagnosis of 603 people with TB (436 per 100,000). 70,040 (50.7%) participants had their blood pressure measured, resulting in the detection of 29,536 (42.2%) people with hypertension. 60,262 (43.7%) participants had their blood glucose levels measured, resulting in the detection of 4,788 (7.9%) with hyperglycemia. 53,565 (38.8%) participants were screened by all three tests, and 25,774 (48.1%) people were diagnosed with at least one of the three diseases.



**Conclusions:** This service delivery model directly addresses the health facility access barriers which participants face and saves them time and money by offering multiple, free-of-cost screening tests in one encounter. For programs, the model improve participant mobilization, maximizes resources (cost per diagnosis) and supports continuity of care across multiple diseases.



## OA41 TB: How much does it cost?

### OA41-521-17 Household and health service delivery costs of pediatric home-based versus facility-based TB preventive treatment in Ethiopia (CHIP-TB)

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**Background:** Pediatric Tuberculosis contact tracing and linkage to TB Preventive Treatment (TPT) is challenging and may incur substantial costs for households of persons with TB. Home-based delivery of health services such as contact tracing and TPT may reduce the financial burden on household members of making monthly clinic visits.

**Design/Methods:** We estimated the patient and health service delivery costs of home-based versus facility-based pediatric (<15 years) contact person management (contact tracing, TPT initiation, and follow-up) in Ethiopia. We used a modified societal perspective (including health systems and patient costs), nested in a pragmatic cluster-randomized trial in nine home-based and nine facility-based clinics (CHIP-TB). Household out-of-pocket costs and lost income were captured from a subset of 125 participants across all clinics. Time-and-motion observations captured health system staff effort for TPT provision.

We estimated ranges for health service delivery costs using trial expense reports and project staff interviews. We estimated costs per household visited and per child completing TPT.

**Results:** The estimated total cost per household was \$19 [95% credible interval: \$15-\$24] for the home-based arm, versus \$27 (\$19-\$37) for the facility-based arm. The estimated total cost per child completing TPT was \$12 (\$8-\$17) for home-based TPT and \$21 (\$12-\$45) for facility-based TPT. From the patient perspective, care-seeking

costs, which included lost income and out-of-pocket costs, were \$1.43 per household in the home-based arm vs. \$12.87 in the facility-based arm. By contrast, health system costs, which included staffing, equipment, and administration and implementation costs, were \$17.18 per household in the home-based arm versus \$14.09 in the facility-based arm. Patient costs accounted for 48% of all costs in the facility-based arm but only 8% in the home-based arm.

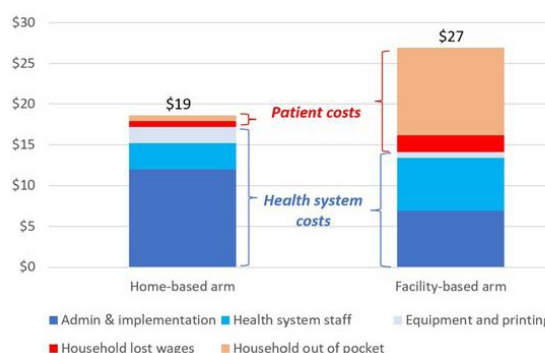


Figure. Split of patient and health system costs per household for TB contact person management in the home-based and facility-based arms.

**Conclusions:** From a societal perspective, home-based child TB contact tracing and provision of TPT is not more costly than facility-based provision and leads to significant cost savings for households.

## OA41-522-17 Cost-effectiveness of interventions to improve diagnosis and preventive treatment for paediatric TB in nine sub-Saharan African countries

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**Background:** Practical interventions are urgently needed to improve diagnosis and anti-tuberculosis treatment (ATT) initiation in children aged 0-14 years, and to increase coverage of tuberculosis preventive treatment (TPT) in children at high risk of developing tuberculosis disease.

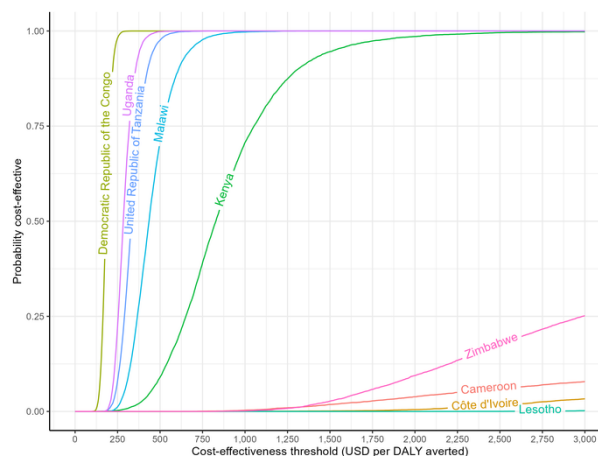
The multi-country Catalyzing Pediatric TB Innovations (CaP-TB) package of interventions scaled up facility-based intensified case-finding and strengthened household contact management and TPT provision at different entry points attended by children.

**Design/Methods:** We analysed clinic-level pre/post data to quantify the impact of the CaP-TB intervention on ATT and TPT initiation across 9 sub-Saharan African countries.

We analysed project expenditure and cascade data to determine unit costs of intervention components and used mathematical modelling to project health impact, health system costs and cost-effectiveness.

**Results:** Overall, ATT and TPT initiation increased, with country-level incidence rate ratios varying between 0.8 (95% uncertainty interval [UI]: 0.7 to 1.0) and 2.9 (95%UI: 2.3 to 3.6) for ATT, and between 1.6 (95%UI: 1.5 to 1.8) and 9.8 (95%UI: 8.1 to 11.8) for TPT.

We projected that for every 100 children starting either ATT or TPT at baseline, the intervention package translated to between 1 (95%UI: -3 to 1) and 42 (95%UI: 23 to 57) deaths averted, with a median incremental cost-effectiveness ratio (ICER) of US\$640 per disability-adjusted life-year (DALY) averted. ICERs were below US\$1,000/DALY averted in 5 countries.



**Conclusions:** In most countries, the CaP-TB intervention package improved tuberculosis treatment and prevention services for children aged under 15 years and would be considered cost-effective at thresholds of US\$1,000/DALY averted or higher.

Differences in estimated ICERs reflect a range of factors including varying baseline coverage of services, the impact of the intervention, resource use and costs in different contexts. Setting-specific intervention adaptation may be required to improve cost-effectiveness in some environments.

## OA41-523-17 The impact and cost of using mobile digital X-ray units to detect pulmonary TB in South Africa

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**Background:** The 2018 South African tuberculosis (TB) prevalence survey identified poor knowledge and awareness of TB symptoms in communities, leading to delayed healthcare-seeking and undiagnosed TB. Digital chest X-ray (dCXr) with computer-aided detection tools can assist in the early diagnosis of TB if deployed using the right care model.

**Design/Methods:** We analysed the costs of dCXr alongside a pilot study using 9 dCXr units (4 mobile vans, 5 shipping container clinics) deployed in 4 districts across 2 provinces (Western Cape, KwaZulu-Natal) in South Africa for 1-19 months per district in 2020-2022.

Sites were selected based on high TB prevalence using GIS mapping. Outcome data were collected electronically; economic costs were calculated based on a combination of ingredients-costing and expenditure analysis. We estimated the provider costs of two models (dCXR container placement adjacent to health-facilities versus community-outreach using mobile vans) and adjusted costs from this pilot study for routine-implementation based on expert input (“Routine-care” scenario). Costs are presented in 2022 US\$.

dCXR unit	Number of persons screened	Cost per category (% of total cost)					Average cost per person screened	TB cases found (% positivity)	Average cost per TB case found
		Staff	Equipment	Consumables	Demand creation	Media			
<b>Pilot-study scenario</b>									
Mobile van	7,459	\$50 (27%)	\$4 (2%)	\$10 (5%)	\$18 (9%)	\$108 (57%)	\$189	197 (1.78%)	\$8,689
Container	21,946	\$453 (63%)	\$36 (5%)	\$29 (4%)	\$202 (28%)	\$0 (0%)	\$721	451 (2.03%)	\$931
<b>Routine-care scenario</b>									
Mobile van	7,459	\$27 (18%)	\$2 (2%)	\$10 (6%)	\$7 (4%)	\$108 (70%)	\$154	197 (1.78%)	\$6,301
Container	21,946	\$451 (87%)	\$36 (7%)	\$29 (6%)	\$0 (0%)	\$0 (0%)	\$516	451 (2.03%)	\$666

Table 1. Average economic cost of dCXR screening by scenario in 2022 US\$.

**Results:** A total of 29,405 clients were screened using dCXR; 2,541 had abnormal X-rays suggestive of TB, and 648 tested positive for TB in sputum testing (TB positivity 2.2%) (see Table). Across scenarios, the average cost ranged from \$154 to \$721 per person screened, and from \$666 to \$8,689 per TB case found, with differences driven by the extent of media use, demand-creation activities and different staff contingents. While mobile clinics reached underserved rural populations, containers adjacent to facilities yielded higher screening volumes and TB positivity, leading to lower cost per TB case found despite higher cost per person screened.

**Conclusions:** Our analysis suggests that DCXR units collaborating with partners and facilities and using GIS hotspot for site selection to obtain highest possible screening yield can identify significant numbers of undiagnosed TB cases in short periods of time efficiently, especially when using containers.

### OA41-525-17 Apples and oranges: comparison of cost per case detected for three active TB case-finding strategies

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**Background:** To achieve Viet Nam’s goal ending tuberculosis (TB) by 2030, active case finding (ACF) should be one of the key priorities. However, many people have reservations about the cost to implement ACF.

We compared the cost per case detected through three simultaneously deployed ACF strategies on the USAID-funded Erase TB project.

**Design/Methods:** Erase TB operated in 10 districts of Ha Noi and Ho Chi Minh City. This study encompassed results from 2020-Q1 to 2022-Q2. ACF strategies included household and close contact investigation (ENHANCE), community-based X-ray screening (SWEEP) and private-sector engagement for facility-based screening and private TB treatment reporting (REPORT).

To calculate marginal cost per case detected by ACF strategy, we compiled three levels of costs: L1: Field costs; L2: Direct costs (L1+supervisors); and L3: fully-loaded organizational costs (L2+shared cost centers). Costs were incurred in VND and translated to USD using a rate of USD1=VND23,000.

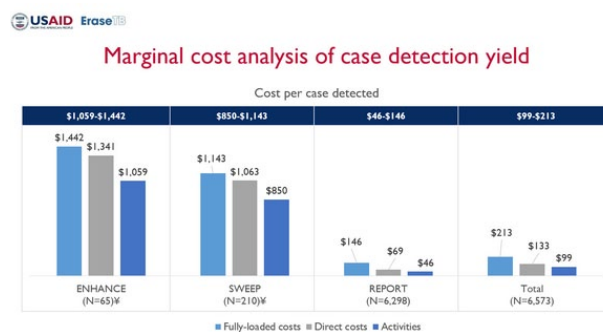


Figure. Marginal cost analysis of case detection yield.

**Results:** Erase TB detected 6,573 persons with TB through ENHANCE (n=65), SWEEP (n=210) and REPORT (n=6,298). The aggregate marginal costs per case detected across the four cost levels were L1=\$99, L2=\$133 and L3=\$213. The marginal cost per case detected through ENHANCE was L1=\$1,059, L2=\$1,341, and L3=\$1,442. Similarly, the marginal costs of case detection through SWEEP was L1=\$880, L2=\$1,063, and L3=\$1,143. Given the high number of persons with TB detected through REPORT, the marginal costs were much lower at L1=\$46, L2=\$69, and L3=\$146.

**Conclusions:** Marginal costs differed substantially across ACF strategies. The highest costs were incurred when reaching into the community to diagnosed people with TB early in their disease course. Meanwhile, REPORT was the most cost-effective, as people with TB had already taken the initiative to seek care with a provider. Ending TB requires application of all strategies, but also requires great care and discernment when evaluating their effectiveness and sustainability.

### OA41-526-17 A risk-benefit and cost analysis of different TB preventive therapy regimens in two high-risk populations: a modelling study

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**Background:** Household contacts (HHC) of people with infectious tuberculosis and people living with HIV (PLHIV) are at increased risk of developing tuberculosis (TB) disease and may benefit from TB preventive therapy (TPT). We conducted cost and risk-benefit analyses comparing three TPT regimens to no TPT, incorporating recent estimates of TPT-related AE, as well as post-TB disability and mortality.

**Design/Methods:** We developed a state-transition, Markov microsimulation model with a 20-year time horizon, without discounting. We modelled HHC or PLHIV with a positive IGRA who were aged 35 years and living in a high-income setting who did not receive TPT or received one of three regimens: four months of rifampin (4R), three months of isoniazid and rifapentine under DOT (3HP-DOT) and nine months of isoniazid (9H). Outcomes included health system costs, quality-adjusted life years (QALYs), and the proportion of patients developing tuberculosis, experiencing a TPT-related adverse event (AE), developing severe respiratory disability after TB treatment, and dying from TB. Cost and transition probabilities were from the published literature.

**Results:** Without TPT, 6.4% and 49.9% of HHC and PLHIV developed TB, respectively, while 1.6% and 12.1% had post-TB respiratory disability, and 0.3% and 2.5% died of TB (Table).

Moreover, without TPT, costs and QALYs associated with TB were \$1,709 and \$13,368, and 18.62 and 13.89, per HHC and PLHIV, respectively. All TPT regimens resulted in lower costs, rates of TB, post-TB disability, and TB deaths, though safety varied. Of all TPT regimens, in both populations, 4R was safest, with the largest gain in cost savings, QALYs, and reduction in TB disease and disability.

	% with TPT-related AE	% developed TB disease	% post-TB respiratory disability*	% Died due to TB	QALY (over 20 years)	Costs (2020 USD)
HHC received 4R	2.1%	2.3%	0.6%	0.1%	18.73	\$956
HHC received 9H	4.7%	2.9%	0.7%	0.2%	18.70	\$1226
HHC received 3HP-DOT	7.1%	2.5%	0.6%	0.1%	18.71	\$1246
HHC -No treatment provided	0.0%	6.4%	1.6%	0.3%	18.62	\$1709
PLHIV received 4R	2.1%	21.1%	5.0%	0.9%	14.22	\$6045
PLHIV received 3HP-DOT	7.1%	22.0%	5.3%	1.0%	14.20	\$6463
PLHIV received 9H	4.7%	25.8%	6.2%	1.2%	14.15	\$7270
PLHIV - No treatment provided	0.0%	49.9%	12.1%	2.5%	13.89	\$13368

Abbreviation: HHC- household contacts, PLHIV: people living with HIV, 4R: four months rifampin, 9H: nine months isoniazid, 3HP-DOT: three months of isoniazid and rifapentine under directly observed treatment

\*Severe respiratory disability: walks slower than people of the same age on the level because of dyspnea or stops for breath after walking 100 meters or after a few minutes on the level or too dyspneic to leave the house or breathless when dressing. For all outcomes: 20-year time horizon

**Conclusions:** Among PLHIV and HHC with a positive IGRA, TPT resulted in improved outcomes, including lower post-TB disability and mortality, improved QALYs, and lower costs, compared to no TPT. Of regimens considered, 4R was associated with greatest gains relative to no TPT.

### OA41-527-17 Economic burden of multidrug-resistant TB on patients and households: a global systematic review and meta-analysis

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**Background:** Multidrug-resistant tuberculosis (MDR-TB) is a major health threat worldwide, causing a significant economic burden to patients and their families. We conducted this systematic review and meta-analysis to determine the global burden of catastrophic costs associated with MDR-TB on patients and their households.

**Design/Methods:** We systematically searched five databases (CINHAL, MEDLINE, Embase, Scopus, and Web of Science) from inception to September 02, 2022, for studies reporting catastrophic costs on patients and affected families of MDR-TB.

The primary outcome of our study was the proportion of patients and households with catastrophic costs. Costs were considered as catastrophic when a patient spends 20% or more of their annual household income on their MDR-TB diagnosis and care.

The pooled proportion of catastrophic cost was determined using a random-effects model. Publication bias was assessed using visualization of funnel plots and the Egger regression test. Heterogeneity was explored with subgroup meta-analyses and meta-regression.

Finally, we used Preferred Reporting Items for Reporting Systematic Review and Meta-Analysis-20 (PRISMA-20). The research protocol was registered in PROSPERO (CRD42021250909).

**Results:** Our search identified 6,635 studies, of which 11 were included after the screening. MDR-TB patients incurred total costs ranging from \$650 to \$8,266 during treatment. The mean direct cost and indirect cost incurred by MDR-TB patients were \$USD 1,936.25 (SD  $\pm$  \$USD 1897.03) and \$1,200.35 (SD  $\pm$  \$USD 489.76), respectively. The overall burden of catastrophic cost among MDR-TB patients and households was 81.58% (95% Confidence Interval (CI), 74.13-89.04%). The overall pooled prevalence of catastrophic cost among Drug Susceptible (DS)-TB patients was 46.03% (95% CI, 21.34-70.71%).

**Conclusions:** The catastrophic costs incurred by MDR-TB patients were significantly higher than the catastrophic costs incurred by DS-TB. MDR-TB patients incurred more expenditure for direct costs than indirect costs. Social protection and financial support for patients and affected families are needed to mitigate the catastrophic economic consequences of MDR-TB.

### OA41-528-17 Catastrophic costs of drug-resistant TB for urban people in Indonesia: an expenditure approach

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**Background:** Drug-resistant Tuberculosis (DR-TB) remains a significant health problem in Indonesia. In 2021, there were 8,268 DR-TB cases, while only 62% enrolled in treatment. West Java and East Java were two provinces with a relatively low percentage of DR-TB case notifications (West Java 45% of 3,747 estimated cases; East Java 37% of 2,807 estimated cases).

This study aimed to explore the catastrophic cost among people with DR-TB in Bandung, West Java, and Surabaya, East Java.

**Design/Methods:** Quantitative analysis through micro-costing was utilized on 100 DR-TB patients selected by purposive sampling. In micro-costing, we identified the catastrophic cost by calculating the ratio of costs incurred in treating DR-TB and annual household expenditure (more than 20%).

The calculation was conducted by utilizing a questionnaire adapted from Tuberculosis patient cost surveys: a handbook published by WHO.

**Results:** This study showed that 81% of respondents experienced a catastrophic failure. People with DR-TB tend to experience economic pressure due to job loss (60% stopped working) or loss of productive time during DR-TB treatment. Patients who experience catastrophic failure do various ways to cover catastrophic costs, from getting social assistance (28%), borrowing money (28%), to selling assets (28%).

Some respondents sold assets of up to USD 6300 to overcome the economic impact of DR-TB. Not all people with DR-TB get economic assistance from the government.

**Conclusions:** People with DR-TB in Indonesia are still facing catastrophic financial burdens that result in poorer TB treatment outcomes. A clear scheme of social protection for people with DR-TB is needed to reduce the catastrophic impact of DR-TB.

## OA42 Management of TB during war

### OA42-529-17 The “one-stop shop” medical initiative for TB, HIV and viral hepatitis care in the Odesa Region, Ukraine during the reform, the pandemic and the war

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**Background and challenges to implementation:** Odesa region has the highest burden of TB in Ukraine. The incidence of TB rate is two times higher than the national rate, and the rate of TB/HIV co-infection is four times higher. Due to the provision of medical services for TB, HIV, and viral hepatitis by different providers, low coverage of ART and hepatitis treatment reduced the effectiveness of TB treatment.

To this purpose, a “one-stop shop” for TB, HIV, and viral hepatitis diagnosis and treatment approach was developed.

**Intervention or response:** In 2018-2019, the TB service in Odesa Region was reformed, inter-district offices were established, and certified training was provided to TB doctors. Patient routes have been updated to reflect a people-centered approach and expand services to the general population (including infection control). This model had proven sustainable during the COVID-19 pandemic and during the war when patient movement was restricted. Thanks to the implementation of the model, the appointment time has been significantly reduced, the percentage of ART coverage has increased, and access to hepatitis treatment has expanded. Currently, patients receive diagnosis and treatment of TB, HIV, and HBV from one doctor in one place throughout the region.

Years	TB/HIV co-infection, ART coverage and timing of prescription					All TB/HIV	HCV treatment Number of people	HBV treatment Number of people
	ART before TB	Without ART	ART for up to 14 days	ART on the 15-30th day	ART beyond the 30th day of TB treatment			
2017	336 (25,5%)	214 (15,4%)	95 (6,8%)	295 (18,6%)	470 (33,7%)	1394 (100%)	0	0
2018	434 (26,1%)	200 (12%)	218 (13,1%)	470 (28,3%)	341 (20,5%)	1663 (100%)	0	0
2019	464 (27,7%)	121 (7,2%)	495 (29,5%)	446 (26,6%)	150 (8,9%)	1576 (100%)	0	0
2020	296 (31%)	63 (6,6%)	393 (41,2%)	150 (15,7%)	52 (5,5%)	954 (100%)	438	98
2021	303 (32,5%)	41 (4,7%)	392 (45,4%)	104 (12%)	23 (2,7%)	864 (100%)	1072	128
2022	285 (34,9%)	40 (4,9%)	379 (46,4%)	92 (11,3%)	20 (2,5%)	816 (100%)	1030	234

Table.

**Results/Impact:** During the period of model implementation, the percentage of ART coverage in patients with HIV/TB co-infection increased by 10.5%.

In 2022-2023 it will be more than 95%, with ART prescription within the first two weeks of treatment (excluding TB and cryptococcal meningitis). Hepatitis treatment has become accessible to everyone.

**Conclusions:** A comprehensive and integrated approach to receiving medical services from a single provider has made it possible to target diagnosis and treatment to all those in need, including vulnerable groups, offering people-centered services. Modern treatment approaches have made it possible to expand access to quality medical services.

### OA42-530-17 The impact of war on the treatment capacity of regional TB centres in Ukraine: main challenges and ways to overcome them

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**Background:** 25 regional TB centers in Ukraine coordinate TB response at the regional level. In 2022, the National TB program of Ukraine faced unprecedented challenges due to the war: the destruction of facilities, active military actions, temporary occupation, migration processes among medical staff and people with TB, and limited funding. These challenges cause violations of human rights.

**Design/Methods:** An online survey among management staff was conducted on the activities of TB centers in context of the crisis caused by war. The questionnaire consisted of several parts related to the infrastructure of institutions, human resources, the main difficulties in working with internally displaced persons, and problems at the outpatient and inpatient stages of TB care.

**Results:** Currently, of 25 regional TB centers, only Luhansk was relocated to another region, and two TB centers do not provide medical care in total.

Among main challenges identified by the management staff of the centers: 44% (11 centers) are related to complicated logistics and transportation, 40% (10 centers) to migration, and only 20% (5 centers) complain about the lack of staff. Temporary difficulties, such as frequent air alerts, lack of electricity, and mobile/Internet connection, did not significantly affect centers' work (4% in 1 center). Factors that allowed to overcome the challenges: 84% (21 centers) coordinated cooperation of medical staff, 80% (20 centers) assistance of partners (international organizations, business), 60% (15 centers) assistance of volunteers, 44% (11 centers) support of the state at the level of the Ministry of Health of Ukraine and local governments.

**Background and challenges to implementation:** 25 regional TB centers in Ukraine coordinate TB response at regional level. In 2022, the National TB program of Ukraine faced unprecedented challenges due to the war: destruction of facilities, active military actions, temporary occupation, migration processes among medical staff and people with TB, and limited funding. These challenges violate human rights.

**Intervention or response:** An online survey among the management staff was conducted on the activities of TB centers in the context of the crisis caused by the war. The questionnaire consisted of several parts related to the infrastructure of institutions, human resources, the main difficulties in working with internally displaced persons, and problems at the outpatient and inpatient stages of TB care.

**Results/Impact:** Currently, of 25 regional TB centers, only Luhansk was relocated to another region, and two TB centers do not provide medical care in total.

Among the main challenges identified by the management staff of the centers: 44% (11 centers) are related to complicated logistics and transportation, 40% (10 centers) to migration, and only 20% (5 centers) complain about the lack of staff. Temporary difficulties, such as frequent air alerts, lack of electricity, and mobile/Internet connection, did not significantly affect centers' work (4% in 1 center).

Factors that allowed to overcome the challenges: 84% (21 centers) coordinated cooperation of the medical staff, 80% (20 centers) assistance of partners (international organizations, business), 60% (15 centers) assistance of volunteers, 44% (11 centers) support of the state at the level of the Ministry of Health of Ukraine and local governments.

**Conclusions:** The most significant challenges were direct destruction of infrastructure, complicated logistics, and migration processes among people with TB. No doubt, the work of the TB center staff has been the principal value that has helped to counteract this, but it is necessary to pay attention to the problem of burnout among TB workers.

### OA42-531-17 Special interventions on contact tracing in Ukraine during the war: programmatic results

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**Background and challenges to implementation:** During the full-scaled war in Ukraine the access to TB diagnostics for population is limited. The reasons are: lack of clinics and medical professionals in occupied regions and those with hostilities; lack of priority of TB diagnostics in medical professionals; care for wounds and combat injuries is prioritized; health issues are not the priority for population in conditions when survival in hostilities and in the regions of arrival are prioritized.

At the same time staying in bomb shelters, moving in evacuation trains led to increased number of TB contacts among general population of Ukraine.

In Ukraine, medical professionals conduct contact tracing routinely. However, taking into account the large proportion of missing TB cases in Ukraine - 41% (WHO, 2021), the number of contacts screened for TB should be increased.

**Intervention or response:** There are two interventions on contact tracing provided by Alliance in Ukraine. The first one - optimized TB case finding (OCF- TB) is aimed at social contacts of vulnerable populations search; the second one (Contact tracing MPSS) searches for additional contacts (those who were not found and screened by the healthcare system) of TB/DR-TB patients who are on medical-psychosocial support provided by Alliance. The last one started in July 2022. All diagnostics procedures are in line with National TB protocol. Alliance's interventions contribute to reaching additional contacts and increasing access to TB diagnostics for them.

**Results/Impact:** We compare the outcomes of Alliance's interventions and the routine contact tracing:

Intervention	Geography	# of contacts examined	# of contacts examined per 1 index-case	# of TB cases diagnosed, absolute number	per 1000 contacts	Number needed to investigate (NNI) <sup>1</sup>
Routine contact tracing, 2021	entire Ukraine (governmental-controlled area)	27,677	2	429	15.5	65
Contact tracing (MPSS), 2022	6 regions	3,515	4	174	48.7	20
OCF TB, 2022	4 regions	3,324	8	271	81.5	12

<sup>1</sup> Number of contacts are examined in HCF to diagnose 1 TB case.

**Conclusions:** TB diagnostics among contact persons in Alliance's interventions significantly exceeds the same indicator within the routine contact tracing. These in-

terventions should be scaled up to the entire Ukraine despite the ongoing war. This will allow to decrease the number of missing TB cases caused by the COVID-19 epidemic and the war.

### OA42-532-17 Post-conflict response to ensure continuity and resuming interrupted TB services, a lesson from Amhara Region, Ethiopia

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**Background and challenges to implementation:** The conflict in Ethiopia has mainly affected the health system, compromising the capacity to ensure service continuity, particularly for patients who need long term treatment, like TB patients. Interruption of TB diagnosis, care and treatment, not only worsen the health of patients who were on treatment, but also increase the chance of drug-resistance TB and transmission to the community.

**Intervention or response:** The USAID eliminate TB project conducted a rapid assesment in 169 health facilities and identified the damaged In TB services and designed a four-month period post conflict response plan (PCRP)  
**Implementation:** The project deployed seven consultants and vehicles to support the technical working groups (TWG) established at each zone, and 1359 health workers were provided a counselling support and resumed routine work. TB screening and tracing lost TB patient campaigns were conducted in all districts. The project distributed 9 GeneXpert machines and 40 microscopes, established a locally adapted sample transport system and link health facilities to the nearest diagnostic facility; distributed 5 computers, 749 recording and reporting materials to resume the information system; and conducted a follow-up support to ensure service resumption in the following three months.

**Coordination and monitoring:** The projects and regional task force conducted a biweekly virtual meeting, and the challenges identified were forwarded to responsible expert and leadership and response evaluated in the next meeting. The TWGs also conducted a six round biweekly Review meeting with TB officers 53 district.

**Results/Impact:** Results: A total of 171,583 people screened, and 53 Positive including 1 DR-TB TB positive were linked to treatment, 85 lost TB patients traced and linked to treatment.

**Conclusions:** The coordinated PCR was effective. By the end of the PCRP implementation period, 218 HFs resumed TB service, 92 districts resume TB information system and all districts resumed routine Joint supportive supervision to support the health facilities.

### OA42-533-17 "Runaway TB kits": strategy to avert unfavourable TB treatment outcomes in a conflict-affected part of Ethiopia

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**Background and challenges to implementation:** Amhara region was affected by conflict during June–November 2021. Anti-TB drug supply and drug administration under supervision is usually disrupted during a war.

**Intervention or response:** The USAID Eliminate TB Project supports the Amhara region to ensure the anti-TB drug supply and improve quality of care for TB patients in terms of successful treatment completion. The project collaborated with the regions, trained clinicians, and undertook supportive supervision to monitor activities at TB clinics where TB medication is served in full for six months or in TB patient kit forms. During trainings and supportive supervisions, it was advised to issue a full TB patients kit for patients on medication during the conflict, "runaway" TB kits. The project assessed the role of runaway kits in terms of anti-TB drug stock-outs and treatment success rate (TSR) after the conflict.

**Results/Impact:** During the initial peak conflict period (October–December 2020), about 1.4% of 120 assessed health facilities experiences anti-TB drug stock-outs whereas this proportion was less than 1% in the second round of the conflict (June–November 2021). Of 6,109 TB cases in the cohort of July–September 2021, 94.6% successfully completed their treatment, and of 5,563 cohort TB patients in October–December 2021, 95.6% were either cured or completed. The TSRs were not different from the usual 96% success rate in the region ( $Z = 0.6, p = 0.87$ ).

**Conclusions:** The introduction of runaway kits left only 2% of health facilities with stock-outs and averted potentially high unfavorable outcomes for TB patients in the conflict-affected areas. This seems a good experience worth sharing in similar settings and shock conditions.



**OA42-534-17 Active TB case-finding among internally displaced persons in Ukraine during the military conflicts: five-year experience**

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**Background and challenges to implementation:** Since 2014, two waves of population migration was fixed in Ukraine due to russian aggression. First migration was from non-governmental controlled areas (two eastern regions) in 2014-2015; the second one started in 2022.

These led to increase in the numbers of IDPs, that are considered as key affected population to TB. According to official data there are 4.893k IDPs in Ukraine now.

**Intervention or response:** Alliance started ACF TB initiative among IDPs in 2018 in three regions with the highest number of IDPs. State social services (SSS) were engaged, since IDPs apply to them for registration and social support.

Screening for TB symptoms, support of screening-positive people during TB diagnostics process up to treatment enrollment of those with diagnosed active TB is provided by SSS. Since the full-scaled invasion in 2022, the initiative was scaled-up to the central and western regions where IDPs were arriving from the regions with hostilities and/or occupied.

**Results/Impact:** Our experience showses TB notification among IDPs is the highest in the first years after the migration’s start and decreases as IDPs are socialized at the regions of arrival. As mass migration subsides, TB is concentrated among IDPs who were not able to get socialized. After the registration of less number of TB cases among IDPs (2019-2020) our efforts were shifted from total IDPs to those who were still in duffcult life circumstances (since 2021).

After the war start we got back to ACF TB among total IDPs. We expect higher number of TB in IDPs in 2023 (lower NNI).

Year	# of the year after mass migration start	NNI (number needed to investigate) <sup>1</sup>
2018	5	356
2019	6	423
2020	7	421
2021	8	218
2022	1	206
Q1 2023	2	152

<sup>1</sup> NNI- number of patients that should be examined in HCF to diagnose 1 TB case.

**Conclusions:** Active TB case finding among IDPs should be included in the activities for their social adaptation in the places of their arrival. These measures can mitigate the impact of TB spread during hostilities.

**OA43 Strategies to strengthening Health System for TB prevention and care**

**OA43-535-17 The centralised online TB/DR-TB Consilium: supporting clinicians’ capacity to manage difficult-to-treat cases and facilitating effective drug-resistant TB care throughout Uzbekistan**

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**Background and challenges to implementation:** Despite its progress in TB control, Uzbekistan remains a high burden country for multi drug-resistant TB (MDR-TB) [1]. TB specialists based at remote regional and peripheral facilities often lacked expert advice in managing complex TB/DR-TB cases. This was exacerbated by COVID-19 restrictions on gathering and travel.

**Intervention or response:** The USAID Eliminating TB in Central Asia (ETICA) Activity and the NTP initiated a weekly, centralized countrywide online DR-TB consilium in early 2022. USAID ETICA provided technical and financial support to establish centers of innovative distance learning and monitoring in the NTP and regional TB facilities to provide easy access to online TB/DR-TB consilium. Internet connectivity at all medical facilities in Uzbekistan allowed TB specialists at every level to participate and receive expert input from NTP specialists. Discussion at the Consilium address clinical decision-making for complex TB cases, diagnostic cases, and patients with comorbidities.

**Results/Impact:** From January 2022–February 2023, on-line consilium participants discussed 405 cases, including 92 DR-TB cases (61 MDR-TB and 31 XDR-TB), 56 DS-TB cases, and 257 diagnostic and other cases from all over the country. The number of cases presented at the online TB/DR TB consilium has grown over time (see Figure) as the number of participants has increased. More than 300 participants from all regions of Uzbekistan now regularly join to discuss patient management and exhibit increasing interest in learning through case discussions. Most TB specialists in the country have improved their knowledge and skills while presenting cases or receiving feedback on their management of TB/DR-TB cases.

**Conclusions:** The countrywide online TB/DR-TB consilium plays an important role in supporting TB specialists in managing difficult-to-treat TB and DR-TB cases, while building the capacities of regional and peripheral/district level specialists. The online Consilium model is effective for improving DR-TB care throughout Uzbekistan and could be replicated in other countries.

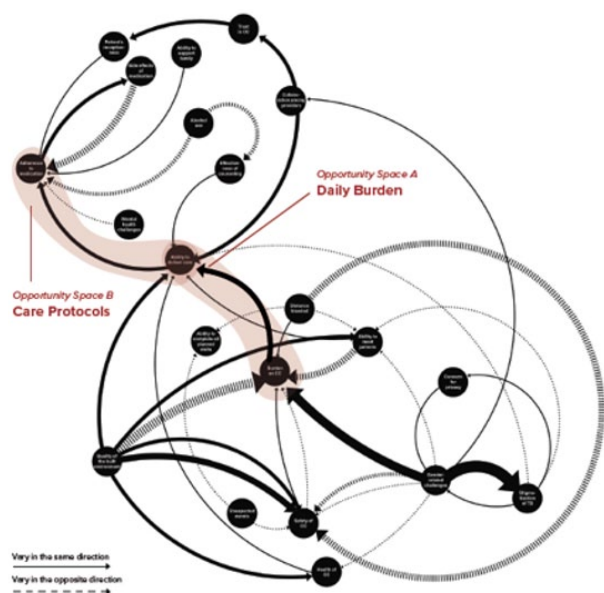
## OA43-536-17 Applying a behavioural design lens to strengthen health systems

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**Background:** Health worker staff act as care coordinators (CCs) who provide various services to people affected by TB. Health systems view CCs as “task-runners” as opposed to users of a system that require appropriate support. Training protocols and digital interfaces are often not aligned with CC daily experiences.

**Design/Methods:** 14 CCs in the Indian districts of Surat and Ranchi were invited to photograph their daily experiences. Subjects were asked open-ended questions about their photos in the form of stories. 365 stories and over 220 photos were documented over three weeks. We applied network science to generate a systems dynamics map that visualizes connections across variables. An algorithmic model measured connections across parameters of connectivity, frequency, influence, and efficiency to estimate a variable’s importance and strength of association.



**Results:** One of the two opportunity spaces identified for action is described below:

### A. How can we better support CCs in their planning activities?

*“We are routinely asked to do urgent tasks such as share data, visit stakeholders, attend meetings, document activities—it interferes with our daily plan—and we are unable to meet patients that we committed to.”*

### B. How can we apply a gender lens to protocols?

*“This area is full of textile factories. I have many patients there. It is an area where no woman can go.”*

*“There is no place in the field where women can find a washroom.”*

### C. How can we adapt protocols to the unique conditions of the built environment?

*“There was a tenement at the top of a factory where workers lived. There were 20-25 congested, tiny and noisy rooms. There was no ventilation and a very damp, foul smell.”*

**Conclusions:** Care Coordinators are increasingly tasked with more work with the expansion of TB initiatives. A design framework can better prototype protocols and products that motivate effective care delivery.

## OA43-537-17 Diagnostic network and route optimisation as a guide to implementing a cost-effective sample transportation system in the hilly areas of Uttarakhand, India

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**Background and challenges to implementation:** Specimen referral and transportation system is an essential mechanism to improve access to TB testing. Under India’s National TB Elimination Program (NTEP), the existing referral systems are ad-hoc and unstructured resulting in minimal or no impact. Diagnostic network and Route optimization (DNO) was taken up for Uttarakhand, a district that faces logistic challenges due to its hilly terrain.

**Intervention or response:** The TB molecular diagnostic network (Xpert and Truenat®) was restructured in 5 districts of Uttarakhand using supply chain network optimization analytics using the OptiDx Diagnostic Network Optimization Tool. The possible routes and resources required for implementing a sample transportation system were explored using RO techniques. The analysis considered optimal utilization of existing devices, cost efficiencies and access to TB testing.

**Results/Impact:** The annual molecular TB diagnostic capacity in 2021-22 (23 micro-PCR devices, Xpert and Truenat® at 19 testing sites) for these districts is 52,500 tests where the devices were under-utilised at 12.72% of total capacity.

The DNO analysis decentralised the devices thereby reducing average sample transportation distances from 29 to 18 kms (38% reduction). It identified 78 peripheral health institutions that could be linked to sample transportation system where total facilities increased by 132% contributing to additional access to TB testing through sample collection.

This addition is likely to support improvement in utilization of testing devices to 54% (4.25 times). The cost of transportation is projected to be reduced to 38%. The implementation of a sample transportation system

based on this DNO analysis can result in a projected increase in testing from 1.72% of population to 4.5% of population annually. RO analysis supported implementation of sample transportation by identifying number of routes, vehicles, and human resources per district.

**Conclusions:** DNO and RO analysis are effective tools for planning efficient sample transportation systems leading to improved access to TB testing.

### **OA43-538-17 Leveraging the integrated specimen and results transportation network to improve access to TB molecular testing: a case study of Mukono District, Uganda**

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**Background and challenges to implementation:** Improving access to molecular diagnostics, like GeneXpert testing, is crucial for enhancing TB diagnosis especially in high TB burden settings. In Uganda, these diagnostic services are mainly available at high-level health facilities, placing a significant burden on patients who must travel long distances to access them.

An audit in March 2022 found out that only 38% of all notified TB patients were tested with a molecular test against a target of >71% while 54.2% of all sputum samples had a turnaround time (TAT) longer than 72 hours at 15 non-GeneXpert sites.

We aimed to improve access to molecular testing and reduce TAT by leveraging the integrated specimen and results transportation network.

**Intervention or response:** In April 2022, the USAID LPHS-TBA project recruited two additional motorcycle riders to support specimen and results transportation bringing the total number of motorcycle riders to four. Using the hub and spoke model, we assigned 15 health facilities without GeneXpert testing services (spokes) to three health facilities with GeneXpert testing onsite (hubs).

We then re-designed routing schedules for motorcycle riders to ensure that each of the 15 spokes is reached at least 3 days a week and revised specimen shipment registers to track specimen referral and TAT. At each of the spokes, line lists were made for notified TB patients who had missed a molecular test who were later contacted and asked to provide sputum samples for GeneXpert testing.

**Results/Impact:** By December 2022. The proportion of patients tested with a molecular test improved from 38% (115/301) to 77.5% (300/387) while the proportion

of GeneXpert results released in less than 72 hours improved from 45.8% (604 out of 1318) to 71.5% (802 out of 1121).

**Conclusions:** Through leveraging the integrated specimen and results transportation network, we were able to improve the proportion of patients that received molecular testing for TB.

### **OA43-539-17 Addressing the gap in finding missing TB cases among TB contact persons: introduction of a contact investigation master-list, a methodical approach for documenting contact investigation**

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**Background and challenges to implementation:** Despite recommendations to improve contact investigation (CI) for early identification and treatment of Tuberculosis (TB) and prophylactic therapy for Latent TB Infection (LTBI), screening of TB contact persons remains a challenge in the Philippines.

Patient leakages in the CI cascade are associated with an inadequacy of tools to document and follow up contact persons of TB patients.

**Intervention or response:** USAID's TB Platforms for Sustainable Detection, Care and Treatment Activity (TB Platforms) implemented a CI master list to the City Health Office (CHO) of Lipa, Batangas, as part of a comprehensive technical assistance package to scale up CI and TB Preventive Therapy (TPT) coverage. TB Platforms oriented healthcare workers (HCWs) on the CI master list and led a practical exercise demonstrating proper recording of contact details.

A consensus was reached to initially prioritize documentation and screening of contact persons of bacteriologically confirmed (BC) cases to serve individuals with higher TB risk.

**Results/Impact:** The LIPA CHO reported 34% (381/1,112) CI coverage over a six-month period before implementation. In the first six months of utilizing the CI master list, the CHO documented 1,121 contact persons with BC cases. The tool allowed the tracking of each contact person as they received TB services across the care cascade, resulting in 100% CI coverage (1,121/1,121). Increased CI coverage led to the identification of four active BC and 81 latent TB cases, with all individuals enrolled into appropriate treatment regimens.

**Conclusions:** Utilizing the CI master list increased CI efficiency by providing a methodical approach for documenting and tracking TB contact persons. It helped re-

duce initial lost-to-follow-up with individuals tracked as they completed the care cascade. However, TB services and logistics must be available, accessible, and affordable for optimal contact investigation.

### OA43-540-17 Tech-enabled self-learning interventions for upskilling community outreach workers: experience from India

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**Background and challenges to implementation:** With India alone contributing ~30% to the global total TB-affected individuals, urgent action to improve early identification and case-management is warranted. Decentralizing care through government-led Ayushman Bharat Health and Wellness Centres (AB-HWCs) can help bring services closer to the communities.

However, Community Health Officers (CHOs) at these centres lack necessary technical skills for TB, which hinders decentralization. Further, empowering TB Champions can also aid community engagement for effective case-management

**Intervention or response:** Jhpiego's USAID-funded-NISHTHA program developed and delivered self-learning modules on Tuberculosis (TB), in local languages, for key cadres across India from Jan-Dec'21. The program included a 12-module model on *i-learn* (learning management system for CHOs), and an Interactive Voice Response (IVR) based platform called *Swasthya Vani* with 14 bite-sized episodes for TB Champions using feature phones.

Training modules were prepared in consultation with the government and focused on TB basics, roles/responsibilities, gender-responsive approach, social equity, community engagement, health education, and stigma. *i-learn* included pre-and post-tests with certificates awarded upon successful completion. Performance dashboards were created for monitoring activities.

**Results/Impact:** As of March'23, 1,563 CHOs used *i-learn* from 11 Indian states, of which 69% started new modules and ~20% completed all 12 modules. CHO knowledge scores increased in post-test compared to pre-test (Relative change: 29%). *Swasthya Vani* was used by 1,203 unique callers from six states who called a total of 3,973 times. The average call length was 9.1 min (SD±14.6min) and a total engagement of 605.2hrs on all learning modules. Further, ~80% of the enrolled participants completed at least seven episodes. Ready adoption of the models by government stakeholders, reach of IVR to remote areas, and CHOs' tech familiarity ensured models' sustainability and acceptance.

**Conclusions:** Empowering and building capacities of these cadres can strengthen community engagement for TB. Tech-based self-learning platforms hold promise in training young individuals and reaching hard-to-reach areas; however, maintaining participant engagement in such models necessitates attention

### OA43-541-17 Revolutionising TB patient care: how the public-private mix model and district health information software are changing the dynamics

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**Background and challenges to implementation:** Pakistan is a high-burden TB country (5<sup>th</sup>). A significant aspect of the fight against tuberculosis in Pakistan is engaging the large and diverse private healthcare sector. More than 86% of the population seeks healthcare in the private sector. There have been more than 20 years of actively working towards ending TB.

However, the public and private sectors remain unregulated and capturing real-time data and patients presents a critical issue.

**Intervention or response:** To overcome these challenges, Mercy Corps Pakistan initiated the digitalization of TB recording and reporting tools by custom-designing the District Health Information Software (DHIS2). The plan is to implement it as a central system for digitalization in the 120 TB-PPM districts of Pakistan. The digitalization pilot, which started in October 2022, has been conducted in 6 geographically spread districts.

**Results/Impact:** A total of 4772 patient records have been entered, and the acceptability of software and technology was very high (95%).

The use of digital systems identified gaps which had never been identified before, i.e., 89% of the patient's follow-ups were not conducted in time, resulting in a treatment gap the follow-up testing results were not available for 49% of the patients, making it difficult to declare their outcomes.

Some mandatory fields were missing, like contact number and national ID card number, which are essential to identify the duplication. Also, the staff's field visits did not follow the program guidelines, highlighting implementation challenges. Overall, data quality was low compared to the perceived quality based on the paper system.

**Conclusions:** Pilot results highlighted implementation realities and acted as reminders/nudges for teams' responses while entering the data. They are used to the old methods and cannot fully adapt.

For the program, comprehensive monitoring is needed, and new ways of capacity building are required to focus on gaps identified by the system.

### OA43-542-17 Scaling up intensified case-finding through the adoption of the FAST Plus strategy in “Tuberculosis Alisin Natin (Eliminate TB)” campaign in Quezon Province, the Philippines

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**Background and challenges to implementation:** In 2022, Quezon province reported a TB Treatment Coverage Rate of 77%, below the national target of 85%, despite a concerted effort to accelerate TB elimination strategies, including finding missing TB cases and intensifying infection prevention control in health facilities to eliminate TB.

**Intervention or response:** The USAID’s TB Platforms for Sustainable Detection, Care and Treatment Activity conducted a series of advocacy activities in 41 public and private hospitals and primary care facilities to promote the adoption of the FASTPlus strategy and scale up intensified case finding and infection prevention and control. FASTPlus is a practical approach to finding missing TB cases and infection prevention and control through screening all individuals coming to the health facility, regardless of the reason for the consult. The active identification of persons presumed to have TB, their separation from others, and the provision of prompt and effective treatment prevents the spread of TB.

**Results/Impact:** To support a 100% adoption rate, USAID’s TB Platforms helped develop a provincial ordinance, providing for a province-wide campaign to eliminate TB, known as “*Tuberculosis Alisin Natin*” (Eliminate TB), with provisions on the mandatory implementation of FASTPlus in all healthcare facilities.

Between 2021 and 2022, FASTPlus was adopted by 53 facilities and led to a 131% increase in TB screening (65,131 in 2021 to 150,660 in 2022).[GU1] [SJ2] The total number of TB cases diagnosed increased by 8% (1197 vs 1287). Among drug-sensitive TB cases, the increase was equivalent to 7% (1185 vs 1266) while among drug-resistant TB (DR-TB) cases, the increase was 75% (12 vs 21).

**Conclusions:** The FASTPlus strategy offers opportunities to strengthen systematic intensified case-finding, especially in the detection of DR-TB and enhance IPC in health facilities to prevent the spread of TB among patients and healthcare workers. The strategy also provides opportunities to increase TB service coverage.

### OA44 TB Modeling

#### OA44-543-17 Natural history of TB disease according to disease severity at presentation

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**Background:** There is substantial heterogeneity in disease presentation for individuals with tuberculosis disease. While this could impact disease outcomes, there are limited data to support such an association. We aimed to estimate disease outcomes by disease severity at presentation among individuals with tuberculosis during the pre-chemotherapy era.

**Design/Methods:** We extracted data from studies of patients enrolled 1917-1948 in the United States, stratified by three categories of disease severity at presentation defined using the U.S. National Tuberculosis Association diagnostic criteria. These criteria were based largely on radiographic categories (“minimal”, moderately advanced”, and “far advanced”) established by the U.S. National Tuberculosis Association.

We used Bayesian parametric survival analysis to model the survival distribution overall and stratified by disease severity. We used Bayesian logistic regression to estimate the severity-level specific odds of natural recovery within three years.

**Results:** People with minimal tuberculosis at presentation had a 2% (95% credible interval: 0%-11%) TB mortality probability within five years versus 40% (95% credible interval: 15%-68%) for those with far advanced disease. Individuals with minimal disease had 13.6 times the odds (95% CI: 9.87-19.1) of natural recovery within three years compared to those with far advanced disease.

**Conclusions:** Mortality and natural recovery vary substantially by disease severity at presentation. Practical radiographic stratification of patients presenting with pulmonary tuberculosis can provide insight into the expected trajectory of disease.

Our results suggest that people with minimal disease at presentation have low mortality and high rates of natural recovery. These results are consistent with current initiatives to evaluate individualized treatment regimens (e.g. shortened or longer) based on the severity of disease.

### OA44-544-17 Preventing TB with community-based care in an HIV-endemic setting: a modelling analysis

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**Background:** Antiretroviral therapy (ART) and tuberculosis preventive treatment (TPT) both prevent tuberculosis (TB) disease and deaths among people living with HIV. Differentiated care models, including community-based delivery, can increase uptake of ART and TPT in settings with a high burden of HIV-associated TB, particularly among men.

**Design/Methods:** We developed a gender-stratified dynamic model of TB and HIV transmission and disease progression among 100,000 adults ages 15-59 in Kwa-Zulu-Natal, South Africa. We drew model parameters from a community-based ART initiation and resupply trial (Delivery Optimization for Antiretroviral Therapy, DO ART) and other scientific literature.

We simulated the impacts of community-based ART and TPT delivery programs over ten years, assuming community-based ART and TPT could be scaled up to similar levels as in the DO ART trial (*i.e.*, ART coverage increasing from 49% to 82% among men and from 69% to 83% among women) and sustained for ten years. We projected the number of TB cases and deaths averted relative to standard, clinic-based care.

**Results:** If community-based ART could be implemented with similar effectiveness to the DO ART trial, increased ART coverage could reduce TB incidence by 27.1% (range 21.3% - 34.1%) and TB mortality by 34.6% (range 24.8% - 42.8%) after ten years.

Increasing both ART and TPT uptake through community-based delivery was projected to reduce TB incidence by 29.5% (range 23.9% - 36.0%) and TB mortality by 35.9% (range 26.9% - 43.8%). Community-based

ART and TPT reduced gender disparities by reducing TB mortality among men by a projected 39.7% (range 30.0% - 48.5%) and 30.7% (range 23.0% - 38.4%) among women.

**Conclusions:** By substantially increasing coverage of ART and TPT, community-based care for people living with HIV could reduce TB incidence, mortality, and gender disparities in settings with high burdens of HIV-associated TB.

### OA44-545-17 HIV and antiretroviral treatment as drivers of rifampicin-resistant TB in South Africa: insights from mathematical modelling

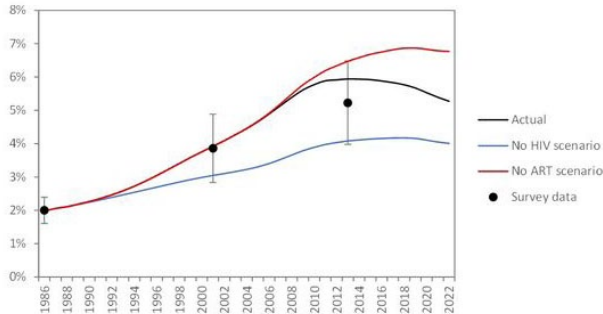
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**Background:** Rising levels of multidrug and rifampicin resistant tuberculosis (MDR/RR-TB) are a global concern, with several modelling studies predicting continued increases in coming years. TB patients are at increased risk of acquired rifampicin resistance if they have HIV coinfection, especially at low CD4 counts, but this dynamic has not previously been modelled.

**Design/Methods:** We extended a previously-developed model that simulates HIV and TB in South African adults, to include the acquisition and transmission of rifampicin resistance. In line with systematic reviews, the risk of acquiring RR with TB treatment is modelled as being negatively associated with patients' CD4 counts. We allow for temporal changes in drug susceptibility testing, both before treatment initiation and at treatment failure, as well as other changes in TB prevention and treatment. The model is calibrated to data from national TB drug-resistance surveys, and recorded numbers of MDR/RR-TB laboratory diagnoses and patients initiating second-line TB treatment, using a Bayesian approach.

**Results:** The model estimates that the proportion of South African TB patients with rifampicin resistance at diagnosis increased from 2.0% (95% CI: 1.7-2.3%) in 1986 to 5.9% (5.2-6.9%) in 2013, in line with survey data (Figure). In the absence of HIV, the prevalence of MDR/RR-TB would have increased to 4.1% (2.7-5.1%) in 2013, suggesting a third of rifampicin resistance in

2013 was attributable to HIV. In the absence of antiretroviral treatment (ART), the prevalence of rifampicin resistance would have been higher (6.5% [5.6-7.6%] in 2013, rising to 6.9% [5.7-8.2%] in 2019). ART reduced the prevalence of rifampicin resistance in 2019 by 17%, and greater reductions are projected over the longer term.



**Figure: Rifampicin resistance prevalence in South African tuberculosis patients at diagnosis**  
 The 'No HIV' scenario is one in which there is assumed to have been no HIV epidemic historically, and the 'No ART' scenario is one in which we simulate the HIV and TB trends that would have been expected if no antiretroviral treatment (ART) programme had been introduced. Lines represent the average estimates from 1000 posterior distribution samples (95% confidence intervals not shown).

**Conclusions:** In countries with high HIV prevalence, HIV may be a major driver of rifampicin resistance in people with TB. ART programmes have the potential to reduce the emergence of resistance substantially.

**OA44-546-17 Spatiotemporal modelling of *M. tuberculosis* transmission risks using environmental, clinical and patient movement data**

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**Background:** In countries with high tuberculosis (TB) incidence, congregate settings such as healthcare facilities carry a considerable risk of *Mycobacterium tuberculosis* (*Mtb*) transmission. The risk of indoor airborne infection is often estimated with the Wells-Riley equation – an epidemiological model based on the ventilation rate and the duration of exposure to infectious doses (so-called quanta). The concentration of infectious quanta is often assumed to be constant in airspace and time. Here, we developed a spatiotemporal extension of the Wells-Riley model that uses patient movements to estimate indoor transmission risk.

**Design/Methods:** We collected environmental (CO<sub>2</sub>), clinical (from electronic patient registries), and patient movement data (video sensors; see tracking examples in Figure 1a) for 8 days between October and November 2021 in a primary care clinic in South Africa. Our model relates the risk of infection (P) to the infectious quanta concentration (N), which can vary over time and

airspace. We assume that the newly emitted quanta decrease exponentially with distance to infectious individuals, and we estimate the removed quanta via time-varying air exchange rates based on indoor CO<sub>2</sub> levels. We performed 1,000 Monte Carlo simulations, considering uncertainty in all modeling parameters and assuming similar numbers of masked and unmasked TB patients among clinical attendees.

**Results:** Video sensors recorded 2,645 clinical attendees of whom 925 were linked to patients records. Across simulations, we estimated a daily mean P of 0.9% (95%-limits: 0.2%-2.1%). On average, there were 9 (95%-limits: 0-19) patients with P>1% per day. N was higher in the morning and waiting room (Figure 1b).

**1a | Subset of patient movement data**

Examples of trackings from 40 patients in the clinic



**1b | Estimated quanta concentration in the clinic by daytime**

Average concentration in the morning (7:30 to 12am) and afternoon (12am to 4pm)



**Conclusions:** Combining environmental, clinical, and patient movement data allowed spatiotemporal modeling of *Mtb* transmission risks. This approach could identify hotspots and high-risk patients in indoor settings, measure the effects of control measures, and guide optimization of person flows.

## OA44-547-17 Sub-country level variation in TB healthcare service disruptions due to COVID-19 in South Africa: a model-based analysis

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**Background:** Tuberculosis (TB) healthcare service disruptions, due to stringent measures to contain the spread of SARS-CoV-2 (COVID-19), have been reported by countries worldwide. The extent to which these disruptions can vary at sub-country level is currently not known. We aimed to estimate TB healthcare service disruptions during the COVID-19 epidemic at the provincial level in South Africa.

**Design/Methods:** We used autoregressive integrated moving average (ARIMA) time-series models to estimate healthcare service disruptions in the nine South African provinces. TB testing, case notification and treatment outcome data for the years 2017-2021 were provided by the National Institute for Communicable Diseases and National Department of Health.

We quantified disruptions as the percentage difference between data observed during the COVID-19 epidemic (Apr2020-Dec2021) compared with expected values derived through predictions from the pre-Covid-period (Jan2017-Feb2020). Estimated monthly percentage differences were aggregated for Apr-Dec 2020 and Jan-Dec 2021.

**Results:** At country level, we estimated that Xpert Ultra tests performed during 2020 (Apr-Dec) were 32% (95% uncertainty interval: 26%-37%) lower and TB case notifications were 27% (18%-34%) lower than predicted. The proportion treatment success and proportion death during TB treatment among patients with reported outcomes were 4.1% (1.9%-6.1%) lower and 21% (11%-32%) higher than predicted, respectively. At province level, reductions in Xpert Ultra tests performed (range 26%-41%), TB case notifications (range: 16%-47%) and proportion treatment success (range 0.2%-9.3%) as well as increases in proportion death (range: 0.4%-43%) varied considerably (Figure). In 2021, percentage differences in Xpert tests performed and TB case notifications were variable but more modest overall (Figure).

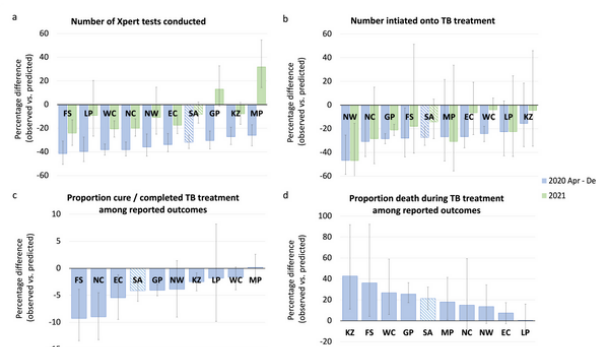


Figure. Average percentage differences between observed and predicted TB indicator values for the periods April-December 2020 and January-December 2021 among the 9 provinces of South Africa: Eastern Cape (EC), Free State (FS), Gauteng (GP), KwaZulu-Natal (KZ), Limpopo (LP), Mpumalanga (MP), Northern Cape (NC), North West (NW) and Western Cape (WC). TB treatment outcome data was only available until December 2020. Error bars: 95% uncertainty intervals. Striped bars: national estimates for South Africa (SA). Negative percentage differences represent reductions in observed data during the COVID-19 epidemic compared with expected values derived through predictions from the pre-Covid-period.

**Conclusions:** Our analysis demonstrates considerable sub-country level variation in TB healthcare service disruptions during 2020-2021, suggesting that COVID-19 response measures had a differential impact on TB health services in the nine South African provinces. Sub-country level analysis in high TB burden countries can help target recovery measures towards areas at highest need.

## OA44-548-17 Using facility-level notification data to predict TB hotspots at the community level: challenges and experiences from Bangui, Central African Republic

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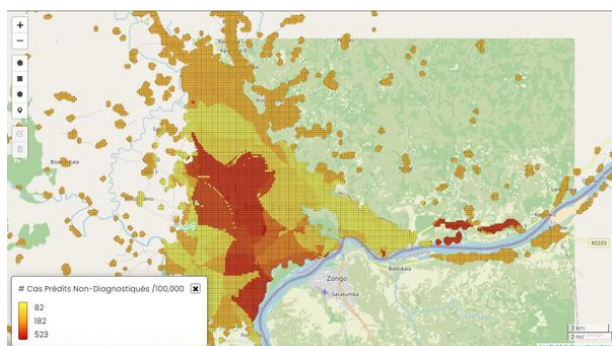
**Background and challenges to implementation:** Central African Republic (CAR) with the TB incidence rate of 540 per 100,000 people in 2020, is among the 4 highest TB incidence countries in the central region of Africa. More than 50% of the estimated cases remain undiagnosed/unreported in the country, with 13,428 new TB cases reported in 2021.

In this resource limited setting we tested an innovative approach for predicting hotspots of TB using facility level TB notification data. The idea was to overcome limitations of notification data (under-reporting, under-diagnosis) and identify underserved areas at the highest resolution for optimizing TB treatment services.



**Intervention or response:** We used open source data to map population settlements in Bangui, overlaid by a grid of 100m resolution to get ‘tiles’ of 100x100m. We estimated the number of individuals with potentially undiagnosed TB using incidence and notification data and weighted their distribution by population density within the catchment area (20 min walking distance). We then used the ratio of estimated undiagnosed TB to tile population combined with high resolution contextual data like sociodemographic and indicators of human development to train a Bayesian model which predicted the number of undiagnosed TB potentially present across the whole city. Virtual meetings were regularly organized to follow and discuss the process with local teams.

**Results/Impact:** We predicted number of undiagnosed TB per 100,000 population in Bangui at a resolution of 100m. The overall region could be categorized in 3 groups: High, Moderate and Low rates of potentially undiagnosed TB. Of the 12 facility catchment areas which provide treatment services, two, seven and three were classified as high, medium and low risk regions respectively.



**Conclusions:** Predictive modelling techniques combined with high resolution contextual data can be used to target underserved populations in a more effective manner. Discussions are ongoing to implement an active contact investigation in these prioritized hotspots.

### OA44-549-17 Accelerating TB case-finding through targeted community active case-finding using artificial intelligence hotspot mapping: TB LON experience in Sagamu Local Government Area, Ogun State, Nigeria

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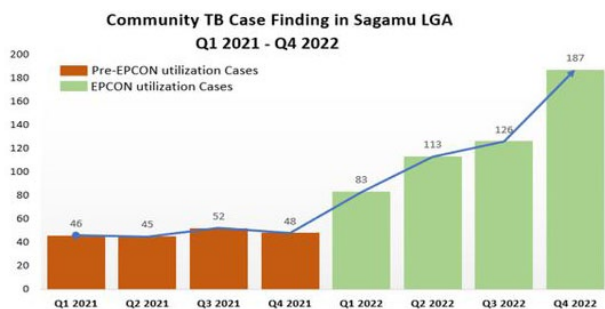
**Background and challenges to implementation:** Epidemic Control Systems Artificial Intelligence (EPCON AI) quantifies TB risks in population groups by capturing, combining, analyzing health records, lifestyle, and contextual data to estimate disease burden. EPCON plays a pivotal role in finding missing TB cases in Nigeria by modeling infectious diseases with its predictive model based on Bayesian Inference.

The USAID-funded TB-LON 3 project aims to find the missing TB cases in the community using this innovative platform to optimize community interventions. Before EPCON, community outreaches and house-to-house TB case searches were carried out in predetermined community areas within the LGA based on the intuition of the Health Care workers with no scientific basis and outcomes characterized by low case findings.

**Intervention or response:** EPCON AI hotspot mapping guides identifying specific hotspot community areas where TB cases can be found based on contextual indices and historical TB case-finding data.

As a result, outreaches and house to house ACF were carried out at targeted communities as predicted by AI hotspot mapping and the corresponding TB case finding has been highly significant in contrast to the pre-EPCON low TB case yield.

**Results/Impact:** There has been an exponential and steady, stepwise rise in TB case finding since the introduction of EPCON-AI guided community ACF with about a 290% increase in TB case detection in Q4 2022 in comparison with Q4 2021, as shown in the chart above.



**Conclusions:** The use of artificial Intelligence aided hotspot mapping to determine TB-burdened communities within local government areas for targeted outreaches to find missing TB cases is a scientific and cost-effective technology that has proven to deliver good returns on investment as evidenced by better utilization of available resources to produce a more efficient performance yield and could be a game changer in rapidly breaking the chains of community transmission of Tuberculosis, through accelerated TB case detection.

### OA44-551-17 Can we reach TB elimination? Modelling the impact of public health interventions on TB burden in England

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**Background:** England has a low incidence of TB, with an estimated incidence of 7 per 100,000 population in 2021, 76.4% of which were amongst the foreign-born. Mathematical modelling can help to anticipate what is needed in order to reach the 2035 End TB goals.

**Design/Methods:** We developed a deterministic, compartmental model of TB transmission dynamics in England, distinguishing 'domestic' and 'foreign-born' populations. We calibrated the model to available epidemiological data for TB in England.

We then simulated the following interventions:

- Active case-finding (ACF), for example through contact tracing,
- Tuberculosis preventive therapy (TPT) amongst those with evidence of latent TB infection, and;
- Monthly follow-up post-treatment.

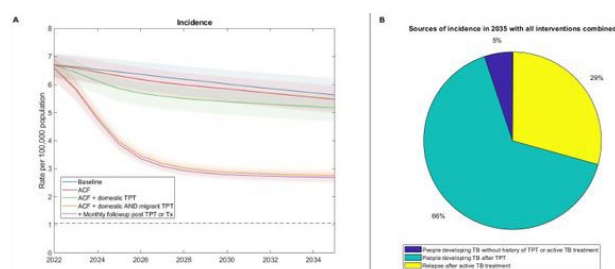
We assumed TPT to have 60% efficacy in reducing incidence, consistent with the current 3HP regimen, and also drew from the literature for relapse rates following treatment of active TB. We modelled all interventions

separately in domestic and foreign-born populations, assuming them to be scaled up in a linear way from 2022 to 2025.

**Results:** Of all interventions, increasing TPT coverage amongst migrants would lead to the greatest reduction in incidence (Figure 1A).

However, a combination of all these interventions falls short of reaching the TB reduction target by 2035 (Figure 1A).

Figure 1B illustrates the remaining sources of incidence by 2035, highlighting that the vast majority comes from individuals who have already been treated, either for TB infection (66%) or for active TB (29%).



**Conclusions:** Combined interventions in both domestic and foreign-born populations could see substantial reductions in TB incidence and mortality, by 2030. However, meeting the elimination goals will be challenged by the limitations of current treatments: namely, the imperfect efficacy of preventive therapy, and the potential for post-treatment relapse of active TB treatment. Post-treatment follow-up may play an important role towards mitigating these challenges.

## OA45 Can we find everyone by 2030? Missing TB Cases!

### OA45-552-17 Community TB detection model to find TB missing cases – experiences from Tanzania

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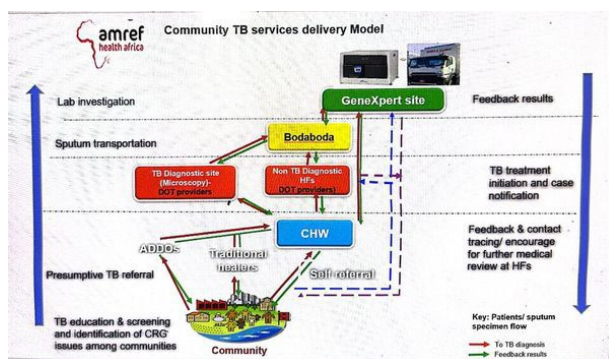
**Background and challenges to implementation:** Tanzania is among the 30 high TB burden countries with the incidence of 208/100,000 with the treatment coverage of 65%, which indicates (35%) of estimated cases remained undiagnosed<sup>1</sup> (WHO,2022).

Amref and its partner MDH under HIV/TB Global-Fund grant (2021- 2023) are implementing interventions to find TB-missing cases through community TB detection Model in 8 regions.

[1] World Health Organization (2021). Global Tuberculosis report. Geneva.

**Intervention or response:** In community TB detection model, the key player is Community Health Worker (CHW) who provide TB education, screening through door to door visits, community campaigns and outreach services including contact investigations; and refer TB presumptive cases to health facilities for diagnosis. Occasionally, mobile-van-TB clinics are used in hard-to-reach areas.

Through trained Motorcyclists, samples have been transported from non-diagnostic facilities to GeneXpert sites. A total of 1920 CHWs are linked to trained 960 Accredited Drug Dispensing Outlets and 640 Traditional healers to provide thorough TB screening and referrals among their clients.



**Results/Impact:** Between Jan 2021 and June 2022, TB notified cases were increased by 52% from 4,796 (Q1, 2021) to 9,254 (Q2,2022) in implementation area.

During the same period, community contribution in TB case notification increased to 61% compared with the baseline of 23% which is greater than the national target of 30%. Transportation of sputum samples has increased bacteriological confirmed TB cases to 54.2% compared to 35% baseline (2020)[1].

[1] NTLP data, 2021 and 2022

**Conclusions:** Community engagement through different community entry points is a key for finding missed TB cases. With the huge magnitude of missed TB cases at 35% (2020), the country should think of investing more on community-based interventions to achieve END TB targets.

Transportation of specimen from Non-TB diagnostic sites and communities to diagnostic sites increases access to molecular tests.

### OA45-553-17 Community influencers as key drivers of community mobilisation: learnings from Aashwasan, a 100-day active case-finding campaign in the tribal districts of India

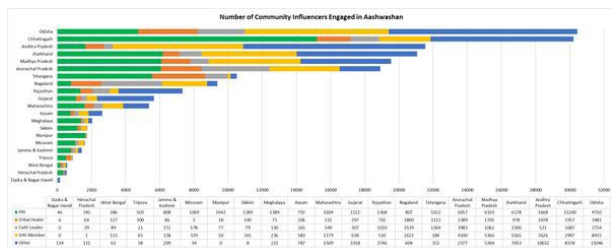
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**Background and challenges to implementation:** India's current health system relies heavily on accredited social health activists (ASHA) for all the health programs. The task of taking every health service or information to each household, even in the remotest of geographies, is on ASHA.

The evidence of leveraging influential people from the community for improving the health outcomes is limited and is restricted to the members of Panchayati Raj Institutions (PRI) and Self-Help Groups (SHGs). Role of influential people from the same community, called community influencers, is crucial to drive any behaviour change or to provide an environment that positively influences the health of its members.

**Intervention or response:** Aashwasan, a 100 days active case finding campaign for pulmonary tuberculosis (TB), was implemented across 68,413 villages of 174 tribal

districts in 21 States/UTs of India between January and August 2022. The first step of village-level outreach under Aashwasan was engaging with and getting the buy-in from the community influencers. Once the influencers understood the objectives of the campaign and were willing to support, they were onboarded.



**Results/Impact:** A total of 193,406 community influencers (including, PRI members: 58,368, Tribal Healers: 19,058, Faith leaders: 19,066, SHG: 41,018, Others 55,896) supported Aashwasan through various communication activities on multiple platforms in their villages. This helped in achieving 280,259 persons with presumptive pulmonary TB getting tested and diagnosing an additional 10,249 TB cases.

**Conclusions:** Community influencers played a crucial role in mitigating the challenge of stigma associated with TB and convincing communities to take part in screening and testing for TB.

Along with helping in achieving the immediate objectives of the campaign, engagement with community influencers ensured an enhancement in the collective awareness of TB and available services and building trust between the community and public health system.

**OA45-554-17 Strengthening knowledge and skills among civil society organisations in mobilising domestic resources against TB-HIV and malaria**

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**Background and challenges to implementation:** Health is a devolved function in Kenya, with county governments prioritizing access to health and provision of healthcare services. Most counties allocate up to 75% of resources to recurrent expenditure, leaving preventive, promotive, and rehabilitative health services underfunded.

To address this issue, Amref Health Africa in Kenya, with support from the Global Fund, has been working to enhance domestic resource mobilization through civil society organizations (CSOs) in 10 high burden counties to advocate for increased budgetary allocation to HIV, TB, and Malaria that rely heavily on donor funding.

**Intervention or response:** To strengthen domestic resource mobilization, Amref Health Africa’s project aimed to create an inclusive environment. 300 CSOs were trained between August and October 2022 on budgeting processes, effective monitoring of health budgets, collaborating with partners, and holding stakeholders accountable. This training equipped the CSOs to make meaningful inputs into county budget formulation and review processes.

**Results/Impact:** CSOs’ advocacy efforts in three counties have contributed to the significant increase in funds towards the fight against HIV, TB, and malaria in the 2023-2027 CIDP. To ensure improved health outcomes for communities, CSOs have developed an accountability structure, addressing the previous lack of systems and structures for tracking expenditures, which resulted in low expenditure and absorption rates in the previous cycle of implementation.

However, there was a reduction in the TB and HIV resources invested in some of the counties as the gaps and needs analysis done during the process showed an increase in partner contribution for the interventions. This resources were in turn allocated and prioritized for other needs including Malaria.

**CIDP Estimates - Amount in Million Ksh**

County	TB		HIV		Malaria	
	2018/2022	2023/2027	2018/2022	2023/2027	2018/2022	2023/2027
Vihiga	250	128	500	149	NA	181
Homa Bay	25	150	25	433	15	885
Kisumu	4.5	11.25	117	39	28	31.7

**Conclusions:** The outcomes demonstrate that with adequate training and support, CSOs can advocate for budgetary allocation towards eradicating TB at the county level. The CSOs’ training empowered them to engage in budgetary processes, make meaningful inputs, and champion budgetary allocation to health services.

**OA45-555-17 Role of family members of patients with TB compared to traditional healers in TB case detection in 86 health facilities in seven provinces, Afghanistan, 2020-2022**

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**Background and challenges to implementation:** Due to low awareness and lack of knowledge of tuberculosis (TB), it is estimated that 30% of the population with TB signs and symptoms do not go to health facilities for care, particularly in rural areas resulting in delays in diagnosis and treatment and increasing the risk of

TB transmission within communities. Awareness raising and community-level case finding in rural areas is a national priority.

**Intervention or response:** The USAID AFIAT project collaborated with local NGOs to strengthen the community-based DOTS (CB DOTS) program in seven provinces.

In addition, to engage 1,318 CHWs in CB DOTS, from 2020 to 2022, a total of 86 community health supervisors (CHSs) were trained on CB\_DOTS in turn, these CHSs trained 110 TB patients' family members and 100 traditional healers to support community mobilization on identifying and referring presumptive TB patients (PTB) to selected 86 diagnostic HFs

**Results/Impact:** From 2020 to 2022, TB patients' family members referred 5,381 PTB, which is five times higher compared to PTB referred by traditional healers (922). Among referred PTB by TB patients' family members 397 were diagnosed with TB which is 4 times higher compared to traditional healers (85). The number of PTB patients who were notified of their TB status due to TB patients' family members' referrals steadily increased by 52% starting in 2020 with 1499 and ending in 2022 with 2282 (See Table 1).

Year	Presumptive TB cases referred by traditional healers	Presumptive TB cases referred by TB patients' family members	All forms of TB notified among those referred by traditional healers	All forms of TB notified among referred TB patients' family members
2020	235	1499	6	108
2021	324	1600	12	129
2022	363	2282	67	160
Total	992	5381	85	397

Table 1: Engagement of TB patient's family and traditional healers in CB DOTS in 86 HFs of seven provinces- Afghanistan

**Conclusions:** The involvement of TB patients' family members in identifying and notifying TB patients showed an increase in TB case notification in the selected HFs. The involvement of TB patients' family members in community-based DOTS in other rural provinces is recommended.

### OA45-556-17 Tapping into latent local resources for meeting additional nutritional needs of people with TB in Tamil Nadu, India

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**Background and challenges to implementation:** National TB Elimination Program (NTEP) India data and other studies estimate that 55% of annual TB incidence in India suffer from malnutrition. Observed in Tamil Nadu as well, lack of nutritious diet leads to poor treatment outcomes and increases the probability for people with TB (PwTB) to relapse. NTEP provides a support of INR 500 for each PwTB per month as Direct Benefit Transfer (DBT).

**Intervention or response:** USAID supported Accountability Leadership by Local communities for Inclusive, Enabling Services (ALLIES) Project, implemented by REACH, trained TB Champions to implement a Community Accountability Framework (CAF), where challenges faced by PwTB in TB care and services are discussed and recorded for addressal. As part of the CAF process, in selected facilities of six districts in Tamil Nadu, the need for additional nutritional support was expressed by PwTBs. TB Champions identified a local solution - they prepared a list of PwTB requiring support and list of potential donors who could provide the same. They sensitised the donors about the challenges faced by PwTB. Donations by willing donors were collected and rations were distributed to the PwTB. Based on requirement, one-time nutritional support and support for the entire treatment duration was provided. This included protein-rich food items with longer shelf life.

**Results/Impact:** 79 TB Champions mobilised over 250 local donors including elected representatives, members of NGOs, faith-based organisations, shopkeepers, teachers, rotary clubs. Additional nutrition support of an estimated value of USD 10000 was provided to 2254 PwTBs over a period of 21 months. 89% (2006) of the PwTB received one-time nutritional support and 11% (248) received nutritional support for the entire treatment duration.

**Conclusions:** Through a systematic process, TB Champions identified the needs of PwTBs such as requiring additional nutrition support, and effectively tapped into locally available resources to support the PwTBs.

### OA45-557-17 Innovative community-based approaches doubled TB case notification in the Sagamu Local Government Area, Ogun State: A TBLON3 Project experience in Nigeria

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**Background and challenges to implementation:** According to the World Health Organization (WHO), Nigeria has the highest burden of TB in Africa, ranking 6th globally with incidence at 219/100,000 population. The USAID TBLON 3 aimed at finding the missing TB cases and scaling up TB services especially in targeted hotspots and hard-to-reach communities.

Prior to the project, general healthcare workers rely heavily on passive case-finding, conducting occasional TB screening in selected locations. Sagamu Local Government Area was not known as high TB burden and there is a gap in the estimated TB burden and TB notification.

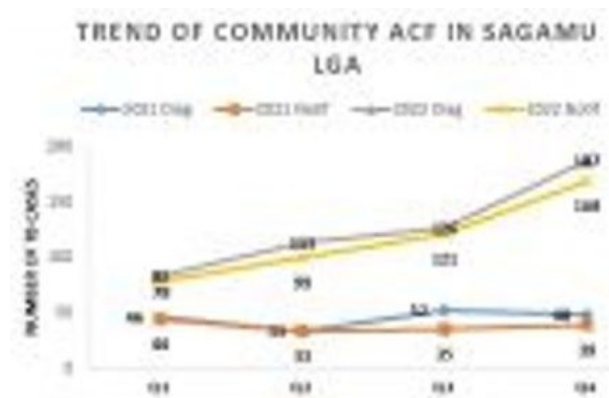
**Intervention or response:** This is a retrospective comparison of community active case finding in Sagamu Local Government Area between year 2021 and 2022.

In October 2021, 25 community volunteers were selected to work within their communities of residence. This was to ensure familiarity with the terrain and build trust from community members.

They conduct TB awareness, sensitization and screening activities as well as mobilized for outreaches. They collect sputum samples from persons presumed to have TB, identified by using the WHO symptom (W4SS) checklist before referral to minimize the losses in that step of the TB care cascade.

The samples were logged into a facility presumptive register prior to movement to for GeneXpert Rif assay to facilitate efficient result retrieval.

The volunteers also render escort services to diagnosed patients to healthcare facilities for enrollment into care and act as treatment supporters throughout treatment course.



**Results/Impact:** In 2021, a total of 17,773 persons were screened and 2080 presumed to have TB were identified against 34,711 and 4475 in 2022 respectively. There was also 6% increment in the proportion of diagnosed cases that were notified between 2021 and 2022. The total number of TB cases notified in 2021 more than doubled at the end of 2022.

**Conclusions:** Community-based approaches complement case-finding efforts.

### OA45-558-17 Ukrainian refugees in host countries: barriers, coping strategies and community response to provide effective access to HIV and TB treatment and prevention

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**Background:** TB incidence rate in Ukraine was 45 people per 100 thousand people in 2022, whereas the number of newly registered cases of tuberculosis, including relapses, was 18,500 people. Existing TB rates in Ukraine are on average 10 times higher than in Central and Western Europe. The Public Health Center of Ukraine registered slightly over 200 Ukrainian refugees who have continued TB treatment in receiving countries whereas we estimate this number to be much higher.

**Design/Methods:** A qualitative study was carried out with Ukrainian refugees in 6 receiving countries: Germany, Poland, France, Lithuania, Georgia, and Moldova. We interviewed Ukrainian refugees living with HIV and/or affected by TB as well as care providers and public health experts.

The aim of the study was to explore barriers in access to care, the role of stigma and of discrimination, formal

and informal strategies for overcoming the barriers, success stories, including civil society practices.

**Results:** The key barriers were low awareness of medical personnel in the EU countries about TB, low access to community groups and TB civil society organizations in receiving countries, stigma in refugees' reception centers and lack of mental health services. The best practices include hotline support services, including remote case management and transnational support from the public health center of Ukraine and Ukrainian TB care NGOs.

**Conclusions:** EU countries set an unprecedented benchmark for Ukrainian refugees implementing the "temporary protection" policy although not fully in line with the specific needs of key populations. However these measures did not include Ukrainians who arrived before February 24, 2022, and citizens of third countries who resided in Ukraine.

### OA45-559-17 Positioning TB Champions in TB Units to provide treatment support services to people with TB in India

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**Background and challenges to implementation:** TB treatment, care, and support are the core elements of the TB elimination process. The rapid expansion of TB care services and the introduction of innovative models of service delivery are aiding their uptake across the country under the National TB Elimination Programme in India.

Adopting person-centered approaches and fostering greater community participation can further strengthen person centered care services.

**Intervention or response:** In 2022, drawing on the philosophy 'When TB Champions (TBCs) talk about TB, communities listen', the Unite to ACT (UTA) project rolled-out a facility-based intervention - TB Support Hubs - across 10 states of India. TBCs were trained to provide a comprehensive package of support services, including treatment literacy, individual and family counseling and follow-up of public health actions such as contact tracing, comorbidity screening etc.

Five high-burden TB facilities were identified in each district and 5 trained TB Champions placed at the facility, to provide this set of services to all people with TB enrolled there. Job aids for TB Champions and educational materials for PwTB were developed and disseminated.

### Results/Impact:

Number of TBC engaged in TBSH	Total PwTB reached out			PwTB reached out as per type of TB		PwTB reached out as per site of disease	
	Male	Female	Transgender	DS TB	DR TB	Pulmonary	Extra Pulmonary
400	13749	9555	6	22922	388	17994	5316

Between September and December 2022, TBCs reached out in-person, primarily at the point of treatment initiation, to more than 23,000 PwTB. Of this, nearly 41% were women, and 5% children below 14 years. In addition, TBCs are presently supporting about 380 people with drug-resistant TB. TB Unit staff ensure that all newly diagnosed PwTB meet TBCs for peer counseling. The Support Hub model has emerged as a robust community support system through the treatment regimen period.

**Conclusions:** TBSH is an initiative to provide inclusive, value-added holistic care and rehabilitative services for PwTB, and strengthen the interface between the health system and communities.

### OA46 Finding TB cases among vulnerable populations

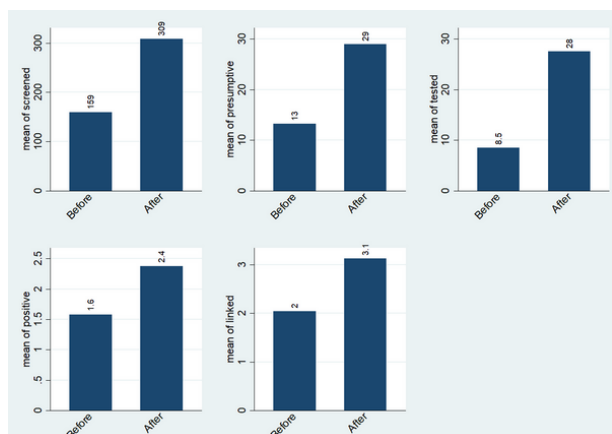
#### OA46-560-17 Strategies to resolve the gap in adolescent TB care in Uganda: The TEEN TB Project

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**Background:** Strategies to promote health care-seeking behavior among adolescents are urgently needed. We piloted a project (TEEN TB project) aimed at improving uptake of tuberculosis (TB) care services among adolescents at Ugandan health facilities.

**Design/Methods:** We developed an adolescent TB awareness and screening package using the human centered design. The package had 3 interventions: TB screening cards, TB awareness poster messages and a local song deployed in project health facilities and surrounding communities. Data on socio-demographic & clinical characteristics of adolescents were collected between October 2021 & March 2022 at Kawolo, Iganga,

Gombe and Kiwoko hospitals. Before and after intervention data from facility records was collected and analyzed using logistic regression to determine the effect of the package.



**Results:** A total of 394 adolescents were included and the majority (76%) were school-going. Overall, the intervention improved adolescent TB care in the four project health facilities. The average number of adolescents screened increased by 94% from 159 to 309, with an incidence rate ratio (IRR) of 1.9 ( $p < 0.001$ , 95% CI 1.9-2.0), there was a 2 fold increase among those presumed to have TB; from 13 to 29, (IRR of 2.2,  $p < 0.001$ , 95% CI 1.9-2.5) and those tested with Gene-Xpert increased more than 3 times from 8 to 28 (IRR of 3.3,  $p < 0.001$ , 95% CI 2.8-3.8). There was a minimal increase in the average monthly number of adolescents with a positive result from 1.6 to 2.4 and linkage to TB care services from 2 to 3.1. These were not statistically significant at  $p=0.170$  and  $p=0.154$  respectively.

**Conclusions:** The project improved uptake of TB services among adolescents along the TB care cascade (screening, TB testing and linkage to care). We recommend a robust and fully powered randomized controlled trial to evaluate the effectiveness of the package.

### OA46-561-17 Evaluating the efficiency of active case-finding interventions to improve childhood TB in Nigeria

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**Background and challenges to implementation:** Infants and young children exposed to tuberculosis (TB) face a high risk of TB infection, disease and death. It is estimated that TB in children accounts for a third of all TB case notifications. Despite the recent progress in TB notification in Nigeria, improving childhood TB case-

finding remains one of the leading concerns of the national TB program. The USAID-funded TB LON 1 & 2 project instituted targeted interventions that ensure active screening for TB among children attending health facilities and community events to increase case-finding in Nigeria.

**Intervention or response:** The impactful facility and community-based interventions involved engagement and training of healthcare workers and ad hoc staff as TB screening officers, continuous capacity building, and provision of laboratory consumables and logistics for sample movement. The screening officers actively screened children attending healthcare facilities and community health outreaches, identified presumptive clients and ensured diagnostic evaluation and linkage to TB treatment for diagnosed TB cases. The intervention efficiencies were assessed and compared using TB yield, the number needed to screen (NNS) and the number needed to treat (NNT).

**Results/Impact:** From January to December 2022, 2,211,486 children were screened for TB across the five different intervention types, and 128,791 presumptive TB were identified with a 6.3% diagnostic drop-out. In all, 5,272 TB cases were confirmed, giving a TB yield of 4.4% (Table 1). The TB yield of community-based interventions (6.1%) was higher than those of the facility-based interventions (3.6%),  $p < 0.001$ . The average NNT for community-based interventions was 16 (range: 12 – 17), while for facility-based interventions was 28 (range: 25 – 36).

Intervention category	Facility-based Screening Interventions			Community-based Screening Interventions			Total	
	ICF Public	ICF Private	All facility-based Intervention	Community ACF	Contact Investigation	ACF-special pop.		All community-based Intervention
Persons screened	1,342,554	529,115	1,871,669	285,911	51,459	2,447	339,817	2,211,486
Presumptive identified	60,774	29,379	90,153	23,762	14,424	452	38,638	128,791
Presumptive evaluated for TB	55,975	28,101	84,076	22,465	13,700	448	36,613	120,689
Cases diagnosed	2,265	780	3,045	1,294	895	38	2,227	5,272
Cases put on treatment	2,173	744	2,917	1,284	895	38	2,217	5,134
NNS	593	678	615	221	57	64	153	419
NNT	25	36	28	17	15	12	16	23
TB patient yield	4.0%	2.8%	3.6%	5.8%	6.5%	8.5%	6.1%	4.4%

ICF – Intensified case-finding, ACF – active case-finding

Table: Facility and community-based interventions TB cascade summary.

**Conclusions:** Active case-finding in targeted populations is critical to improving TB case-finding in children. Interventions utilizing community structures for active TB screening among children were more efficient regarding TB case yield when compared with facility-based interventions.



### OA46-562-17 Active case-finding at textile spinning mills and sugar cane factory in Solapur, India

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**Background and challenges to implementation:** The spinning mills of Solapur and Sugar factories employ contractual and day wage labourers coming from lower socio-economic status with poor health seeking behaviour. Workers working in spinning mills are exposed to fine microfibers. Similarly, sugar factory workers are exposed to chemicals, dust, and bagasse. The occupational hazard with both these industries are poor lung health making them vulnerable to acquiring TB.

**Intervention or response:** The health department in collaboration with Directorate of Industrial and Safety Health, Solapur Regional office undertook an active case finding campaign among workers employed in textile spinning mill and sugar factory. This ACF was a one-day activity in the month of December 2022 in both the factories wherein 1620 employees attended awareness session. This was followed with screening of 4 symptom (cough, fever, weight loss and night sweats), spot sputum sample were collected and Xray was done for presumptive cases. Samples of all presumptive cases were subjected to sputum microscopy/NAAT.

**Results/Impact:** The retrospective data from the intervention was analysed. Of the 1620 employees 585 (36%) attended the screening camp. Among those screened for symptoms, 320 employees (55%) were presumptive TB cases and of them 16 (5%) patients were additionally identified as active TB. All the TB cases identified were put on treatment, who would have gone unidentified without this campaign. (Figure 1)

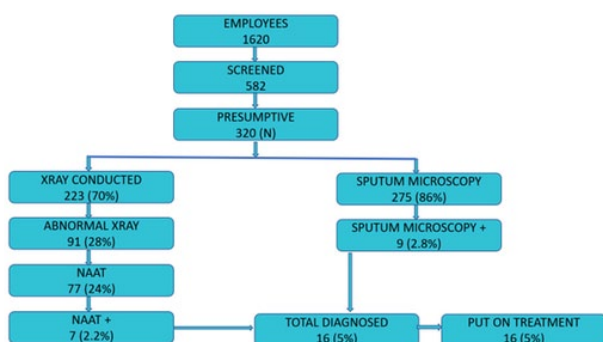


Figure 1. ACF at high-risk workplace in Solapur.

**Conclusions:** This study demonstrates the potential and effectiveness of ACF among vulnerable workplaces thereby helping in identification of missed TB cases.

A collaborative approach with industrial health regulatory body to identify, map vulnerable workplaces and further execute strategic and regular ACFs should be a consistent practice. It can further be incorporated into policies to fortify END TB strategies.

### OA46-563-17 Incorporating the next generation in the fight to end TB: a case study of TB service provision by peer support groups among secondary school students

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**Background and challenges to implementation:** Children can play a crucial role in ending TB by raising awareness about the disease and promoting healthy behaviors among their peers. Engaging children in ending TB requires a child-friendly approach and platforms such as the schools which recognizes their unique needs and perspectives.

The aim of this study is to determine the impact of peer education on the uptake of TB screening and on TB case finding among secondary school children in Badagry LGA area of Lagos State.

**Intervention or response:** Between October 2021 and March 2022, 50 senior students were selected from 7 secondary schools and trained as TB peer educators. These students were tasked with the responsibility of increasing awareness of Tuberculosis among the students and to also facilitate their access to TB testing services. Data was collected over a six-month period before and after the initiation of the process.

**Results/Impact:** t-test analysis was used to compare the screening and TB case finding data before and after the intervention with level of significance set at <0.05 to determine the level of association of peer education on uptake of TB screening and TB case finding in the schools over this period. The results showed a statistically significant association with p-value < 0.05 for TB screening and TB diagnosis.

There was a 1000% increase in the number of students screened for TB (from 4699 to 49198 clients) and 400% increase in TB case finding (from 23 to 93 cases) among secondary school students.

The table below summarizes the findings of this study.

Indicators	Before the intervention (April-Sept 2021)	During the period of intervention (Oct-March 2022)
Total school children Screened for TB	4699	49198
Total school children presumed to have TB	586	2868
Total school children evaluated for TB	585	2845
Total school children diagnosed with TB	23	93
Total school children enrolled on treatment	17	87

**Conclusions:** In conclusion, schools can program for engaging children in TB prevention and care activities, such as screening, testing, and linkage to treatment. Involving children in TB activities is crucial to the success of ending the tuberculosis epidemic and achieving the END TB goal.

### OA46-564-17 Finding the missing persons affected by TB through successful active case-finding means being organised and patient-friendly

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**Background:** To achieve goals of ending tuberculosis (TB), activities which increase the number of individuals diagnosed and treated for TB is needed as well as strengthening prevention services. We describe active case finding (ACF) activities and results from Manila, Philippines.

**Design/Methods:** Retrospective and prospective analysis of ACF activities May 2022 until February 2023. After mobilization activities and communication in the community and health structures, participants from the general population over 15 years were invited for free chest Xray (CXR). ACF circuit included 6 stations each with trained staff including registration and consent, symptom screening, CXR (including interpretation), sample collection, doctor consultation as required and exit interview.

Education was provided and confidentiality respected. Planning and organization of activities was necessary to ensure high numbers of participants could flow quickly through each step. Participants with abnormal CXR or symptoms had sputum collected, which was transported for Xpert testing. If diagnosed with TB, participants were referred to local health centre for treatment. Followup and support was provided to families and participants with TB.

**Results:** A total of 5663 persons were screened with CXR, 1957 (35%) screened positive on CXR and another 433 with symptoms only (8%). Xpert testing was performed for 2308 participants (95% of positive screened), of which 301 (13%) had results of confirmed TB.

Overall, 5.3% (301/5663) of all persons screened had confirmed TB. Another 121 participants were clinically diagnosed with TB. Of the total 422 participants diagnosed with TB, 283 (67%) started TB treatment.

**Conclusions:** Successful ACF activities can identify high rates of TB in the general population. With organization and planning, high numbers of participants can be screened in a patient friendly model. Comprehensive care is required to ensure linkage to care post ACF activities.

### OA46-565-17 COVID-19 pandemic, an opportunity to find people with TB: a TB intervention in Nairobi slums, Kenya

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**Background:** The COVID-19 pandemic had a damaging impact on finding people with tuberculosis (TB). To help mitigate this, the Kenya Ministry of Health (MOH) instituted bidirectional TB and COVID-19 screening and testing. We describe processes and outcomes of this intervention for clients attending 14 Eastern Deanery Aids Relief Program (EDARP) supported sites in Nairobi slums.

**Design/Methods:** Based on WHO criteria, the MOH developed tools for bidirectional TB and COVID-19 screening for all clients in health facilities. All clients were offered COVID-19 and TB screening. People presumed to have either or both diseases were subjected to relevant tests including COVID-19 polymerase chain reaction (PCR) and rapid antigen tests, Gene-Xpert, smear microscopy or chest radiograph. EDARP incorporated key TB/COVID-19 indicators in their electronic medical record systems for documentation.

We analyzed program data on TB and COVID-19 case finding for October 2020–September 2022. We calculated frequencies, proportions, and crude odds ratios (COR) with 95% confidence intervals (CI) for variables along the TB screening and diagnostic cascade among people with presumptive and those without presumptive COVID-19.

**Results:** Overall, 177,477 clients were screened for COVID-19 and 2,527 (1%) were COVID-19 presumptive. Of these, 2,053 (81%) were screened for TB, and 1,242

(60%) screened positive. Among clients who screened positive, 963 (78%) underwent diagnostic evaluation and 242 (25%) were diagnosed with TB. Of the 174,950 (99%) clients without COVID-19 symptoms, 138,743 (79%) were screened for TB. Of these, 12,423 (9%) screened positive and 8,263 (67%) were diagnostically evaluated, with 1,004 (12%) diagnosed with TB. People with presumptive COVID-19 were more likely than those non-COVID-19 presumptive to have presumptive TB, [COR,15.6, 95%CI:(14.2-17.0)], undergo diagnostic evaluation [COR,1.7, 95%CI:(1.5-2.0)] and be diagnosed with TB [COR,2.4, 95%CI:(2.1-2.8)].

**Background and challenges to implementation:** The COVID-19 pandemic had a damaging impact on TB case finding and treatment outcomes. To help mitigate this, the Kenya Ministry of Health (MOH) instituted bi-directional TB and COVID-19 screening and testing. We describe processes and outcomes of this intervention for clients attending 14 Eastern Deanery Aids Relief Program (EDARP) Presidential Emergency Fund for Aids Relief -supported sites in Nairobi slums.

**Conclusions:** People with presumed COVID-19 are a high-yield population for TB. Integrating TB case-finding into COVID-19 and other respiratory disease screening could improve identification of people with TB.

**OA46-566-17 Yield from active TB case-finding activities in prisons: implications for routine TB screening in Nigerian penitentiary institutions**

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**Background and challenges to implementation:** Prisons and other penitentiary institutions represent a high-risk population for TB compared with the general population, and they often have limited access to health care services. In the Nigerian context most prisons are overpopulated due to poor infrastructure and the slow system of justice.

This further increases the risk of spread of Tuberculosis among prisoners suggesting that prisons represent a significant reservoir of tuberculosis.

**Intervention or response:** USAID funded TB LON 1 and 2 project implemented by KNCV Nigeria conducted TB screening in 17 prisons across Nigeria. Following advocacy to the authorities, the prison health teams were trained to be part of the TB screening intervention. The best spot for screening was identified and a workflow drawn up. The workflow specified the sequence for screening cell inmates. TB Screening was done using digital chest Xray with Computer aided detection

for TB (CAD4TB) or by applying the WHO 4 symptom screening (W4SS). Samples were collected from identified presumptive TB and evaluated. All diagnosed TB patients were then linked to treatment.

**Results/Impact:** From January- August 2022, a total of 26,615 prison inmates, were screened, 4,162 presumptive TB were identified (presumptive TB yield of 16%); Of the identified presumptive TB 4,158 were evaluated (Evaluation rate of 99.9%); a total of 468 TB cases were diagnosed with a TB yield of 11%; Of the diagnosed TB cases, 456 were successfully enrolled on treatment (enrolment rate 97.4%). There was a higher TB yield (17%) from screening done with the digital chest Xray with CAD4TB compared to screening done with W4SS (TB yield of 5%).

Type of Screening	# Screened	# Presumptive identified	# Presumptive evaluated	# TB patients diagnosed	# Put on Treatment	NNS	NNT	Presumptive TB yield	TB Yield
Digital Chest Xray with CAD4TB	20,847	2,016	2,012	344	340	61	6	10%	17%
W4SS	5,768	2,146	2,146	118	116	49	18	37%	5%
Total	26,615	4,162	4,158	462	456	58	9	16%	11%

Table 1. Active TB case finding in prisons screening cascade.

**Conclusions:** Given the high yield of TB cases, it is inferable that prisons are hotspots for Tuberculosis. Three times more TB cases were diagnosed with digital Xray screening with CAD4TB. We propose routine biannual screening using Chest Xray with CAD4TB in Nigerian penitentiary institutions.

**OA46-567-17 The yield of community-based TB services targeting migrant workers in the South of Mozambique, 2022**

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**Background and challenges to implementation:** The incidence of tuberculosis is observing a slow reduction in Africa, however, TB among migrant workers is still a key gap for TB control in the region.

This study explored the difference of TB incidence between miners, ex-miners, migrant workers and general population in three provinces of Mozambique in 2022.

**Intervention or response:** This is a retrospective cohort study carried out in Mozambique to compare the yields of TB screening among migrant workers, miners, ex-miners and the general community conducted by the International Organization for Migration in migrant-sending communities. The approach included:

1. Community engagement and awareness-raising
2. Mapping
3. Screening for TB symptoms

4. Referral of presumptive cases to TB testing (molecular or smear test)

5. The clinical diagnostic criteria were applied for those unable to provide sputum.

TB case notification rates from January to December 2022 were computed to evaluate the screening outcome among migrant workers, miners, ex-miners and the general population. A chi-square test was applied to compare the incidence proportion of TB cases including demography and the other characteristics of the cases detected.

**Results/Impact:** Of the 10,217 people screened for TB symptoms, 430 TB cases were diagnosed with TB and linked to care. There was a significant difference ( $X^2 = 72.86$ ;  $P < 0.000001$ ) in the TB incidence proportion between migrants workers (5,777.8 per 100,000), miners (8,823.5 per 100,000), ex-miners (7,163.5 per 100,000) and the general population (3,210 per 100,000) during the period of analysis.

The incidence proportion of TB among migrant workers was significantly 70% higher than in the general population (OR: 1.6 95% CI: 1.3,2.1). Similarly, significant differences were observed in the number needed to screen ( $p < 0.00001$ ).

**Conclusions:** Target TB community-based services are the key approach to finding missing TB cases among vulnerable populations. The migrant population has a higher rate of TB compared to the general population. Further investigation and screening are warranted.

## OA47 Multidrug-resistant TB management: transmission, contact investigation, programmatic treatment

### OA47-568-17 Short-term drug-resistant TB treatment regimen is associated with favourable treatment outcomes in KwaZulu-Natal, South Africa, 2015-2020

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**Background:** South Africa introduced the all-oral short treatment regimen in 2018. The Bedaquiline (BDQ) and linezolid containing regimen replaced the previous injectable containing regimen.

With the introduction of the new 6-month treatment regimen which includes BDQ, pretomanid, linezolid and/moxifloxacin (BPAL/M) in the country, this study

through the USAID supported TB LON programme aimed to assess treatment outcomes associated with the current short treatment regimen.

**Design/Methods:** A retrospective cohort analysis of routinely collected data from public health facilities, 2015 to 2020. Descriptive analysis was used for summary statistics and generalised linear models were used to determine the relationship between treatment outcomes (death, lost to follow-up [LTFU], treatment success and failure) and regimen type (short vs. long).

**Results:** 20,128 DR-TB clients were included in this analysis, males constituted 57% and were significantly older at 36 years (IQR: 30-44). 32% of clients were initiated on the short regimen and significantly older, 35 years (IQR; 28-45). HIV co-infection (73% vs. 77%) and retreatment (31% vs. 37%) were significantly lower among clients on the short regimen compared to those on the long regimen.

In clients on short regime, significantly lower proportions of LTFU (12% vs. 17%) and treatment failure (1% vs. 3%) were observed including higher proportion of treatment success (70% vs. 62%) compared to clients on long regimen. Clients on short regimen had lower risk of unfavourable treatment outcomes, LTFU [aRR 0.76; (95% CI: 0.70-0.83)] and treatment failure [aRR 0.64; (95% CI: 0.33-0.92)] but a higher risk of treatment success [aRR 1.26; (95% CI: 1.18-1.35)]. No significant difference in death by regimen type [aRR 0.96; (95% CI: 0.89-1.03)] was observed.

	Short regimen No. (%)	Long regimen No. (%)	p-value
<b>Overall</b>	6,351 (32%)	13,777 (68%)	0.001
<b>Sex</b>			
Female	2,628 (41%)	6,052 (44%)	
Male	3,723 (59%)	17,725 (56%)	0.001
<b>Median age (IQR)</b>			
	35 years (28-45)	34 years (27-43)	<0.001
<b>HIV status</b>			
Negative	1,687 (27%)	3,107 (23%)	
Positive	4,618 (73%)	10,551 (77%)	<0.001
<b>Treatment history</b>			
New	3,995 (69%)	7,606(63%)	
Retreatment	1,827 (31%)	4,527 (37%)	<0.001
<b>Treatment outcomes % (Numerator/Denominator)</b>			
Treatment success	70% (4,448/6,351)	62% (8,544/13,777)	<0.001
Lost to follow-up	12% (753/6,351)	17% (2,375/13,777)	<0.001
Treatment failure	1% (90/6,351)	3% (384/13,777)	<0.001
Died	16% (991/6,351)	16% (2,185/13,777)	0.643

\*p-value: Pearson chi-square for binary variables

Wilcoxon rank-sum (Mann-Whitney) for continuous variables

Table 1. Demographic and treatment outcome summary statistics by regimen type, KwaZulu-Natal, 2015 - 2020.

**Conclusions:** This study provides empirical evidence of short regimen benefits on DR-TB treatment outcomes from a large TB control programme in an HIV and TB endemic setting.

### OA47-569-17 Treatment outcomes in the first BPaL patients in the Philippines under operational research

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**Background:** The treatment success rate of rifampicin-resistant TB (RR-TB) patients given standard program regimens in the Philippines ranged from 54% to 74% from 2015 to 2019 even with the introduction of the 9 month bedaquiline-containing shorter regimen. In 2019, loss to follow-up (LTFU) was 12%, death 11%, failure 3%.

In 2020, WHO recommended 6 months BPaL with bedaquiline, pretomanid and linezolid 1200 mg/d under operational research (OR) for fluoroquinolone-resistant, intolerant and non-responsive MDR-TB patients. The Philippines was among the early adopters and implemented the BPaL OR under LIFT-TB in Dec 2020 with strengthening of laboratory capacity, clinical management and active TB drug safety monitoring and management.

**Design/Methods:** This is a descriptive study using OR data in the Philippines entered to data collection forms, REDCap and excel databases, and programme data from the National TB Program describing treatment outcomes.

**Results:** The BPaL OR in the Philippines enrolled 103 patients from June 2021-December 2022, of whom 58 finished 6 months of treatment (Linezolid 1200 mg/d) by June 2022. Mean age was 58 years; 64% (37) male; 9% (5) people living with HIV; 31% (18) with diabetes mellitus. BPaL eligibility included 48% (28) fluoroquinolone resistance; 48% (28) intolerance and 3% (2) non-response to previous MDR regimens.

The BPaL OR success rate was 97% (56), 1.7% (1) death from a cardiac cause and 1.7% (1) not evaluated due to protocol violation. There was no LTFU nor treatment failure. There were 16 patients assessed for the 6<sup>th</sup> month post-treatment follow-up with 100% sustained success.

**Conclusions:** Outstanding treatment outcomes of patients on the BPaL regimen should encourage countries to transition to programmatic use of WHO-recommended BPaL-based regimens for MDR/RR-TB while strengthening both clinical and programmatic aspects.

Aside from a shorter treatment duration, the pill burden is lower, transmission of MDR/RR-TB would be less, and patients can return to economic productivity earlier.

### OA47-570-17 Yield of systematic household contact investigation for drug-resistant TB cases in selected districts of Bangladesh

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**Background and challenges to implementation:** Contacts of people with active drug-resistant (DR) tuberculosis (TB) are more likely to be exposed to DR-TB than others in the population. Contact investigation (CI) among households of individuals with DR-TB is an important intervention for early diagnosis of DR-TB and to reduce infection and disease transmission in the community. The USAID's Alliance for Combating TB in Bangladesh (ACTB) Activity supported the National Tuberculosis Control Programme (NTP) to perform systemic CI at household level in 22 high TB-burden districts of Bangladesh.

**Intervention or response:** Lists and personal details of individuals who were newly detected with DR-TB (index) were collected from DR-TB Treatment Initiation sites (Chest Diseases Hospitals). Field health workers (FHW) visited household contacts, counselled the families and performed CI. Symptomatic contacts were referred to Directly Observed Treatment, short course (DOTs) centers for consultation and GeneXpert<sup>®</sup> testing. If any presumptive individual was diagnosed as TB, FHWs ensured that they are enrolled for appropriate treatment in their respective DOTs center.

**Results/Impact:** From October 2021 to September 2022, the houses of 923 index individuals with DR-TB were visited for CI. Through CI, 6,648 contacts were screened; 660 (10%) presumptive were identified; 477 (72%) presumptive were tested; and eventually, 14 persons were diagnosed with drug-sensitive (DS) TB and 1 with DR-TB.

Among those diagnosed with DS-TB, 8 were children (7 clinically diagnosed [CD] and 1 bacteriologically positive [B+] case) and 6 were adults (4 B+ & 2 CD). The lone individual with DR-TB case was the mother of the index case.

**Conclusions:** Contact investigation of individuals with DR-TB leads to identification of DS-TB more than DR-TB. Children account for over 50% of those diagnosed with TB. Further study to understand the transmission dynamics of DR-TB is needed to inform policy.

### OA47-571-17 Household contact investigations of drug-resistant TB in Viet Nam

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**Background and challenges to implementation:** In 2022, Vietnam ranked 11<sup>th</sup> among the 30 countries with the highest TB and multidrug-resistant TB burden. Early household contact investigations of drug-resistant TB (DR-TB) patients are essential to avoid the risk of community transmission of DR-TB strains and are crucial in the fight to end TB.

**Intervention or response:** As part of a TB REACH-funded project, large-scale household contact investigations were conducted in three provinces: Ha Noi, Ho Chi Minh City, and Can Tho. When index DR-TB patients were notified at Provincial Lung Hospitals or District TB Units in the intervention area, household contacts were enumerated and then screened for TB symptoms. All DR-TB contacts were eligible for testing with the Xpert MTB/RIF Ultra assay. DR-TB contacts diagnosed with TB were linked to appropriate TB treatment.

**Results/Impact:** During the project implementation period, a total of 1,579 DR-TB index patients were notified and 92.2% received a contact investigation. 3,167 contacts were enumerated (average of 2.18 contacts per index patient). 3,081 contacts were screened for TB symptoms, of whom 2,809 (91.2%) were tested with the Xpert MTB/RIF Ultra assay. This resulted in the detection of 57 contacts with TB (yield of 1.9%, 10x Viet Nam's national incidence rate), including 30 (52.6%) with drug-sensitive TB, 25 (43.9%) with multidrug-resistant TB, and 2 (3.5%) with pre extensively drug-resistant TB. The median time from index patient treatment start date to a contact's TB diagnosis was 45.5 days.

**Conclusions:** Prompt DR-TB contact investigations were very high yielding, but the major discordance in drug-resistance profile between DR-TB index patients and their household contacts with TB needs further investigation.

### OA47-572-17 Contact tracing among paediatric and adolescent household contacts of drug-resistant TB patients in a high TB burden ward in Mumbai, India

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**Background and challenges to implementation:** Children and adolescents exposed to drug-resistant TB in the household are often missed by TB programmes. Médecins Sans Frontiers (MSF) in collaboration with the India National TB Elimination Programme (NTEP) implemented a contact tracing intervention in a high-burden urban slum setting in Mumbai, India.

**Intervention or response:** Household contacts are identified within 7 days of treatment initiation of the index patient by community health workers (CHW). All the children (<10 years) and adolescent (11 to 19 years) contacts identified are given vouchers for X-rays to be done at designated facilities followed by medical consultation at primary health centres and at a district hospital. The contacts with suspicion of disease on clinical and or radiological assessment are subjected to microbiological evaluation with rapid molecular test. Microbiologically and/or clinically diagnosed contacts are put on treatment. Contacts with no active TB disease are followed up every 6 months for a period of 2 years.

**Results/Impact:** In the period of June-December 2022, 281 paediatric and 299 adolescent contacts were screened. In total, 1 paediatric and 8 adolescent contacts were diagnosed and put on treatment with yield of 0.4% (1/281) and 3% (8/299) respectively. During the period review only 30% (174/580) of the children completed full TB screening assessment. We experienced gap in implementation across every step of contact tracing process.

**Conclusions:** We identified gaps in different points of the screening cascade, mainly difficulty accessing X-ray screening, medical assessment, and un-willingness to seek health care. Targeted health promotion activities to reduce stigma can improve health seeking behaviour. Solutions to make TB screening more accessible (e.g.

Portable X-ray) with child friendly diagnostic tools (e.g. Stool gene-expert) are urgently needed to reduce the gap in child TB diagnosis.

Area of gap	Gap	Challenges identified	Proposed solution
Home identification of contacts (580)	48%	Unwillingness among parents to screen children (fear of TB stigma)	TB health education
Radiological screening (302)	(278/580)	Insufficient X-ray vouchers for children compared to sample size considering patient from private sector	Partner support in X-ray voucher for all children Portable digital X-ray modalities
Radiological screening (302)	37%	Health seeking behaviour	Health promotion
Medical consultation (189)	(113/302)	Consultation with private practitioners outside the programme	Training of private practitioners
Medical consultation (189)	8%	Out - of pockets expenditure due to transportation (medical consultation)	Transport vouchers/ decentralisation of diagnostic services at primary health centre
Complete evaluation (174)	(15/189)	Lack of child friendly diagnostic tools	Less invasive and child friendly test (like stool gene-expert)
		Difficulty in diagnosis	Improve access to facilities
		Financial constrains (travel cost/loss of daily wage)	providing fine needle aspiration/ biopsy/gastric lavage especially in public sector
			Transport voucher for families to complete screening.

Table 1. Gaps in implementation of the contact tracing with proposed solutions.

### OA47-573-17 Increasing access to drug-resistant TB services through decentralised care delivery in Bangladesh

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**Background and challenges to implementation:** In Bangladesh, a significant number of drug-resistant tuberculosis (DR-TB) cases (over 64% of an estimated 4,500 cases) remained undetected and untreated in 2021. Further, several access barriers prevent patients from seeking timely diagnostic care and appropriate treatment.

**Intervention or response:** To address this issue, we implemented a holistic approach that included active case finding (ACF), active contact investigation (ACI), and strengthening of public-private referral systems to increase DR-TB case detection and notification in the Chattogram and Khulna Divisions. Private providers (PP) and health workers received rigorous training for the effective management of DR-TB and were linked with the supportive mentorship program to facilitate remote consultations by a multidisciplinary medical

board. This program utilizes digital platforms like video conferencing and WhatsApp to support junior physicians in diagnosing DR-TB patients. The project also undertook a community campaign to raise awareness about DR-TB through advocacy, counseling.

**Results/Impact:** Between January and December 2022, we diagnosed 211 DR-TB patients through facility-based ACF and community-based ACI, and 186 DR-TB patients were diagnosed through active referral system. Of 397 patients diagnosed with DR-TB, 98.7% (n=392) patients were initiated on all-oral DR-TB treatment regimens, surpassing our project targets of enrolling 314 patients. Compared to 2021 notifications data (n=278), our interventions resulted in a 43.0% increase in DR-TB notifications in intervention divisions. Further, our efforts led to the detection of 3 children with DR-TB which was zero in previous years. Of 392 DR-TB individuals who initiated treatment, 23% (n=91) were diagnosed with diabetes. Moreover, through ACF and ACI interventions we diagnosed 1,004 DS-TB (952 adults; 52 children) and all were initiated on treatment.

**Conclusions:** This project has demonstrated that engaging all care providers, creating context-specific TB care pathways, empowering providers, and strengthening local capacity can potentially improve access to services, increase TB case detection, and effectively link patients to the appropriate care and treatment.

### OA47-574-17 Network analysis of close contacts of children, adolescents and young adults with drug-resistant TB, South Africa

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**Background:** Children, adolescents, and young adults typically interact with similar-aged individuals through school and friendship networks. However, it remains uncertain whether their unique social structure may be shaping drug-resistant tuberculosis (DR-TB) transmission. We examined social networks of children, adolescents, and young adults with DR-TB in South Africa and compared them to older adults' social networks.

**Design/Methods:** During Jan-2019 to Dec-2022, we enrolled people with extensively drug-resistant TB (XDR-TB) and pre-XDR TB from four districts in KwaZulu-Natal province, South Africa, and interviewed

them about close contacts over the preceding two years. Contacts shared between participants were identified by matching first name, last name, age, and gender. Ego-centric networks (i.e., networks centered around each participant) were created to characterize contacts' age groups. Network analysis compared betweenness (i.e., how often a participant lies on the shortest path between two other participants in the network) and degree centrality (i.e., number of direct connections a participant has in the network) between younger and older participants (<25 vs. ≥25 years).

**Results:** We enrolled 238 participants with pre-XDR/XDR TB, including 29 participants aged <25. There were a total of 2474 close contacts across all participants: younger participants had significantly more close contacts than older participants (mean: 14.1 vs. 9.9;  $p < 0.001$ ). Younger participants reported a significantly higher proportion of younger people among their close contacts than older participants (45.6% vs. 29.4%;  $p < 0.001$ ). Network analysis revealed that younger participants had significantly higher betweenness centrality (mean of 437 vs. 285;  $p = 0.001$ ) and degree centrality (mean of 14.1 vs. 9.9;  $p < 0.001$ ) (Figure).

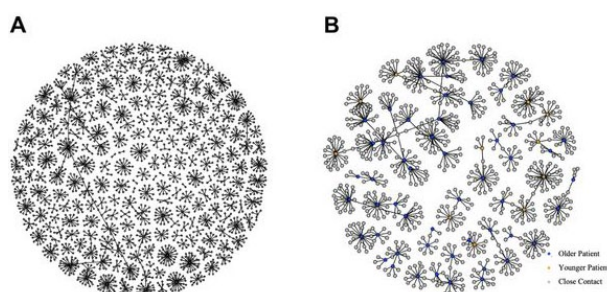


Figure. Overall network (A) and selected network (B) of participants with XDR/pre-XDR TB from KwaZulu-Natal, South Africa. Betweenness centrality and degree centrality for younger and older participants in the overall network (Graph A,  $n = 238$ ). Selected visualization of highly connected nodes in the network (Graph B,  $n = 62$ ).

**Conclusions:** Social networks of younger people with DR-TB are larger and more inter-connected than those of older individuals, suggesting there may be more opportunities for transmission within these networks. Contact tracing that expands beyond household contacts to social networks may be important for case-finding and prevention efforts for DR-TB.

### OA47-575-17 Multidrug-resistant TB clusters and transmission in Taiwan: a population-based cohort study

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**Background:** Multidrug-resistant tuberculosis (MDR-TB) remains a challenge in the control program of Taiwan, where 0.5% of new and 2.1% of previously treated cases were resistant to at least both rifampin (RIF) and isoniazid (INH). Since >80% of our MDR-TB are new cases, genotyping of MDR *Mycobacterium tuberculosis* is implemented to facilitate contact investigation, cluster identification, and outbreak delineation.

**Design/Methods:** This was a population-based retrospective cohort study analyzing MDR-TB cases from 2019 to 2021. Whole genome sequencing (WGS) was performed using the Illumina MiSeq and analyzed using the TB Profiler. Single nucleotide polymorphisms thresholds of  $\leq 12$  and phylogenetic methods were used to identify putative transmission clusters. An outbreak was confirmed using genomic data and epidemiologic links.

**Results:** Of the 237 MDR-TB cases, 190 (80.2%), 42 (17.7%), and 5 (2.1%) were simple MDR, pre-XDR and XDR-TB, respectively. The predominant lineages were 2.2 (113, 47.7%) and 4.5 (53, 22.4%). Phylogenetic reconstruction identified 62 (26.2%) isolates in 17 clusters, ranging 2-10 isolates.

Nevertheless, only 2 clusters, one household and one community, were confirmed outbreaks. MDR-TB cases from eastern Taiwan [odds ratio (OR) 5.16, 95% confidence interval (CI) 1.62-16.45], and those infected with lineages 2.1 (OR 2.39, 95% CI 1.12-5.13) isolates had high risk of transmission.

Besides, MDR isolates harboring INH/*fabG1* t-8c (OR 33.46, 95% CI 4.18-267.54) and RIF/*rpoB* S450L (OR 6.35, 95% CI 2.59-15.53) mutations were significantly associated with clusters.

Furthermore, we found 166 (70.0%) isolates harbored compensatory mutations in the RIF/*rpoA*, *rpoB*, and *rpoC* genes. We observed that MDR isolates concurrently harboring RIF/*rpoC* E750D and INH/*fabG1* t-8c mutations were significantly associated with clusters.

**Conclusions:** Routine and continuous surveillance using WGS-based analysis is recommended to warn risks and delineate transmission clusters of MDR-TB. We proposed to observe genetic markers, INH/*fabG1* t-8c, INH/*fabG1*t-8c with RIF/*rpoC* E750D, and RIF/*rpoB* S450L, of *M. tuberculosis* for interruption of putative MDR-TB transmission.



## OA48 Infection Control

### OA48-576-17 Producing evidence to inform healthcare worker protection against TB: An assessment of infection prevention and control practices in selected health facilities in Taguig City, the Philippines

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**Background and challenges to implementation:** Healthcare workers (HCWs) have five to ten times higher risk of TB infection compared with the general population. In the Philippines, HCWs could account for almost 20% of the national TB incidence.

While effective Infection, Prevention, and Control (IPC) measures can reduce healthcare-associated infections by at least 30%, many health facilities still have poor IPC practices. Inadequate IPC implementation puts the lives of HCWs and their patients at risk of TB and other nosocomial diseases.

**Intervention or response:** In February 2022, USAID's TB Platforms for Sustainable Detection, Care and Treatment Activity assessed IPC implementation in 26 health facilities.

The assessment was guided by the WHO's three-level hierarchy of IPC protocols: Administrative, Environmental and Respiratory Protection, including HCW TB screening and treatment. IPC interventions under each protocol were graded vis-a-vis IPC guidelines. A composite scoring system was used, with a passing mark of  $\geq 90\%$ .

**Results/Impact:** While health facilities are already implementing IPC activities, only a few adhere to guidelines. Only six (23%) facilities scored 90% or more. While, 25 (96%) report a TB screening program for HCWs, only 13 (50%) screened staff for TB at least annually. In nine (35%) facilities, at least one HCW was diagnosed with TB. In 3 (11%) facilities, staff have no access to routine TB IPC training and occupational health services. In 8 (29%) of the facilities, ventilation systems are irregularly maintained; 15 (59%) have no Ultraviolet Germicidal Irradiation units. Seven facilities (27%) are not implementing respiratory protection programs.

**Conclusions:** IPC implementation needs significant improvement in many health facilities. Additionally, protection and care schemes for HCWs against TB need strengthening. HCWs are the most valuable resource in the fight against TB. We must protect their needs and safeguard their health.

### OA48-577-17 Environmental infection control measures for prevention of TB cross-transmission at HIV care settings in India: a cross-sectional study, 2021-2022

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**Background:** HIV persons with undiagnosed TB can lead to cross-TB acquisition among other HIV persons and Health workers. Airborne infection control guidelines (AIC) suggest environmental measures to prevent cross-TB transmission.

**Design/Methods:** A cross-sectional study was conducted in HIV care settings at 14/37 high HIV-TB burden states and from each state, 10% of high HIV burden ( $>75$  percentile caseload) Antiretroviral treatment centers (ARTC) were selected randomly. From each of the ARTCs, a maximum of two peripheral link ART centers (LAC) were also selected randomly.

Assessment pertaining to the measurement of Air changes per hour (ACH) with the help of an anemometer, air flow direction with the help of an incense stick, cross ventilation by measuring the floor, window, and door dimensions, the seating arrangement of HCW-patient with respect to airflow directions were done in each room of these centres.

Obstruction and further improvement with regard to ventilation were also noted. As per AIC guidelines, ACH  $> 12$ , open ventilation area of more than 20% of the floor, and perpendicular seating arrangement with respect to airflow direction were considered appropriate ventilation measures.

Rooms were considered ill-ventilated with a high risk of TB cross transmission if both ACH and ventilation were inadequate along with inappropriate seating arrangement. SPSS 28.0 was used for analysis.

**Results:** A total of 595 rooms were assessed across 95 facilities. Adequate cross ventilation was observed in 63.2% of rooms, adequate ACH at 56%, and appropriate seating arrangement in 46% of rooms. 98/533 (18.4%) rooms were ill-ventilated with a high risk of TB cross-transmission. At these 98 rooms, overhead vents were closed at 39 (40%) rooms and it was partially opened at 4 rooms which can be opened for ventilation improvement.

**Conclusions:** Around one fifth of the rooms were ill-ventilated and were amenable for further ventilation improvement to prevent cross TB transmission.

## OA48-578-17 Building momentum in TB infection control practices at PEPFAR-supported sites

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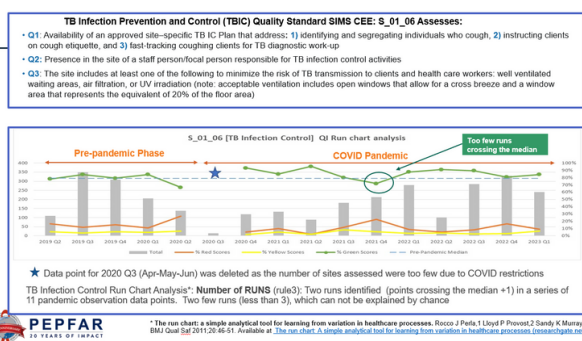
**Background and challenges to implementation:** We present TB infection prevention and control (TBIC) performance to quality standards in 3,094 facilities in 28 countries supported through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) from March 2019-January 2023. PEPFAR prioritized intensive integrated IPC activities by implementing standard and transmission-based precautions in all supported sites.

**Intervention or response:** COVID-19 mitigation activities sparked a renewed focus on facility-wide Infection Prevention and Control (IPC) activities. The effect on TBIC was assessed in PEPFAR programs through SIMS (Site Improvement Monitoring System) quality assurance (QA) assessments. TBIC quarterly performance during the COVID-19 pandemic was compared to pre-pandemic performance median.

Data was analyzed by identifying if too few/many runs crossing the median line, an established quality improvement (QI) methodology that identifies if observations divert from random data behavior.

**Results/Impact:** COVID-19 movement restrictions negatively impacted the number of sites receiving SIMS assessments; however, the COVID-19 response improved TBIC practice as measured by SIMS QA scores (red-yellow-green).

Acceptable green-scores increased from 80% pre-pandemic to 85% average during COVID pandemic, a finding not due to chance per QI runs analytics (The-run-chart-a-simple-analytical-tool-for-learning-from-variation-in-healthcare-processes. Perla-et-al. BMJ-Qual-Saf-2011;20:46-51).



**Conclusions:** Pandemic associated changes included new IPC assessment modules for IPC program implementation, environmental cleaning procedures, availability of PPE and decontamination of medical devices.

These new standards complement ongoing TBIC, waste management, lab biosafety and injection safety QA efforts. SIMS IPC data is now required from a specific number of sites in all PEPFAR country supported programs. Data is analyzed at a granular level, in addition to general scores, to inform targeted improvement activities at the site level. This will strengthen countries' public health emergency preparedness for endemic and pandemic threats.

Limitations to analysis: sites assessed pre-and-post pandemic were not the same and were not stratified by location/size for comparison. Despite this, the standard QI methodology used validates the identified trend.

## OA48-579-17 Ventilation adequacy at tertiary healthcare institutions serving as nodal drug-resistant TB centres in India

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**Background and challenges to implementation:** Optimizing ventilation in health facilities is an essential airborne infection control (AIC) measure to reduce transmission risk. Standards for adequate ventilation measured as air changes per hour (ACH) were introduced in the national AIC guidelines in 2010. From 2007-2013, nodal DR-TB centres were assessed for AIC compliant when established in India. National TB Elimination Programme (NTEP) India conducted AIC re-assessments at 76 nodal DR-TB centres with support from WHO, CDC and FIND. We report ventilation adequacy and proposed interventions to address this.

**Intervention or response:** The assessments were conducted during Sep'22 to Mar'23 using a structured AIC checklist. After orientation, teams of experts comprising of chest/infectious disease physician, public health specialist, microbiologist and biomedical engineer conducted assessments over 3 days in each institute covering various departments known to have high transmission risk. Ventilation adequacy was assessed by observing overcrowding, air-flow directions using vaneometer and measuring ACH per hour using anemometer.

**Results/Impact:** In the 76 sites assessed, a total of 296 out of 561 departments (53%) had adequate ventilation (Table-1). About one third of TB wards and bronchoscopy rooms; and about half of registration and OPD waiting areas assessed had adequate ventilation. TB labs and radiology rooms were better ventilated. In remaining departments, corrective measures including civil works to optimize ventilation with or without UVGI installations, etc. were recommended.

Department assessed	Total number assessed	Adequate Ventilation (N)	Adequate Ventilation (%)
TB Wards	160	56	35.0
Bronchoscopy	36	12	33.3
Registration/ Waiting area	55	29	52.7
OPD/ Waiting area	154	88	57.1
TB Lab	62	41	66.1
Radiology/ Waiting area	63	48	76.2
Other*	31	22	71.0
TOTAL	561	296	52.8

\*Other included PFT/ procedure room, Non-TB wards, EP Ward, DOT Center, other waiting areas, etc.

Table-1: Adequacy of ventilation in various departments of institutes serving as Nodal DR-TB Centres.

**Conclusions:** Optimizing ventilation with or without UVGI installation need to be considered in institutes managing DR-TB based on periodically AIC assessment by a multi-disciplinary team to reduce the risk of transmission as well as their sustained impact to accelerate ending TB in India

### OA48-580-17 Employer-led model for ending TB: a workplace policy intervention for BEST, Mumbai’s bus transport system

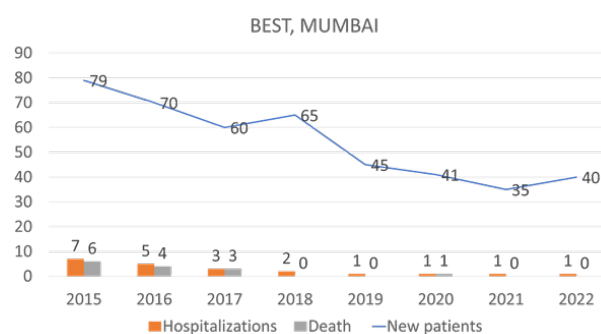
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**Background and challenges to implementation:** People spend majority of their time at workplace. Employers are responsible for creating and providing a safe and healthy work environment. Employees are compliant to healthy and progressive workplace policies promoted by their employers, including interventions for controlling TB. Management of TB requires social, emotional, financial approach along with correct information dissemination to patients and their contacts. However, a comprehensive workplace policy for Tuberculosis and associated comorbidities are rarely implemented by companies.

**Intervention or response:** BEST is a public sector enterprise in Mumbai employing over 30000 employees with a network of 26 dispensaries. BEST has designed and implemented an integrated workplace model to comprehensively End TB since 2012.

The activities conducted are awareness sessions about TB prevention and importance of healthy lifestyle to all employees; mass screening for TB and comorbidities; bi-directional testing for Covid, Diabetes, HIV, and Vit D deficiency; group discussions for Tobacco cessation followed by screening for TB; differentiated TB treatment services and patient and family counselling for prevention of TB.

**Results/Impact:** The retrospective data was analysed from 2015 to 2022. The intervention over a period of 8 years has shown a gradual decline in incident TB cases and reduced the hospitalization and mortality. For last 6 years 100% patients were adherent to treatment. BEST workplace policy has also shown a significant improvement in reducing absenteeism due to TB, with an average reduction from 18 months to 8 months from 2015 to 2022.



**Conclusions:** BEST advocates for implementing this model at all workplaces to achieve End TB goals. A comprehensive and integrated workplace policy can be beneficial to both employer and the employees. Employees benefit by easily accessible, appropriate care and feel more inclusive at the workplace. Simultaneously the employer’s benefit from reduced absenteeism and highly efficient workforce. The entire approach helps reduce stigma and promote health seeking behaviour.

### OA48-581-17 Improving infection control measures for the reduction of TB cases among TB personnel in Ukraine, 2018-2022

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**Background and challenges to implementation:** Health workers in TB settings are exposed to a higher risk of acquiring TB. The study aims to evaluate the impact of the Infection Prevention Control (IPC) measures in reducing TB cases among the health staff in Ukraine, during 2018-2022.

**Intervention or response:** A retrospective analysis of the TB cases was carried out to compare the TB notification among the TB staff and the other health staff, during 2018-2019. Inclusion criteria were “being TB Health staff/health staff” and “new/relapse cases of TB”. A national Policy on IPC was adopted in 2021.

**Results/Impact:** The total number of TB cases notification is higher among the TB staff compared to the other health staff in Ukraine. TB cases among the TB staff, compared to TB cases among the other Health staff per 10.000 was as follows: 2018- 85.0 % higher (40.0 vs 6.0), 2019- 82.2% higher (29.7 vs 5.3), 2020- 83.2% higher (25.0 vs 4.2), 2021- 77% higher (14.3 vs 3.3), 2022- 71% higher (11.7 vs 3.4).

While comparing the TB data of 2018 (when IPC was not implemented) and 2021 (when IPC was adopted) among TB staff and other health staff, TB reduction was observed:

For the TB staff, it was a 64.3 % reduction (40.0 in 2018 vs 14.3 in 2021) for the other health staff it was a 45% reduction (6.0 in 2018 vs 3.3 in 2021).

Besides, TB cases in 2022 vs 2021 revealed: among TB staff 18.2% reduction (11.7 in 2022 vs 14.3 in 2021) among the other health staff which increased by +3.0 % (3.4 in 2022 vs 3.3 in 2021). Meaning that IPC is firmer for TB facilities.

**Conclusions:** TB staff is exposed to a higher risk of acquiring TB, strict IPC measures are essential for TB risk reduction and allow for a safer work environment for the healthcare personnel.

(Mtb) infection with progression and regression across minimal (pathological damage but not infectious), sub-clinical (pathological damage and infectious) and clinical (infectious and reporting symptoms) TB disease, acknowledging natural recovery, treatment, and mortality. Transition parameters were informed by historical and contemporary data, and subclinical disease was assumed 50% as infectious as clinical disease.

We grouped individuals based on whether they contributed to transmission and whether or not they progressed to clinical disease. The main outcome was the proportion of all transmission attributable to each pathway group.

**Results:** We estimate that 93.5% (95% credible interval, CrI, 93.1-94.0) of Mtb-infected individuals will not contribute to transmission within 10 years of Mtb infection. 51.9% (95% CrI 48.4-55.7) of those that do contribute will never progress to clinical disease, driving over one third (35.5%, CrI 29.5-43.1) of all transmission over a 10 year period. This increased to 50.3% (95% CrI 42.0-61.2) if we assumed no difference in relative infectiousness for subclinical TB.

**Conclusions:** Our findings suggest that at least one third, and up to half, of transmission following Mtb infection comes from individuals who will never progress to clinical disease, and are left undiagnosed by current policies. If we are to End TB and halt transmission, TB care and prevention policies need to consider all infectious TB, not just who report to a clinic.

### OA48-582-17 Transmission pathways across the spectrum of TB disease – how much transmission are we missing?

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**Background:** As new technologies are developed to diagnose and treat tuberculosis (TB) disease before individuals self-report to a clinic, it is key to understand how much transmission is left undiagnosed by current policies. Here we extended a data-driven, mathematical modelling approach to quantify different pathways through the spectrum of TB disease in terms of transmission contribution.

**Design/Methods:** We simulated 10-year pathways for 1,000 cohorts of 10,000 individuals using a deterministic modelling framework of *Mycobacterium tuberculosis*

## OA49 Engaging private sector agencies to end TB

### OA49-583-17 High TB case detection yields of an intermediary agency for private sector engagement in Viet Nam

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**Background and challenges to implementation:** Private sector engagement remains a critical component in a country's TB response. Over the past decade, intermediary agencies have demonstrated the ability to yield substantial case detections and improve TB treatment coverage at a national scale.

**Intervention or response:** Between January 2020 and March 2023, the National TB Program (NTP) and Friends for International TB Relief (FIT) scaled an intermediary agency model to 10 provinces of Viet Nam. The model employed two strategies:

S1. Referral of persons with suspected TB for diagnosis, and;

S2. Notification of persons privately treated for TB.

For S1, health-seeking individuals were screened using chest X-ray (CXR) followed by testing with a molecular assay. Individuals with TB choose treatment at NTP sites or with a private provider.

For S2, providers reported new TB treatment and outcomes of previously reported patients monthly. Treatment data had to meet NTP standards for official notification.

**Results/Impact:** Through S1, 843,699 persons underwent CXR screening and sputum was tested from 11.7% (98,840/843,699). The all forms TB yield was 2.1% (2,149/100,000), of whom 4.4% had drug-resistant TB. Approximately 91.4% (16,572/18,128) had a documented linkage to care, of whom 74.6% (12,356/16,572) took treatment with the NTP. For S2, 132 providers reported 11,007 persons receiving private TB treatment.

After data quality control, 91.5% (10,073/11,007) were entered into VITIMES, the NTP's surveillance system, and thus included in the official national notification figures. After removing 2,727 individuals detected through S1 but treated and reported via S2, the intermediary agency detected 29,135 persons with TB, while 22,429 individuals with TB were linked to care and officially notified on VITIMES.

PPM M5 results in 10 provinces of Viet Nam		01-01-2020 to 31-03-2023	
S1	Diagnostic referral strategy	#	%
1	Verbally screened	862,496	--
2	Screened by chest x-ray (CXR)	843,699	97.8%
3	Sputum tested for TB	98,840	11.7%
4	Diagnosed with TB	18,128	2.1%
4.1	- Bacteriologically-confirmed with TB	15,441	85.2%
4.1.1	-- Drug-susceptible TB	14,759	95.6%
4.1.2	-- Drug-resistant TB	682	4.4%
4.2	- Clinically diagnosed	2,687	14.8%
5	Initiated on treatment	16,572	91.4%
5.1	- Treatment with the NTP	12,356	74.6%
5.2	- Treatment in the private sector†	4,216	25.4%
S2	Private treatment report strategy	#	%
1	Private providers reporting TB treatment	132	--
2	Private treatment reports‡	11,007	--
3	Number of people entered into VITIMES	10,073	91.5%

Notes: † S2 & out-of-network providers; ‡ Includes 2,727 individuals detected through S1 and choosing private treatment;

**Conclusions:** Private sector engagement through the intermediary agency model in Viet Nam has generated substantial yield and notifications over the past three years. The model should be scaled nationally and tested in other high TB burden settings.

### OA49-584-17 Engaging private sector agencies in ending TB: a public-private partnership intervention in Bihar, India

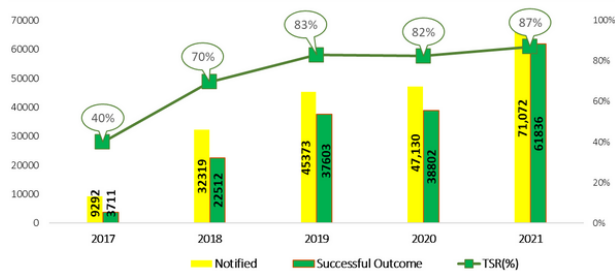
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**Background and challenges to implementation:** Control of tuberculosis (TB) in India is complicated by the presence of a large, disorganised private sector where most patients first seek care. Collaboration between the National TB Elimination Program (NTEP) and private sector has been recognized as key to India's TB elimination goals by 2025. The Patient Provider Support Agency (PPSA) model is the most commonly implemented partnership option, where private intermediary agencies are contracted to work closely with NTEP resources and engage private providers.

**Intervention or response:** The learnings of public private interface agency (PPIA) pilot in Patna district during 2014-2018 was the basis to scale up engaging private health care providers through support of private agency in increasing TB notification and quality of care to patients seeking treatment from private sector. Bihar state government selected two non-government organizations as PPSA through competitive bidding to map the private health care providers, chemists and laboratories, arrange orientation of providers in standards of tuberculosis care in India (STCI) and started implementing in 14 districts since June 2020.

The scope of work included TB notification, bank account seeding and validation for providing benefits of nutritional support through direct benefit transfer (DBT), universal drug susceptibility test, screening for HIV and diabetes and treatment adherence resulting into desirable treatment outcome.

**Results/Impact:** Total TB patient notification from private sector has increased from 6987 (in 2017) to 77368 in 2022, and contribution of private sector has been 82179 (51%) of all TB cases notified (161146) in 2022. Testing for HIV and Diabetes of the TB patients notified from private sector has increased to 91% (HIV) and 79% (Diabetes), from 5% and 4 % respectively in 2017. The treatment success rate of private TB patients increased from 40% to 87%.



**Conclusions:** PPSA with government support marks an important milestone for scaled-up, sustainable private sector engagement in India.

### OA49-585-17 Potential to engage private providers for public-private mix approaches: insights from Myanmar

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**Background:** Private providers are critical in Tuberculosis (TB) diagnosis and treatment as they serve as primary point-of-care. Despite significant private providers engagement in Myanmar over the past decade, there is a need to understand their affiliation status, behaviors, and involvement in TB care as a whole.

**Design/Methods:** A cross-sectional mixed-method study was conducted with 674 private providers (51 private hospitals and polyclinics, 260 general practitioners, and 363 pharmacies) to assess their interest, challenges, and successes in engaging TB program for scale-up of PPM in Myanmar.

The selected providers were categorized as either affiliated or non-affiliated based on their collaboration with an organization to provide TB care. 193 affiliated and 481 non-affiliated providers completed a quantitative survey, which was followed by 45 qualitative in-depth interviews (IDIs).

**Results:** Majority, 89.3% of providers reported correct initial response for a person with presumed TB, i.e., explaining about TB and referral with DOTS form and sputum request form. Diagnosis was primarily through chest X-ray (87.8%) and sputum examination (87.0%). 37.3% of affiliated providers reported that they tested and treated presumptive TB, while 55.4% of non-affiliated providers referred clients to public TB centers. 51.2% of non-affiliated providers were willing to participate in TB program, mainly through making TB referrals and raising awareness. IDIs revealed that lack of time and limited confidence to manage TB were the main barriers for non-affiliated providers to participate.

The engagement of providers in PPM-TB program depended on awareness of PPM networking in operating township, linkage to TB service facility nearby, technical training and providing support for clients' transportation.

**Conclusions:** Engaging private providers who were not yet affiliated could help identify presumptive TB and reduce missed people with TB. Thus, comprehensive engagement strategies are needed to engage non-affiliated providers with existing PPM network and supports should tailor on particular needs and challenges of these providers.

### OA49-586-17 Private health sector engagement in TB services in Afghanistan, 2018-2022

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**Background and challenges to implementation:** Although Afghanistan has a large private sector, its coverage for tuberculosis (TB) is low. Only 5% (811/16,000) of private general practitioners (GPs) and 23% (100/430) of private hospitals are currently engaged in TB control. Additionally, the private sector is unregulated and there is weak coordination with the public sector.

**Intervention or response:** Since 2018, GPs and private hospitals are engaged in TB control activities in 24 provinces through two piloted interventions:

a. Public-private mix: 811 GPs across 24 provinces received a range of TB services including identification and referral of presumptive TB patients, diagnosis, and treatment of TB. The Global Fund (GF) alongside United States Agency for International Development (USAID)-funded projects (e.g. Challenge TB, Assistance for Families & Indigent Afghans to Thrive (AFIAT), Urban Health Initiative (UHI)), and TB Program have supported this intervention.

b. Urban DOTS program: 100 private hospitals in nine cities received a full package of TB services including screening, testing, treatment, recording and reporting, awareness, and referrals. The required capacity-building, reagents, anti-TB medicines, recording and reporting tools, alongside information, education, and communication materials were provided by the GF, US-AID-funded projects (CTB, AFIAT, UHI), and the TB Program.

**Results/Impact:** Presumptive TB patients (PTB) identified by the private sector increased by 78% (35,868) in 2022 compared to 2018 (20,074). Contribution to the national level was 6% in 2022. All form TB cases notified by the private sector increased by 60% in 2022 compared to 2018. Contribution to national level was 16% in 2022.

Indicators	2018		2019		2020		2021		2022	
	Total private	National	Total private	National	Total private	National	Total private	National	Total private	
# of total presumptive TB patients (PTB)	20,074	861,131	27,222	460,406	25,875	500,124	29,198	587,818	35,868	
# of all form TB cases	5,232	52,770	6,532	46,058	5,434	50,710	8,126	52,405	8,377	
% of PTB referred by the private sector	5%		3%		5%		6%		6%	
% of diagnosed TB cases referred by the private sector	10%		12%		12%		16%		16%	

Table 1 Contribution of the private sector in TB control. 2018-2022.

**Conclusions:** Despite the challenging environment, engaging the private health sector in TB services significantly improved case notification. Given the proportion of private hospitals and GPs still unengaged, this provides a unique opportunity to expand private sector engagement in TB management and reduce the gap in TB case detection countrywide.

### OA49-587-17 Role of the private sector in TB service provision during COVID-19 and political instability in Myanmar

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**Background:** The dual crises of COVID-19 and political instability have had significant impacts on basic health care in Myanmar, including tuberculosis (TB) case notification and TB service provision. PATH conducted a study to better understand the role of private sectors in filling crises-driven TB service gaps as part of the US-AID-funded HIV/TB Agency, Information, and Services Activity.

**Design/Methods:** A cross-sectional, mixed-methods situational analysis was conducted focusing on Yangon, Mandalay, Sagaing, Kachin, and Northern Shan. It included a desk review, descriptive analysis of TB data (2019–2021), and stakeholder consultations (June–September 2022).

**Results:** In comparison to 2019 data, quantitative analysis showed a significant reduction in TB case notifications: 23% in 2020 and 51% in 2021 due to travel restrictions and an abrupt paucity of public sector healthcare providers. Even though the private providers were also affected by these dual crises, they were able to intensify efforts to continue providing TB services through private-private partnerships. The private sector contributed 15% of the total TB case notifications in 2019, reaching 17% and 38% in 2020 and 2021, respectively, while overall TB case notifications decreased significantly.

The stakeholder consultations revealed that private providers were able to fill gaps in the continuum of TB service provision through private-private and public-private mix models in a variety of geographical areas, including conflict-affected areas.

Furthermore, private-private partnerships were crucial during times of crisis. Through private-private partnerships, uninterrupted services were provided, including: (a) the delivery of a continuous supply of anti-TB drugs and (b) TB diagnostic services through private laboratories.

**Conclusions:** While COVID-19 and political instability hampered TB service provision in the public sector, the private sector played a crucial role in the continuation of TB service provision. As evidenced by improved partnership models, Myanmar needs to continue and scale up private-sector engagement to strengthen its contribution to end TB.

### OA49-588-17 Integrating public-private mix (PPM) TB service into primary healthcare units as a solution for PPM TB operational challenges in Ethiopia

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**Background and challenges to implementation:** The PHCU is the smallest division in the Ethiopian health tier system including primary hospitals or health centers with five satellite health posts. However, there is no integrated PPM service in the PHCU. Since 2020, the USAID Eliminate TB Project has been working to integrate PPM TB sites into the PHCU. All facilities within the PHCU are supported by a single team that supports both private and public facilities, known as the “one visit, one team, one PHCU” approach.

**Intervention or response:** PPM TB facilities are made to benefit from available GeneXpert sites and the national sample referral network of the postal courier system. The project team makes sure that all PPM TB sites have a health information system code to generate reports from 1,000 PPM sites.

Also, the project holds orientations, trainings, and review meetings. The change in PPM contribution and treatment outcomes because of the integration is presented and compared with overall national figures for July 2020 to June 2022.

**Results/Impact:** The introduction of PPM TB service at the primary health care level suggests a contribution to the increase in national TB case detection from 15% to 20%. This is significantly demonstrated in big towns, such as Adama (20.2% to 56.4%) and Bahir Dar (19.9% to 43.9%).

Also, the cure rate in project-supported private facilities increased by 23% (63% to 86%) as compared to the change in the overall cure rate at national level of 1% (83% to 84%). Treatment success increased from 88% to 92%, and the national figure remained the same at 95%.

**Conclusions:** Operational challenges at private health facilities can be mitigated by integrating PPM sites into PHCU. This enables the PPM TB sites to find more missed TB cases and deliver quality TB care services with better treatment outcome.

### OA49-589-17 Enhancing the contribution of private health providers to TB case-finding in Southwest Nigeria – the USAID TB-LON 3 project experience

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**Background and challenges to implementation:** Private healthcare providers are critical in detecting and treating tuberculosis (TB) in countries like Nigeria with a private sector-driven healthcare system. There has been a systematic engagement of formal and informal private healthcare professionals in providing TB services in Nigeria.

This study presents the contribution of private providers to the diagnosis and treatment of tuberculosis under the USAID TB Local Organizations Network, Region 3 (USAID TB-LON 3) in Southwest Nigeria.

**Intervention or response:** This intervention was implemented through a partnership with the private sector (formal and informal). In FY22 (October 2021 to September 2022), USAID TB-LON 3 developed and rolled out the implementation of a public-private mix optimization plan in Lagos State to improve TB service coverage in already engaged private health facilities and facilitate systematic expansion into unengaged facilities. Lessons learned were adapted to impact scaleup in Ogun, Oyo, and Osun states. In all, 492 Private Hospitals, 77 Community Pharmacies, 139 Stand Alone Labs, 378 patent and proprietary medicine vendors, and 133 traditional birth attendants/traditional medicine practitioners facilitated the screening.

**Results/Impact:** A total of 1,918,336 individuals were screened, 90,545 (5.0%) presumptive were identified, and among these, 85,828 (95.0%) were tested/evaluated. The private sector improved the screening rate from 32% to 69% and the presumptive yield from 2% to 4.2%. Consequentially, in FY22, the private sector contributed 8% (diagnosed 6,881 TB cases) to TB case finding on the TB- LON 3 project. In comparison, 6,431 (93.0%) TB cases were notified through the private sector during FY22.

**Conclusions:** This intervention effectively enhanced Private Health Providers' contribution to tuberculosis case finding in Southwest Nigeria. However, there is a need to design innovative approaches and rapidly scale up these providers' engagement, strengthening their capacity and monitoring their adherence to tuberculosis guidelines.



**OA49-590-17 Business-not-as-usual: impact of an intermediary agency on national public-private mix notifications in Viet Nam**

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**Background and challenges to implementation:** Public-private-mix (PPM) innovations such as private provider interface agencies (PPIA) in India have shown sustained positive impact on TB case notifications at a national scale. It is unclear, however, if the model and its benefits are replicable in other high tuberculosis (TB) burden countries, such as Viet Nam.

This study analyzed trends in official PPM notification data reported by the NTP following the scale-up of a local PPIA pilot.

**Intervention or response:** Between 2020 and 2023, the National TB Program (NTP) and Friends for International TB Relief (FIT) scaled a PPIA first to five and then 10 provinces of Viet Nam. The PPIA employed a sales force to engage private providers with a value proposition of free Xpert testing, technical capacity building and financial incentives in exchange for systematic screening and diagnostic referrals and reporting of privately treated persons with TB, if applicable. The PPIA also managed recording and reporting on behalf of the providers.

**Results/Impact:** In 2021, PPM notifications in the intervention provinces rose by +273% year-on-year, driven by a +1,408% rise in private-sector notifications and +92% in notifications from non-NTP public-sector providers. In contrast, all other provinces recorded respective declines of -22% to -37%. The contribution from five provinces resulted in a +31% increase in national PPM notifications. This trend continued in 2022, as national PPM notifications rose by +62%. These trends led to a more than doubling of PPM contribution to national notifications from an average of 11.1% in 2017-2020 to 19.0% in 2021 and 25.0% in 2022.

**Conclusions:** The PPIA has made a profound impact on PPM in Viet Nam despite a limited geographic scope, suggesting that additional expansion can further optimize treatment coverage among health-seeking persons with TB. However, as the model continues to scale, concrete plans are needed for transitioning its financing to sustainable, domestic sources.

**OA50 Digital methodologies in TB prevention and care**

**OA50-591-17 The future of TB active case-finding in Pakistan: embracing self-learning artificial intelligence tools for better yield and cost-effectiveness**

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**Background and challenges to implementation:** Despite the widespread implementation of Active Case Finding (ACF) interventions globally, the evidence for effectiveness and the optimal approaches to target populations is uncertain, whereby targeting people for screening can be challenging. Thus, efficiently identifying the hotspots for screening camps is of utmost importance.

**Intervention or response:** Mercy Corps uses two ways to select the hotspots: MATCH-AI and traditional. The MATCH AI model predicts at the community level using a machine learning algorithm based on tuberculosis notifications, laboratory data, socio-demographic information, access to health services, spatial patterns, and TB risk factor data. Whereas the traditional method uses caseload from the site per public sector TB reports in the last quarter; caseload from the site in the previous quarter; distance from the health facility, and the last screening camp conducted at the same location. The

Categories	Number of notifications in 2020			Number of notifications in 2021			Change from 2020 to 2021		
	Total	Private	Non-NTP Public	Total	Private	Non-NTP Public	Total	Private	Non-NTP Public
PPIA provinces (5/63 provinces)	2,305	318	1,987	8,608	4,795	3,813	+273%	+1,408%	+92%
Remaining 58 provinces	9,713	2,904	6,809	7,122	1,832	5,290	-27%	-37%	-22%
<b>Total</b>	<b>12,018</b>	<b>3,222</b>	<b>8,796</b>	<b>15,730</b>	<b>6,627</b>	<b>9,103</b>	<b>+31%</b>	<b>+106%</b>	<b>+3%</b>
	100%	27%	73%	100%	42%	58%			

Categories	Number of notifications in 2021			Number of notifications in 2022			Change from 2021 to 2022		
	Total	Private	Non-NTP Public	Total	Private	Non-NTP Public	Total	Private	Non-NTP Public
PPIA provinces (10/63 provinces)	8,608	4,795	3,813	15,810	7,487	8,323	+84%	+56%	+118%
Remaining 53 provinces	7,122	1,832	5,290	9,600	2,385	7,215	+35%	+30%	+36%
<b>Total</b>	<b>15,730</b>	<b>6,627</b>	<b>9,103</b>	<b>25,410</b>	<b>9,872</b>	<b>15,538</b>	<b>+62%</b>	<b>+49%</b>	<b>+71%</b>
	100%	42%	58%	100%	39%	61%			

Table.

total population (twelve camps) of MATCH-AI-selected hotspots in the province of Punjab was included. For the traditional camps, a sample of twelve hotspots was calculated based on the same implementing partner but different districts and tehsils, and then randomly selected every fourth camp till it reached the required number.

**Results/Impact:** A comparative analysis based on the yield was conducted. In MATCH-AI, the ratio is 10:1. So, for every 10<sup>th</sup> screened people, there was 1 TB patient. For traditional ways, the ratio is 24:1, implying every 24<sup>th</sup> screened patient, there was 1 TB patient. The comparison showed a difference between the selection of the screening camps. The yield per camp is 4.5 and 1.8, indicating that MATCH-AI is 1.5 times better than the traditional methods.

Method	All forms Yield	Average Camp Yield	TB Positivity Rate
MATCH-AI	10:1	4.5	10%
Traditional	24:1	1.8	4%

**Conclusions:** Based on the limited available data, we conclude the method of MATCH-AI is a better identifier for screening camps and TB patients and should be used more. Diagnosing more cases reduces the cost of intervention. However, additional analysis with more data is required to conclude further.

### OA50-592-17 Digital tracking of the care cascade in programmatic TB preventive treatment

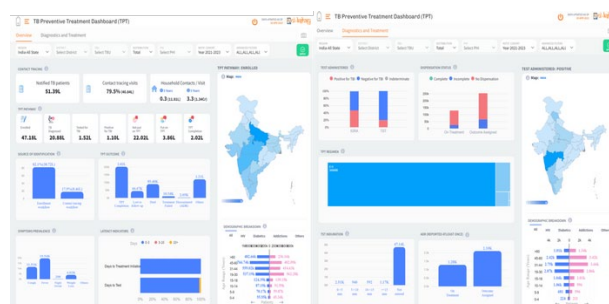
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**Background and challenges to implementation:** Ni-kshay is India's web enabled patient management system for tuberculosis (TB) under National TB Elimination Programme (NTEP) since 2012. We describe rapid progress made in transitioning from aggregated and paper-based system to an integrated digital TB Preventive Treatment (TPT) module within Ni-kshay infrastructure.

**Intervention or response:** Until 2021, aggregated and paper-based systems were used to record and report TPT data with its own intrinsic challenges of completeness, correctness, and consistency. While India's national guidelines for programmatic management of TPT were prepared and introduced in 2020-21, NTEP adapted WHO's prevent-TB-app and applied its learnings to developed the Ni-kshay TPT module with life-cycle approach linking an individual's information through their disease course from TB infection (TBI) to

disease to drug-resistance care cascade till they survive. This enabled users to enrol TPT beneficiaries including high-risk population, add TBI tests, trigger TPT-specific workflow, initiate TPT, dispense drugs, monitor adherence and TPT completion. An interactive TPT dashboard was also introduced in early 2022 to monitor the TPT care cascade till TPT outcomes, disaggregated by public/private sector, geography, turn-around times, drug dispensation and adverse drug reaction monitoring.

**Results/Impact:** A policy of 'digital-first-and-paper-second' envisaged in India's national TPT guidelines has been implemented with introduction of Ni-kshay TPT module and dashboard that has data on >4.7 million enrolments, >0.15 million TB infection tests, >0.3 million put on TPT, >0.2 million TPT completion captured. The monitoring of care cascade was possible in >25,000 health facilities and disaggregated through TPT dashboard to prompt corrective actions at all levels.



**Conclusions:** TPT policy and Ni-kshay TPT module cum dashboard has been a major milestone under NTEP. The information captured by health facilities serves for surveillance and monitoring the trend of TB infection care cascade across diverse geographies in India to accelerate ending TB.

### OA50-593-17 The impact of hot-spot mapping on TB yield from community case-finding interventions: Experience from Nigeria

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**Background and challenges to implementation:** In light of the high burden of tuberculosis (TB) in Nigeria and the urgency to improve case notification, innovative strategies to find the missing TB cases are highly needed. However, questions remain about TB epidemiology, including how adaptation and targeting of response efforts could improve case-finding, given ongoing transmission, a high HIV burden, and other social and economic factors.

**Intervention or response:** The USAID-funded TB LON project led by KNCV Nigeria deployed an Early Warning Outbreak Recognition System (EWORS) to inform targeted community TB response for impactful case-finding. EWORS used an advanced surveillance mechanism to identify TB patients' residences in clusters, enabling it to predict areas with elevated disease spread (hotspots) at the community level. TB screening activities were targeted at such hotspot locations.

Trained community health workers conducted mass TB screening at EWORS-predicted hotspot locations. Presumptive TB cases identified were evaluated for TB using the GeneXpert instrument or Truenat. Confirmed TB cases were linked to treatment.

**Results/Impact:** From January to December 2022, EWORS identified 96 TB hotspot areas. Of the 114,935 persons screened for TB in the hotspot areas, 10,594 (9%) presumptive TB identified and 10,580 (100%) were further evaluated for TB using GeneXpert.

All the 1,874 (17%) TB cases diagnosed were linked to treatment. The number needed to screen (NNS) to find TB was 61 persons, and the number needed to test (NNT) was 6 persons compared to the 152 and 13, respectively, in the general population.

**Conclusions:** Active TB case-finding intervention conducted in the TB hotspot areas yielded high TB cases. As the intervention showed good efficiency, this approach can be deployed on a large scale to improve TB case-finding and is recommended for scale-up in Nigeria.

**OA50-594-17 Impact of real-time surveillance system on programme efficiency: USAID TB-LON 3 Project experience**

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**Background and challenges to implementation:** Stakeholders in the National TB Program have implemented several interventions to reach, treat, and cure TB cases. However, there is room for improvement in using the resulting implementation data for decision-making, policy-making, and corrective measures to enhance the effectiveness of these efforts. In Lagos, Ogun, and Oyo states of Nigeria, the USAID TB-LON 3 project encountered challenges due to poor reporting rates of sup-

ported sites and gaps in the reported TB cascade data. To address these issues, a real-time surveillance system was developed.

**Intervention or response:** In response to data use challenges, the Strategic Information unit of the USAID TB LON 3 project implemented by the Institute of Human Virology, Nigeria (IHVN) developed a real-time dashboard using a Google form and populated sheets by field staff to capture relevant TB cascade indicators. The dashboard highlights efficiency levels in colors, from "green" as efficient to "amber" as above average, "yellow" as below average, and "red" as not efficient.

It also displays weekly and biweekly achievements against their respective project targets across tuberculosis (TB) cascade and all project interventions. These reports were reviewed by the team every week and presented to the USAID team on a bi-weekly basis for program review

**Results/Impact:** The dashboard availed the opportunity to promptly identify implementation gaps, verify reporting completeness and prioritize interventions and strategies for improved program implementation efficiency. Consequently, on average, the facility reporting rate improved from 56% to 98%, the evaluation rate improved from 72% to 90%, and the treatment enrolment rate improved from 76% to 89%.

STATES	Efficient		Above Average		Below Average		Not Efficient		MHO	NNT	
	# screened (screening coverage)	%	# presumptive (consumption TB yield)	%	# evaluated with result (evaluation rate)	%	# TB patients (TB test diagnosis)	%			
Lagos	61,029	23.0%	2,573	4%	1,768	69%	160	3%	56	100%	10
Ogun	15,377	11.0%	1,024	7%	803	78%	101	13%	81	82%	6
Osun	25,437	22.0%	1,509	6%	1,301	73%	141	9%	111	51%	8
Oyo	22,648	11.0%	1,584	7%	1,340	72%	97	6%	82	85%	2
Achievement	124,501	23.2%	7,690	6%	5,193	72%	499	7%	392	78%	26
1 Weekly Target	48,220	6.1%	4,017	8.3%	4,023	100%	478	12%	411	86%	109
% Achievement	146%	100%	79%	83%	82%	43%	63%	63%			

**Conclusions:** Real-time surveillance systems help to improve project performance and swift decision-making. Consequently, resource utilization is optimized. The project developed a web-based application on Demographic Health Information System (DHIS) platform based on the same concept.

**OA50-595-17 Information-based microplanning for enhancing TB case-finding and monitoring: experience from a community engagement initiative in Karnataka, India**

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**Background and challenges to implementation:** Active community engagement is recognised by National Strategic Plan for Tuberculosis (2017-25). Enhanced TB case finding as part of community engagement initiative to achieve goal to 'End TB' by 2025 is being implemented

through USAID supported Breaking the Barriers (BTB) project, rolled out in Karnataka among key vulnerable populations. As the first step, in the project we conducted an extensive mapping exercise to identify vulnerable sites, community structures and prepared them for community engagement. In the initial phase of the project we learnt that outreach activities were not yielding desired results.

**Intervention or response:** As a response, a bottom-up planning approach called ‘microplanning’, was done in Bangalore district, covering an urban metro population of 7,58,698 during July-September’21. Microplanning is a dynamic process, done on a quarterly basis using management information system, to categorize vulnerable sites based on population coverage, performance of TB indicators and access to health system and prioritize its outreach activities to render support to the neediest. In this process, the high priority sites were identified, community-based leaders were supported through handholding meetings, perspective-building workshops. Also, the community-based leaders were supported to prioritize awareness campaigns, health camps, verbal screening, referrals of TB-presumptive and provide non-medical support to persons with TB.

**Results/Impact:** After microplanning the active CS number went from 28% to above 80%, the proportion of the population screened went up to 74%, from 11% with corresponding enhancements in referrals, tests and diagnosis within 6 months’ time. (Figure 1).

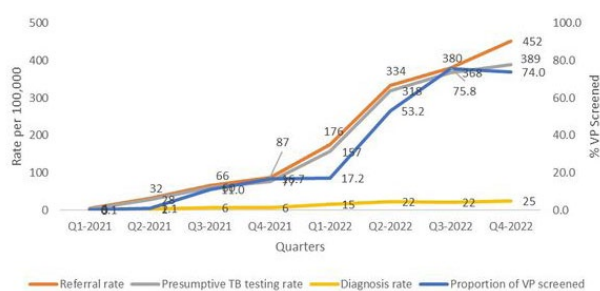


Figure 1. Quarterwise trend of TB case finding: Pre and post microplanning in Bangalore district, Karnataka, India.

**Conclusions:** Microplanning had supported in increasing the engagement of community structures and enhanced TB case finding. In large-scale implementation, microplanning has a crucial role to improve and sustain community participation within the vulnerable population.

## OA50-596-17 Improving quality TB care through digital transformation in the Kyrgyz Republic

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**Background and challenges to implementation:** According to WHO, the Kyrgyz Republic has 130 cases of tuberculosis (TB) per 100,000. The USAID Cure Tuberculosis project, implemented by JSI, explores how patient-centered information systems support improvements in TB services in the Kyrgyz Republic, to strengthen care quality, ensure treatment continuity, and reduce barriers to care.

Prior to implementation one key barrier involved clinicians’ waiting more than two months to receive laboratory test results, making it difficult to initiate patients on the appropriate treatment.

**Intervention or response:** The project worked with the National TB Program to develop several electronic TB medical information systems to develop patient-level information systems including an electronic TB register, laboratory data management information system, pharmacy module, electronic medical record, and treated cases payment verification system.

**Results/Impact:** The information systems create a longitudinal record of care across multiple organizations, allowing clinicians to provide more coordinated care. Aided by an improved sample transport system, the testing turnaround time went from 90 days to as little as 5 days, quickly kick-starting patients on TB treatment. Other improvements included the ability to provide more comprehensive case management.

Outpatient providers and TB Concilia now have access to treatment provided in inpatient settings and other facilities, enabling them to use more comprehensive information in making decisions about the course of treatment, which reduces the risk for acquiring drug-resistant TB.

### Conclusions:

The following approaches strengthened the information systems for improved use by clinicians and improved TB care quality:

- Digitized business processes allow for better TB care workflow and easy-to-access records.
  - Data shared easily between government entities through integrated systems, reducing duplication of records.
  - Seamlessly exchange data between systems and facilities enabling faster information access.
- Future attempts to develop patient-level information systems for TB care should incorporate these approaches to maximize TB patient care benefits.

**OA50-597-17 Using spatial analysis of routine data through MATCH and AccessMod to inform sub-national TB programme planning in Lesotho**

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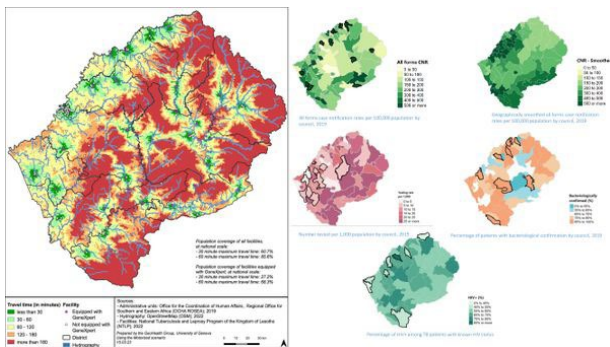
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**Background:** According to WHO estimates, 14000 people fell ill with TB in Lesotho in 2020, of whom only 4624 were notified, leaving over 60% of estimated cases undetected by the national health system. The National Leprosy and TB programme (NLTP) identified various factors contributing to the low case detection and high mortality, including poor financial access to services, low health literacy but also under-identification of people with presumptive TB by health care workers.

A geo-epidemiological analysis using integrated MATCH and AccessMod approach was applied to obtain a better understanding of areas where people with TB might be missed and to support subnational program planning.

**Design/Methods:** We performed a descriptive spatial analysis based on facility level TB surveillance data, HIV prevalence survey data, TB prevalence survey data, publicly available subnational poverty estimates and various sources of geospatial data including land cover and road network data. Relevant indicators along the care cascade were mapped on community council level. Access to TB services within 30 and 60 minutes travel time were estimated with AccessMod using two different travel scenario's: horseback and walking.

All outputs were jointly interpreted during a triangulation workshop to identify subnational gaps in TB program planning and prioritize areas for selected interventions.



**Results:** We identified a number of districts and community councils where people with TB might be missed or not notified for one of the following reasons:

1. Disruptions due to the COVID-19 pandemic,
2. Low prevalence to notification ratio,
3. Low spatial outliers.

A number of community councils were prioritized for interventions aimed to improve TB screening, testing and diagnosis based on spatial patterns. Finally, recommendations were made to optimize the location of GeneXpert machines to shorten referral times.

**Conclusions:** Geo-epidemiological approaches, such as MATCH and AccessMod, support the planning of locally relevant activities and a more effective allocation of resources.

**OA50-598-17 Inclusion of digital technologies to support TB treatment adherence under routine practice in Ukraine**

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**Background and challenges to implementation:** In Ukraine, the COVID-19 epidemic and health reform accelerated the demand for outpatient care. The burden of the war affected both patients and health care providers making it necessary to use more treatment observation options as an alternative to directly observed treatment (DOT).

**Intervention or response:** To ensure quality of care, STBCEU introduced DATs in 6 oblasts as additional treatment observation option. Smart pill boxes and video-observed treatment (VOT) with the use of the SureAdhere mobile app were included into routine practice. The USAID-funded Support TB Control Efforts in Ukraine Project (STBCEU) supplied TB facilities with smart pill boxes, trained health care providers on both DATs, introduced DAT standard operation procedures, and provided ongoing technical support.

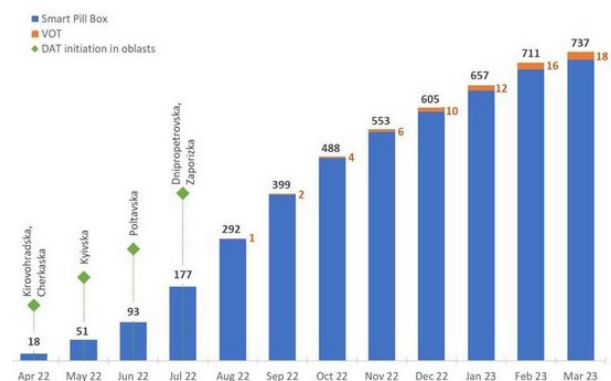


Figure 1. Patient enrollment on DATs in 6 oblasts of Ukraine (2022-2023)

**Results/Impact:** Since April 2022, 737 TB patients have used DATs during their treatment (719 on smart pill boxes; 18 on VOT). In March, 421 patients (including 170 DR-TB) continued DAT-supported treatment; 225 TB patients (including 26 DR-TB) have successfully completed treatment; and 31 patients had unfavorable outcomes. The average treatment adherence rate was 88.9% for all oblasts based on the platform data.

**Conclusions:** STBCEU's DAT intervention has helped to ensure people-centered TB care by offering an additional method for supervision of TB patients which provided real-time adherence data while allowing patients to engage in their routine lives. SureAdhere app was not as widely used by health care providers as a tool for VOT arrangement, as they preferred to continue VOT practices previously included in the standard of care.

## OA51 Rapid tests for all TB cases

### OA51-599-17 Next-generation sequencing-based TB diagnostics

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**Background and challenges to implementation:** The commercial availability of numerous Next-Generation Sequencing (NGS)-platforms poses challenges to clinical laboratories to choose the best solution. We summarize our comparison of Illumina (MiniSeq MiSeq), MinION (Oxford Nanopore Technologies, ONT), WGS, and tNGS in all possible combinations under the conditions of middle- and high-income countries. We have all implemented the technologies in-house (SRL Gauting) and at the NRL in Almaty, Kazakhstan. Furthermore, we compared different software packages for bioinformatics and report generation.

**Intervention or response:** For WGS on Illumina platforms, we prepared libraries with Nextera XT (FC-131-1096, Illumina), for ONT with Rapid Barcoding 96 (SQK-RBK110.96, ONT). For tNGS on Illumina, we prepared libraries using Deeplex® Myc-TB (Geno-

screen), and for tNGS on MinION the ONT-CUST-KIT/SQK-RBK110.96. Sequencing platforms and NGS types were evaluated with regard to their capital investment, required infrastructure, operation costs, maintenance, sequencing capacity per run, availability of free and user-friendly bioinformatics software, capacity building, supervision, and M&E.

**Results/Impact:** Based on our evaluation study and experience, we recommend to use the NGS platform/assay that is most appropriate for the workload and goals of diagnostic routine, surveillance, and clinical research planned to be performed.

The Illumina platform, coupled with the Deeplex tNGS kit, shows best performance with high-throughput, i.e. particularly large numbers of tests, provided that maintenance of equipment is assured that is quite costly.

The MinION requires the lowest seed capital, zero maintenance, and the shortest NGS libraries preparation time. Capacity building is similarly intense with both solutions.

**Conclusions:** The course should be set based on the number of tests that shall be performed and on available budget. When investment and long-term maintenance can be afforded, Illumina MiniSeq or MiSeq is an option for high throughput labs. For lower numbers of tests under resource-limited conditions, ONT provides optimal solutions. Special considerations should be given to the proper choice of data analysis software.

### OA51-600-17 High TB case notification through improved use of GeneXpert testing in Ethiopia

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**Background and challenges to implementation:** GeneXpert is a molecular diagnostic test that detects the genetic material for *Mycobacterium tuberculosis* and associated rifampicin resistance (RR). It has been underutilized, starting from the advent of the COVID-19 pandemic to September 2022. In high TB-burden countries like Ethiopia, underutilization of existing GeneX-

pert machines means that presumptive TB cases must be diagnosed by clinical judgment and less sensitive tests, which impacts case notification.

**Intervention or response:** An optimization plan was developed and implemented across 140 GeneXpert sites. A total of 842 non-GeneXpert sites were networked for specimen referral and result delivery by official telegram. Clinicians from 140 sites attended the “Xpert for all” sensitization workshop, and job aids were printed and distributed to increase awareness and demand. Supply was monitored from the central hub to facility level, and regular and intensive technical support to GeneXpert sites was performed by regional and zonal USAID Eliminate TB staff. Implementation was monitored through data collection from 140 GeneXpert sites every month through LabXpert and GxAlert connectivity solutions and verified from health facilities’ GeneXpert registration book and by exporting performance data from GeneXpert software. Data was double-entered and analyzed using SPSS.

**Results/Impact:** Increased GeneXpert utilization from 64.8% (49,947) to 81.6% (71,467); the number of bacteriologically confirmed cases from 4,538 to 6,700; and a number of RR cases from 161 to 250. An interventions package was developed and implemented and was easy and cost-effective to integrate with the existing system.

**Conclusions:** Targeted implementation of intervention packages for optimized GeneXpert utilization increased TB case notification significantly. Improved specimen referral networking and result delivery, clinician sensitization, job aid distribution, and regular supportive supervision are key elements for the optimization of GeneXpert utilization.

### OA51-601-17 Task shifting of Xpert Ultra testing to nurses for improved access to childhood TB diagnosis in primary health centres and faster testing in paediatric wards

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**Background:** Task shifting of Xpert Ultra testing from laboratory technicians to nurses in Primary Health Centers (PHC) and pediatric wards could increase access to rapid molecular testing for tuberculosis (TB) diagnosis and ensure rapid results for hospitalized patients.

We assessed the detection yield and feasibility of Ultra testing on nasopharyngeal aspirate (NPA) by nurses and laboratory technicians in children with presumptive TB at PHCs and in hospitalized children with severe pneumonia within the TB-Speed project in seven countries.

**Design/Methods:** Of 23 PHCs and 15 pediatric wards, 9 and 4 respectively had trained nurses perform Ultra using the battery-operated GeneXpert Edge. We assessed the proportion of samples tested, TB detected, invalid results and turnaround time between sample reception and result and between sample collection and result delivery to clinicians. External Quality Assessment (EQA) was conducted using proficiency testing on two panels. We documented nurses’ experiences and perceptions using self-administered questionnaire and during individual interviews.

**Results:** Ultra results were valid in 244/253 (96.4%) and 250/258 (96.9%) tests for nurses at PHC and hospital wards versus 880/895 (98.3%) and 867/874 (99.3%) for laboratory technicians, respectively. Testing time was close between nurses and laboratory technicians at PHC, and test delivery time was shorter for nurses at pediatric wards (Table). Low EQA results (<85%) by nurses were mostly due to processing errors (17/22). In-ward nurses reported technical difficulties during the procedure in

18/155 (11.6%) questionnaires. PHC nurses appreciated the value of Xpert in their facility but underlined the issue of time consumption and risk of errors due to few samples.

	Primary health centers			Reference hospitals		
	Nurse (9 sites)	Laboratory technicians (14 sites)	p value	In-ward nurse (4 sites)	Laboratory technicians (11 sites)	p value
Samples received, N	254	897	NA	258	874	NA
Samples tested, n (%)	253 (99.6)	895 (99.8)	0.637	258 (100)	874 (100)	NA
MTB detected, n (%)	2 (0.8)	3 (0.3)	0.348	1 (0.4)	20 (2.3)	0.047
MTB not detected, n (%)	242 (95.7)	877 (98.0)	0.037	249 (96.5)	847 (96.9)	0.748
Invalid/Error, n (%)	9 (3.6)	11 (1.2)	0.012	8 (3.1)	7 (0.8)	0.005
TAT (sample reception to test results) – hours, median [interquartile range, IQR]	1.13 [1.08; 1.79]	1.10 [1.07; 1.45]	<0.001	NA	NA	NA
TAT (sample collection to result delivery) – hours, median [IQR]	NA	NA	NA	1.95 [1.5; 2.87]	2.87 [1.97; 4.81]	<0.0001
External quality assurance (EQA) results	3 sites with EQA ≥90% and 6 with EQA <85%	11 sites with EQA ≥90% and 3 with EQA <85%	NA	3 sites with EQA results: 2 with EQA ≥90% and 1 with EQA 85-90%	10 sites with EQA ≥90% and 1 with EQA 85-90%	NA

Not applicable (NA)

Table. Yield and feasibility of Xpert between nurses and laboratory technicians

**Conclusions:** Task shifting of Xpert Ultra testing to nurses can be feasible. High number of processing errors may be due to overwhelmed PHC nurses and lack of practice, highlighting the importance of training and supervision.

## OA51-602-17 Improving the use, optimisation and turnaround time for modular replacement of GeneXpert platforms: the experience from Kaduna State, North West Nigeria

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**Background and challenges to implementation:** In 2016, Nigeria adopted the WHO-recommended rapid molecular diagnostic test for Tuberculosis using GeneXpert as first-line diagnostic test for TB. Despite support for its use, the GeneXpert platforms were fraught with systemic and operational challenges. Frequent modular failures coupled with long delays in replacement of faulty modules hampered the achievement of the full testing potentials of machines in various parts of the country including Kaduna state. The state TB program embarked on a multi-stakeholder Laboratory systems strengthening strategy aimed at improving the TAT for supply and replacement of faulty GeneXpert modules.

**Intervention or response:** As part of a five-year quality improvement strategy embarked upon between 2018 and 2022, all Laboratory focal persons from the 20 Gene Xpert sites were progressively trained on regular machine maintenance, generation of mandatory documents for faulty modules, and replacement of such modules. KNCV/Cepheid and NTBLCP supported to develop clear SOPs for these tasks as well as strict maintenance of minimum Xpert cartridge stock balance and adequate forecasting. Following high level advocacy, the Kaduna state government and Global Fund installed solar-powered back-up for all sites and procured 15 additional GeneXpert machines with 10 installed in mobile diagnostic trucks.

**Results/Impact:** Significant improvement in the response time whenever faulty modules is reported from an average of 20 - 30 days or beyond in 2017 to between 7-14 days from the time mandatory documents were generated and submitted in 2022. TAT for results improved from 2-4 weeks to 24-72 hours in 2017 and 2022 respectively. A steady increase in proportion of persons with presumptive TB tested using gene Xpert from 44% in 2017 to 72% in 2022 is reported.



**Conclusions:** Consistent engagement with the government at all levels, representatives of Cepheid, capacity building of the end users, power backup contributed to a significant reduction in equipment down-time with overall strengthening of the Laboratory capacity.

**OA51-603-17 Increased sensitivity of molecular TB diagnostic assays: the importance of good laboratory practice in minimising contamination**

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**Background and challenges to implementation:** South Africa transitioned to Xpert® MTB/RIF Ultra (Ultra) as the screening molecular test for detecting *Mycobacterium tuberculosis* complex (MTBC) in 2017 due to its improved sensitivity. Ultra provides an additional result category ‘MTBC trace detected’ (‘trace’) representing the lowest detectable amount of genetic material. Of 10.4 million Ultra tests performed since 2017, 1.5% reported ‘trace’. Programmatic monitoring using the centralised laboratory information system and Cepheid’s C360 remote-monitoring software determined provincial ‘trace’ baseline-trends with Western Cape reporting the highest (~2%) and KwaZulu-Natal province, the lowest (~1%). However, in October 2020, Mpumalanga province reported ‘trace’ rates >2%.

**Intervention or response:** Within Mpumalanga, a single laboratory was identified as the main contributor to the provincial rise in ‘trace’ rates, >4%. Further analysis of testing sequence isolated the majority of MTBC-detected and ‘trace’-results to sequential batches processed between 04h00-07h00, on specific days, suggesting contamination events.

Analysis of the laboratory’s External Quality Assurance (EQA) performance records demonstrated three EQA-specimens where expected result ‘MTBC-not detected’ had been reported incorrectly as either ‘trace’ or ‘MTBC-detected’. Onsite visits were conducted to observe the laboratory’s testing procedures/workflows. Type of specimen jar in-use, spillages, single-use buffers applied to multiple specimens, increased workload, multitasking across diagnostic benches and staffing constraints were identified as contributing factors to the surge in likely false ‘trace’ results.

**Results/Impact:** Good laboratory practice (GLP) was reinforced through retraining, workflows adjusted, staffing constraints addressed and daily review of all ‘trace’ and MTBC-detected results implemented. With continued reinforcement of interventions, the laboratory’s ‘trace’ and consequently provincial rates returned to expected levels.

**Conclusions:** Despite Ultra being marketed as a closed-system that minimizes cross-contamination, with its higher sensitivity, non-adherence to GLP may lead to false ‘trace’ results directly impacting patient care and clinical management. Centralised monitoring of trends allows for implementation of real-time interventions to further minimise false-positive results.

**OA51-604-17 Comparing TrueNat and GeneXpert results from the same patients to determine concordance rate**

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**Background:** KNCV through USAID funding introduced the use of the Portable Digital xray (PDX) machine for TB screening in communities. In Cross River, PDX has been used to conduct screening especially in hard to reach communities where there is very limited access to health care. The proportion of clinically diagnosed cases is expected to be around 50%. Clinical Diagnosis in Cross River was at 86% in May 2022 and 100% in June 2022. Low bacteriologic diagnosis prompted the need to verify results from the Truenat machine used for bacteriological evaluation.

This study compared results derived from the Truenat diagnostic machines with genexpert results from same patients to determine concordance rate

**Design/Methods:** This was a quantitative study conducted between 1<sup>st</sup> of July and 31<sup>st</sup> of July 2022. Two sputum samples were collected from each presumptive client identified from PDX screening. One was sent for Genexpert and the other for Truenat testing. To eliminate bias, the two sputum specimens were randomized by a toss of a coin to either be used for GeneXpert or Truenat. Samples were transported to laboratories accordingly.

Number of persons Screened	Number of presumptive TB cases identified	Number of presumptive TB cases that could produce 2 sputum samples	Number of presumptive TB cases sent for testing		Number of positive TB cases diagnosed	
			Genexpert	Truenat	Genexpert	Truenat
1238	72	40	40	40	3	3

**Results:** 1238 clients were screened and 72 presumptive TB cases were identified. 8 patients were unable to produce any sputum and 24 others could produce only 1 sputum sample hence they were excluded from the study. Of the eligible 40 patients, parallel testing was done using both genexpert and the Truenat machine and 3 TB cases were diagnosed by both diagnostic machines (Genexpert and Truenat simultaneously) in the same samples.

**Conclusions:** Findings from this study have demonstrated that the TB positivity rate from Truenat and GeneXpert machines are similar implying that Truenat has capacity to correctly detect TB from Sputum Specimens. Other reasons for low TB yield from community active case finding in Cross river should be explored.

### OA51-605-17 Improving efficiency of the TB screening cascade: utility of a one-stop shop for TB diagnosis in the community

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**Background and challenges to implementation:** Nigeria ranks 6th among the high burden countries for TB with an estimated incidence of 219/100,000 and accounts for 6.3% of the gap of unidentified TB cases globally. One major reason for the gap between notified and estimated cases is under diagnosis.

To address this, KNCV Nigeria on the USAID-funded TB LON 1 and 2 project introduced a one stop shop for TB screening and diagnosis in the community.

**Intervention or response:** Piloted during the world TB day celebration in 2022 and subsequent scale up to all 14 states of implementation, KNCV Nigeria deployed mobile teams for community outreaches in identified TB hotspots. A molecular WHO-recommended rapid diagnostic (mWRD) platform- TB LAMP or Truenat was coupled to a specially configured tricycle. The mobile teams screened for TB using WHO four Symptom Screening (W4SS). All identified presumptive TB had on-site testing of samples collected. All diagnosed TB cases were then linked to TB treatment. Data was analyzed using the TB Screening efficiency cascade and findings compared to outreaches conducted without on-the-spot TB diagnosis with mWRD.

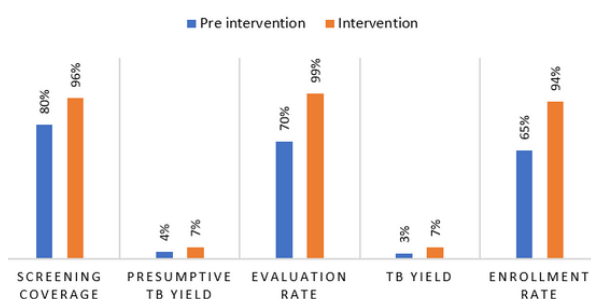


Figure. Improvement in community TB screening cascade.

**Results/Impact:** Compared to the period prior to intervention, Screening coverage -proportion screened out of the total attendees improved from 80% to 95% (35% in-

crease). Presumptive TB yield -proportion of Presumptive TB identified out of the number screened increased from 4% to 7% (75% increase); Evaluation rate- proportion of presumptive TB identified successfully tested increased from 65% to 99% (52% increase), Turn-around time for test results was same day compared 3 days or more, TB yield -proportion that tested positive for TB increased from 3% to 7% (133% increase in TB yield); Treatment Enrollment rate increased from 65% -90% (38% increase).

**Conclusions:** Having a diagnostic platform to test identified presumptive TB on-site during community screening improves the efficiency of the TB screening cascade.

### OA51-606-17 Pre-treatment attrition after rifampicin-resistant TB diagnosis with Xpert MTB/RIF and/or Ultra in high-burden countries: a systematic review

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**Background:** With the introduction of rapid molecular testing for rifampicin-resistant tuberculosis (RR-TB), such as Xpert (MTB/RIF or Ultra), pre-treatment attrition should be minimal. However, no previous review summarized pre-treatment attrition after RR-TB diagnosis using Xpert in high burden countries.

**Design/Methods:** Medline, Web of Science and EMBASE were searched for studies published between January 2011 and June 2022 reporting original data on RR-TB diagnosis using Xpert MTB/RIF and treatment initiation. Two researchers screened and extracted data on the proportion of RR-TB patients who did not initiate treatment (due to pre-treatment loss to follow up or mortality). We assessed heterogeneity and calculated a pooled estimate with random effect meta-analysis in STATA. A modified Newcastle-Ottawa scale and Cochrane tool were used to assess study quality.

**Results:** Thirty-three eligible studies (19 from Africa, 13 from Asia, one from Latin America and one from Europe) were included out of 2509 identified. Seventeen studies were retrospective, 14 were prospective cohorts, and two were randomized clinical trials.

The estimated pooled proportion of pre-treatment attrition was 17% (95% confidence interval (CI): 11-25%,  $I^2=98.54%$ ,  $p=0.00$ ) overall, 9% (95% CI:6-12,  $I^2=59.25%$ ,  $p=0.00$ ) in 13 studies using only active

case-finding versus 24% (95%CI:14-34, I<sup>2</sup>=98.91%, p=0.00) in 20 studies using passive case finding (in-between group heterogeneity p=0.001). Twenty-four, four and three studies were rated respectively of fair, good, and poor quality among the cohort studies. Both trials included were rated of fair quality.

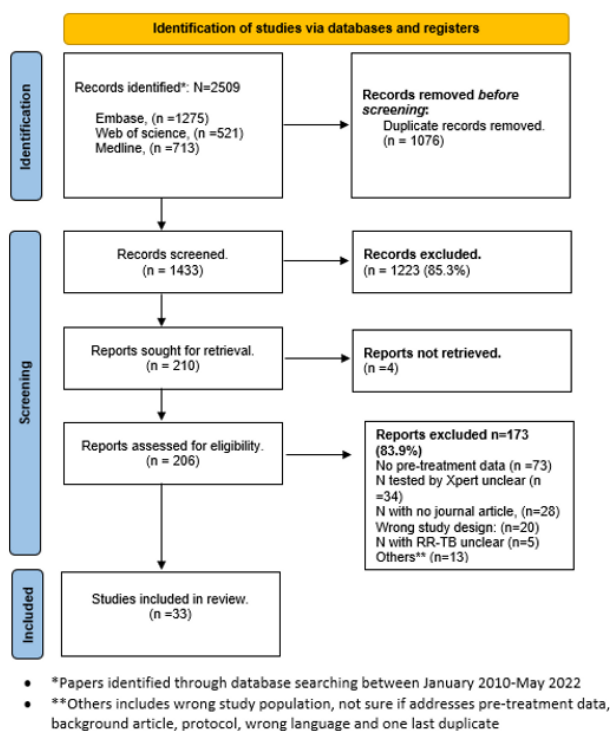


Figure. Prisma flow chart.

**Conclusions:** Pre-treatment attrition after RR-TB diagnosis on Xpert MTB/RIF was common in studies included and lower when using active case finding. However, studies were heterogenous and of limited quality overall. This study highlights the importance of actively reporting outcomes of all patients diagnosed with RR-TB using Xpert MTB/RIF.

## OA52 TB treatment: regimen, tools for monitoring and outcome

### OA52-607-17 Retreatment with new anti-tuberculosis drugs is associated with worse clinical outcomes in patients receiving treatment with combined bedaquiline- and delamanid- containing regimens

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**Background:** Data on patients with drug-resistant tuberculosis who are retreated with new anti-tuberculosis drugs: bedaquiline, delamanid, linezolid, and clofazimine are limited. We sought to evaluate the efficacy and safety of regimens combining bedaquiline and delamanid and compare the outcomes between persons with and without a history of new drugs exposure.

**Design/Methods:** A retrospective cohort study was conducted among patients with pulmonary drug-resistant tuberculosis who received bedaquiline and delamanid combination in Georgia between 2017 to 2020 as a part of salvage regimens in programmatic settings.

**Results:** Overall, 106 mostly male (75%) patients with a median age of 39 years received bedaquiline and delamanid concurrently. Among them, 39 (37%) had prior exposure to new drugs with higher rates of baseline resistance compared to those without exposure to new drugs (bedaquiline 15% vs 2%, linezolid 25% vs 16%). Sputum culture conversion (SCC) rates among patients with and without prior new drugs exposure were 64% vs 96%, respectively and the median (IQR) time to SCC was 62.0 (33.0-110.0) vs 36.0 (21.0-67.0) days. Among patients exposed and not exposed to new drugs, favorable outcome rates were 41% and 79% respectively (p<.001). Out of 39 patients with a history of new drugs use, 8 (21%) developed acquired bedaquiline resistance during or after treatment, and 3(8%) developed resistance to delamanid. No patients without prior exposure to new drugs acquired drug resistance. There were no significant differences in adverse events between the two groups of patients and QTc prolongation (>500 ms) was rare (3%).

**Conclusions:** Prior exposure to new anti-tuberculosis drugs was associated with worse clinical outcomes and acquired drug resistance. Rapid tests for new drugs, novel drugs and regimens are needed to improve outcomes in this important population.

### OA52-609-17 Risk of the emergence of rifampicin-resistant TB after incomplete first-line treatment

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**Background and challenges to implementation:** Drug-resistant tuberculosis can emerge during tuberculosis treatment. However, the risk of resistance emergence and its relationship with incomplete treatment (loss to follow-up) have not been well characterized.

**Intervention or response:** We carried out a cohort study using tuberculosis surveillance data from Ukraine, January 2015 – November 2018, to identify people initially diagnosed with rifampicin-susceptible tuberculosis (RS-TB) and a treatment outcome of lost to follow-up or successful treatment.

We did two analyses:

1. A logistic regression to estimate the association between recurrence (defined as being diagnosed with TB again within 18 months of initial diagnosis) among these patients and incomplete treatment, and;
2. Among patients that experienced recurrence, a logistic regression to estimate the association between rifampicin-resistant tuberculosis (RR-TB) at recurrence and incomplete treatment.

**Results/Impact:** We included 30,053 RS-TB episodes, of which 1,166 (3.9%) had a recurrence within 18 months; of those, 254/1,166 (21.8%) had RR-TB on recurrence. Odds of recurrence decreased with increasing length of treatment (e.g. odds of recurrence following 3-4 months of treatment was 30% lower [95% CI: 1-50% lower] versus with <1 month of treatment (Figure 1a). For people who experienced a recurrence, odds of RR-TB diagno-

sis at recurrence increased with increasing amounts of treatment received (e.g. OR=2.28 [95% CI 0.99, 5.68] following 3-4 months of treatment versus <1 month of treatment); odds for those with 5-6 months of treatment then dropped to being similar to those with less than one month of treatment (Figure 1b).

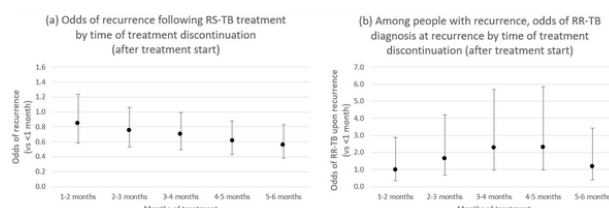


Figure 1.

**Conclusions:** Failure to complete the intended course of treatment is a major risk factor for recurrence and the emergence of drug resistance. These results indicate that the continuation phase of treatment needs to be carefully monitored and special attention paid to finding and returning to care those who are lost to follow-up.

### OA52-610-17 Understanding self-adaptive behaviours and practices of people with drug-resistant TB to cope with drug side effects: findings from a qualitative positive deviance study in South India

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**Background and challenges to implementation:** Despite introduction of newer and shorter regimens, treatment for drug- resistance tuberculosis (DR-TB) remains challenging in terms of pill burden and side effects associated with it.

Understanding self-adaptive behaviors and practices of persons affected by DR-TB in overcoming drug side-effects could be useful for advising other persons with TB (PwTB).

**Intervention or response:** This qualitative study was conducted under USAID supported Breaking the Barriers project between 2019-2022 in Hyderabad and Bengaluru of Telangana Karnataka States of South India. Criterion sampling was used to recruit positively deviant adult DR-TB PwTBs (n=20) who completed DR-TB treatment with maximum adherence (< 2 days of missed

drug intake), along with their family caregivers (n=20). Semi structured interviews in local language inquired about practices, behaviours, which enabled coping of DR-TB drug side effects. Thematic analysis using inductive approach was used for data analysis.

**Results/Impact:** Themes explanatory of self-adaptive behaviours and practices of DR-TB person's in mitigating pill and injection side-effects were identified, include:

1. Using adjuvants and special nutritional diets to improve pill palatability, suppress gastric intolerance and withstand power of pills
2. Staggered pill consumption based on its size and perceived power
3. Adapting a daily fixed routine for pill consumption to normalize drug intake
4. Home-made topical application for mitigating injection pain
5. Planning convenient timings and place for injection administration to overcome pain and immobility
6. Natural adaptation towards drug intake during later treatment phases.

**Conclusions:** A range of self-adaptive practices and behaviours by DR-TB persons provided a window of choices for them to confront intolerant and inescapable side-effects created by pills and injections.

These adaptations served a cognitive purpose for DR-TB persons by providing instant but vital relief for their mind and body. These self-adaptions could be peer-taught for benefit of other DR-TB persons, building resilience towards treatment demands and psycho-social challenges of DR-TB persons.

## OA52-611-17 Determinants of adherence to drug-susceptible TB treatment in a South African cohort: a focus on HIV infection, antiretroviral therapy, care access and stigma

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**Background:** Suboptimal adherence to tuberculosis (TB) treatment is common and puts individuals at increased risk of treatment failure. Identifying risk factors for poor adherence may help better target individuals and improve resource allocations.

We assessed potential determinants of poor treatment adherence: HIV status; antiretroviral therapy; time to clinical care access; and perceived stigma among drug-sensitive TB patients.

**Design/Methods:** This is a secondary analysis of the "TB Mate" cluster randomised controlled trial, which implemented a TB treatment adherence intervention in three South African provinces (PACTR201902681157721). Medication monitors were used to measure patient treatment adherence; each time the monitor was opened, medication intake was recorded, as a proxy to evaluate adherence. Adults enrolled in the control arm, using the pillbox without a daily reminder and without differentiated care, were included in this analysis. Logistic regression was used to model poor adherence (defined as <80% doses taken) and negative binomial regression was used to study adherence quantitatively, as a count of doses taken. Directed acyclic graphs were used to guide the selection of covariates in the model.

**Results:** Out of 1,213 participants from 9 clinics, 51% (614) had adherence of <80%. 63% (769) of participants were living with HIV, of whom 66% (507/769) were taking antiretroviral therapy. Median time to access clinical care was 127 minutes. 95% (1151/1213) reported no perceived stigmatisation at the time of starting TB treatment. Living with HIV was identified as a strong determinant of poor adherence to TB treatment. Being on antiretroviral therapy, time to clinical care access and perceived stigma were not associated with adherence.

Variable	Coding	Poor adherence: (<80%) Adjusted OR (95%CI)*	P-value	Adherence count: Adjusted RRs (95%CI)*	P-value
HIV-status (n=1209):	Negative	1	<0.001	1	0.005
	Positive	1.68 (1.27-2.22) <sup>1</sup>		0.90 (0.83-0.97) <sup>1</sup>	
Antiretroviral therapy (n=769):	HIV+ not on ART	1	0.65	1	0.26
	HIV+ on ART	1.09 (0.75-1.57) <sup>2</sup>		0.95 (0.86-1.04) <sup>2</sup>	
Time to access care, minutes** (n=1213):	<60	1	0.73	1	0.87
	60-119	0.83 (0.48-1.42) <sup>3</sup>		1.02 (0.88-1.18) <sup>3</sup>	
	120-179	0.84 (0.47-1.48) <sup>3</sup>		1.00 (0.86-1.16) <sup>3</sup>	
	180-239	1.08 (0.59-1.98) <sup>3</sup>		1.00 (0.85-1.18) <sup>3</sup>	
Perceived stigma: (n=1209)	No stigma reported	1	0.94	1	0.74
	≥1 point of stigma	1.02 (0.58-1.82) <sup>4</sup>		0.97 (0.84-1.14) <sup>4</sup>	

\* adjusted for sex, age, clinic, country of origin, ethnicity, education level, occupation, marital status, household status, tobacco, alcohol and illicit drug consumption, socio-economic position, plus: 1 time to access clinical care; 2 time to access clinical care, perceived stigma; 3 previous TB, HIV status, diabetes; 4 previous TB, time to access clinical care, HIV status. RR rate ratio. CI confidence interval

\*\*Time to access care was based on the addition of the travel time to clinic and the waiting time inside the clinic

*Table. Adjusted odds ratios and incidence rate ratios for the association between exposures of interest and adherence to TB treatment (binary adherence and adherence count).*

**Conclusions:** Very low adherence reported highlights the need for TB treatment support interventions and especially among those living with HIV. The lack of association found with previously identified risk factors may be due to differences in setting, study design and adherence measurement method.

## OA52-612-17 Low sensitivity of self-report to identify sub-optimal adherence in people with multidrug-resistant TB and HIV in South Africa (the PRAXIS study)

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**Background:** Drug-resistance during the treatment of multidrug-resistant tuberculosis (MDR-TB) and HIV highlights the need to support medication adherence. Patient self-report, such as 30-day recall, is commonly used in research and clinical practice, to monitor medication adherence.

**Conclusions:** While participant self-report was highly specific for non-adherence, most episodes of non-adherence were not identified due to the low sensitivity. Cumulative 6-month self-report measures identified a larger proportion of non-adherent participants versus monthly account.

The EDM device identified more episodes of non-adherence compared to the self-report and may be a critical component in an adherence support program for MDR-TB HIV in this setting.

While electronic dose monitoring (EDM) devices measure adherence in real-time and are less subject to recall and social desirability bias, they are expensive.

The purpose of this study was to evaluate the accuracy of self-reported adherence compared to EDM-measured adherence in patients with MDR-TB and HIV.

**Design/Methods:** A prospective observational cohort of patients co-infected with MDR-TB and HIV receiving a bedaquiline-containing treatment and ART, enrolled from 2016-2018 in Durban, KwaZulu Natal, South Africa using two separate EDM devices for ART and bedaquiline. Medication adherence was measured daily with EDM, and at monthly study visits through 6 months by self-report. Three different self-report tools were used: 7-day recall, 30-day recall and a 30-day visual analogue scale.

**Results:** Of 199 enrolled patients, 198 provided adherence data for both bedaquiline and ART. Through six months 29/198 (14.6%) participants self-reported sub-

Patients reporting suboptimal adherence by self-report (Visual Analogue Scale (VAS), 7-day Recall, and 30-day Recall) compared to Wisepill RT2000 electronic dose monitoring device measured adherence (7-days and 30-days prior to monthly study visit)

Self-report data is recorded as number of respondents reporting <100% adherence over number of total respondents at each time point. Wisepill data is reported as number of participants with calculated adherence <100% during the specified time period. \*Cumulative 6-month self-report adherence is reported as the number of unique participants reporting non-adherence to any of the self-report measures during the 6-month period. Cumulative 6-month Wisepill adherence is reported as the number of participants where at least one missed dose was detected by the Wisepill device during the 6-month study period.

Monthly Visit	Bedaquiline					ART				
	VAS	7-day Recall	30-day Recall	Wisepill (7-days)	Wisepill (30-days)	VAS	7-day Recall	30-day Recall	Wisepill (7-days)	Wisepill (30-days)
1	0/193 (0%)	0/195 (0%)	1/195 (0.5%)	13/194 (6.7%)	60/195 (30.8%)	2/182 (1.1%)	3/191 (1.6%)	5/179 (2.8%)	80/192 (41.7%)	135/193 (70.0%)
2	1/189 (0.5%)	5/192 (2.6%)	2/193 (1.0%)	19/188 (10.1%)	57/190 (30.0%)	2/188 (1.1%)	1/192 (.5%)	2/191 (1.1%)	95/189 (50.3%)	146/191 (76.4%)
3	1/184 (0.5%)	6/187 (3.2%)	3/188 (1.6%)	23/182 (12.6%)	57/184 (31.0%)	0/185 (0%)	2/188 (1.1%)	3/188 (1.6%)	107/184 (58.2%)	148/184 (80.4%)
4	2/176 (1.1%)	6/183 (3.3%)	5/183 (2.7%)	20/171 (11.7%)	50/176 (28.4%)	0/177 (0%)	1/182 (.6%)	3/182 (1.7%)	107/175 (61.1%)	149/179 (83.2%)
5	1/175 (0.6%)	2/180 (1.1%)	0/181 (0%)	34/165 (20.6%)	63/172 (36.6%)	3/175 (1.7%)	4/181 (2.2%)	6/181 (3.3%)	115/174 (66.1%)	153/175 (87.4%)
6	1/173 (0.6%)	3/178 (1.7%)	3/178 (1.7%)	36/129 (27.9%)	67/160 (41.9%)	1/174 (0.6%)	2/178 (1.1%)	4/178 (2.3%)	161/171 (94.2%)	168/171 (98.3%)
Participants with any reported non-adherence through 6 months*	29/198 (14.6%)		151/198 (76.3%)			21/198 (10.6%)		198/198 (100%)		

OA52-612-17 Table.

optimal adherence to bedaquiline at any point and 21/198 (10.6%) participants reported suboptimal adherence to ART.

Comparatively, by EDM, 151/198 (76.3%) participants missed at least one dose of bedaquiline and all participants (100%) missed at least one dose of ART during the six-month period. Using EDM as the reference standard, a composite score of the three self-report tools was highly specific (98.2%), but not sensitive (4.8%).

### OA52-613-17 Evaluating the efficacy, feasibility and acceptability of a video-observed therapy strategy for TB patients in Senegal during the pandemic

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**Background:** The COVID-19 pandemic has had a negative impact on TB control indicators in Senegal. In order to maintain the continuity of TB treatment and care in the context of COVID-19, a novel intervention to provide virtual directly observed therapy, short-course (VOT, or VOT) using an online, video-enabled social media platform (WhatsApp) was implemented and evaluated among TB patients in the Dakar region in Senegal.

**Design/Methods:** A mixed-methods study was undertaken among patients recruited between January and March 2021 who received daily video calls via WhatsApp over a six-month period. Adherence levels, clinical and treatment outcomes were collected and compared to data extracted from clinical records of DS-TB patients receiving standard DOTS. Feasibility and acceptability were assessed through interviews with TB patients and TB centre staff to assess attitudes and perceptions of VOT.

**Results:** 97 patients were enrolled in VOT from five clinics and 146 patients on DOTS during the study period and acted as the controls. Participants were predominantly male, with an average age of 32.5 years. At the end of month 2, adherence was observed among 73% of patients in the DOTS group and 78% in VOT group and more patients receiving DOTS were AFB+ (17% vs 14%). By the end of month six, a similar proportion of patients were cured in both groups. VOT was acceptable and feasible among patients and providers with barriers related to internet connectivity and concerns for privacy. VOT could be an effective alternative to standard DOT to improve treatment adherence, particularly in the context of public health crises when access to services may be restricted.

**Conclusions:** A scaling up of VOT with a robust evaluation, including an evaluation of costs, in Senegal should be conducted to inform future national guidelines, particularly as a tool to maintain continuity of care during COVID-19 and future public health emergencies.

## OA52-614-17 Analysis of healthcare workers' levels of engagement with digital adherence technologies for TB before and during the war in Ukraine

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**Background:** In implementing digital adherence technologies (DATs), healthcare workers' (HCWs) interaction with patients' engagement data is essential for monitoring and implementing differentiated care. The impact of the full-scale Russian invasion of Ukraine on TB service delivery is assumed to be negative.

Overall 9/18 months of the Adherence Support Coalition to End TB study in Ukraine coincided with the war. We aimed to evaluate if levels of HCWs' engagement with DATs have changed in wartime.

**Design/Methods:** A digital platform recorded patients' daily engagement with the DAT by receiving a signal that a patient opened their smart pillbox, assumed to indicate that the patient had taken their medication dose. If no signal was received, a HCW was asked to contact the patient and confirm manually whether the dose had been missed or taken. We defined a dose as having 'no information' when either no manual dose was added or it was added >7 days after the treatment-day (long delay).

We grouped facilities into regions directly affected by the war (Mykolaiv, Donetsk) and those less affected in Southern (Odesa) and Western (Lviv, Zakarpattia) Ukraine, and time periods into pre-war (14 Jun 21 - 23 Feb 2022), the early phase of the war (24 Feb - 30 Apr 2022), and later phase (1 May - 28 Oct 2022).

Using a negative binomial model with random effects for a facility, we evaluated the proportion of 'no information' days across regions and time periods, adjusting for age, sex and treatment phase.

**Results:** Digital engagement data for 816 drug-susceptible-TB participants were included (111,667 treatment days). Of all participants, 69% were male and median age was 44 years. Pre-war treatment days with no information ranged from 6.8%-8.7%, by region. Following the start of the war, this increased to around 30% in Mykolaiv/Donetsk, 16% in the Southern, and 12% in the Western regions. (Table)

Region	Time period	Total treatment days	Total days no information	%	RR*	95% CI	RR**	95% CI
Directly affected by the war (Mykolaiv/Donetsk)	before war	9454	825	8.7%	1		1	
	24/2-30/4/2022	3183	1193	37.5%	3.71	(3.37, 4.61)	3.71	(3.17, 4.33)
	1/5-28/10/22	2632	724	27.5%	3.06	(2.56, 3.65)	2.71	(2.27, 3.24)
Southern (Odesa)	before war	12662	1053	8.3%	1		1	
	24/2-30/4/2022	5751	951	16.5%	1.99	(1.73, 2.30)	1.95	(1.68, 2.25)
	1/5-28/10/22	11900	1930	16.2%	1.85	(1.64, 2.09)	1.72	(1.52, 1.93)
Western (Lviv and Zakarpattia)	before war	28692	1964	6.8%	1		1	
	24/2-30/4/2022	13706	1364	10.0%	1.66	(1.50, 1.84)	1.69	(1.52, 1.87)
	1/5-28/10/22	23687	3307	14.0%	2.00	(1.83, 2.18)	1.86	(1.70, 2.02)

\* adjusted for age and sex; \*\* adjusted for age and sex and treatment phase (intensive or continuation). RR rate ratio. CI confidence interval

**Conclusions:** The war's physical proximity severely affected patient-provider interaction and HCWs' engagement with DATs.



## OA53 Identification & Management of TB Infection

### OA53-615-17 Integrating interferon-gamma release assay testing in the TB infection care cascade: experience from the Joint Effort for Elimination of TB project, India

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**Background and challenges to implementation:** Diagnosis of tuberculosis infection (TBI) and provision of TB preventive therapy (TPT) are critical to control TB transmission. Evidence on the feasibility of integrating the Interferon-Gamma Release Assay (IGRA) tests for diagnosing TBI in TPT interventions in India is limited.

This abstract documents the experience of testing household contacts (HHC) of pulmonary TB patients (PTB) with IGRA in a TPT initiative from India under programmatic conditions.

**Intervention or response:** Under the aegis of the National TB elimination Program (NTEP), FIND, through the Joint Effort for Elimination of TB initiative, is implementing IGRA testing for TBI (QuantiFERON-TB Gold Plus test) in two districts (Bagalkot, Karnataka state; Mahbubnagar, Telangana state) of India.

The HHCs of notified index PTB cases were screened for TB and IGRA was done for all eligible ( $\geq 5$  years of age) and consenting HHCs. A third-party agency was hired for end-to-end IGRA testing services. Dedicated phlebotomists collected blood samples for testing.

Results were classified as IGRA positive/ negative/indeterminate. Data from project initiation (Oct'21) till Dec'22 were analysed.

**Results/Impact:** Overall, 10,836 HHCs of 2,767 index pulmonary TB patients were identified. Among those HHCs who consented for screening (99.5%, N=10,779), N=10,328 (96%) were  $\geq 5$  years of age. Approximately 10% (N=1,025) of these HHCs did not consent for IGRA testing. Among those who consented, IGRA was performed on 85% (N=7,916) HHCs (Figure 1).

Of those who underwent testing (56% females, median age=29 years (IQR:16,43), N=2,802 (35.4%) had a positive IGRA result. Hesitancy among HHCs to undergo IGRA testing, and difficulty in reaching to all eligible HHCs were key challenges to implementation.

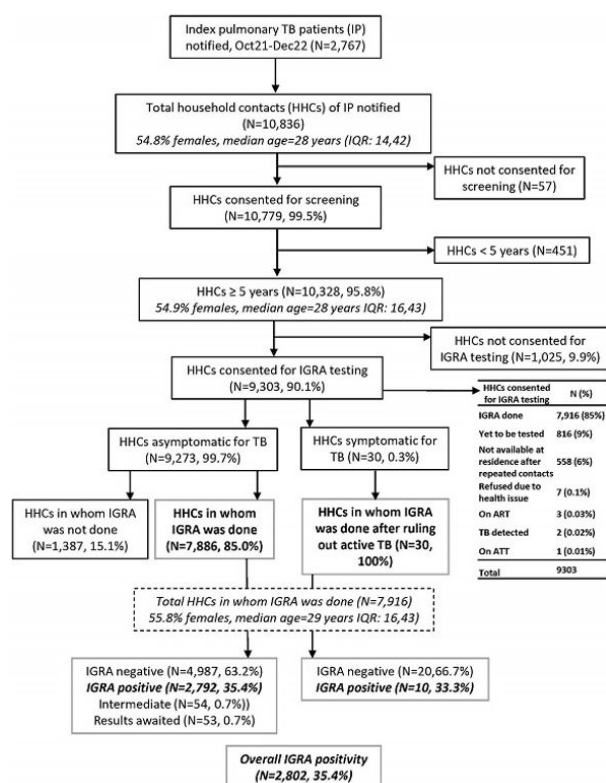


Figure 1. IGRA testing in JEET TBI project, FIND, India, Oct 2021 to Dec 2022.

**Conclusions:** The project successfully tested nearly three-fourth of the HHCs of index TB patients identified. The initiative demonstrates the feasibility of integrating IGRA diagnostic in the TBI care cascade to identify individuals who would benefit most from the TPT.

### OA53-616-17 Pragmatic cluster-randomised trial of home-based preventive treatment for TB in Ethiopia (CHIP-TB)

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**Background:** TB preventive treatment (TPT) is highly effective at preventing TB disease but remains poorly implemented; two-thirds of children are not linked to TB preventive services. We aimed to determine whether home-based contact management improves TPT uptake among contact persons aged <15 years compared to the facility-based standard of care.

**Design/Methods:** A cluster-randomized trial was conducted in 18 facilities in Oromia, Ethiopia from September 2021 through December 2022. The intervention was task-shared by health extension workers (HEWs) and facility-based TB focal persons. The primary outcome is the ratio of children initiating TPT per TB patient. A key secondary outcome is the ratio of children identified per TB patient. Analysis used Poisson regression, accounting for the cluster-randomized design.

**Results:** The home-based and facility-based arms identified 280 children from 167 TB patients and 246 children from 186 TB patients, respectively (cluster-adjusted ratio 2.03 vs 1.52 children per TB patient;  $p=0.27$ ). In the home-based intervention, 272 children initiated TPT compared with 244 children in the facility-based arm (cluster-adjusted ratio 1.70 vs 1.34 children per TB patient;  $p=0.27$ ; Table 1).

Inter- vention Facilities	Number of Children <15 years Initiating TPT	Number of TB Patients	Ratio of Children Initiated on TPT per TB Patient	Mean Ratio (cluster- adjusted)	Control Facili- ties	Number of Children <15 years Initiating TPT	Number of TB Patients	Ratio of Children Initiated on TPT per TB Patient	Mean Ratio (cluster- adjusted)
1	32	31	1.03		10	9	12	0.8	
2	100	50	2.00		11	35	31	1.1	
3	27	16	1.69		12	8	34	0.2	
4	18	11	1.64		13	28	22	1.3	
5	40	22	1.82	1.70	14	55	34	1.6	1.34
6	10	5	2.00		15	26	15	1.7	
7	18	6	3.00		16	72	29	2.5	
8	16	16	1.00		17	6	3	2.0	
9	11	10	1.10		18	5	6	0.8	

Table 1. Cluster-level Data for the Ratio of Children Initiating TPT per TB Patient.

Among those initiated on TPT, 258 (80%) and 235 (87%) completed treatment in the two arms, respectively. There were no child deaths. One child (0.3%) failed TPT, requiring a change from TPT to TB treatment, after initiation by an HEW. Only 2 (0.01%) children discontinued TPT due to drug-related adverse events, both from the facility-based arm.

**Conclusions:** Home-based TPT initiation and follow up by HEWs was a successful, person-centered alternative TB prevention care model. HEWs successfully identified, initiated and followed children on TPT. Though not statistically significant, the home-based intervention identified and initiated more children on TPT per TB patient.

## OA53-617-17 Outcomes among incarcerated people treated for active and latent TB infection in Uganda, 2020

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**Background:** Incarcerated persons (IPs) are at higher risk for active TB (ATB) and unsuccessful treatment outcomes. We studied correlates of unsuccessful treatment for ATB and latent TB infection (LTBI) among IPs in Uganda.

**Design/Methods:** In a cross-sectional study, we analyzed data on demographics, length of incarceration before treatment, and HIV status among IPs treated for ATB or LTBI in 27 prisons during 2020. Successful outcomes included treatment completion (for both ATB and LTBI) or confirmed cure (for ATB). Unsuccessful outcomes included lost to follow-up (LTFU), transfer out and death and, for ATB, treatment failure.

**Results:** Among 1,117 IPs treated for ATB, 1,099 (98.0%) were men, median age was 34-years, 340 (30.4%) were HIV-positive. Overall, 985 (88.1%) had successful outcomes. Of the 132 with unsuccessful outcomes, 36 [27.2%] were LTFU, 35 [26.5%] died, 5 [3.7%] failed treatment, while 56 [42.4%] had no documented outcome. Having bacteriologically-confirmed (AOR: 2.3, 95% CI: 1.00–6.30,  $p=0.05$ ) or extra-pulmonary (AOR: 1.6, 95% CI: 1.06–2.40,  $p=0.09$ ) compared to clinically-diagnosed TB and, being in prison  $\leq 6$  months before ATB treatment initiation (AOR: 3.13, 95% CI: 1.60–6.11,  $p=0.0008$ ) correlated with unsuccessful outcomes. Among 2,672 IPs treated for LTBI, 2,337 (87.5%) were men, median age was 30-years, 2,468 (92.5%) HIV-positive. Overall, 2,117 (79.2%) completed treatment and 555 (20.8%) with unsuccessful outcomes (248 [44.6%] transferred, 207 [37.2%] LTFU, 98 [17.6%] stopped, and five [0.2%] died). Being in prison  $\leq 6$ -months before LTBI treatment initiation (AOR: 1.78, 95% CI: 1.28–2.48  $p=0.0006$ ), male (AOR: 1.58; 95% CI: 1.10–2.27;  $p=0.014$ ), or HIV-positive (AOR: 2.13, 95% CI: 1.42–3.21,  $p=0.0003$ ) correlated with unsuccessful outcomes.

**Background and challenges to implementation:** Incarcerated persons (IPs) are at higher risk for active TB (ATB) and poor treatment outcomes. We conducted a cross-sectional study to better understand correlates for unsuccessful treatment for ATB and latent TB infection (LTBI) among IPs in Uganda.

**Intervention or response:** We analyzed data on ATB or LTBI treatment among IPs during 2020 at 27 prisons including demographic characteristics, treatment initia-

tion date, length of incarceration before initiation, and HIV status. Successful treatment included completion (for both ATB and LTBI) or bacteriologically confirmed cure (ATB). Unsuccessful treatment included lost to follow-up (LTFU) and death and, failure (ATB).

**Results/Impact: Results:** Among 1,117 IPs treated for ATB, 1,099 (98.0%) were men, median age was 34 years, and 340 (30.4%) were HIV-positive. Overall, 985 (88.1%) had a successful outcome. Of the 132 with unsuccessful outcomes, 36 [27.2%] were LTFU, 35 [26.5%] died, 5 [3.7%] failed treatment, while 56 [42.4%] had no documented outcome. Having bacteriologically confirmed (AOR: 2.3, 95% CI: 1.00–6.30, p=0.05) or extra-pulmonary (AOR: 1.6, 95% CI: 1.06–2.40, p=0.09) compared to clinically diagnosed TB and being in prison ≤6 months before ATB treatment was initiated (AOR:3.13, 95% CI: 1.60–6.11, p=0.0008) correlated with unsuccessful treatment. Among 2,672 IPs treated for LTBI, 2,337 (87.5%) were men, median age was 30 years, and 2,468 (92.5%) were HIV-positive. Overall, 2,117 (79.2%) completed LTBI treatment and 555 (20.8%) had unsuccessful treatment 248 [44.6%] transferred, 207 [37.2%] LTFU, 98 [17.6%] stopped treatment, and five [0.2%] died. Being in prison ≤6-months before LTBI treatment (AOR: 1.78, 95% CI: 1.28–2.48 p=0.0006), male (AOR: 1.58; 95% CI: 1.10–2.27; p=0.014), or HIV-positive (AOR: 2.13, 95% CI: 1.42–3.21, p=0.0003) correlated with unsuccessful treatment.

**Conclusions:** ATB and LTBI treatment outcomes among IPs remain sub-optimal, correlated with short prison stays. Bacteriologically confirmed or extra-pulmonary-TB was a risk factor for unsuccessful outcomes for ATB while male and HIV-positive IPs were at a higher risk of unsuccessful LTBI treatment.

### OA53-618-17 Preventive TB treatment for household contacts of TB patients: experience from India

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**Background and challenges to implementation:** Tuberculosis prevention strategies for household contacts (HHCs) of TB patients (a known risk group for TB) are key to limit the global TB burden. In India, Joint Effort for Elimination of Tuberculosis (JEET) has been implementing TB Infection (TBI) component in collaboration with National TB programme (NTEP) since September 2021. This document describes the 15-month implementation of JEET project.

**Intervention or response:** The JEET project provides door-step TB screening, linkage for diagnosis of TBI; and TPT initiation for HHCs of pulmonary TB patients, in 22 districts of four states in India, covering a population of 68.7 million. In two districts 3HP, while in 20 districts 6H is administered as TPT regimen.

In addition, the project liaises with healthcare providers for TPT initiation and linkage for adverse-events management. The TPT follow-up and adherence-support are being provided through fortnightly telephonic calls and monthly in-person visits. Stakeholder meetings are organised monthly for collaborating action.

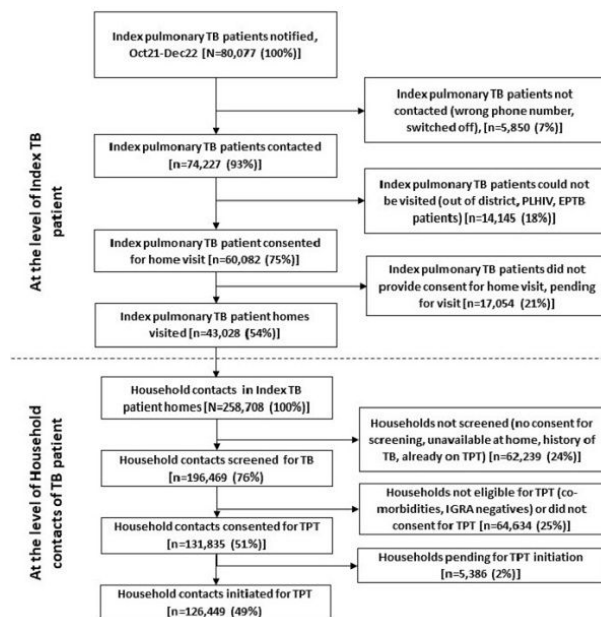


Figure 1. TB preventive treatment for household contacts of pulmonary TB patients in JEET project, India, 2021-22.

**Results/Impact:** During October 2021-December 2022, a total of 80,077 patients with pulmonary TB were notified, of whom 74,227 (93%) were contacted telephonically to schedule screening visits for their HHCs at home (Figure 1).

A total of 60,082 (75%) consented for home visit, of whom 43,028 (54%) were visited. Subsequently, 196,469 HHCs were screened and of these 126,449 (49%) were put on TPT (including 125,198 on 6H and 1251 on 3HP).

Of those initiated on TPT, <2% HHCs reported any adverse-events. Among 52,502 initiated on TPT between Oct 2021-June 2022; 45,393 (86%) successfully completed TPT.

**Conclusions:** Project JEET demonstrates the feasibility of further scale up in similar contexts in India. Expanding the involvement of healthcare providers (including traditional healers and grass root providers) in TB prevention strategies will help in meeting the targets of ending TB in the country.

### OA53-619-17 Xpert testing, chest-X-ray or tuberculin skin testing for household contact assessment: preliminary findings from a cluster-randomised clinical trial

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**Background:** Chest X-ray (CXR) and TST are potential barriers for tuberculosis preventive therapy (TPT) initiation in low-resource settings. We conducted a multi-centre cluster-randomized clinical trial in Benin and Brazil, comparing three strategies for household contact (HHC) assessment prior to TPT initiation.

**Design/Methods:** HIV uninfected persons aged 5-50 years who were HHC of persons with newly diagnosed microbiologically pulmonary tuberculosis were randomized by household in equal numbers to one of three arms:

1. TST followed by CXR, if TST positive (standard),
2. TST followed by Xpert-MTB/RIF if TST positive, and;
3. CXR performed for all HHC, and no TST.

In strategies 1 and 2, TPT was recommended for TST positive participants in whom tuberculosis disease was excluded by CXR or Xpert-MTB/RIF.

In strategy 3, participants without radiological evidence of tuberculosis disease were offered TPT. The primary outcome was the number of eligible HHCs that started TPT within three months of randomization.

**Results:** Out of 1,590 randomized participants, 1,273 were from Benin and 317 from Brazil. 475, 583 and 532 participants were assigned to strategies 1, 2, and 3, respectively.

Overall, 434/475 (91%), 550/583 (94%) and 494/532 (93%) completed the related investigations of each strategy, respectively, and 151/166 (91%), 187/199 (94%), 447/475 (94%) initiated TPT. In Brazil, the completion of assessment was lower (range 73%-79%) compared to Benin (95%-98%) (Table).

In Brazil, the lowest proportion initiating TPT was in strategy 3 (74%) and the highest in strategy 2 (82%). In Benin, TPT initiation was above 95% in all strategies.

	Strategy 1	Strategy 2	Strategy 3
<b>Brazil</b>			
Completed assessment for TB infection and TB disease	81/102 (79%)	79/101 (78%)	83/114 (73%)
Participants eligible for TPT initiation*	48/81 (59%)	33/79 (42%)	76/83 (92%)
Started TPT within three months of randomization	37/48 (77%)	27/33 (82%)	56/76 (74%)
<b>Benin</b>			
Completed assessment for TB infection and TB disease	353/373 (95%)	471/482 (98%)	411/418 (98%)
Participants eligible for TPT initiation*	118/353 (33%)	166/471(35%)	399/411 (97%)
Started TPT within three months of randomization	114/118 (96%)	160/166 (96%)	391/399 (98%)

Notes: \*In strategies one and two, TPT was recommended if the participant had a TST positive and TB disease was excluded. In strategy three, TPT was recommended after the exclusion of TB disease

Table.

**Conclusions:** Assessment completion and TPT initiation proportions were higher than reported in routine conditions in low-income settings, regardless of the strategy. Benin had higher rates of complete assessment of HHC and TPT initiation than Brazil. Our results suggest that testing to detect TB infection and exclude TB disease is not a substantial barrier to TPT initiation.

### OA53-620-17 The burden of chronic conditions associated with increased risk of TB among members of TB-affected households in southern Africa

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**Background:** Tuberculosis (TB)-affected communities are often highly vulnerable, with social, economic, and biological factors increasing risk of both TB and other chronic conditions, whilst impeding healthcare access. The prevalence of chronic conditions among TB household contacts in Africa is unknown.

**Design/Methods:** Within a TB household contact cohort study (ERASE-TB), we offered screening for HIV, diabetes (HbA1c), underweight (body mass index), lung impairment (spirometry), and alcohol use disorder (AUDIT-C) at three sites in southern Africa (Maputo, Mozambique; Mbeya, Tanzania; Harare, Zimbabwe).

Missing data for screening tests were handled by multiple imputation by chained equations and prevalence estimates calculated in the multiply imputed dataset.

**Results:** Overall, 2101 TB household members have been enrolled (2021-2023); 2094 with complete demographic data were included in this analysis.

A quarter were adolescents (10–17 years), median age was 27 (IQR 17–42 years) and 62% were women (reflecting that most of the people with TB were men). Six percent had a previous history of TB. Less than 1% had co-prevalent TB.

Prevalence of HIV was 16% (9% newly diagnosed through screening) and prevalence of elevated HbA1c was 9% (86% newly diagnosed). 22% of people had lung impairment (mostly a restrictive pattern).

Alcohol use disorder was more common among men (20% vs. 9% of women;  $p < 0.001$ ). 7% of people were underweight. Risk factors varied by age, sex, and study site.

Overall, 62% of participants had at least one potentially modifiable TB risk factor identified through screening.

	Overall (N=2094)	Mozambique (n=710)	Tanzania (n=685)	Zimbabwe (n=699)
HIV	16% (14–18%)	17% (14–20%)	14% (11–16%)	16% (13–19%)
Elevated HbA1c	8.6% (7.0–10%)	6.1% (4.1–8.2%)	9.4% (6.6–12%)	6.7% (4.5–8.8%)
Underweight	6.6% (5.5–7.7%)	7.7% (5.8–9.7%)	5.9% (4.1–7.6%)	6.4% (4.6–8.3%)
Lung impairment	22% (19–24%)	25% (21–29%)	13% (9.7–16%)	26% (22–30%)
AUDIT-C+	13% (11–14%)	13% (10–15%)	13% (10–15%)	13% (11–16%)
Current smoker	5.1% (4.2–6.1%)	2.8% (1.6–4.0%)	3.7% (2.3–5.1%)	8.9% (6.8–11%)

*Table: Prevalence of chronic conditions and selected TB risk factors among members of TB-affected households aged ≥10 years in southern Africa (N=2094). Presented as prevalence estimate (95% confidence interval).*

*Abbreviations: AUDIT-C = Alcohol Use Disorder Identification Test (3 question version). Underweight defined as body mass index <18.5kg/m<sup>2</sup>. Lung impairment defined as any spirometric impairment (against Global Lung Initiative ‘other’ reference standard).*

**Conclusions:** These findings illustrate a high burden of chronic conditions among members of TB affected households. Whilst most people with HIV were diagnosed and on treatment, most other conditions were previously unrecognised and untreated. Inclusion of strategies to identify and address these factors within TB screening programmes may reduce TB incidence and improve the overall health of this vulnerable community.

### OA53-621-17 Integrating interferon-gamma release assay testing with routine CD4 and viral load monitoring to scale-up TB preventive therapy for people with HIV in Brazil: the PREVINE-TB study

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**Background:** In Brazil, annual screening for tuberculosis infection (TBI) is recommended for people with HIV (PWH) with CD4>350 cells/mL to guide tuberculosis preventive therapy (TPT). However, challenges with tuberculin skin testing (TST)—the most used tool to assess TBI—have resulted in undertesting.

We hypothesized that a strategy pairing screening via interferon-gamma release assay (IGRA) with routine CD4 and/or viral load (VL) monitoring could improve TBI screening and TPT uptake.

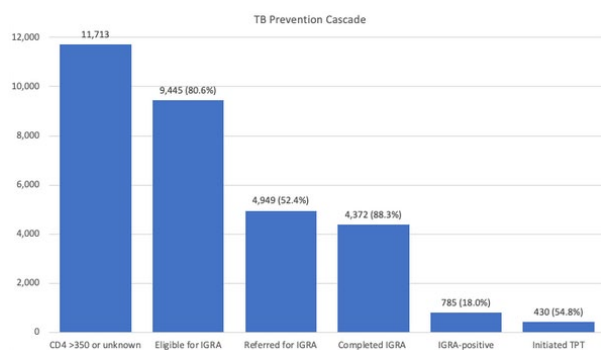
**Design/Methods:** PREVINE-TB was conducted at clinics in Rio de Janeiro, Manaus, and São Paulo, Brazil. We integrated an IGRA assay (QuantiFERON-TB Gold Plus) at routine CD4/VL blood draws.

We consented and enrolled PWH presenting for routine care who were eligible for TBI evaluation according to Brazilian national guidelines (CD4>350; no negative TST within 12-months; no history of a positive TST, TPT, or TB treatment).

Clinicians were trained to order IGRA for asymptomatic PWH referred for routine CD4 and/or VL testing. We assessed the TBI cascade following IGRA implementation: numbers and proportions eligible for TBI screening, referred for IGRA, IGRA performed, IGRA-positive, and initiating TPT.

**Results:** From 06/2020-10/2022, 11,713 PWH with CD4>350 presented for routine HIV care. Of these, 2,268 (19%) were not eligible for TBI evaluation (268 [19%] TST-negative within 12-months, 1,301 [57%] previous TB, 523 [23%] previous TPT) and 4,494 (38%) were not referred for IGRA.

Among 4,949 referred, 4,372 (88%) completed IGRA testing. Of these, 785 (18%) were IGRA-positive (392/1,254 [31%] in Rio, 151/924 [16%] in Manaus, 240/2,194 [11%] in São Paulo), of whom 430 (55%) initiated TPT.



**Conclusions:** Integration of IGRA in routine HIV care was feasible in Brazil, and prevalence of TBI was high. Referral for TBI screening and TPT remains a challenge; nevertheless, IGRA successfully identified many PWH with TBI who would benefit from TPT. Continued efforts are needed to further scale-up TBI screening and TPT in Brazil.

## OA53-622-17 QIAreach QuantiFERON-TB and QuantiFERON-TB Gold Plus concordance to detect TB infection among people living with HIV in Brazil: a prospective study

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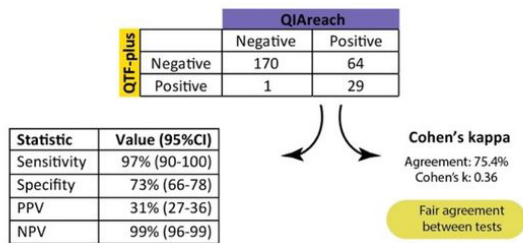
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**Background:** Testing for tuberculosis infection (TBI) should be performed in individuals with an increased risk of developing active TB. QIAreach QuantiFERON-TB (QIAreach), a novel Interferon Gamma Release Assay (IGRA) assay that can be deployed in resource-limited settings, has been shown to have high accuracy and concordance with QuantiFERON-TB Gold Plus (QTF-Plus) in non-immunosuppressed persons. However, the performance of QIAreach in people living with HIV (PLHIV) remains undetermined. We assessed the concordance between QIAreach and QTF-Plus in a high TB/HIV burden setting.

**Design/Methods:** We prospectively assessed QIAreach in an HIV reference center in Manaus, Brazil. After excluding active TB and other opportunistic infections, we collected blood samples from PLHIV ≥18 years with CD4 count >350 cells/mm<sup>3</sup> or unknown. Samples were processed concurrently for each assay following the manufacturer's instructions. We analyzed the diagnostic accuracy (sensitivity, specificity, predictive values) of QIAreach in reference to QTF-plus and used Cohen's kappa coefficient to determine the degree of agreement between the tests. A logistic regression model was performed to identify factors potentially associated with increased odds of false positive QIAreach results.

**Results:** Among 268 study participants, the median age was 39 years (IQR: 29-48 years), 70% were male, and the median CD4 count was 537 cells/mm<sup>3</sup> (IQR: 362-714). Compared to QTF-Plus, QIAreach sensitivity, specificity, and NPV (95% CI) were 0.97 (0.90-1.00), 0.73 (0.66-0.78), and 0.99 (0.96-0.99), respectively. The proportion of divergent tests was 17.9% and agreement using the Kappa statistic was 75.4%. Sex, age, alcohol, tobacco use, contact with a confirmed TB case, CD4, and detected viral load were not associated with increased odds of a false-positive result.



*Figure. Diagnostic test evaluation. Upper panel: contingency table with the rate of positive and negative results for each test. Bottom left panel: sensitivity and specificity measurements, as well as positive predictive value (PPV) and negative predictive value (NPV). Bottom right panel: Cohen's kappa statistics.*

**Conclusions:** In PLHIV, QIAreach had high sensitivity and negative predictive value. However, concordance with QTF-Plus was suboptimal, with increased false-positive results. Due to high NPV, the role of QIAreach as a Point-of-Care triage test for TBI requires further determination.

## SHORT ORAL ABSTRACT SESSION (OA)

### SOA16 Achieving results through community interventions

#### SOA16-919-17 Gender-responsive TB care: Review of a systematic male-targeted screening initiative in Lagos State, Nigeria

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**Background and challenges to implementation:** Previous research has identified that a lower proportion of men are reached during active case-finding despite TB being commoner in them. This underscores the need to have activities that would specifically target men in a bid to find all missing people with TB. This is part of the USAID funded TB-LON 3 project being implemented in Lagos State.

**Intervention or response:** A ranking of all Local Government Areas (LGAs) in Lagos State was done and top 9 high TB burden LGAs were purposively selected for this initiative.

Hubs where higher number of men are most likely to be found were mapped in each selected LGA. This included transportation hubs, beer parlors, sports bars, meetings of male-dominated trade unions/associations, brothels, drug addicts' hide-outs e.t.c. Females present were screened and recorded separately.

The TB screening was integrated with HIV counseling and testing and conducted during peak period of human traffic to the identified places. WHO 4-symptom checklist and CAD enabled ultra-portable digital X-ray (where available) was used to identify people presumed to have TB while their sputum samples were collected and analyzed with the GeneXpert Rif Assay afterwards.

**Results/Impact:** The results presented are over an 8-month period between July 2022-February 2023. A total of 3,372 adult males were screened with a presumptive TB and TB yield of 14% and 15% respectively was recorded. This resulted in number needed to screen

(NNS) and number needed to test (NNT) of 50 and 7 respectively. These indicators are way higher for the general populace at 254 and 10 respectively on the same TB-LON 3 project.

**Conclusions:** Deliberate efforts to target men would ensure that no one is left behind in the search for missing TB cases. This provides a useful guide especially in resource constrained settings where it important to target activities towards areas of prospective high yield.

#### SOA16-920-17 Engaging with the community for TB response: experience from a tribal district in India

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**Background and challenges to implementation:** World TB Report 2020 show 10.4% of TB notification are from tribal communities. Prevalence is 2.7 times higher than national average (256/100,000), possibly due to remote location, inaccessible to health-facility and lack of diagnostic-facility. A focused intervention strategy is essential to tackle the multidimensional issues among the tribals. This paper highlights the role of community-structures (CS) in TB-response.

**Intervention or response:** USAID supported Breaking-The-Barriers (BTB) project implemented in three-districts of Assam viz. Baksa, Dibrugarh and Kamrup-Metropolitan since October'21 through community-engagement approach. Engaging with CS play a catalytic role for creating-awareness, mitigating-stigma, promoting positive-health-seeking behaviour and enhanced-case-detection. Mushalpur, a BTB intervention TB-unit in Baksa, with the highest notification in the district since 2019, peaking its notification in 2022 (388) (31% increase from 295 in 2021). In Mushalpur, 72 intervention sites were identified covering 55,625 vulnerable population. Through a collective effort of trained project-staff, 80 CSs (Self-Help-Groups, Village-Health-Sanitation-and-Nutrition-Committee, Senior-Citizen-Club, Youth-Organisation, Labour-Union etc) were identified. Key leaders (83) from the CS were trained through perspective building workshops (3) and regu-



lar handholding meetings (118) to empower them for conducting TB-response activities viz. awareness-campaigns, advocacy-meeting, health-campaigns, screening, referrals for tests, and supporting persons with TB (PwTB) for non-medical and other needs.

**Results/Impact:** During Jan-Dec'22, participation of CS in TB-response activities increases. 59 CS conducted 557 awareness-camps, 17 health-camps, screened 81787 people, referred 1403 presumptive for test, and 90% tested with 7% positivity-rate. The community-engagement approach contributes to 23% of total TU-notification and 70% of vulnerable-population mapped. Findings also show 86% of the diagnosed PwTB were tested on the same-day and 98% initiated-treatment within 7 days.

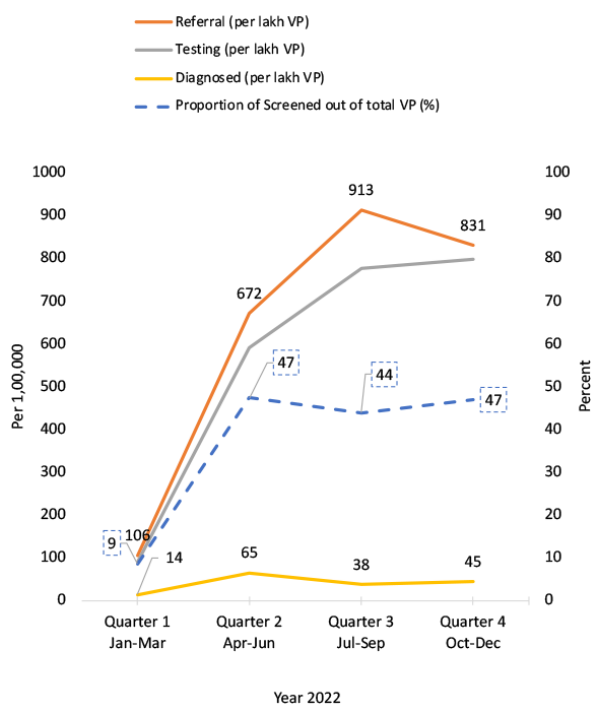


Figure 1. Trend in screening, referral, testing and diagnosed in Mushalpur TU.

**Conclusions:** Community-engagement approach in tribals have contributed immensely in TB-response activity. These learnings reinforce, need for a wider uptake of community centric models in India's national TB programs to reach the missing millions and achieve the goal to 'End TB' by 2025.

## SOA16-921-17 Engaging youth to #END\_TB to encourage desired social and behavioural change regarding TB in the Kyrgyz Republic

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**Background and challenges to implementation:** Kyrgyzstan is one of 18 high-priority countries for tuberculosis (TB) in the WHO European Region. Around 53% of people with TB are aged 18 to 44, and there are many cases of TB among adolescents. Formative research conducted by the USAID Cure Tuberculosis project, led by JSI, shows a low level of knowledge about TB among the young, causing problems with health-seeking behavior, including in TB.

**Intervention or response:** We developed a youth engagement approach to inform young people about TB on a peer-to-peer basis and promote health-conscious behavior among the young population.

We engaged student movements and designed targeted training and tools to build the capacity of young volunteers in TB basic information and behavior change communication.

**Results/Impact:** From February 2022 till March 2023, we trained 183 journalism and medical student volunteers who reached over 7,000 university and high school students in areas of high concentration of migrants and socially disadvantaged groups in the cities of Bishkek and Osh, and Chui oblast with information about TB.

**Conclusions:** Engaging and reaching the young generation with key TB messages is critical to improving TB care and encouraging desired social and behavior change to #END\_TB.

The youth engagement approach helps young people develop leadership and communication skills, build sustainable knowledge about TB, and contribute to reducing stigma and discrimination and strengthening health-conscious behavior in the population.

### SOA16-922-17 TB active case-finding in communities: Lessons from an integrated community engagement approach

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**Background and challenges to implementation:** The annual incidence of TB in Malawi in 2021 is estimated at 132 per 100,000. Low awareness about TB and its associated risk in the community contributes to low health-care-seeking behaviour and TB detection gaps. DAPP Malawi is implementing the USAID-supported “Mobilizing Local Entities to Improve the Quality, Scale and Sustainability of the TB Response in Malawi,” (Project QSS) which engages a range of community stakeholders to increase TB awareness and supports active TB case finding.

**Intervention or response:** DAPP Malawi employs an integrated approach to engage communities in active case finding. Through Project QSS, DAPP Malawi built the capacity of Community Health Workers (CHW), Community Health Volunteers (CHVs), Community-Based Organizations (CBOs), local and religious leaders, and youth clubs to perform different but complementary roles. DAPP CHWs mentor community stakeholders on TB messaging, systematic screening, sample collection, psychosocial counselling, stigma reduction and contact tracing. Volunteers who manage Community Sputum Collection Points (CSPCs) conduct systematic TB screening, sputum sample collection and transportation, referrals, and contact tracing. CBOs, youth clubs, mother groups, and local and religious leaders complement CHW and CHV efforts by disseminating TB messages and referring people to either CSPCs or the nearest health facility. Local and religious leaders act as influencers to offset misinformation and promote community TB screening services.

**Results/Impact:** Between January and December 2022, 320,694 people were reached in the communities served by CSPCs volunteers and 52.9% (169,771) were screened for TB; 7.4% (12,557) had symptoms presumptive and; 1.9% (233) were diagnosed with TB and notified compared to only 36 TB cases in 2021.

**Conclusions:** The integrated and coordinated community-based approach with strong links to local health facilities increased TB awareness, facilitated active case finding and increased case detection by over 6-fold in 2022 compared to 2021.

### SOA16-923-17 Issues and challenges of early diagnosis of TB in children aged 0-14 years in Cameroon: The experience of the “Women’s Voices” campaign

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**Background and challenges to implementation:** In 2019 in Cameroon, out of 6,000 children expected to be suspected of having TB, only 1,261 (21%) were identified, a detection gap of 78% according to the WHO (WHO Report, 2020).

In order to contribute to the improvement of TB detection in this particularly vulnerable group, the NGO, For Impacts in Social Health, launched in 2020 the advocacy Campaign “Women’s voices” on the issue of TB in children in Cameroon. The implementation of this campaign was confronted with restrictions due to the COVID-19 pandemic.

**Intervention or response:** Ten “Women Champions” were identified and trained to carry out advocacy with the support of Allies. This was done through communication campaigns to saturate the public space and advocacy meetings organised with officials and Technical Departments of the Ministry of Public Health.

**Results/Impact:** A total of 1100 women joined the “Women’s Voices” Campaign. 09 key messages were disseminated, on the targets of the national TB strategy for children and the commitments of the Political Declaration of the 2018 UN High Level Meeting on TB. 21 media outlets were used to enhance the advocacy campaign. This campaign helped to enrich the TB modules in the national IMNCI guides. The “Women’s Voices” advocacy campaign contributed to making paediatric TB a priority in the national TB response.

**Conclusions:** The “Women’s Voices” advocacy campaign on the issue of tuberculosis among children in Cameroon has made it possible to revise the IMNCI guides by integrating specific modules on paediatric tuberculosis.

For a better appropriation of the systematic screening of TB in this target group, it is recommended to Disseminate the revised guides and to train health care providers to look for signs and symptoms of TB.

## SOA16-924-17 Bolstering the capacity of the TB community to support people with TB for improved treatment adherence and treatment outcomes

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**Background and challenges to implementation:** In Kazakhstan, COVID-19 pandemic restrictions made it harder for people to access TB services, leading to an increase in drug-resistant TB (DR-TB) cases. TB treatment coverage fell from 100% in 2010 to 74% in 2020 (Global Fund Results Report 2022).

As a result, the already-crucial role of non-governmental organizations (NGO) and community-based groups in linking vulnerable populations (VP) to health services has gained additional importance.

**Intervention or response:** To help Kazakhstan accelerate progress toward ending TB, the USAID Eliminating TB in Central Asia Activity collaborated with the National TB Program (NTP) to develop a peer counseling training course for community groups and peer counselors (PC). In 2021, 10 NGO social workers participated in the “First Among Peers” training course and learned how to reach and support VP and connect them with health services and how to facilitate TB peer support groups.

After completing the course, the trainees led TB support groups and provided peer counseling, psychological and social support to PWTB.

**Results/Impact:** Over 12 months, PCs provided support to a total of 180 PWTB who were experiencing difficulty in adhering to treatment. PCs helped 20 PWTB return to treatment; 11 register for disability and receive benefits; 15 get registered at their place of residence; and 5 restore their identity documents.

Of the 180 PWTB peer support group attendees, none have stopped treatment and 11 have already successfully completed treatment. In 2023, the trained community leaders organized a new NGO and won a Global Fund grant to continue providing services to VP.

**Conclusions:** These innovative approach to bolster the capacity and boost involvement of the TB community contributed to the creation of TB support groups and a new NGO, have strengthened the country’s DR-TB response, and created a sustainable resource within the TB community for future work.

## SOA16-925-17 OneImpact: Improving TB treatment and care services using community-led monitoring

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**Background and challenges to implementation:** Putting people at the heart of the TB response is critical for ending TB. Every year, Cambodia’s National TB Program (NTP) reports missed TB cases that went undiagnosed or lost from the health system because of barriers to health services, human rights violations, stigma, and a lack of access to support services.

**Intervention or response:** The CLM-OneImpact application is a digitalized solution tool that empowers people affected by TB to access TB information, human rights, key messages from TB survivors and champions, and TB care and support services. It also provides them with accurate and actionable information, and links with nearby health facilities, peer support groups (PSG), and health service providers.

KHANA has introduced the CLM-OneImpact to the NTP and implemented it in five selected operational health districts in Cambodia with a rising TB burden. The PSG leaders were recruited and trained to facilitate the implementation of CLM-OneImpact at the target sites.

When barriers were reported by people with TB using OneImpact App, the PSG leaders were the first respondents to validate and resolve cases on drug-side effects, TB stigma, quality of services, treatment adherence and support, and social support services.

**Results/Impact:** As of 31 December 2022, 918 cases have been reported through the CLM-OneImpact. Amongst the cases, 419 were barriers to TB services, 185 were barriers to TB support services, 130 were barriers related the human rights violation, and 184 were barriers arising from TB Stigma. The CLM-OneImpact data helps to inform local health services providers, NTP, and CCC in ways to improve programs and policies relating to TB care and treatment services.

**Conclusions:** CLM-OneImpact has enabled community-driven responses and allowed the users of TB services to input, gather, and use the information on services provision to collect feedback on barriers. The data will help improve TB services’ quality, effectiveness, equity, and efficiency.

## SOA16-926-17 Multisectoral engagement and accountability to end TB in the Eastern Europe and Central Asia Region: A civil society and community perspective

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**Background:** Multi-drug resistant TB remains public health crisis in EECA region. Civil society and community (CSO/CO) engagement has been crucial to tackling the neglected TB social determinants and supporting multisectoral actions.

However, efforts to meaningfully engage CSOs, TB affected communities remain nascent in most high-incidence settings. Drawing on World Health Organization multi-sectoral accountability framework to accelerate progress to end TB by 2030, we undertook a baseline assessment of approaches adopted and challenges in the EECA region.

**Design/Methods:** A mixed methods design was used for the study. Data have been virtually collected between January 2021 to June 2021 via a standardized survey, in-depth interviews, and country-specific focus group discussions: 53 organizations completed the survey, 31 organizations' leads participated in interviews. Participants included 24 TB survivors and representatives of 35 diverse CSOs/COs working with national TB programs of five countries: Belarus, Kazakhstan, Moldova, Tajikistan, Ukraine. Organizations ranged from large NGOs to grass-root initiatives. Quantitative data were analyzed using descriptive statistics and triangulated with themes derived from qualitative data.

**Results:** Fundamental elements to "meaningful engagement" in TB response include a favorable environment for CSOs/COs to voice suggestions and concerns on barriers in access to care for people they serve; seats at the decision-making table, beginning from the conceptualization phase and with a tangible impact on the decisions; and sustainable public financing to support operational activities. Multisectoral collaboration activities have been closely linked to Country Coordination

Mechanisms, which are key platforms engaged with the grants from the GF. The hierarchy in accountability actions of the CSOs/COs have been unpacked.

**Conclusions:** Findings of this study lend voice to CSOs/COs' perspectives in EECA region about integral elements of their meaningful engagement in the TB response, accountability; and needed conditions to ensure their financial, operational and programmatic sustainability in multisectoral collaboration.

## SOA16-927-17 Community-led monitoring for equitable health service delivery in Tanzania

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**Background and challenges to implementation:** The COVID-19 pandemic greatly hampered TB treatment services due to requirements of social distancing and reallocation of staff. TB patients also experienced increased stigma and discrimination owing to similarity of symptoms between the two diseases. Consequently, a set of new challenges to TB patients on treatment, especially in the context of Community, Rights and Gender (CRG), were realized.

As a result, through Community-Led Monitoring approaches were implemented to overcome gender and human rights related barriers to TB care in Tanzania.

**Intervention or response:** MKUTA, in collaboration with the Stop TB partnership, investigated the challenges facing TB patients through CLM using the OneImpact digital application in the context of CRG.

**Results/Impact:** Thirty Community Health Volunteers (CHVs) were trained on basic CRG concepts and using OneImpact mobile application to collect qualitative data using tablets from 2000 patients (1100 male, 900 female), resulting in a total of 4000 TB challenges were documented. The most common reported challenges were stigma (60%), human rights violations such as breach of confidentiality (20%), and lack of treatment support (10%). The most common form of stigma that was reported was self-stigma (59%) and stigma from family members (44%), whereas the most common treatment support challenge was a need for nutrition support (45%).

**Conclusions:** This project highlighted the need for increased advocacy to stakeholders and communities at large on TB-related stigma so as to reduce stigma from

the community and patients themselves. Moreover, experience from the project implies applicability of the digital approach in health care across all communicable and non-communicable disease spectrum. The approach calls for the health system decision makers to routinely seek feedback from service recipients to identify gaps in service delivery and implement corrective measures.

### SOA16-928-17 Preventing silicosis in the stone mines of the Thar Desert in India

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**Background and challenges to implementation:** State of Rajasthan is the second biggest resource in mineral wealth in India after Bihar and large numbers of mines of various minerals exist in the state. An estimate suggests that nearly 2 million people are engaged in the industry of mining in the state. Western part of the state is very famous for its sand stone and marble stone mines. Mineworkers working in these stone mines have a long history of difficult work conditions and poor health due to inadequate health safety arrangements. Caused by consistent inhalation of dust particles, mineworkers suffer with occupational lung diseases, particularly with Silicosis.

A large number of mineworkers suffer with this disease and die at premature ages causing great losses to their families.

**Intervention or response:** In past, very little interventions have been made in the region to prevent this problem. GRAVIS, an NGO working in the region, has initiated the process on advocacy on health safety of mineworkers in the region.

The organization is engaged in organizing health-screening services for the mineworkers, in promoting use of respiratory masks and wet drilling, facilitating referrals of patients to the hospital, advocate with the government and mine owners to ensure safety and organize trainings on silicosis prevention and control.

Research on occupational lung diseases in the region and develop preventive measures is also an important part of GRAVIS work. GRAVIS' work reaches over 200,000 mineworkers.

**Results/Impact:** As a result of GRAVIS' interventions, there is a greater awareness generated on silicosis. A large number of mineworkers use masks and work under safer conditions. Wet drilling in many mines has started to reduce the air pollution and health screening activities have started.

**Conclusions:** Silicosis is major public health problem in India and in many other settings where stone mining is prevalent. There is a need of a comprehensive approach to combat silicosis.

### SOA17 Imaging for a TB free world

#### SOA17-929-17 Impact of artificial intelligence on chest radiography reporting: a multi-reader, multi-centre study of automatic detection of multiple abnormalities and generation of a diagnostic reporting system

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**Background:** Radiology report writing is a time-consuming task that also requires experience from the radiologists. This study developed and tested a novel AI system (MOM-ClaSeg) to assess its performance in assisting radiologists to automatically detect multiple abnormalities and generate diagnostic report on chest x-ray (CXR).

**Design/Methods:** MOM-ClaSeg has been developed by applying augmented Mask-R-CNN based Generative Pre-trained Text content generation networks. From 5/22/2022 to 7/22/2022 and 7/22/2022 to 9/22/2022, over 36,000 PA/AP-CXR from 12 hospitals were retrospectively collected and used as experiment group (G2) and control group (G1), respectively.

A group of 11 radiologists were involved in this study: 6 junior radiologists (5~10 yr-experience) generating initial diagnostic reports, 2 senior radiologists (>15 yr-experience) reviewing initial report from either junior radiologist (G1) or MOM-ClaSeg (G2) to generate final reports, and 3 consensus expert radiologists (>25 yr-experience) as gold standard to evaluate the accuracy of final reports.

Comparison of (G1) double reading, where two radiologists interpret CXR to generate a final report, and (G1) single reading, where single radiologist generates final reports based on MOM-ClaSeg generated reports, were conducted to evaluate senior radiologist's performance.

**Results:** Compared with double reading, accuracy and sensitivity of single reading with MOM-ClaSeg have increased by 1.49% (from 96.60% to 98.09%,  $P<0.001$ ) and 10.95% (from 87.07% to 98.02%,  $P<0.001$ ), respectively. Specificity has increased by 0.22% without statistical significance (from 97.89% to 98.10%,  $P=0.255$ ). Total reading time of single reading using AI has reduced by 213.70% (from 8.56s to 17.09s).

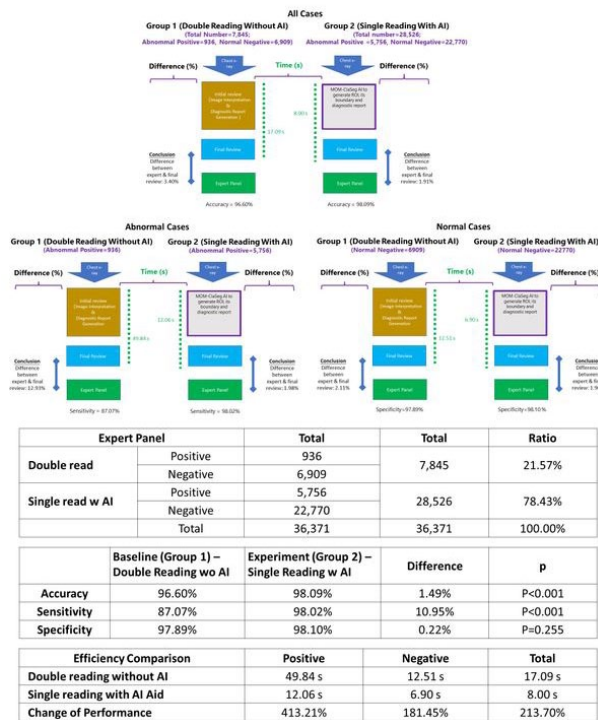


Figure 1. The image review comparison testing flowchart (upper) and results of double reading without AI aid vs. single reading with AI aid (lower).

**Conclusions:** This MRMC study shows that a multi-disease detection and report generation AI can potentially serve as the first reader to generate the initial diagnostic report and radiologist only reviews its diagnostic reports to make final decision. It also shows that single reading with AI can reach much higher accuracy and efficiency than double reading by two radiologists.

### SOA17-930-17 Novel, non-18F-FDG tracers used in positron emission tomography-computed tomography studies of TB

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**Background:** Positron Emission Tomography coupled with computed tomography (PET-CT) has the potential to revolutionise tuberculosis research. It provides a three-dimensional view of the structural and spatial distribution of tuberculosis and functional data on changes in metabolism, drug penetration and immune-control within tuberculous lesions. Here we summarise alter-

native labels to 18F-FDG that could change our understanding of tuberculosis and could fuel more effective drug development.

**Design/Methods:** We identified articles published in the scientific and medical literature from 1 January 1979 through 31 December 2022 that described the use of novel labels in PET to evaluate tuberculosis in animal models and in human studies. Articles in English were included. PubMed was searched using the terms “tuberculosis,” “PET,” “novel label”, “hypoxia imaging”, “molecular imaging”, “noninvasive imaging.”

Bibliographies of the articles were reviewed for additional relevant publications. For this review, we included studies where PET was coupled with magnetic resonance imaging (MRI) as well as CT, and excluded all single person case reports.

Group	Label	Model	Findings
Radio-labelled TB drugs	<sup>68</sup> Ga-nitroimidazole	Human	Localisation and quantification of hypoxic lesions in lungs. Pretomanid shown to have excellent penetration in brain parenchyma and the CSF.
	<sup>18</sup> F-Pretomanid	C3HeB/FeJ mice	
		Rabbit	
	<sup>11</sup> C-Rifampicin	Human	Description of the temporal and spatial evolution of RHZ. Necrotic lung tissue, cavity walls and brain lesions have low R exposure. Ability of drugs to cross blood brain barrier decreases in order of Z > H > R. Poor correlation between rifampicin concentrations in CSF and brain lesions. 2-F-Isoniazid rapidly accumulates at sites of infection including necrotic lesions. 5-F-PZA is not a suitable surrogate label of PZA distribution.
	<sup>11</sup> C-Isoniazid	Rabbit	
Repurposed from cancer	<sup>68</sup> Ga-DOTATOC	Human	Higher relative uptake of <sup>68</sup> Ga-DOTATOC in lymph nodes compared to <sup>18</sup> F-FDG. <sup>18</sup> F-FDG has increased sensitivity over <sup>68</sup> Ga-DOTANOC in the detection of tuberculous lesions
	<sup>68</sup> Ga-Citrate	Human	Ability to distinguish between active and inactive tuberculosis disease, as well as identify extrapulmonary sites of disease, and monitored response to treatment. May be particularly useful for defining intracranial pathology.
	<sup>64</sup> Cu-ATSM	C3HeB/FeJ mice	<sup>64</sup> Cu-ATSM can detect hypoxic tuberculous lesions that develop in C3HeB/FeJ mice. Treatment with a TNF inhibitor reduces [ <sup>64</sup> Cu]-ATSM uptake in tuberculous lesions, suggesting that TNF inhibition disrupts granuloma organisation to increase oxygen permeability.
	<sup>11</sup> C-methionine	Human	<sup>11</sup> C-methionine was superior to <sup>18</sup> F-FDG in the delineation of intracranial tuberculomas and may be more sensitive in assessing therapeutic response.
Immune cell receptor labels	<sup>11</sup> C-JNJ-28312141	C3HeB/FeJ mice	Label binds to CSF1R+ macrophages and delineated granulomas in a mouse model
	<sup>64</sup> Cu-FLFLF <sup>64</sup> Cu-LLP2A	Macaques	Correlation with macrophage and neutrophil abundance in granulomas but <sup>64</sup> Cu-FLFLF was less-specific for neutrophils than anticipated. <sup>64</sup> Cu-LLP2A uptake was related to macrophages and T cells activity in granulomas. Dynamic changes in affinity for <sup>64</sup> Cu-LLP2A relative to <sup>18</sup> F-FDG uptake over 12 weeks of infection was reflective of the dynamic changes in cellular architecture and metabolism within granulomas.
	<sup>125</sup> I-DPA-713 in SPECT	Human	<sup>125</sup> I-DPA-713-SPECT a macrophage-specific radioligand has improved signal-to-noise ratio compared to FDG-PET. <sup>125</sup> I-DPA-713-SPECT discriminated between bactericidal activity of (RHZ Vs. Bedaquiline-Z-Clotazimine) as early 4 weeks into treatment. <sup>125</sup> I-DPA-713 demonstrated high signal intensity in TB lesions on PET-CT in humans.
	<sup>124</sup> I-DPA-713 in PET-CT	C3HeB/FeJ mice BALB/c mice	

Table.

**Results:** Alternative labels to 18F-FDG hold substantial promise. These include three major groups; radio-labelled tuberculosis drugs, radiopharmaceuticals repurposed from cancer research and immune cell receptor labels. Studies of radio-labelled drugs have characterised the temporal and spatial distribution of standard drugs and newer agents, in particular their ability to penetrate into necrotic, hypoxic lesions and intracranial lesions. Labels based on immune cell receptors characterised the dynamic immunological changes within granulomas. Of particular interest, a macrophage-specific radioligand discriminated between the bactericidal activity of a highly active regimen from standard tuberculosis therapy, from as early as 4 weeks into treatment. Table 1 summarises non-18F-FDG tracers investigated in TB research.

**Conclusions:** The use of labels other than 18F-FDG has increased our understanding of drug distribution, host-pathogen interactions in tuberculosis. It has the potential to transform PET-CT's diagnostic and predictive capacity as a biomarker in tuberculosis research.

### SOA17-931-17 Iterative threshold score calibration for statistically rigorous, operationally unobtrusive threshold selection for artificial intelligence systems

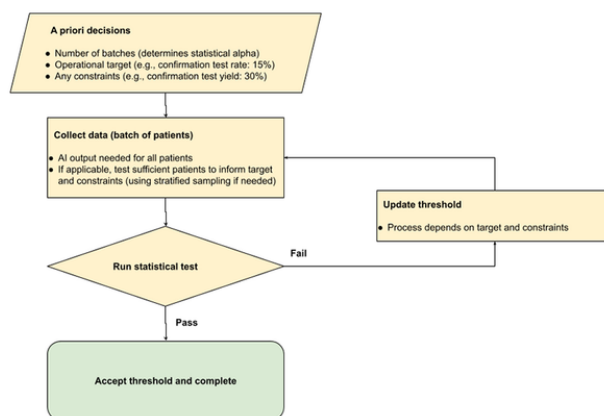
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**Background:** Artificial intelligence (AI) algorithms have been recommended to triage chest X-rays for pulmonary tuberculosis (TB) screening. These AI systems output a continuous range of numerical scores [0,100] requiring thresholding for binary (yes/no) classification. Optimal thresholds vary based on factors such as demographics, TB and HIV prevalence, and clinical characteristics. Several AI systems permit a user-defined threshold, both empowering and challenging, requiring balance sensitivity and specificity themselves. Users often rely on default thresholds or costly trials for optimization.

**Design/Methods:** We developed a cost-efficient method, Iterative Threshold Score Calibration (ITSC) that statistically adjusts the threshold over a user-defined number of iterations (batches of people screened) to achieve an operational target (e.g., confirmation test rate) within defined constraints (e.g., confirmation test yield). Evaluations after each iteration determine if the threshold meets the desired target, and updates the threshold if not. ITSC enables AI systems to triage TB diagnosis during calibration and can be customized for multiple sites with unique characteristics. In simulations, we compared ITSC to calibrating the AI threshold to a prospective calibration trial, where all patients re-

ceive confirmation tests. We simulated different cohorts using a population of over 20,000 unique retrospective TB screening images, artificially constructed to have an assumed TB prevalence between 1-10%.



**Results:** We observed that ITSC was able to optimize the threshold while maintaining the same level of type 1 error and consuming only 20-40% of the negative confirmation tests needed by a prospective confirmation trial.

**Conclusions:** We present a statistically rigorous approach to iteratively testing and optimizing the threshold for an AI model, reducing the costs of deployment while improving screening performance. This approach may be applicable in other non-TB screening settings as well.

### SOA17-932-17 Portable digital X-ray and dynamics in active TB case-finding

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**Background and challenges to implementation:** According to WHO, in 2021, an estimated 10.6 million people fell ill with Tuberculosis (TB) worldwide. Nigeria is ranked sixth nation with the highest number of TB cases globally. The country contributed 4.4 percent to the total TB cases globally. The high burden in Nigeria might be largely due to diagnosis gap, hence, the introduction of portable digital x-ray (PDX) with computer aided detection (CAD); an innovative and sensitive tool by KNCV Nigeria to help close the TB detection, notification, and treatment gaps.

**Intervention or response:** The PDX with CAD was used for active TB case finding in rural communities, urban slums, hard-to-reach areas, health, and correctional facilities between January 2022 to December 2022. PDX was deployed to 20 out of the 34 LGAs in Katsina state.

Advocacy and mobilization were done to screen consenting individuals from 4 years and above, with presumptive TB identified using artificial intelligence (AI) and TB symptoms. On-the-spot sputum samples were collected in sputum cups and transported in cold packs to the laboratory and tested using Genexpert or truant machines. TB cases were diagnosed from the presumptive TB and placed on treatment via the local government TB focal person.

**Results/Impact:** The PDX with CAD screened a total of 14,231 clients, identified and tested 926 presumptive and diagnosed 342 TB cases; the number needed to test (NNT) was 3, and number needed to screen (NNS 41). These patients were diagnosed mostly in the communities as they were not too ill to have sort help in the hospitals, they would have remained as reservoir for TB for long if not for PDX intervention.

**Conclusions:** This result have shown the contribution of 1 PDX unit in closing the TB diagnostic gap in Katsina state and also revealed the need for upscale of PDX intervention within the state as LGA coverage stands only at 58% in 1 year.

### SOA17-933-17 The added value of computer-aided detection software for external quality assessment at a private clinic in Viet Nam

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**Background:** The WHO recently recommended the use of computer-aided detection (CAD) software as a radiologist replacement during TB screening. However, using CAD software in conjunction with radiologists is likely to be a more acceptable chest X-ray (CXR) interpretation scenario in settings where radiology services already exist.

**Design/Methods:** We assessed the added value of using qXR v3 CAD software (Qure.ai, India) as an external quality assessment (EQA) check on radiologist CXR in-

terpretations during TB screening at a private clinic in Ho Chi Minh City, Viet Nam. The CAD software's utility was to identify people with TB whose abnormal CXR image, and thus opportunity for diagnosis, was missed by the radiologist. CXRs were interpreted by the clinic's on-site radiologist and processed by the qXR CAD software in parallel.

Participants with any abnormal CXR result, either by the radiologist and/or the CAD software (qXR score  $\geq 0.50$ ), were eligible for sputum testing using the Xpert MTB/RIF Ultra (Ultra) assay.

**Results:** Between June 2022 and February 2023, a total of 4,116 participants were screened by CXR at the clinic, resulting in the detection of 41 people with Ultra-positive TB (total yield of 1.0%). The qXR CAD software indicated an additional 39 participants (+21.7%) for sputum testing above/beyond the radiologist.

If only the radiologist had interpreted the CXR images, 31 people would have been diagnosed with Ultra-positive TB (sensitivity = 75.6%), whereas if only the qXR CAD software had interpreted the CXR images, 40 people would have been diagnosed with Ultra-positive TB (sensitivity = 97.6%). The qXR CAD software missed just one person with Ultra-positive TB, whose qXR score was 0.36.

		CAD Software Interpretation	
		TB Presumptive (qXR score $\geq 0.50$ )	TB Negative (qXR score $< 0.50$ )
Radiologist Interpretation	<b>Any Abnormal</b>	158 (3.8%)	22 (0.5%)
	Sputum tested	115 (72.8%)	18 (81.8%)
	Ultra-positive	30 (26.1%)	1 (5.6%)
	<b>Normal</b>	39 (0.9%)	3,897 (94.7%)
	Sputum tested	29 (74.4%)	N/A
	Ultra-positive	10 (34.5%)	N/A

Table. Crosstab of radiologist and CAD software CXR interpretations and follow-on sputum collection and Ultra testing yields.

**Conclusions:** This CXR interpretation scenario resulted in a +29.0% sensitivity gain in screening yields, and proved to be acceptable with clinic staff, as sputum collection and testing rates were similar across all screening cohorts.



## SOA17-934-17 Calibration and evaluation of two computer-aided detection software products for improving pulmonary TB case detection in two districts of Pakistan

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**Background:** Pakistan is increasingly turning to CXR for TB screening as it can identify asymptomatic people requiring diagnostic testing. Several CAD software now interpret TB-related CXR abnormalities. This study determined optimal abnormality score thresholds for TB screening concerning two CAD products: Lunit IN-SIGHT CXR version3.0 and qXR version3.

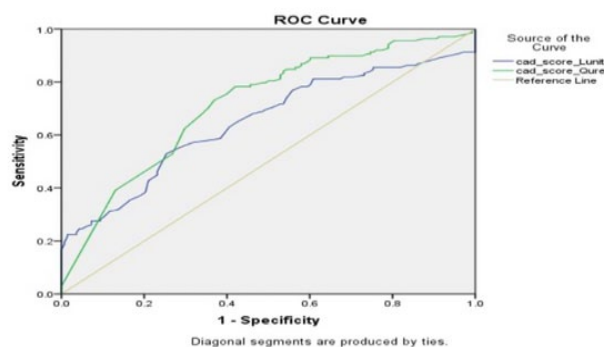
We aimed to achieve high sensitivity and specificity to minimize confirmatory testing costs. We calculated the optimal abnormality score consistent with achieving the best sensitivity and specificity to meet the WHO target product profile for triage tests, and modeled costs for Xpert tests based on screening 100,000 people.

**Design/Methods:** This one-to-one case-control study included 276 participants (138 with Xpert-confirmed TB and 138 with Xpert negative results). Individuals underwent digital CXRs using Fujifilm Calneo Xair read by two AI algorithms. The performance of both software was tested with WHO's tools with different abnormality scores.

Calibration thresholds were determined by correlating CAD readings with Xpert results and performance evaluated using sensitivity and specificity. ROC determined the ideal threshold score for CAD implementation consistent with accuracy and yield, enabling calculating cost implications on Xpert cartridges.

**Results:** Among 276 participants (212 male and 64 female), all were HIV-ve, 44 had diabetes, and 83 were smokers. For qXR and Lunit, achieving 90% sensitivity resulted in specificities of 25% and 5.8%. To achieve 70% specificity, the sensitivities for qXR and Lunit were 57.6% and 55%.

To meet the TPP sensitivity threshold scores were 30 for qXR and 19 for Lunit, with sensitivities of 90.6% and specificities falling to 26.1% and 4.3%, respectively. Incremental costs would be entailed for additional GenXpert testing.



**Conclusions:** The study provides new insights into maximizing TB case detection in Pakistan demonstrating the utility of the WHO toolkit for new CAD users though limited across diverse settings. While future research is recommended, sacrificing specificity for sensitivity appears inevitable.

## SOA17-935-17 Concordance rate of expert reviews of PDX-CAD radiograph and molecular WHO-recommended rapid diagnostics for TB active case-finding in Delta State, Nigeria

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**Background and challenges to implementation:** The persistent gap between TB identification and incidence is a major barrier to achieving TB elimination. Artificial intelligence (AI) algorithms can be trained to recognize tuberculosis-related abnormalities on chest radiographs. Various AI algorithms are available commercially, yet there is little impartial evidence on how their performance compares with other diagnostic methods of molecular WHO recommended rapid diagnostic (mWRD) tests.

Hence, this study is aimed at determining the concordance rate of expert review of PDX-CAD radiograph and mWRD test in tb active case search.

**Intervention or response:** KNCV Nigeria is implementing community active case search in Delta state Nigeria using a PDX-CAD. In 2022, clients were screened and presumptive were identified using PDX-CAD and symptomatically. Radiographs of clients with screening scores of 50 and above were sent to experts for further evaluation, also, radiographs of clients who have low screening score but have major signs and symptoms of TB were sent for expert review, these clients underwent mWRD test. Data was obtained from KNCV Nigeria

intervention data base. Information on number of Persons screened, number Presumptive identified, number of presumptive evaluated and number of diagnosed TB cases was extracted and used for this study. Analysis was done using descriptive statistics.

**Results/Impact:** A total of 14280 clients were screened for TB. Presumptive clients identified with radiograph sent for expert review were 1426 (10%). Client with result from radiograph review and mWRD test were 92% (n=1426; 1317). Concordance was 63% (n=1317; 827).

**Conclusions:** In the result, a 63% concordance rate shows a substantial significant potential of the PDX-CAD to detect TB. The availability of CAD will help in scaling up active case finding for TB and thus contribute to TB elimination in these settings, even though threshold setting and cost-effectiveness modeling are required to guide the optimum implementation of CAD products as part of screening programs.

### SOA17-936-17 18F-FDG positron emission tomography-computed tomography as treatment outcome parameter in patients with drug-susceptible pulmonary TB

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**Background:** Optimal treatment duration for drug-sensitive pulmonary tuberculosis (DS-PTB) is unknown. We assessed the clinical value of the 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) scan as a radiological biomarker to predict the risk of relapse in patients with DS-PTB at the end of treatment (EOT).

**Design/Methods:** We performed a retrospective analysis of patients treated for DS-PTB with at least one 18F-FDG PET/CT at EOT at the Kepler University Hospital in Linz, Austria between 2011 and 2019. Images were assessed for residual metabolic activity (RMA) to compare patients with RMA to patients with complete metabolic response (CMR).

**Results:** Out of 236 patients with at least one 18F-FDG PET/CT, 35 DS-PTB patients had at least one 18F-FDG PET/CT scan at EOT. Almost two thirds (63%; 22/35) of DS-PTB patients showed RMA at EOT, while 37% (13/35) showed a CMR. None of the DS-PTB patients developed a relapse during follow-up neither in the RMA- nor in the CMR group. Median follow-up period was 14 months (IQR 2-94) in the RMA group and 12 months (IQR 6-74) in the CMR group. Median treatment duration was 357 days (IQR 312-376) and 369 days (IQ 274-428), respectively.

**Conclusions:** In our cohort RMA at the EOT was not associated with higher risk of tuberculosis relapse while current literature suggests that negative 18F-FDG PET/CT findings after ATT might have a protective effect against tuberculosis relapse.

## SOA18 Tobacco Industry

### SOA18-937-17 Article 5.3 policy audacity in India: analysis of enablers and supportive factors in policy processes

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**Background and challenges to implementation:** Following the unanimous adoption of a series of guidelines and recommendations for the implementation of Article 5.3, (Conference of Parties, 2008), success stories from India seem to follow a 'domino' effect, wherein precedents in one sub-national jurisdiction are followed by others. This review scrutinizes Indian tobacco control policy audacity in terms of Article 5.3 of WHO-FCTC to explore enablers that facilitated it.

**Intervention or response:** A census approach-all sub-national Article 5.3 documents (circulars/letters/notifications/orders) were mapped from various sources and summarised. Key themes were identified and compared across jurisdictions: eligible Indian states/Union territories (UTs), to identify similarities and differences.

**Results/Impact:** More than 50% of Article 5.3 policy coverage is evident on India's map, till April 13, 2023. Analyzed documents reveal notable omissions across states/UTs in the adoption of key Article 5.3 guidelines: only some districts and state governments refer to regulating 'socially responsible' industry activities, while none include pre-emptive measures preventing the industry from receiving preferential treatment.

Government(s) of Assam, Karnataka, Kerala, Tamil Nadu, Meghalaya, Uttar Pradesh, Puducherry, Manipur, and Uttarakhand have issued detailed notifications including a protocol, procedure for a meeting (if at all necessary), code of conduct, and empowered committee constitution. Following clustering across the states/UTs, the Ministry of Health was found to be the major

enabler; with the Ministry of Higher Education as an outlier (Madhya Pradesh) and Uttar Pradesh en route for a “top-down” model.

**Conclusions:** Lessons from India reveal that civil societies, along with policy actors and local governments have been integral in following the “bottom-up” Article 5.3 policy adoption process. ‘Whole of government approach’, intersectoral and multi-jurisdiction collaboration, and lessons learned from previous policies with proactive advocacy strategies are additional drivers that the states/UTs in India and other Parties to the FCTC can employ in adopting and implementing Article 5.3 policy, as they embark upon similar efforts.

### SOA18-938-17 An assessment of tobacco advertising, promotion and sponsorship legislations in Africa

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**Background:** Article 13 of the WHO Framework Convention on Tobacco Control (FCTC) recommends complete ban on all forms of tobacco advertising, promotion, and sponsorship (TAPS). The tobacco industry sees Africa as a place to expand their business through aggressive marketing of their products.

This study aimed to assess legislative compliance to Article 13 in the WHO AFRO region.

**Design/Methods:** Document analysis of TAPS provisions in national laws from 18 countries in the WHO AFRO region was conducted. Laws were sourced from the Campaign for Tobacco-Free Kids’ Global Resources database. Eight TAPS components in line with the guidelines to the implementation of Article 13 were extracted into a spreadsheet including:

1. Direct and indirect mass media advertising;
2. Promotion;
3. Point-of-sale product display and promotion;
4. Packaging and product design;
5. Internet sale and promotion;
6. Sponsorship;
7. Corporate social responsibility activities; and
8. Cross-border TAPS.

For each of these components, Information on whether the target country had a full ban, partial ban, no ban, or if the status was uncertain were coded. Extracted data were then sent to an identified tobacco control stakeholder in the country for verification.

**Results:** Our results reveal that among the 18 countries surveyed, a total ban on TAPS activities were found to be 75% in Uganda (6/8 and 62.5% in Nigeria, The Gambia and Togo (5/8). There are partial bans on 2 TAPS com-

ponents in Uganda and Nigeria; and 3 components in Togo and The Gambia. Tanzania and Senegal have no provisions for 3 and 2 TAPS components respectively.

**Conclusions:** The study found that none of the 18 countries assessed has a comprehensive ban on TAPS. Partial bans allow the tobacco industry to take advantage of legal gaps deploy strategies to target youth. Countries need to review their laws and institute full TAPS bans to comply with Article 13 of the WHO FCTC.

### SOA18-939-17 Tobacco vendor licensing in Ranchi, India: A potential strategy to reduce point-of-sale tobacco advertising and promotions, and product display

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**Background:** In India, provisions of the Cigarettes and Other Tobacco Products Act, 2003 (COTPA) prohibits direct and indirect advertisement, promotion, and sponsorship of tobacco products (TAPS) at points-of-sale (POS). The local government in Ranchi has adopted policies to strengthen enforcement of COTPA through tobacco vendor licensing. A baseline survey (wave1), assessing compliance with TAPS policies at POS, was conducted in 2020. Our objective was to assess and compare compliance with TAPS policies post the implementation of vendor licensing (wave2) in 2022.

**Design/Methods:** Data collectors conducted observations at tobacco vendors identified along pre-determined stretches of road, ranging from 500-1000m in each of the 53 wards in Ranchi. The geographic location of each tobacco vendor was recorded. For each POS data collectors noted the presence of tobacco advertisements, tobacco product display, and if tobacco products were within reach of minors.

**Results:** The study conducted observations in N=374 locations in wave1 and N=350 in wave2. Approximately 15% of tobacco vendors (n=54) had outdoor tobacco advertisements in wave2, versus 29% (n=108) during wave1. Indirect outdoor advertisements showed an overall decrease of 16% between the two waves (wave1: 25%, n=93; wave2: 9%, n=31).

Similarly, indoor advertisement was observed in 14% of tobacco vendors (n=53) in wave1 and 8% (n=28) in wave2. While tobacco product display at POS remained almost the same across the two waves (wave1: 17%; wave2: 18%); of those that had products on display, there was an overall reduction of 14% of display within the reach of minors (wave1: 89%; wave2: 75%).

**Conclusions:** There was an overall decrease in tobacco advertisements at POS in Ranchi, from 2020 to 2022. These findings suggest that regular state-level enforcement efforts, including adoption of tobacco vendor licensing, can be effective in implementation of COTPA.

### SOA18-940-17 Tobacco industry's tax evasion through price mechanisms in Bangladesh

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**Background and challenges to implementation:** To make Bangladesh tobacco-free before 2040 it is necessary to raise the price of tobacco products above the purchasing power of the consumer. But due to the price mechanism of the tobacco company, the price of the tobacco product is constantly getting cheaper to the consumer even if the tax increases.

Besides, for the abnormal price hike of daily necessities the general people are reducing the consumption of eggs, milk and other nutritious foods to cope with this expenditure. Overall procedure is facing some serious challenges in its implementation mentioned below:-

1. Political and social challenges,
2. Weak regulatory framework,
3. Limited access to healthcare,
4. Tobacco farming.

**Intervention or response:** Prices of tobacco and daily necessities has been collected through random sampling from the markets of Dhaka, Jessore, Jhenaidah, and Satkhira districts. Moreover we have collected the price information of cigarettes and regular commodities of the last 5 years from 2018 to 2023 from the Govt. tariff commission. In addition secondary data and the opinions of public health and tobacco control experts were obtained and analyzed.

**Results/Impact:** In contrast to the 57%-119% increase in prices of basic commodities like rice, milk, egg, meat, the price of cigarettes increased by only 8%, 3.2%, 19.35%, and 15.5%, respectively, by 4 different tiers. Apart from this, taking advantage of not mentioning 'maximum retail price' on the packaging of tobacco products and the opportunities of selling single stick cigarettes priced at Tk. 4, Tk. 6.50, Tk. 11.10 and Tk. 14.20 are being sold at Tk. 5, Tk. 7, Tk. 12, and Tk. 16 respectively. The government is losing about Tk. 5000 crores of revenue every year due to the non-taxation of this additional value.

**Conclusions:** Taking into account GDP growth and inflation rate tax raise on tobacco products will play an important role in revenue generation, tobacco control and health promotion.

### SOA18-942-17 Impact of price and tax changes in the national budget on the retail prices of tobacco products (cigarettes) in Bangladesh

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**Background and challenges to implementation:** The multi-tier tax structure makes tobacco products very cheap and readily available in Bangladesh. So, it is important to reveal that the current tax structure helps control of retail cigarette price after the sixth month of national budget. So determining the difference between Maximum Retail Price (MRP) printed on the package and the actual selling price.

**Intervention or response:** Data has been collected from the 48 retail outlets (points of sales) in 12 cities. This includes the divisional cities of Dhaka, Barisal, Khulna, and Mymensingh, as well as two other district towns from each division. Data has been collected from four retail outlets in each city. Data has been collected from June to December 2022 for this study.

**Results/Impact:** According to the data collected in the survey, the maximum retail price printed on the 20-stick cigarette pack of the premium tier was BDT 284. But retailers are selling for BDT 306.13. The study also found that the maximum retail price printed on 20 stick packets is BDT 222 and BDT 130 in high and medium tiers, respectively. But the average selling price is BDT 237.55 and 136.96 taka. The maximum retail price is BDT 80 printed on a 20 sticks packet of low tier, but it is sold at an average of BDT 95.96 for a 20-stick pack.

Tier	MRP Printed on the pack	Average Retail Sale Price	Price Difference	Price Difference Rate	Total tax Rate (SD-VAT+HDS)	Government Part from Excess Price	Amount of Sale in FY 2021-22 (20 stick pack in crore)	Tax Evasion (in crore BDT)
Premium	284	306.13	22.13	7.8%	81%	17.93	14.04	251.74
High	222	237.55	15.55	7%	81%	12.6	9.69	122.09
Medium	130	136.96	6.96	5.14%	81%	5.64	16.32	92.04
Low	80	95.96	15.95	20%	73%	11.64	134.85	1569.65
<b>Total</b>								<b>2038.52</b>

Table. Potential loss of government revenue in FY 2022-23.

As such, if taxes could be levied on the highest retail price, the government could get an additional revenue around BDT 20.35 billion from last six months of FY 2022-23.

**Conclusions:** The government is losing thousands of crores of revenue every year due to lack of oversight in the tobacco sector. Therefore, in addition to effective tobacco control, it is important to stop extorting cigarette companies from the public. This will play an important role in stopping tax evasion by tobacco companies.

## SOA19 Air quality and lung health

### SOA19-943-17 Tupumue, a study of asthma, lung function and air pollution exposures in schoolchildren in an informal (slum) settlement and a more affluent area of Nairobi, Kenya

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**Background:** Although one billion people live in slums, the consequences for respiratory health of living in these settlements remain largely unknown. An unanswered question is whether the 350-500 million children living in informal settlements are at increased risk of asthma, the commonest childhood non-communicable disease. The aim of the Tupumue study was to determine whether children living in an informal settlement in Nairobi, Kenya are at increased risk of asthma and to identify pertinent environmental exposures.

**Design/Methods:** Children attending schools selected at random in Mukuru (a large slum) and the neighboring more affluent residential area of Buruburu were compared. Questionnaires quantified respiratory symptoms and environmental exposures; lung function was measured; personal exposure to particulate matter (PM<sub>2.5</sub>) was measured in a subset and used to estimate exposure for all participating children.

**Results:** 2373 children participated, 1277 in Mukuru (median, interquartile range, age 11, 9-13 years, 53% girls), and 1096 in Buruburu (10, 8-12 years, 52% girls). Mukuru schoolchildren had greater exposures to air pollution sources (median 39µg/m<sup>3</sup>, IQR 35-43) than in Buruburu (median 22µg/m<sup>3</sup>, 20-25), p<0.001.

When compared with Buruburu schoolchildren, Mukuru schoolchildren had a greater prevalence of the symptoms, 'recent wheeze' (9.5% vs 6.4%, p=0.007) and 'trouble breathing' (16.3% vs 12.6%, p=0.01), and these symptoms were more severe (sleep disrupted by

wheeze, 6.9% vs 4.2%, p=0.005) and problematic. Diagnosed asthma was more common in Buruburu schoolchildren (2.8% vs 1.2%, p=0.004). In multivariate analyses, significant adverse associations were observed with self-reported exposure to 'vapours, dusts, gases, fumes' ('trouble breathing'), use of mosquito coils ('wheeze'), adult smoker(s) in the home ('trouble breathing'), and living <500m from a major road.

**Conclusions:** Children living in informal settlements are more likely to develop symptoms consistent with asthma that are more severe but less likely to be diagnosed as asthma.

### SOA19-944-17 Ambient air pollution and risk of active TB: a nationwide population-based cohort study in Taiwan

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**Background:** Available evidence on the relationship between long-term exposure to particulate matter with aerodynamic diameter of ≤ 2.5 µm (PM<sub>2.5</sub>) and tuberculosis (TB) has been limited and inconsistent. This study aimed to investigate this association using a nationally representative sample from Taiwan.

**Design/Methods:** We conducted a longitudinal cohort study of individuals aged ≥12 years who participated in 5 rounds of the National Health Interview Survey between 2001 and 2017. Each participant was followed up until the incidence of active TB, death, or 31 December 2020, whichever came first.

The incidence of TB was identified based on ICD code and prescription of anti-TB drugs. The PM<sub>2.5</sub> exposure was estimated using air quality monitoring stations and microsensors data, which has been previously published.

We conducted time-dependent Cox regression, using the average PM<sub>2.5</sub> level in the preceding two years as the exposure window. Restricted cubic splines were used to measure the nonlinear association.

**Results:** Among the 72,180 individuals with a median follow-up time of 11 years, 488 TB cases were reported. The mean annual PM<sub>2.5</sub> level during the follow-up period was 26.8 µg/m<sup>3</sup> (SD: 8.9 µg/m<sup>3</sup>).

After adjusting for sex, age, body mass index, cigarettes smoking, alcohol use, education level, household income, living in mountain administrative areas, TB history, and secular trend of TB, the adjusted HR was 0.95 (95% CI: 0.85-1.06) for every 10 µg/m<sup>3</sup> increase in annual average of PM<sub>2.5</sub>. We found evidence for effect modification by age (p-value = 0.048), and the adjusted HR

was higher among people > 65 years (aHR 1.09, 95% CI 0.91-1.31). No significant non-linear relationship was found ( $p$ -value = 0.063 for linearity).

**Conclusions:** In the large population-based cohort study, there was no strong association between long-term exposure to PM<sub>2.5</sub> and risk of active TB. The elderly population might be the vulnerable subgroup for the effect of air pollution.

### SOA19-945-17 Spatio-temporal trends of air pollution in Kampala City, Uganda, 2020–2022

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**Background and challenges to implementation:** Fine particulate matter (PM<sub>2.5</sub>) is an air pollutant that poses greatest health risk to humans, with levels >15 µg/m<sup>3</sup> being associated with serious health effects. PM<sub>2.5</sub> is a measure of air quality associated with such health effects and its major route of entry is respiratory tract. Cities are more prone to poor air quality compared to non-urban areas. We assessed the spatio-temporal trends of air quality concentrations in Kampala City in order to determine the exposure to risk for lung disease.

**Intervention or response:** PM<sub>2.5</sub> concentration data for January 1, 2020–June 30, 2022 from Clarity Node Solar-Powered monitors were analyzed using STATA 14. We computed 24-hour mean PM<sub>2.5</sub> concentration at city and city division levels by combining data from all monitors in the respective areas. Average PM<sub>2.5</sub> concentrations were compared by hour of the day and diurnal variations in air quality throughout the day determined. We used the Seasonal Mann-Kendall statistical test to assess trends in 24-hour average PM<sub>2.5</sub>.

**Results/Impact:** Overall, the 24-hour average PM<sub>2.5</sub> from January 1, 2020–June 30, 2022 was 59 µg/m<sup>3</sup> (range: 18–182 µg/m<sup>3</sup>) in Kampala City. PM<sub>2.5</sub> concentrations exceeded 15 µg/m<sup>3</sup> in all city divisions: Kawempe (63 µg/m<sup>3</sup>), Central (61 µg/m<sup>3</sup>), Rubaga (60 µg/m<sup>3</sup>), Nakawa (55 µg/m<sup>3</sup>) and Makindye (53 µg/m<sup>3</sup>). PM<sub>2.5</sub> concentration peaked from 10am–noon (74–73 µg/m<sup>3</sup>) and 8pm–9pm (73–77 µg/m<sup>3</sup>). There was a small decline in PM<sub>2.5</sub> from January 2020 to June 2022 ( $r = -0.27$ ,  $p < 0.001$ ). PM<sub>2.5</sub> increased during April–June [2020 ( $r=0.56$ ,  $p=0.006$ ), 2021 ( $r=0.26$ ,  $p=0.030$ ), and 2022 ( $r=0.37$ ,  $p=0.030$ )] and declined during July–September, 2021 ( $r=-0.43$ ,  $p=0.008$ ) and January–March, 2022 ( $r=-0.41$ ,  $p=0.011$ ).

**Conclusions:** Unhealthy PM<sub>2.5</sub> levels were observed even during times of less traffic and economic activity in Kampala City; predictable annual patterns in high PM<sub>2.5</sub> were seen. This may worsen lung health for city residents.

### SOA19-946-17 Exposure to air pollutants increases risk of pulmonary TB due to DNA methylation

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**Background:** Exposure to particulate matter (PM) increases the risk of tuberculosis, but the mechanism is not fully understood. Genomic DNA methylation could be modified when exposed to air pollutants, which may be an essential molecular mechanism. We measured the organic and metal pollutants in the bronchoalveolar lavage fluid (BALF) of patients with pulmonary tuberculosis and further evaluated the effect of DNA methylation and cytokine levels.

**Design/Methods:** The concentration of organochlorine pesticides (OCPs), polycyclic aromatic hydrocarbons (PAHs), and metal elements of BALF samples was detected by gas chromatography-mass spectroscopy (GC-MS) and inductively coupled plasma mass spectrometry (ICP-MS). We employed the Luminex 200® platform to determine the cytokines (IFN- $\gamma$ , IL-10, IL-12, IL-17A, IL-2, IL-23, IL-4, IL-8 and TNF- $\alpha$ ) in plasma. The Illumina HiSeq platform was used to assess DNA methylation at 99 CpG sites in the promoter regions of the immunity-related gene.

**Results:** We found that  $\gamma$ -HCH and Bap increased tuberculosis risk, with adjusted Odds Ratios (aORs) of 1.781 (95% CI: 1.398-2.334) and 3.456 (95% CI: 2.208-6.445), respectively.

For metal elements, Sr, Ag and Sn were risk factors for tuberculosis (aOR=1.781, 3.456 and 4.319, respectively), while Cu (aOR=0.540) and Ba (aOR=0.510) exposure could decrease the risk of tuberculosis.

Cytokines, such as IFN- $\gamma$ , IL-17A, IL-2 and IL-23, were higher in the tuberculosis group, while the level of IL-4 was lower.

The methylation at the IL-4\_06\_121 site showed a significant mediating role of  $\gamma$ -HCH, Sr and Sn in the risk of tuberculosis, with the aOR of 1.215 (95% CI: 1.006-1.759), 1.215 (95% CI: 1.006-1.759) and 1.148 (95% CI: 1.005-1.550), respectively. The IL-4 mediated the association between IL-4 gene methylation and tuberculosis risk.

**Conclusions:** Various organic and metallic contaminants could be observed in BALF, affecting DNA methylation of immune-related genes and cytokines. DNA methylation played a mediating role in the association between PM and pulmonary tuberculosis.

## SOA19-947-17 Challenges and opportunities for implementing cotton dust control interventions in textile mills of Karachi, Pakistan: a qualitative study

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**Background:** Cotton dust exposure is a significant occupational hazard in the textile industry, that can cause respiratory problems such as bronchitis, byssinosis and asthma. Despite efforts to control exposure, textile workers continue to experience adverse health effects. This work was part of the MultiTex randomized controlled trial designed to test interventions for improving respiratory health of textile workers in Karachi, Pakistan. We conducted end line qualitative interviews to explore experiences and opinion of study participants and stakeholders regarding the intervention package. Understanding their experiences and perspectives is essential for developing effective interventions.

**Design/Methods:** This qualitative study used 15 in-depth interviews with managerial staff, 11 key-informant interviews with the relevant stakeholders from public and private organizations and 14 focus group discussions with textile workers to explore their experiences regarding the intervention. Of the 38 textile factories that participated in the trial, 14 were purposively selected for this study. The interviews were audio-recorded, transcribed, translated and analyzed using thematic analysis.

**Results:** Four main themes emerged from the data:

1. Perceived health effects,
2. Coping mechanisms,
3. Organizational support, and;
4. Perceived barriers to reducing exposure.

Participants reported various respiratory symptoms such as coughing, wheezing, and shortness of breath, which they attributed to cotton dust exposure. Coping mechanisms included wearing facemasks and seeking medical advice. Participants reported limited organizational support and identified barriers, such as the cost and inconvenience of implementing control measures. Most participants reported that refresher trainings conducted at the factories were very helpful and that Multi-Tex committee (responsible for compliance and sustainability) was a great initiative.

**Conclusions:** There is a need for comprehensive and effective interventions to reduce cotton dust exposure and improve the health and well-being of textile workers. Organizational support, including education and training, is crucial in the design and implementation of such interventions.

## SOA20 Person-centred care

### SOA20-948-17 "Throughout the treatment, you continue to pamper and give them attention": healthcare workers' behavioural adaptations to retain men in TB care

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**Background:** Men and women face gender-specific challenges in accessing and remaining in TB care. Key bottlenecks faced by men along the TB care cascade are embedded in male gender norms and roles, and their subsequent struggle to meet the expectations of their families and communities. For many men in informal work situations, seeking care usually implies forfeiture of income with potential concomitant effects on their household's food intake and indeed survival.

We undertook a qualitative inquiry to understand healthcare workers' (HCWs) perspectives and experiences of gendered barriers to being retained in TB care.

**Design/Methods:** This qualitative research was developed through the LIGHT Consortium's DESTINE research in Nigeria. We conducted semi-structured key informant interviews with 13 purposively selected HCWs (Females=7, Males=6) involved in delivering TB services at various levels.

Content analysis framed from an interpretative perspective was utilized: naturalized transcription of KII recordings was followed by descriptive first-order coding and interpretative second and third-order coding.

**Results:** Participants perceived that, compared to women, successful retention of men in TB care generally required more time (to build trust), more resources (to support care), more information (to enable empowerment and cooperative decision-making), and more flexibility of service delivery (opening hours).

To be successful in retaining men, HCWs reported adaptations including '*baiting and negotiations*' to ensure individualized care tailored to each man's need. This required extra commitment beyond what is considered official job expectations.

The ability of individual HCWs to recognize and respond to the gendered needs and agency of men and women seeking care differed amongst HCWs.

**Conclusions:** Informally, HCWs do perceive differences between the needs of men and women seeking care and do informally change the way they offer care to meet

these needs. There is a need to re-orientate the health-care-delivery system and build the capacity of HCWs gender-responsive care delivery.

### SOA20-949-17 Nationwide TB stigma assessment in Mongolia: results of qualitative interviews with people diagnosed with TB

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**Background and challenges to implementation:** This study is a part of the nationwide Tuberculosis Stigma Assessment in Mongolia, which aimed to assess the extent and dimensions of stigma related to tuberculosis (TB), to understand stigma as a barrier to accessing care, and to develop strategies with an action plan to address it.

**Intervention or response:** Interviews with people with TB (PWTB) from all 21 provinces and eight districts of the capital city were included, as well as specific vulnerable populations such as mental health patients, prisoners and homeless people. 54 community-based HCWs were trained using the STOP TB Partnership's "TB Stigma data collection tools".

Semi-structured questionnaires containing validated TB stigma scales and additional questions targeting a better understanding of where stigma is being experienced, observed and how it manifests along the TB journey. Transcripts were analyzed using thematic analysis.

**Results/Impact:** Between 21 February and 2 April 2022, 460 participants were interviewed. Self-stigma was reported by 44% of PWTB and it has inhibited 16% to seek care.

Hiding having TB and depression were common, as well as being ashamed of having TB and fear of infecting others. They have also experienced negative encounters with HCWs, family, friends and community, as well as at the workplace.

These experiences manifested mainly through non-verbal communication and they received little support. Majority of participants expressed the critical need for public awareness and advocacy of TB, improved TB health care facilities, knowledge and attitude of HCWs.

Moreover, workplace stigma reduction policies complemented with social and financial support were among the main concerns for PWTB.

**Conclusions:** Both self-stigma of PWTB and perceived stigma of HCWs, family and friends and community are common in the Mongolian society. It is acting as a significant barrier to accessing health care services. Therefore, incorporation of stigma reduction strategies are critically required in the national TB response.

### SOA20-950-17 Differentiated social protection to address the costs of TB care in Viet Nam

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**Background:** Approximately 63% of households affected by TB in Viet Nam experience catastrophic costs. Within the Vietnamese context, provision of financial support to people with TB is most acceptable when it is targeted towards the economically vulnerable, rather than all persons with TB.

**Design/Methods:** A predictive model for catastrophic cost incurrence was developed into a four-question risk assessment tool which could be easily administered by District TB Unit (DTU) staff in order to assess the eligibility of people starting TB treatment for differentiated tiers of socioeconomic support designed to offset direct medical costs. The USAID-funded Erase TB project supported the roll out of this tool at 10 DTUs in Ha Noi and Ho Chi Minh City, as well as the provision of the support packages.

**Results:** Over 4,600 TB patients were screened using the risk assessment tool (83.0% of people starting TB treatment during the intervention period), resulting in the identification of 1,023 (21.8%) who were eligible for at least one kind of support package. 829 (81%) eligible



patients were ultimately enrolled in one of three tiers. 734 patients (88.6%) redeemed at least one transport voucher, with 515 (62.2%) redeemed all six vouchers. 1,384 cash transfers were distributed to 702 patients. Social health insurance premiums were subsidized for 41 patients (69.5% of eligible), which extended insurance coverage to a total of 74 individuals living in TB-affected households. In total, USD 70,444 was provided as socioeconomic support to eligible patients.

	Ha Noi	Ho Chi Minh City	Total
People initiated on TB treatment	1,055	4,600	5,655
PROTECT Assessments completed	970 (91.9%)	3,725 (81.0%)	4,695 (83.0%)
Eligible TB patients	387 (40.8%)	636 (17.4%)	1,023 (21.8%)
Recruited	327 (84.5%)	502 (78.8%)	829 (81.0%)
Tier 1: Transport Vouchers	55 (16.8%)	72 (14.4%)	127 (15.3%)
Tier 2: Transport Vouchers + Cash Transfers	252 (77.1%)	391 (78.0%)	643 (77.7%)
Tier 3: Transport Vouchers + Cash Transfers + SHI	20 (6.1%)	39 (7.6%)	59 (7.0%)
Confirmed non-enrollment	60 (15.5%)	134 (21.1%)	194 (19.0%)

**Conclusions:** This intervention demonstrates the feasibility of stratifying risk and distributing social protection according to socioeconomic vulnerability. Innovative interventions such as this are needed to mitigate catastrophic costs due to TB.

### SOA20-951-17 Breaking barriers to TB-HIV care: Using an integrated community-based approach to reach key populations in Wakiso District, Uganda

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**Background and challenges to implementation:** Integrated community-based services have the ability to improve access to primary health services while reducing costs associated with the provision of these services. We set out to integrate community provision of TB and HIV testing services in order to increase the reach and yield of these two interventions.

**Intervention or response:** In October 2022, the project implemented an integrated community-based approach to provide TB/HIV services at six health facilities in Wakiso district. This was led by the community health workers who worked with clinicians and laboratorians. TB/HIV Hotspot communities were mapped out and the TB/HIV key population living in these communities identified through brainstorming in-line with National guidelines. The teams did TB education and symptom screening. Sputum samples were collected for those presumed to have TB and taken to the laboratory for GeneXpert testing. HIV testing services were provided to those eligible. GeneXpert results were followed up and returned to patients. Those diagnosed with TB and HIV were started on treatment.

**Results/Impact:** A total of 557 individuals were reached. Of these, 115 (20.7%) had presumptive TB and 17 (3.1%) were diagnosed with TB and started on treatment. 16 TB patients had drug susceptible TB and 1 had Multi-drug Resistant TB. The HIV yield was 8/73 (11%), all were linked to treatment services. Among the TB cases diagnosed, 11/17(64.7%) were male. The highest TB yield was among fisherfolk at 5/81(6.2%). Three patients were diagnosed with both TB and HIV. Forty-two presumed TB patients who had a known HIV status or who declined to be tested did not receive HIV testing services.

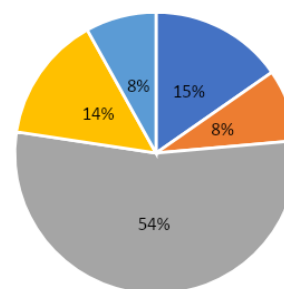


Figure. Pie chart showing categories of key population reached.

**Conclusions:** Using the TB/HIV collaborative model of service delivery provides a people centered and efficient approach to delivery of TB and HIV services.

### SOA20-952-17 Correlates of TB treatment outcome – how supportive are person-centred interventions? Learnings from a community engagement initiative among vulnerable populations in India

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**Background and challenges to implementation:** Key vulnerable groups of National Strategic Plan for Tuberculosis (2017-25) have different levels of knowledge about TB, experienced stigma, and health-seeking behaviour. With the goal to 'End TB' by 2025, it is essential to have a comprehensive person-centred adherence and monitoring support for all persons on anti-TB treatment.

USAID supported Breaking the Barriers project, implemented in Karnataka and Telangana among mining, industrial, tribals and urban-vulnerable, is rolling out care and support group meetings, as a person-centred care model to nudge TB treatment adherence and successful outcomes.

**Intervention or response:** Care & Support Group Meetings, an inclusive gathering of PwTB and caregivers visiting a particular health facility once a month, is a platform to improve communication between PwTB and healthcare providers, support PwTB in overcoming adverse experiences during treatment, mitigate stigma through experience sharing and receive psychosocial counselling, and assistance for nutrition and social entitlements.

We assessed the correlates of treatment outcome and role of CSG meetings, for a cohort of 3,316 PwTB during October 2021-June 2022.

**Results/Impact:** Overall, 84% (2,654) of the PwTB successfully completed their treatment, highest among urban vulnerable (87%) and lowest among industrial (63%). It was found that treatment success was higher among females, in the 15-24 years age group, among persons with drug-sensitive TB and those who attended at least one CSG meeting across all vulnerable groups, as compared to their counterparts.

Controlling for socio-cultural and behavioural factors, it was found that while TB-HIV comorbidity and alcohol use were detrimental, attendance in CSG meetings significantly increased the propensity of successful treatment completion (91%, OR=2.658,  $p<0.001$ ).

		Successful outcome	n=
HIV positive***	No	87.5%	2897
	Yes	79.0% (OR=0.532 $p<0.005$ )	95
	Status unknown	28.6%	154
Alcohol consumption***	No	88.2%	2386
	Yes	82.0% (OR=0.675 $p<0.05$ )	300
	Status unknown	66.0%	460
Attendance in CSG meetings***	No	77.1%	1525
	Yes	91.2% (OR=2.658 $p<0.001$ )	1621

Note: Controlled for = age, sex, education, occupation, religion, caste, type of TB, location of TB and vulnerable groups.

Table 1.

**Conclusions:** Participation of PwTB in CSG meetings during treatment significantly improved treatment outcomes, across all vulnerable groups. National level endorsement for standardization and sustainability of CSG at health facilities is therefore, the need of the hour, to create an enabling environment for PwTB and families.

## SOA20-953-17 'One-stop shop' for TB services: Wellness-on-Wheels is an opportunity to reach vulnerable populations in Zambia

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**Background and challenges to implementation:** Globally, Zambia is one of the countries with a high TB burden. Finding the missing TB patients is a national priority. GeneXpert platforms have been scaled up, especially in urban areas. The coverage of chest-ray services is limited in Zambia. Reaching the rural and hard-to-reach areas with sensitive TB diagnostic services remains challenging.

**Intervention or response:** In 2019, through the Global Fund investment, two mobile vans equipped with digital X-rays and GeneXpert machines were procured and deployed in Lusaka and Copperbelt provinces (two provinces contributing 60% of the total annual national TB notifications in Zambia).

These state-of-the-art mobile TB clinics were explicitly dedicated to active case-finding outreach services in targeted rural and hard-to-reach communities. Before the actual TB screening outreach activity, public awareness was conducted in the respective communities to create demand.

We report the impact of these outreach services on TB notifications and operational challenges associated with mobile TB clinics.

**Results/Impact:** Between 2020 and 2021, a total of 9,264 presumptive TB patients were identified through outreach services. A total of 492 patients were diagnosed with TB and commenced on anti-TB treatment. Females represented 27% of presumptive TB patients and 21% of diagnosed TB cases. Children accounted for 1% (6/492) of diagnosed cases. High operational cost of running mobile clinics is a barrier to reaching more vulnerable populations.

**Conclusions:** Outreach TB services are an important and feasible approach to bringing quality TB services closer to people in hard to reach communities and can save life among vulnerable populations who would go undiagnosed and untreated.

Operational costs should be adequately planned for to sustain outreach activities and to reach more vulnerable communities with quality TB services.

## SOA20-954-17 Nurse case management reduces treatment failure among patients with multidrug-resistant TB in South Africa: results from a cluster randomised trial

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**Background:** There is little evidence describing patient-centered support models for drug-resistant tuberculosis (MDR-TB)/HIV in sub-Saharan Africa. Nurse case management (NCM) models in which a nurse facilitates, and coordinates treatment plans have been shown to provide timely, evidence-based care and to improve treatment outcomes for HIV and TB, yet there is no evidence for MDR-TB infection. We trained professional nurses to provide patient-centered care in support of adherence, engagement and retention in care using the Chronic Care Model.

**Design/Methods:** We conducted a cluster randomized trial among 10 MDR-TB treatment hospital in Eastern Cape and KwaZulu Natal, South Africa between 2014 and 2020 comparing a NCM intervention to usual care (UC). Using generalized estimating equations (GEE) regression analyses for multinomial outcomes, we determine the effects of NCM on final treatment outcome in a modified intent-to-treat analysis (mITT).

	NCM	UC	Total
Enrollment, by arm	N = 1,094	N = 1,042	N = 2,136
Multinomial Outcomes	Adjusted Odds Ratio	P-Value*	95% Confidence Interval
Success (Reference)	--	--	--
Death	0.94	0.81	0.56 - 1.58
Loss to follow-up (LTFU)	0.80	0.37	0.49 - 1.31
Treatment failure	0.55	0.02*	0.32 - 0.92

Legend: \*p<0.05; GEE, generalized estimating equations; adjusted for age, sex, home internet, household number, and number of non-HIV comorbidities

*Table 1: A cluster randomized trial of NCM compared to UC for MDR-TB in SA: enrollment and GEE outcomes.*

**Results:** Among 2,847 enrolled patients, 2,136 (75.0%) were eligible for mITT. Among those, the majority were male (57.9%), unemployed (59.1%) and living with HIV (74.3%). At baseline, mean BMI was 20.4, CD4 was < 200 in 47.7%, with 59.0% on ART and only 20.8% virally suppressed. MDR treatment suc-

cess was 64.5% in the NCM arm and 61.9% in UC. Odds of treatment failure relative to success in NCM intervention were 0.55 times (45%) lower than UC (p=0.023, 95% CI for OR=0.32, 0.92). Odds were not significantly different between arms for death and loss to follow-up (Table 1).

**Conclusions:** Hospitals with NCM support experienced reduced odds of treatment failure, yet we did not find benefit for loss to follow-up, nor death. The NCM supported adherence, preventing treatment failure, however, late presentation to care was a hallmark of death. LTFU is multifaceted, but one central aspect is poverty. Our NCM intervention was unable to provide financial support to overcome barriers to care such as transportation and loss of income.

## SOA21 Global and local policies to Improve TB care and services

### SOA21-955-17 Engaging key stakeholders from high-priority countries for strengthening research capacity to end TB: results from global stakeholder survey

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**Background:** Engagement of investigators and programs from high TB burden countries is essential to ensure the best approaches for designing and conducting TB operational research. In preparation for country partnership through the USAID's Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination (SMART4TB) project, we conducted a global survey to identify priorities of local stakeholders in high-priority countries on studies to help END TB and for strengthening local capacity for research.

**Design/Methods:** A cross-sectional, online survey was administered in February and March 2023. This was preceded by three webinar sessions in which the vision, objectives, and activities of the SMART4TB initiative were presented. The questionnaire included questions about challenges and country capacity building needs and priorities for TB research, the role of regional collaboratives (local organization networks that serve as coordination platforms), willingness of participants to contribute to regional collaboratives, and operational research priorities.

**Results:** Two-hundred thirty-one participants from 38 countries attended the webinars, and 220 people from 23 countries responded to the survey, 52% and 43% from Asia and Africa respectively. Non-governmental organizations and academic/research institutions combined accounted for 75% of the respondents. Several operational research areas were identified, with TB case finding, treatment support and adherence, and prevention being the three top areas (Figure).

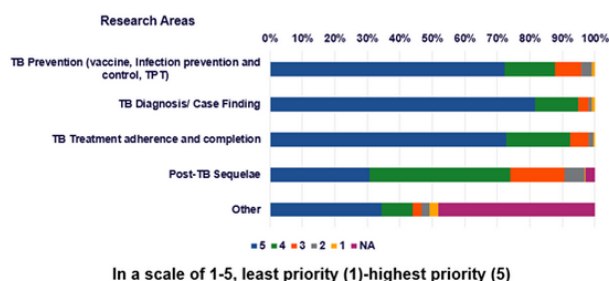


Figure.

Stigma and other structural barriers, limited human resources capacity, inadequate diagnostic capacity, and co-morbidities/co-infections were the top challenges mentioned. Most of the respondents (84%) expressed willingness to collaborate regionally to address these challenges.

**Background and challenges to implementation:** Engagement of investigators and programs from high TB burden countries is essential to ensure the best approaches for designing and conducting TB operational research. In preparation for country partnership through the USAID's Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination (SMART4TB) project, we conducted a global survey to identify priorities of local stakeholders in high-priority countries on studies to help END TB and for strengthening local capacity for research.

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barriers limited human resources capacity, inadequate diagnostic capacity, and co-morbidities and co-infections were the top challenges mentioned. Most of the respondents (84%) expressed willingness to collaborate regionally to address these challenges.

**Conclusions:** The results highlight the importance of engaging all stakeholders at country level to define operational research priorities to accelerate ending TB, and recognizing that operational research should be a spectrum, addressing the cascade of care and social dimensions of TB prevention and care. There was strong support for regional collaboration for facilitating joint capacity building, conducting multi-country studies, and exchange of experience.

### SOA21-956-17 An exploration of sub-national policy, planning and budgeting for TB programmes at 20 districts in Indonesia

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**Background:** Indonesian government demonstrated a solid commitment to end TB through its Presidential Decree on Tuberculosis and national strategic plan. However, efforts to implement public health programs in the country vary for each decentralized district government, which poses a challenge to achieve end TB targets when there are weak enabling policies, inadequate planning and budgeting at local levels.

Therefore, this study aims to map the existing policies and the perspective of local government in the financial planning and budgeting of TB elimination.

**Design/Methods:** The mixed method study explored policies, planning and budgeting, and perspectives of local government stakeholders about the TB program. It was conducted in 20 districts with high TB burden across 14 provinces with cross-sectional design and purposive sample.

Qualitative methods used for desk review and mapping of regulations, policies, and relevant program documents.

Quantitative methods used for descriptive analysis of program indicators achievement, real budget for program, estimation of budget needed, and comparison of estimated needs and estimated notification trend.

**Results:** This study found only 5 districts have TB-specific regulation, 5 districts include TB in their mid-term development plan, and 14 districts that mentioned TB specifically in their budget.

However, across 20 districts, domestic resources for TB is only 0.12% of the overall health program budget. Excluding financing for TB drugs, 10 districts have adequate real budgets for TB programs, this is reduced to

only 3 districts with consideration to financing for medications. Eight districts have an increasing trend of TB notification in 2024. Overall, non-Health governments have yet to prioritize financing for TB due to lack of understanding of the current TB situation in their districts. **Conclusions:** For the district government to fulfill its mandate to contribute in financing for TB, non-Health offices need support to develop local regulations, planning, and budgeting with assistance from national governments.

### SOA21-957-17 Assessing the costs of TB elimination under universal healthcare conditions: application of a TB elimination costing tool in Manila City, the Philippines

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**Background and challenges to implementation:** Universal Health Care (UHC) can create the right conditions for TB elimination. With effective implementation, UHC can improve TB service uptake, increase treatment adherence, and advance treatment outcomes. While UHC can create the needed environment for TB elimination, it will require significant resources.

**Intervention or response:** The USAID's TB Platforms Activity developed a tool to determine the potential costs of eliminating TB under UHC conditions, including costs to TB service providers and patient transportation costs. The tool was developed using Microsoft Excel and provides user-defined inputs and embedded formulas and assumptions based on national standards, considering estimated incident TB cases in the current year and missing TB cases in the previous year. The tool calculates the monetary costs of TB services and patient support, including supplies and logistics. A pilot application of the tool was conducted using 2022 Manila City TB data.

**Results/Impact:** Results show that the potential cost of eliminating TB in Manila City (with an estimated TB incidence of 83,853 cases) within one year is equivalent to PHP 3 billion (~US\$ 55 million). Xpert MTB/Rif cartridges account for the biggest proportion of costs at 27%, followed by patient transportation (25%), and chest x-ray and active TB treatment at 21% each. Five percent were from TB preventive treatment costs, 2% from other logistics. The costs do not include potential additional human resources, equipment and infrastructural needs.

**Conclusions:** Developing and using tools to demonstrate TB elimination costs under UHC conditions is integral in putting the TB elimination agenda at the forefront

of UHC implementation. Amidst health sector-wide reforms such as UHC, commitment is needed from national and local health systems to preserve specialized functions and funding to sustain quality TB care and achieve elimination. UHC implementation can and should go hand-in-hand with the Sustainable Development Goal of ending the global TB epidemic by 2030.

### SOA21-958-17 Role of community health workers in ending TB by reaching out hard-to-reach contact investigation cases: The USAID Afya Shirikishi- Amref Health Africa Project in Tanzania

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**Background and challenges to implementation:** Contact investigation (CI) approach offers an opportunity for early case finding among close contacts of infectious TB patients in their households. Despite the presence of guidelines for CI in Tanzania since 2016, CI is not often conducted due to minimal geographical coverage and inadequate deployment of community health workers (CHWs).

With regards to the WHO's recommendation to actively find the missing people with TB, USAID Afya Shirikishi Activity under Amref Health Africa in Tanzania with support of USAID, is bridging this gap by engaging CHWs to closely conduct CI for TB close contacts of index TB patients within nine project supported regions. Aimed to reach the unreached 41% (54,166 missing people with TB) as reported by the MoH through National Tuberculosis and Leprosy Program.

**Intervention or response:** Given the sensitivity and commitment of volunteerism, it was agreed that at least twice a week, CHWs collect index TB patients' information from DOT health facilities. Visit patients' households to provide TB infection control information, screen contacts, refer for TB testing, and return results. Data collected is submitted to the district TB coordinator for verification, compilation analysis and use.

**Results/Impact:** Retrospective project data from April 2021 to Dec 2022; Indicates 26,417 bacteriologically confirmed TB patients were notified. CHWs were provided with 21,480(81%) index patients for follow up. They found 56,985 close contacts in the households (*Index ratio for CI is 1:2.6 (56985/21480)* of which 54442(96%) were screened for TB. 18626 (34%) were identified as presumptive TB cases. 17932 were referred, while 16,594 (93%) tested and 1781 (11%) diagnosed with TB and started TB medications.

**Conclusions:** Engaging enough and committed CHWs with support from community leaders to support community TB activities will ensure improved TB CI. To improve data collection and follow up, NTLP has to adopt, adapt and reinforce the WHO CI TB Cascade.

### SOA21-959-17 Australian Public Health Legislation: Possible violations of the UN Convention on the Rights of Persons with Disabilities, a TB case study

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**Background:** In Victoria, Australia, the *Public Health and Wellbeing Act 2008 (Vic)* empowers the state to restrict the movement of those with potentially contagious infectious diseases such as tuberculosis and COVID-19. This case report examines the interactions of a refugee living with psychosocial disability and tuberculosis and Victorian public health infrastructure, highlighting the potentially discriminatory consequences of this legislation for people living with disabilities (PLWD).

**Design/Methods:** The case study's interaction with the Victorian *Public Health and Wellbeing Act 2008 (Vic)*, *Public Health and Wellbeing Amendment (Coronavirus) Regulations 2020 (Vic)* and *Mental Health Act 2014 (Vic)* were assessed against the *Charter of Human Rights and Responsibilities (Vic)*, the *UN Universal Declaration of Human Rights* and the *UN Convention on the Rights of Persons with Disabilities (CRPD)*.

**Results:** The case study, a man living with tuberculosis who experienced marginalisation as a result of a number of multiplicative intersectional disadvantages including psychosocial disability, recreational drug use, poverty, racial marginalization and refugee status, experienced three separate instances of involuntary detention, medical treatment and hospital admission over a six-month period, authorised by the aforementioned legislation. In particular, the individual's right to equal recognition before the law (*CRPD Art 12*), liberty and security of person (*CRPD Art 14*) and protecting the integrity of the person (*CRPD Art 17*) were engaged and potentially infringed.

**Conclusions:** Victorian public health legislation disproportionately affects marginalized individuals, particularly those living with psychosocial disability, recreational drug use and poverty, which often co-exist. Despite a requirement for Victorian legislation and public organizations to comply with the *Charter of Human Rights and Responsibilities (Vic)*, this case study demonstrates the discrimination and interference that such individuals experience at the hands of state public health systems, even when legal safeguards are in place.

### SOA21-960-17 Leveraging TB public health messaging to drive vaccination demand in local communities

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**Background and challenges to implementation:** The National Tuberculosis, Buruli Ulcer, and Leprosy Control Program (NTBLCP) in Nigeria has well-established structures for TB case finding and public health messaging. The similarities in the symptoms of Tuberculosis and COVID-19 infection provide an avenue to leverage existing platforms to create demand for COVID-19 vaccination.

This paper aims to showcase how KNCV Nigeria implements the USAID-funded COVID-19 Vaccination Acceleration project which leverages the existing structures of USAID-Funded TB Local Organizations Networks in seven states to support the attainment of 70% vaccination coverage.

**Intervention or response:** The NTBLCP, supported by USAID, launched a unified National TB brand campaign aimed at increasing testing and detection of TB in Nigeria called "Check am o!"

The campaign, spearheaded by Breakthrough ACTION Nigeria included mass media, community, and social media campaigns. The slogan was popularized across the nation, had a wide reach, and was easily recognizable by the public.

By incorporating the "Check am o!" slogan on vaccination paraphernalia as well as providing integrated TB screening, the project leveraged the trust the public has in the slogan to gain acceptability and get communities vaccinated.

Vaccination exercises were carried out by mobile vaccination teams conducting house-to-house vaccinations, mass vaccination sites, and community outreaches.

**Results/Impact:** Between July and October 2022, a total of 1,629,817 doses of COVID-19 vaccines were administered across the seven states for first, last, and booster doses using an integrated service delivery approach.



**Conclusions:** Effective public health messaging is a key driver for TB demand generation in public health interventions. Maximizing integrated health messaging by leveraging on existing platforms can be a tool to drive demand for new health interventions.

### SOA21-961-17 Role of media engagement in disseminating TB knowledge across Meghalaya, India

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**Background and challenges to implementation:** Tuberculosis (TB) is a serious public health problem in India. Strategies to curb the spread of TB must match the multifaceted nature of the epidemic. There is lack of awareness among the general population on TB. The use of mass media is one of the important strategies in inducing behavioral change in relation to TB health seeking and diagnosis, prevention and the treatment. It is an important source of information and through a meaningful engagement about TB can have a long term impact to the general population.

**Intervention or response:** A media sensitization meeting was organized in June 2022 where 35 journalists attended the session. They were provided with information about TB, the burden in the state of Meghalaya, and the need for publishing TB related articles or the services available for TB. The Intervention of Media Engagement is showing a great impact in sharing TB knowledge at the state both rural and urban reached out.

#### Source of data Collection

Primary and Secondary data.

#### Tool for data collection

Interviews and Questionnaires.

**Results/Impact:** After the workshop in June 2022, there was an increase in number of articles of 100 newspapers clip, 120 website including you tube coverage were highlighted on TB programme and services on an average of 3- 30 coverage monthly. These articles and coverage were published on voluntary basis in all languages of the state. More media engagement could lead to increase in TB awareness and contribute towards better health seeking behavior of the population.

**Conclusions:** Media Engagement at the state of Meghalaya has seen a sharp raise after the sensitization workshop. Proper sensitization of media journalists on TB helps in having sustainable engagement. All these media engagement were free, organic and unpaid and thus showing the positive intervention to scale up in different state and country to highlighting the effectiveness of media intervention.

### SOA21-962-17 Optimising the Nigerian National Tuberculosis Call Centre to improve access to TB information and anonymous referral for TB diagnostic services

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**Background and challenges to implementation:** Several factors contributed to low TB case finding in Nigeria, including limited knowledge of the disease and inadequate access to available services. In 2015, USAID supported Nigeria to establish a TB call centre with an 11-digit number. The call centre serves as a digital hub to provide basic information on TB and refer clients to the nearest TB facility.

However, the services of the call centre were not fully optimised as the 11-digit number was not easy to remember and not adequately publicised.

**Intervention or response:** In 2021, Breakthrough ACTION-Nigeria (BA-N) through the support of USAID upgraded the functionalities of the call centre. BA-N replaced the 11-digit number with a short code, 3340, for ease of recall; updated the list of all TB testing centres which enabled prompt referrals for testing; added a call back feature to follow-up referrals, as well as a USSD component which enables self-screening and self-referral for testing.

The call centre was also promoted in the national, multi-media SBC campaign, Check Am O! encouraging anyone coughing for two weeks or more to call 3340 or dial \*3340#.

**Results/Impact:** Between October 2015 to June 2019, the hotline received 149,118 calls and made 5,976 referrals. From January 2021 to December 2022, there was a 530% (790,192) increase in the number of calls received. The hotline made 6145 referrals, and 760 callers self-reported as positive for TB. Over 70% of callers heard about the TB call centre from the mass media campaign. National TB case notification increased by 50% from 2020 (138,591) to 2021 (207,785).

**Conclusions:** A well-structured, well-promoted national TB call centre can contribute to increased access to correct TB information, and referral for TB diagnostic services. Coordinating this service with a multi-media SBC campaign is an effective way to increase the impact of demand creation activities in improving access to TB services.

## SOA21-963-17 Reaching the unreached through social media in India

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**Background and challenges to implementation:** Social media platforms such as Twitter, Facebook, and Instagram can reach large numbers of people with information about tuberculosis -- its symptoms, diagnostics, and available treatments. By sharing information on social media, public health organizations and healthcare providers can educate millions of people about TB and dispel common myths and misconceptions.

**Intervention or response:** With support from the USAID-funded Tuberculosis Implementation Framework Agreement (TIFA) project, led by JSI Research & Training Institute, Inc., the National TB Elimination Program (NTEP) engaged a professional social media agency to steer the programme's communication strategies.

In collaboration with NTEP, the agency created a social media strategy that identifies key objectives, target audiences, and outlines the purpose of different social media platforms. It also focused on creating specialized content for campaigns, key health days, creative experimentation, social media trends, and hashtags. The agency also developed the branding strategies for the NTEP.

**Results/Impact:** The engagement of a professional social media agency improved the reach, engagement, impressions, subscriptions, likes, views, and followers of the NTEP's social media messages. After the engagement of the agency (August 2022 to March 2023), followers on Instagram, Facebook, and Twitter increased from 10 to 300 (2900%), 198 to 1200 (506%), and 3403 to 4618 (36%) respectively.

Overall engagement increased from 8106 to 86878 (971.77%). Social media content on TB awareness, prevention, diagnosis, and treatment were developed and posted on social media platforms including Facebook (>250 posts), Twitter (>300 tweets), and Instagram (>250 posts).

**Conclusions:** Strategic use of social media enabled greatly increased information dissemination, expanded the diversity of facilitated interactive communication, and enhanced public engagement. This enabled people to make more informed decisions.



## E-POSTER SESSION (EP)

### EP17 Immunology for early TB diagnosis

#### EP17-1153-17 Altered interleukin-6 signalling and risk of TB disease: A meta-analysis and Mendelian randomisation study

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**Background:** The role of ubiquitous IL-6 responses in determining human tuberculosis (TB) disease risk is unknown. IL-6 inhibitors, such as tocilizumab, are thought to increase the risk of progression to TB disease, and screening for latent TB prior to using these drugs is widely recommended. We used single nucleotide polymorphisms (SNPs) in and near the IL-6 receptor (IL6R) gene, focusing on the non-synonymous variant, rs2228145, associated with reduced classical IL-6 signalling, to assess the effect of altered IL-6 activity on TB disease risk.

**Design/Methods:** We identified 16 genome wide association studies (GWAS) of TB disease. Effect estimates were extracted for each additional copy of the C allele in rs2228145. We also performed Mendelian randomisation (MR) analyses using rs2228145-C alone, as well as multiple nearby IL6R variants, to assess the impact of reduced IL-6 signalling on odds of TB disease.

**Results:** Sixteen GWAS were included, collating 17,601 cases of TB disease and 977,334 controls across four continents. For each additional rs2228145-C allele, the odds of TB disease reduced (OR 0.94, 95% CI 0.91–0.97,  $p=2.9 \times 10^{-5}$ ). MR analyses, using multiple independent IL6R variants, revealed that reduced classical IL-6 signalling, derived from measurements of two separate exposure variables (serum CRP and plasma IL6R concentrations), was consistently associated with lower odds of TB disease.

**Conclusions:** Our findings establish a causal relationship between IL-6 signalling and the outcome of TB infections, suggesting IL-6 antagonists do not increase the risk of TB disease but rather should be investigated as adjuncts in its treatment.

#### EP17-1154-17 The NTM-iSpot, a diagnostic test for pulmonary non-tuberculous mycobacterial infections for the future?

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**Background:** Nontuberculous mycobacteria (NTM) infections are still a challenge for respiratory and infectious diseases physicians. While their incidence is increasing globally, the standard criteria used for diagnosis remain unchanged since 2007. The guidelines require clinical, microbiological and radiological evidence of disease before the diagnosis can be confirmed.

Further, the clinical relevance of NTM isolations is not fully understood and remains difficult to determine. Keeping in mind the need for better tests to diagnose and determine the clinical relevance of NTM pulmonary infections we assessed the performance of an NTM-specific fluorescent EliSpot in a cohort of people with NTM in pulmonary samples.

**Design/Methods:** Using an NTM-specific 2-color fluorescence EliSpot (NTM-iSpot, AID GmbH, Straßberg, Germany) we evaluated the immune response to NTM-specific antigens (glycopeptidolipids) through T-cell production of IFN- $\gamma$  and IL-2. We tested 44 blood samples: 18 from patients with past or present pulmonary NTM (further classified as NTM-related disease, NTM

colonization, and past NTM related disease), 5 from patients with extrapulmonary NTM, 15 from patients with bronchiectasis with no record of NTM, and 6 from healthy controls.

**Results:** The extrapulmonary NTM group had the highest rate of positive results followed by the group of NTM in pulmonary samples. Within the latter, the majority of positive results were found in the NTM-related disease group (55.5% for IFN- $\gamma$  and 30.0% for IL-2), followed by the colonization group (25.0% for IFN- $\gamma$  and 33.3% for IL-2) (Table 1).

No positive results were obtained in the groups of past and solved NTM-related pulmonary disease, bronchiectasis without record of NTM, and healthy controls.

	Reactive (%)	Reactive/Borderline (%)
Pulmonary NTM + (n=17)	5 (29.4)	7 (41.2)
Disease (n=9)	5 (55.5)	6 (66.7)
Colonization (n=4)	0 (0.0)	1 (25.0)
Past disease (n=4)	0 (0.0)	0 (0.0)
Extrapulmonary NTM + (n=4)	3 (75.0)	3 (75.0)
Healthy control bronchiectasis (n=15)	0 (0.0)	1 (6.7)
Healthy controls (n=6)	0 (0.0)	0 (0.0)

Table 1.

**Conclusions:** The NTM-*i*Spot may have the potential to help guide the clinical evaluation of patients with NTM present in pulmonary samples but of unclear clinical relevance.

### EP17-1155-17 Food insecurity and undernutrition associated with distinct immunologic profiles in people with TB and advanced HIV starting antiretroviral therapy

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**Background:** Food insecurity and undernutrition are related but distinct concepts contributing to poor HIV and tuberculosis outcomes. This may be especially important after ART initiation, a period associated with high rates of morbidity and mortality and key immunologic changes. Their immunologic phenotypes, which may relate to clinical outcomes, remain understudied.

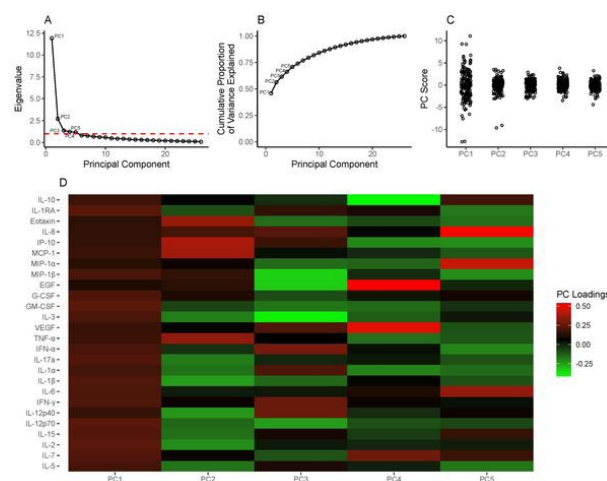
**Design/Methods:** We analyzed data from a cohort of ART-naïve adults with advanced HIV (CD4<125 cells/mm<sup>3</sup>) and newly diagnosed tuberculosis in Botswana 2009-2013. 29 plasma biomarkers were measured pre-ART and 4 weeks post-ART initiation.

We used principal components analysis (PCA) to identify immunological profiles and multivariable linear regression models to assess relationships between pre- and post-ART principal components (PCs) and baseline food insecurity (Household Food Insecurity Access Scale), baseline undernutrition (BMI<18.5 kg/m<sup>2</sup>), and subsequent death.

**Results:** 165 participants had a median age of 35 years (IQR 31-41), 73 (44%) were female, and a median baseline CD4 count of 61 cells/mm<sup>3</sup> (IQR 32-93). 17 (10%) died. PCA identified 5 PCs with eigenvalues >1 (Panels A-C).

After adjustment for confounders, food insecurity was associated with PC3 pre-ART (0.20 per increased category of severity, 95% CI 0.03-0.37) and post-ART (0.25, 95% CI 0.08-0.42), driven by decreases in IL-3 and increases in IFN- $\alpha$ , IFN- $\gamma$ , IL-12p40, IL-8, VEGF, IL-1 $\alpha$ , and IP-10 (Panel D).

Undernutrition was associated with PC5 pre-ART (0.37, 95% CI 0.04-0.70) and post-ART (0.48, 95% CI 0.15-0.81), driven by increases in IL-8, MIP-1 $\alpha$ , and IL-6, and decreases in IP-10 and IFN- $\alpha$ . Post-ART PC3 (4.34 percentage point increased risk per increased score of 1, 95% CI 0.6-8.9) and post-ART PC5 (3.01, 95% CI 0.18-5.58) were associated with death in adjusted models.



**Conclusions:** We identified distinct immunologic profiles associated with food insecurity, undernutrition, and death. Different pathophysiologic processes may link food insecurity and undernutrition with poor outcomes. These profiles might direct interventions to improve outcomes in this precarious clinical setting.

### EP17-1156-17 The impact of polystyrene and polyethylene terephthalate nanoplastics on the growth of *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *M. smegmatis*

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**Background:** Nowadays the problem of biosphere pollution with nanoplastics (NPs) causes serious concerns about their influence on human health. Recent studies demonstrated that people are exposed to NPs through ingestion and inhalation, and these plastic particles can cause respiratory symptoms. Nevertheless, most mechanisms of NPs influence on health remain unclear. As one of the possible ways of impact, NPs could interact with pathogenic microbiota.

This study investigated the effects of NPs on the growth of the common respiratory pathogens *S. aureus* and *P. aeruginosa*. *M. smegmatis* was also used as a model microorganism despite not being considered a human pathogen.

Experiments were aimed to obtain a general understanding of interactions between respiratory pathogens and NPs in their growth environment.

**Design/Methods:** The influence on bacteria was estimated by cultivation with NPs and subsequent growth curve construction. One colony was resuspended in liquid medium, supplemented with 150 ng/ml of polyethylene terephthalate (PET<sub>150nm</sub>) or polystyrene (PS<sub>50nm</sub>), and incubated overnight at 37°C and 170 rpm.

Then, the overnight culture was 10-fold diluted with fresh medium, distributed into a 96-well plate, and incubated in a plate reader under the same conditions.

Optical density measurements at wavelength 600 nm were taken every 30 minutes. Microorganisms cultured without NPs served as control.

**Results:** *S. aureus* grew slower in the presence of PET and PS. Both studied NPs did not influence the growth of *P. aeruginosa*. *M. smegmatis* grew slower with PS and was not affected by PET.

**Conclusions:** NPs influence the growth of respiratory pathogens in a different manner depending on the bacterial species and type of NPs. There are still many unanswered questions about the interactions of different microorganisms and NPs, that require further research.

### EP17-1157-17 Correlating Xpert Ultra cycle threshold values with tuberculous mycobacterial load in a high-burden setting

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**Background:** Identifying and promptly managing infectious tuberculosis (TB) is paramount to curb transmission. However, this is challenging since traditional measures of mycobacterial load, such as smear status and time to TB culture positivity, are often unavailable. Nucleic acid amplification tests, such as GeneXpert Ultra (GXPU), can rapidly provide cycle threshold (Ct) values - a quantitative readout of burden. We investigated the correlation between GXPU Ct values and measures of sputum mycobacterial burden.

**Design/Methods:** We reviewed prospective studies involving symptomatic ambulatory patients presenting to primary healthcare facilities with valid GXPU, smear and TB culture results. High mycobacterial load was defined as any grade of smear positivity and/or time to TB culture positivity  $\leq 7$  days. Ct values were evaluated in raw, mean, and normalized format. Diagnostic accuracy of each measure was evaluated.

**Results:** Of 1178 participants screened across five studies, 171 were GXPU positive and had available Ct values. AUC (95% CI) for raw Ct value was 0.83 (0.76-0.89) in smear-positive persons, and 0.87 (0.80 - 0.93) in those defined as having a high mycobacterial load.

After bootstrapping, a raw Ct value less than 19.2 (as a rule-in marker of high mycobacterial burden) had a specificity of 92.9% (95% CI 80.5 - 98.5), sensitivity of 62.8% (95% CI 53.8 - 71.1), PPV of 96.4% (95% CI 89.9 - 99.3), and NPV of 44.8% (95% CI 34.2 - 55.9). Ct value was not useful as a screening test due to its poor specificity; a cut-off of 23 yielded a sensitivity of 95.8% (95% CI 90.4 - 98.6), but a specificity of 45.3% (95% CI 931.6 - 59.6).

**Conclusions:** A raw Ct value on GXPU is a good marker of mycobacterial load and can be associated with a greater probability of infectiousness and hence transmission potential. These data support using Ct value to direct transmission-interrupting interventions such as patient isolation and contact tracing studies.

### EP17-1158-17 Impact of concurrent cART and 3HP therapy on LTBI reactivation in a non-human primate model for *M. tuberculosis*/SIV co-infection

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**Background:** We have previously shown that earlier initiation of combined antiretroviral therapy (cART) is critical in mitigating chronic immune activation-driven latent TB infection (LTBI) reactivation in rhesus macaque (RM) model of TB/SIV. However, skewed CD4<sup>+</sup> T effector memory (CD4<sup>+</sup> T<sub>EM</sub>) responses persist in the lung and new TB lesions form despite cART treatment. We hypothesize that coadministration of 3HP with cART would result in superior bacterial control and longer lasting functional *Mtb*-specific responses in the lung.

**Design/Methods:** Six RMs were infected with low dose *Mtb* via aerosol and co-infected with SIV<sub>mac239</sub>. They were administered cART+3HP at 2 weeks post-SIV co-infection for 12 weeks. Bacterial burden, PET/CT scans, high parameter flow cytometry, bulk RNAseq, scRNA-seq on longitudinally collected BAL samples were performed.

**Results:** Five out of six macaques treated with cART+3HP were completely devoid of pulmonary bacteria at necropsy with significantly lower lung involvement compared with cART only-treated macaques. The lung tissue in cART+3HP cohort revealed a significant decrease in genes associated with cell proliferation compared to cART only cohort. Though the depleted CD4<sup>+</sup> T cells were replenished to a higher extent than with cART alone, the percentages remained significantly lower than those in LTBI macaques. Importantly, cART+3HP failed to reverse the dysfunctional CD4<sup>+</sup> T<sub>EM</sub> responses in the lungs induced by SIV co-infection, and failed to control inflammation in the lung.

**Conclusions:** Concurrent administration of ART and 3HP improves clinical and microbiological attributes of the co-infection but inflammation in the lung is not ameliorated.

These results suggest that co-infected individuals may remain at risk for progression due to subsequent infections or due to reactivation because of persisting defect in T cell responses.

By identifying systemic and lung-specific immune components in this model, it is possible to identify pathways that can be targeted for host-directed adjunctive therapies for TB/HIV co-infection.

### EP18 Imaging to end TB

#### EP18-1159-17 Comparison of different Lunit INSIGHT CXR software versions when reading chest radiographs for TB

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**Background:** New versions of computer-aided detection (CAD) software for TB screening are regularly released by developers, which purport to have incremental performance gains.

We independently measured the differences in CAD software outputs between INSIGHT CXR versions 3.8.0.4 and 3.9.0.1 (Lunit, South Korea).

**Design/Methods:** A well-characterized chest X-ray (CXR) DICOM test library was compiled using data from community-based active TB case finding activities in Ho Chi Minh City, Viet Nam.

The performance of Lunit CAD software versions was compared by measuring the area under the receiver operating characteristic curve (AUC), stratified by key clinical and demographic variables and using Xpert MTB/RIF Ultra (Ultra) test results as the reference standard. Median Lunit CAD scores were compared using the Wilcoxon signed-rank test.

**Results:** The DICOM test library contained 2,733 participants, of whom 10.4% had Ultra-positive test results. The new Lunit CAD software version had a significantly higher AUC than its predecessor (AUC 0.78 vs 0.76, p=0.020).

There were no significant differences in performance between the software versions among newly diagnosed participants (AUC 0.81 vs 0.81, p=0.574).

However, the new version performed significantly better among people with a past history of TB (AUC 0.73 vs 0.67, p=0.002). The median Lunit CAD score was significantly higher for the new version (0.61 vs 0.35, p<0.001).

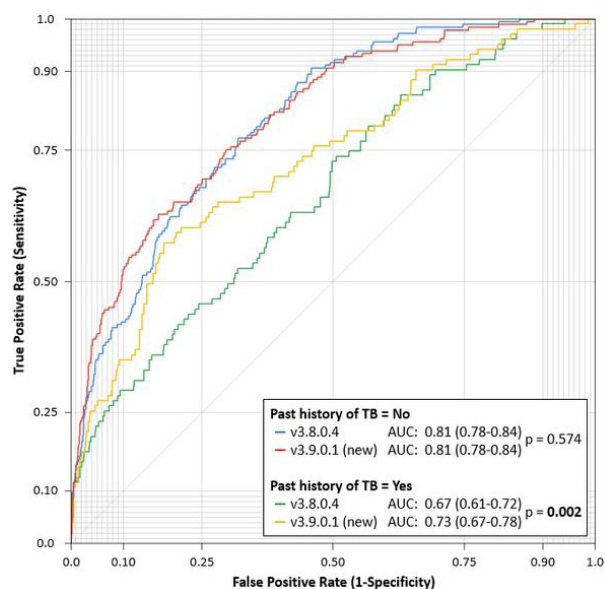


Figure. Comparison of Lunit CAD software versions, stratified by past history of TB.

**Conclusions:** INSIGHT CXR v3.9.0.1 performs significantly better than its predecessor, which has established itself as a top-performing CAD software in multiple independent evaluations. The new version's performance gains were localized in a key sub-population which has traditionally suffered from lower performance across all CAD solutions. The increased median Lunit CAD score in the new version indicates that the software's cut-off score should be reassessed before or in the early days of programmatic deployment in order to optimize detection of TB and utilization of resources.

### EP18-1160-17 Improving TB case-finding using optimised TB screening strategy among at-risk populations in Nigeria

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**Background and challenges to implementation:** Computer-aided detection for TB (CAD4TB) is increasingly being used globally in screening and testing algorithms to increase TB yield. The USAID-funded TB LON project led by KNCV implemented targeted community TB active case-finding (ACF) intervention using chest X-ray TB screening method in Nigeria. The strategy aimed to increase TB case-finding.

**Intervention or response:** We deployed targeted community TB screening interventions in 8 high burden states in Nigeria. At-risk populations were identified using an Early Warning Outbreak Recognition System (EWORS). The intervention used portable digital X-ray (PDX) fitted with artificial intelligence (AI) for TB screening.

Individuals with chest abnormalities were identified as presumptive TB and further evaluated for TB using the GeneXpert MTB/Rif instrument. In a further subcategory, clients who tested negative with GeneXpert were further reviewed by a consultant radiologist for clinical diagnosis. Confirmed TB cases were linked to treatment. Intervention efficiency was assessed using the number needed to screen (NNS) and the number needed to treat (NNT).

**Results/Impact:** From January to December 2022, 114,935 (M 61,817; F 53,118) persons were screened for TB. Of these, 10,594 (9%) presumptive TB were identified and 10,580 (100%) were further evaluated for TB using GeneXpert, resulting in the diagnosis of 2,520 (24%) TB cases. Among the 2,520 (M 1,780; F 740) confirmed TB cases, 2,474 (98%) were linked to appropriate treatment. The NNS and NNT are 46 and 4, respectively. The 2,520 cases put on treatment account for 12% of the 21,192 TB notifications in the 8 states.

**Conclusions:** Our results showed good efficiency in identifying TB cases among at-risk populations, including a higher proportion of TB cases among the male sex, indicating the utility of the strategy in finding the missing TB cases in Nigeria.

### EP18-1161-17 Improving portable digital X-ray-driven active TB case-finding using the X-MAP system in Nigeria

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**Background and challenges to implementation:** With a notification rate of just about 30%, the huge gap in TB case detection and notification in Nigeria has always been a problem and to bridge this gap KNCV Nigeria with funding from USAID introduced the use of Ultra-portable digital X-ray systems with AI coupled to the XMAP which is a real time application that links radiologists to radiographers for review of digital X-rays. We present a 1-year results of the field experience using the PDX and XMAP system in Nigeria.

**Intervention or response:** Targeted community outreaches were conducted using 8 portable digital X-ray machines deployed across 8 states. Identified presumptive were tested using the GeneXpert machine, those that turned out negative and those presumptive that were unable to produce sputum were uploaded onto the XMAP platform for review by consultant radiologists. We present the results of the reviewed reports of the x-ray films uploaded between January and December 2022.

**Results/Impact:** Of the 4,969 films uploaded onto the XMAP platform a total of 2,047 suggestive of TB cases were diagnosed and this gave a 40% TB yield across the

8 machines. The XMAP platforms proves to be very efficient as number needed to review a film was just 2 for the 8 PDX machines in collection.

TB LON PDX Machines	# Uploaded for Review	Suggestive Of T B	Not Suggestive Of T B	Un-confirmed T B	TB yield among Films Reviewed	Number Needed to Review (NNR)
MOB6046 - MOB6046 - DLB 1	913	167	738	8	0.2	5
MOB6066 - MOB6066 - DLB 3	748	372	367	9	0.5	2
MOB6067 - MOB6067 - DLB 4	47	5	42	0	0.1	9
MOB6068 - MOB6068 - DLB 5	988	208	753	27	0.2	5
MOB6069 - MOB6069 - DLB 2	503	408	87	8	0.8	1
MOB6070 - MOB6070 - DLB 6	532	446	76	10	0.8	1
MOB6071 - MOB6071 - DLB 7	494	216	271	7	0.4	2
MOB6072 - MOB6072 - DLB 8	744	225	495	24	0.3	3
TOTAL	4,969	2,047	2,829	93	0.4	2

Table 1.

**Conclusions:** Results from table 1 above has shown that portable Digital X-ray with the XMAP real time reporting system is a game changer to improving clinical TB diagnosis in Nigeria. We would also like to recommend for the deployment of these new tools to KNCV supported and non PDX states in country.

## EP18-1162-17 The value of cavity imaging features in the diagnosis of drug-susceptible and drug-resistant TB

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**Background:** Differential diagnosis of drug-sensitive tuberculosis (DS-TB) and different types of drug-resistant tuberculosis DR-TB patients increases the likelihood of treatment success and reduces transmission. In the study, we explored the differences in cavity imaging features among DS-TB and different types of DR-TB patients.

**Design/Methods:** 160 DS-TB patients and 323 different types of DR-TB patients from Hospital A were retrospectively collected with all their clinical data and CT

scans involved. All CT images were independently reviewed and labeled by two junior radiologists, and if two Dice coefficient values were  $\geq 0.95$ , they would be averaged as the ground truth of the image. Otherwise, a senior radiologist would step in to make the final determination. Cavity imaging features, including the incidence of cavity; the number of involved sextants, cavities and cavities in nodules (masses) or consolidation; the size and roundness of the outer and inner cavities, and the thickness of cavity walls were calculated and statistically analyzed.

**Results:** The comparison test showed that both the incidence and the number of cavities of DR-TB group were significantly higher than the DS-TB group (all  $P < 0.001$ ), and the occurrence of multiple cavities, three or more involved lung lobes and cavities in nodules (masses) were also higher in DR-TB groups ( $P < 0.001$ ;  $P = 0.002$ ;  $P < 0.05$ ). In addition, there were significant differences in other cavity features, including its external and internal diameter and the mean wall thickness among the DS-TB and different types of DR-TB, as well as among within groups of DR-TB (all  $P < 0.005$ ).

Group	Sex			Age				$\chi^2$	
	Male (n=311)	Female (n=172)	$\chi^2$	18-25 (n=118)	26-35 (n=177)	36-45 (n=72)	46-55 (n=72)		$\geq 56$ (n=44)
DS-TB	91 (29.3)	69 (40.1)	5.892 <sup>1</sup> **	36 (30.5)	56 (31.6)	22 (30.6)	25 (34.7)	21 (47.7)	5.074 <sup>1</sup> *
DR-TB	220 (68.1)	103 (59.9)	9.053 <sup>2</sup> *	82 (69.5)	121 (68.4)	50 (69.4)	47 (65.3)	23 (52.3)	20.081 <sup>2</sup> *
-MDR-TB	62 (19.9)	24 (14.0)	3.337 <sup>3</sup> *	23 (19.5)	36 (20.3)	10 (13.9)	11 (15.3)	6 (13.6)	14.862 <sup>3</sup> *
-XDR-TB	16 (5.1)	11 (6.4)		9 (7.6)	9 (5.1)	6 (8.3)	1 (1.4)	2 (4.5)	
-MR-TB	110 (35.4)	47 (27.3)		41 (34.7)	48 (27.1)	27 (37.5)	29 (40.3)	12 (27.3)	
-PDR-TB	32 (10.3)	21 (12.2)		9 (7.6)	28 (15.8)	7 (9.7)	6 (8.3)	3 (6.8)	

<sup>1</sup>Comparison of DS-TB and DR-TB.

<sup>2</sup>Comparison of DS-TB and different types of DR-TB.

<sup>3</sup>Comparison among different types of DR-TB.

\*,  $P < 0.05$ ; \*\*,  $P < 0.01$

Abbreviation: DS-TB, drug-sensitive tuberculosis; DR-TB, drug-resistant tuberculosis; MDR-TB, multidrug-resistant tuberculosis; XDR-TB, extensively drug-resistant tuberculosis; MR-TB, mono-drug resistant tuberculosis; PDR-TB, poly-drug resistant tuberculosis.

Table 1. Patient demographics of DS-TB and DR-TB patients.

**Conclusions:** Cavities were more widely distributed in DR-TB patients compared to DS-TB patients, and the cavity incidence, the number of cavities ( $\geq 3$ ) and involved lung lobes ( $\geq 3$ ), and the proportion of cavities in pulmonary nodules (masses) are significantly higher in DR-TB patients.

### EP18-1163-17 Validation of a computer-aided detection chest X-ray application using the WHO-TDR calibration protocol in individuals with presumptive TB in Delhi State, India

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**Background:** Prior to implementation of computer aided detection (CAD) software for triage in individuals with presumptive tuberculosis (TB), the minimum CAD threshold score needs to be determined. This threshold defines when a patient's CXR is classified as suggestive of TB and hence requires confirmatory TB testing. In this validation study, according to the WHO-TDR calibration protocol, we determined which threshold to use for triaging individuals with presumptive TB visiting primary health centres (PHC) in Delhi, India.

**Design/Methods:** Three PHCs in Delhi State, enrolled consecutive individuals with presumptive TB during three months, took CXR images with a portable X-ray system (FDR Xair XD 2000) and collected sputum specimens for subsequent molecular testing.

Additionally, retrospective data was collected from a separate group of individuals with confirmed TB who had CXR and molecular testing done at a neighbouring chest clinic in the period before portable X-ray systems were installed.

CXR images were independently interpreted by a local radiologist and analysed with qXR version 3.2.9 (qXRv3) using FINDs digital infrastructure that is designed for rapid, independent accuracy assessment of CAD software.

**Results:** Data from 1411 individuals were included, of whom 354 had confirmed TB (43 enrolled prospectively, 311 retrospectively). The area under the receiver operator curve (AUC) of qXRv3 was 0.89 (95% CI 0.87-0.91, Figure).

At the threshold where CAD reaches the same sensitivity as the local radiologist (which is 73%), qXR reached a slightly higher, yet not statistically different, specificity (86% vs 83% by the local radiologist).

At the vendor's recommended threshold of 0.5, the sensitivity reached 82% (95% CI 78-86%) and specificity 76% (95% CI 74-79%).

**Conclusions:** qXRv3 reached a similar performance of that of local radiologist in India, when used in PHCs, but applying the vendors recommended threshold would result in a higher sensitivity and should be considered when resources allow.

### EP18-1164-17 Comparative analysis of the impact of active case-finding: X-ray screening vs. verbal screening for TB diagnosis

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**Background and challenges to implementation:** Pakistan ranks fifth among the thirty countries with the highest TB burden in the world. Approximately 611,000 people are estimated to have fallen ill with TB during the year 2021. Approximately, 339,000 were notified, giving an estimated notification of 55%, with a treatment success rate of 93%<sup>1</sup>.

<sup>1</sup>WHO Global TB Report 2022

**Intervention or response:** Mercy Corps Pakistan, introduced active case-finding (ACF) through chest camps to maximize the outreach efforts for the detection of TB patients amongst the undetected, vulnerable, and marginalized groups.

For this purpose, two types of camps were organized i.e., verbal screening chest camps (where a doctor clinically evaluates the general population), and x-rays screening camps (where a mobile van equipped with X-rays for onsite screening and testing, along with the clinical evaluation by a doctor was used).

**Results/Impact:** In the X-ray screening camps, a total of 151,226 people were screened. The chest X-rays of 108,090 (78%) and sputum samples of 31,342 (22%) people were tested by Gene Xpert systems. A total of 5,978 new TB cases were diagnosed, giving a yield of 2.5 patients per camp and a 7% presumptive positivity rate. In verbal screening camps, 56,754 out of 302,476 people were screened in the OPD and identified as presumptive. A total of 32,231 samples (53%) were tested through acid-fast bacillus (AFB) microscopy and 29,140 samples (47%) by Gene Xpert systems. During testing, 8,740 new TB cases were diagnosed. The yield was 1.5 patients per camp, exhibiting a 7% presumptive positivity rate.

**Conclusions:** Analyzing the results, it is evident that X-ray screening camps had a better yield than verbal screening camps. ACF facilitated strategic access to the vulnerable population, ensuring early diagnosis and the provision of cost-effective treatment. This contributed to an additional 8% of case notifications to the national data, which would otherwise have been missing cases.

## EP19 Dynamics and challenges in DRTB

### EP19-1165-17 Rapid detection of *M. tuberculosis* in sputum using a solvatochromic trehalose probe

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**Background:** Tuberculosis (TB) is the leading cause of death from an infectious bacterial disease. Poor diagnostic tools to detect active disease plague TB control programs and affect patient care. Accurate detection of live *Mycobacterium tuberculosis*, the causative agent of TB, could improve TB diagnosis and patient treatment.

**Design/Methods:** We followed standard chemical procedures for probe synthesis. We performed fluorescence labeling experiments of bacterial cultures in various conditions.

We analyzed the data by fluorescence microscopy and/or flow cytometry. All data were analyzed using GraphPad Prism software's ANOVA (analysis of variance) test.

**Results:** We designed a 4-*N,N*-dimethylamino-1,8-naphthalimide-conjugated trehalose (DMN-Tre) probe that undergoes >700-fold increase in fluorescence intensity when transitioned from aqueous to hydrophobic environments. This enhancement occurs upon metabolic conversion of DMN-Tre to trehalose monomycolate and incorporation into the mycomembrane of Actinobacteria.

DMN-Tre labeling enabled the rapid, no-wash visualization of mycobacterial and corynebacterial species without nonspecific labeling of Gram-positive or Gram-negative bacteria. DMN-Tre labeling was detected within minutes and was inhibited by heat killing of mycobacteria.

Furthermore, DMN-Tre labeling was reduced by treatment with TB drugs, unlike the clinically used auramine stain. Lastly, DMN-Tre labeled Mtb in TB-positive human sputum samples comparably to auramine staining.

**Conclusions:** Collectively, our data suggest DMN-Tre reports both on bacterial identity and on metabolic viability. Indeed, DMN-Tre labeling can report on drug sensitivity. As well, the solvatochromic property of DMN-Tre enables rapid Mtb imaging without washing steps, even in complex samples, such as sputum.

Importantly, the unique mode of fluorescence activation of DMN-Tre allows for an operationally simple procedure—a single incubation step. Thus, the DMN-Tre labeling procedure may translate well both to research and to clinical applications.

### EP19-1166-17 A new stool tool: targeted next-generation sequencing to support treatment monitoring during pulmonary TB treatment

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**Background:** In 2021, 10.6 million people were estimated to develop tuberculosis (TB) with 1.6 million deaths. The burden of drug-resistant TB (DR-TB) is increasing with 3.6% of new TB cases and 18% of previously treated cases. Treatment monitoring is important to promote successful outcomes and to promptly detect emerging drug-resistance in patients who fail therapy.

**Design/Methods:** Stool and sputum samples were analyzed from participants with pulmonary TB and persistent sputum culture positivity completing outpatient treatment in Mbabane, Eswatini from 2014-2021. Persistent sputum culture positivity was defined by MGIT culture positive at baseline and at least one additional timepoint (2, 4, 8, 24 or 56 weeks).

We assessed the potential of targeted next generation sequencing (t-NGS) on an Illumina MiSeq using the Deeplex MYC-TB assay for treatment monitoring and screening for evolution of *Mycobacterium tuberculosis* drug resistance in stool and sputum samples.

**Results:** 11 participants (aged 13-55 years; median 27 years; 64% (7/11) people living with HIV [PLHIV]) provided 47 stool and/or sputum samples for t-NGS. Of these, interpretable sequencing results were obtained in 17/23 stool and 22/24 sputum samples. t-NGS on stool identified mutations during treatment consistent with resistance identified by sputum culture pDST or sputum Xpert in 88% of instances (15/17) along with additional drug resistance mutations.

One participant was identified with a low level mutation (defined by identification in < 5% of the coverage depth of the gene) on stool sequencing (1.8% *ahpC*), which correlated with INH phenotypic resistance from sputum culture. Stool t-NGS also identified the *rpoB* I491F mutation (RIF resistance) not identified on sputum culture pDST or Xpert (stool/sputum).



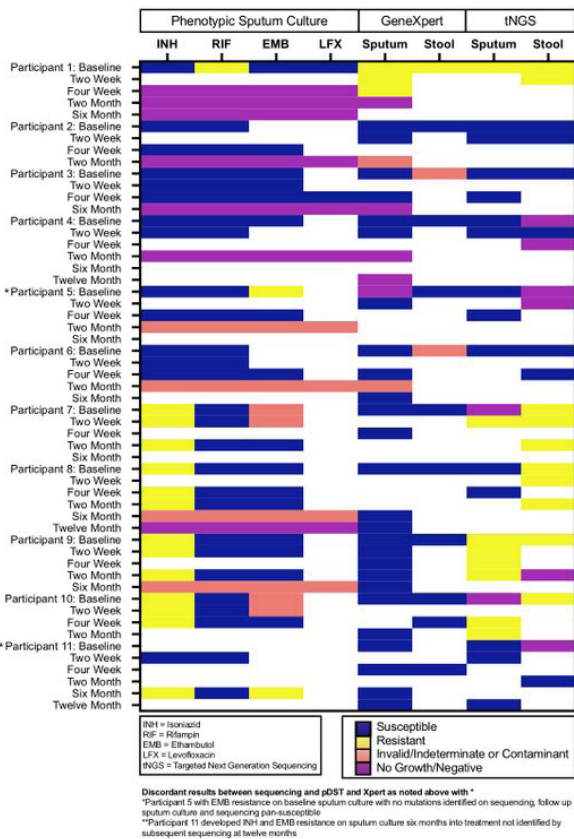


Figure 1. Longitudinal comparison of pDST and GeneXpert vs tNGS.

**Conclusions:** t-NGS is a promising TB treatment monitoring tool to detect the emergence of *M. tuberculosis* drug resistance as a potential cause of treatment failure. Utilizing stool offers an important advantage for individuals with paucibacillary sputum such as children and PLHIV.

### EP19-1167-17 Implementation of PERMYCO, a new 96-well broth microdilution plate for susceptibility testing of *M. tuberculosis*

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**Background:** Improving treatment success rate for MDR-TB involves customizing each patient's antimicrobial regimen to improve efficacy while minimizing toxicity. This requires the Lab ability to analyze MICs in order to affect both drug choice and dosage. The goal of this work is to establish the reproducibility of the

dry 96-well PERMYCO microtiter plate for use in MIC measurements utilizing bedaquiline, delamanid, and other drugs using Sensititre™ plates.

**Design/Methods:** Bacillary suspensions of *M. tuberculosis* H37Ra reference strain ATCC 25177 and drug susceptible clinical isolates has been evaluated. Each mycobacterial isolate has been incubated for 10 to 21 days in a dry customized 96-well broth microdilution plate and then read by the ThermoScientific™ Sensititre™ Vizion™ System. Twelve anti-TB drugs (rifampin, isoniazid, ethambutol, levofloxacin, moxifloxacin, amikacin, kanamycin, ethionamide, clofazimine, streptomycin, delamanid, and bedaquiline) were included, at 5 to 8 two-fold dilutions. The reproducibility of the method was assessed by examining the consistency of repeated readings within the expected range for *M. tuberculosis* H37Ra reference strain. A distribution analysis of MIC values in clinical isolates identified as RIF and INH susceptible by drug sensitivity testing on LJ medium was also performed.

**Results:** The inter-assay consistency in *M. tuberculosis* H37Ra was 100% for all drugs, with the exception of delamanid and isoniazid which showed a concordance of 96% and 92%, respectively. Susceptible clinical isolates showed, in most cases, MICs very close to the critical concentrations of various first- and second-line drugs, but a lower sensitivity was detected in DLM and BDQ, despite assuming that patients have not used these drugs.

**Conclusions:** After 10 to 21 days of incubation, we found that PERMYCO plate is optimally read using the Sensititre™ Vizion™ System. We are providing early evidence that PERMYCO plate may quantitatively evaluate the extent of TB-drug resistance that is linked to genetic variation although it may require further confirmation.

### EP19-1168-17 Implementation of aspect connectivity platform for TrueNat MTB Plus and MTB/RIF Dx: Challenges and early lessons learnt

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**Background:** Truenat *M. tuberculosis* (MTB) and Rifampicin (RIF) diagnostic testing was implemented for the first time in 2022 as part of the USAID/Stop TB Partnership introducing New Tools Project. Implementation of Aspect connectivity for Truenat instruments ensures that patient information and test results from Truenat are integrated with GeneXpert results and are securely

communicated in real time to the national program decision makers and quality indicators are available for Molbio for remote troubleshooting support.

**Design/Methods:** The USAID-funded Infectious Disease Detection and Surveillance (IDDS) project contracted with SystemOne to implement Aspect connectivity solutions for 88 Truenat instruments in Zimbabwe, Tanzania, and Bangladesh. Similarly, Stop TB Partnership contracted SystemOne for connection of 38 instruments in Nigeria. Feedback on implementation was solicited from the IDDS country teams, SystemOne installation engineers, and program staff to identify challenges and early lessons learned.

**Results:** The most frequent challenges identified included optimization of required software upgrade from Molbio, customizing data agreements with SystemOne and Ministries of Health, gaps in data transmission when test results are not reviewed by the end users, the requirement of a subscriber identity module (SIM) data card where Wi-Fi connections are absent, size of data transmission files, and SIM data costs for storage of 300 MB per month on average. Also, there are additional data needs for software upgrades.

**Conclusions:** Training a cadre of superusers to support the Aspect connectivity platform is essential for sustainable support and to ensure successful implementation. Lessons learned included:

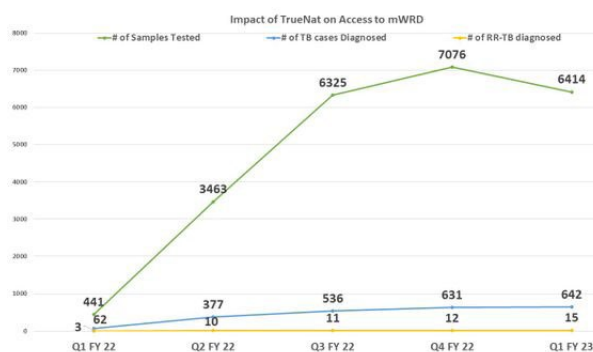
1. Competent superusers are critical to troubleshoot and rapidly resolve glitches and train new end users;
2. Providing SIM cards with sufficient data is necessary to manage result data transmission and software upgrades; and
3. Training Truenat end-users to review all results, including MTB and RIF, is needed to avoid data transmission gaps.

## EP19-1169-17 Using TrueNat to increase access to molecular WHO-recommended rapid diagnostics test for TB in Southwest Nigeria: Implementation results and lessons learnt

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**Background and challenges to implementation:** The role of new innovations in ending TB cannot be over-emphasized. The New Tools Project (iNTP) by USAID/ Stop TB partnership was embraced by the Institute of Human Virology, Nigeria (IHVN) through the USAID TB LON 3 project in four Southwest States in Nigeria. These included donations of 10 battery-powered Truenat Duos workstations that can work at temperatures as high as 40°C, they were deployed to 10 Local Government Areas with high sample testing turn-around-time to improve access to WHO-recommended molecular diagnostic platforms in hard-to-reach areas.

**Intervention or response:** Site selection and stakeholders' engagement was carried out in collaboration with the National and State Tuberculosis Control Program, 16 medical laboratory personnel were trained as end users, and over 300 healthcare workers were sensitized to use the machines. The Project relied on the existing sample referral network to serve the Truenat facilities, while 4 facilities with inadequate human resources were supported with ad-hoc staff.



**Results/Impact:** Access to WHO-recommended molecular techniques increased from 38% to 85% on the project between December 2021 to December 2022. 23,719 samples were tested using TrueNat, from which 2,248 (9.5%) were positive with 51 Rif resistant cases. All the diagnosed patients were placed on appropriate

regimens, and pre-enrolment loss-to-follow-up due to poor access to diagnostics was drastically reduced from 17% to 0% in the supported facilities.

**Conclusions:** TrueNat testing platform has proved itself worthy of its suitability in low-resource tropical settings and hard-to-reach areas because it is battery-powered and can work at 40<sup>o</sup> C. This particularly makes it useful in tropical settings with high burden of TB and limited access to molecular diagnosis. Hence, embracing newer innovations and scaling up with additional TrueNat testing platforms is crucial to finding the missing TB cases globally.

### EP19-1170-17 Improving national access to molecular TB diagnosis using a quality improvement collaborative approach in Uganda

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**Background and challenges to implementation:** Access to molecular test like GeneXpert, by persons with presumptive TB in Uganda remains suboptimal. In October 2021, only 55% of all bacteriologically confirmed TB patients were examined by a molecular test against a recommended 71% national target. Reasons for the gap include; persons with presumptive TB dropping off waiting line before providing sputum sample, delay to examine samples hence discarded and missing test results for samples examined.

**Intervention or response:** USAID LPHS TB activity in collaboration with the national TB program set up a national quality improvement collaborative to address these gaps. A technical working group was established to review national performance data and select high volume sites contributing 80% of the gap. A change package; assigning volunteer to educate patients on sputum production, collect and deliver samples to testing points, relaying test results back from Lab by sms and assigning personnel to examine sputum samples was designed for all these sites. District-based quality improvement teams were oriented on this change package, facilitated to provide onsite mentorship to the health facilities. Periodic virtual meetings were held and a national database created to monitor progress of implementation of the collaborative on access to molecular diagnostic tests

**Results/Impact:** Access to molecular TB tests improved from 54.9% in October 2021 to 80% in December 2022 at the collaborative sites (contributing 80% of the national gap).

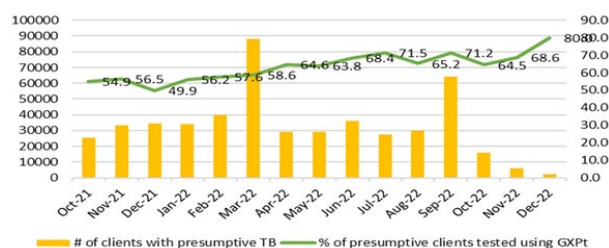


Figure. % of presumptive clients tested using GenXPert.

**Conclusions:** A national level quality improvement collaborative improved access to molecular testing. We recommend adaptation of this approach in similar settings to increase identification of missing TB case globally.

### EP19-1171-17 Use of targeted next-generation sequencing for the diagnosis of drug-resistant TB: A cost-effectiveness analysis

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**Background:** Drug-resistant tuberculosis (DR-TB) is a critical public health threat and typically requires bacteriological confirmation coupled with phenotypic drug susceptibility testing (pDST). Targeted next-generation sequencing (tNGS) can provide comprehensive data on clinically relevant resistance and has emerged as a promising alternative to existing DST.

We assessed the potential cost-effectiveness of tNGS used among individuals with confirmed rifampicin resistance as a replacement for current in-country pDST practice.

**Design/Methods:** We developed a stochastic decision analysis model to assess the cost-effectiveness of replacing current in-country pDST practice with tNGS among individuals with rifampicin resistance. This was done across 3 countries: South Africa, India, and Georgia. Current South Africa and Georgia DST practice is Xpert XDR followed by pDST; LPA and pDST are done in parallel in India. Epidemiological data was sourced from published literature and tNGS diagnostics accuracy data was sourced from an ongoing systematic review. Economic data were sourced from published literature and supplemented with empirical data collection.

**Results:** In South Africa and Georgia, tNGS was cost-effective compared to existing in-country DST practices using a willingness to pay threshold (WTP) of three times the country's GDP per capita. In India, tNGS dominated in-country DST practice resulting in lower

costs and improved health gains. In scenario analysis, when a faster turnaround time for tNGS was assumed to lead to reductions in loss to follow-up, the model led to increased cost-effectiveness of tNGS compared with pDST.

**Conclusions:** This study has shown that using tNGS may be cost-effective depending on the existing pDST practice of the country. It is therefore important to consider the existing standard of care before implementation and scale-up of tNGS.

### EP19-1172-17 Strengthening quantification of TB laboratory supplies to develop a strong TB laboratory network in Bangladesh

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**Background:** Continuous supply and availability of laboratory commodities is crucial in developing a strong laboratory network. The National Tuberculosis Control Program (NTP) of Bangladesh has been facing challenges in forecasting of laboratory supplies owing to lack of standardized methods for quantification. Other factors like varied product list, limited data on consumption status further contribute to delay in finalizing the quantification process.

**Design/Methods:** To overcome this situation, NTP developed a standard excel based quantification tool for TB reference laboratories. Product list was standardized by test category, supply unit, balance stock, monthly consumption status, quarterly forecast assumption and date of expiry.

**Results:** The quantification tool has enabled designing a uniform product list of TB laboratory supplies, improved data quality and saved time. Reference Laboratories have adopted the tool for forecasting and placing demands. Reagent incompatibility due to procurement from different sources is a challenge to the process of quantification.

**Conclusions:** The quantification tool has strengthened the TB laboratory network of Bangladesh. Further development of this tool is recommended to scale up its use in other laboratory programs. A periodic review and update of the quantification process biannually is recommended for any major changes in forecasting or procurement timings.

## EP20 Social protection - the Key solution?

### EP20-1173-17 Assessment of TB-related stigma in Peru

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**Background and challenges to implementation:** Stigma is a very significant social determinant for people affected by TB, as it creates barriers to healthcare services, especially for the most vulnerable populations. Understanding the context of stigma and its impact on people affected by TB, their families, health care providers, and the community at large is key to devising targeted strategies to address it.

**Intervention or response:** Using the stigma assessment tool developed by the Stop TB Partnership (<https://www.stoptb.org/tb-stigma/tb-stigma-assessment-tool>), we measured:

1. Self-stigma among people diagnosed with TB,
2. Secondary stigma among family members,
3. Community stigma, and;
4. Stigma among health personnel.

The study was conducted in the city of Lima, Peru, and was approved by the research ethics committee of Socios En Salud.

**Results/Impact:** Surveys were administered to 377 people affected by TB (171 women, 205 men, 01 defined as other), 30 family members (21 women, 09 men), 30 community members (21 women, 08 men, 01 defined as other) and 30 health professionals (23 women, 07 men). The results of the assessment are shown in Table 1.

In a results socialization workshop, the highest level of stigma in the community was presented and how this impacts the person upon receiving their TB diagnosis (self-stigma). In addition, civil society and the tuberculosis program were able to plan specific activities to address TB-related stigma.

Indicator	Type of stigma	Result %
Level of anticipated self-stigma of PATB	Self-stigma	44.21
Level of secondary family stigma	Secondary stigma	34.75
Level of stigma perceived by the community/neighbors towards PATB	Perceived stigma	64.85
Level of stigma perceived by health care workers towards PATB	Perceived stigma	47.12

Table 1. Level of stigma related to tuberculosis.

**Conclusions:** Assessment is important to propose stigma mitigation activities in tuberculosis, as it allows a better understanding of the extent of stigma and how it is presented in different groups.

Regular measurement is advisable to assess the impact of activities and how stigma barriers to accessing health services are reduced.

### EP20-1174-17 Receipt and utilisation of *Nikshay Poshan Yojana* benefits among patients with TB in India, 2022

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**Background:** *Nikshay Poshan Yojana* (NPY) is a direct benefit transfer (DBT) scheme for nutritional support under the National Tuberculosis Elimination Program (NTEP) in India, offering monthly financial incentive of INR500, to meet additional nutrition requirements of patients with TB.

**Design/Methods:** We conducted this cross-sectional study under USAID funded TIFA project implemented through JSI Research & Training Institute Inc. among patients with TB notified under NTEP and completed treatment between May and October 2022.

We selected nine states by random sampling from strata based on TB score. We used probability-proportionate-to-size sampling, for selection of districts, Tuberculosis Units (TU), Peripheral Health Institutions (PHI) in the subsequent stages. Eligible participants with TB were interviewed from each PHI. We used Open Data Kit for collecting data which was analysed using Stata Version.17.0.

**Results:** The mean(SD) age of the 2061 participants interviewed was 41.23 (16.07) years and 1301 (63.1%) of them were males.

Overall, 1355 (65.7%; 95%CI 63.7,67.8) reported having received at least one NPY benefit, of whom, 1141 (86.3%) had spent it on their own nutritional requirements and 217 (19%) had spent it on the nutritional requirements of their household. Participants with higher educational attainment ( $p=0.003$ ) and favourable treatment outcomes ( $p<0.001$ ) were more likely to have received at least one NPY benefit.

Only 147 (10.9%) were satisfied with the monthly benefit amount of INR500 provided, as they had spent a median (IQR) amount of INR1500 (1000-2500) per month on additional nutritional requirements due to TB.

Variables	Category	Received at least One NPY Benefit		p-value †
		Yes n (%)	No n (%)	
	<b>Total</b>	1355 (65.7)	706 (34.3)	
Age (in Years)	18 to 59	1102 (65.6)	578 (34.4)	0.764
	>= 60	253 (66.4)	128 (33.6)	
Gender	Male	861 (66.2)	440 (33.8)	0.614
	Female	494 (65.1)	265 (34.9)	
Education	Cannot read or write	275 (60.7)	178 (39.3)	0.003*
	Literate without formal schooling	151 (61.6)	94 (38.4)	
	Any formal schooling	737 (67.0)	363 (33.0)	
	Graduate	192 (73.0)	71 (27.0)	
Tuberculosis site <sup>‡</sup>	Extra Pulmonary	294 (66.2)	150 (33.8)	0.959
	Pulmonary	1060 (66.1)	544 (33.9)	
	Not Reported	1 (7.7)	12 (92.3)	
Patient type	New	1168 (65.7)	609 (34.3)	0.269
	PMDT	98 (70.5)	41 (29.5)	
	Retreatment	89 (61.4)	56 (38.6)	
Treatment Outcome	Favourable	699 (70.5)	292 (29.5)	0.000*
	Unfavourable	656 (61.3)	414 (38.7)	
HIV Status <sup>§</sup>	Non-Reactivate	1318 (66.0)	679 (34.0)	0.558
	Reactive	17 (60.7)	11 (39.3)	
	Unknown	20 (55.6)	16 (44.4)	
Diabetes <sup>¶</sup>	Diabetic	166 (72.8)	62 (27.2)	0.031*
	Non-Diabetic	1160 (65.7)	607 (34.3)	
	Unknown	29 (43.9)	37 (56.1)	
Household Income based quintile	First	126 (62.1)	77 (37.9)	0.500
	Second	88 (61.5)	55 (38.5)	
	Third	112 (66.3)	57 (33.7)	
	Fourth	120 (65.9)	62 (34.1)	
	Fifth	91 (58.0)	66 (42.0)	
	Fifth Quintile	91 (58.0)	66 (42.0)	

PMDT- Programmatic Management of Drug-resistant TB  
<sup>‡</sup> Data collection ongoing in three states, hence, results from six states are presented  
<sup>§</sup> Calculated only among reported  
<sup>†</sup> Chi-square test/Fisher's Exact test used  
<sup>\*</sup> p value < 0.05

Table 1. NPY benefit receipt status among patients with TB from six<sup>@</sup> states of India, 2022 (n=2061).

**Background and challenges to implementation:** *Nikshay Poshan Yojana* (NPY) is a direct benefit transfer (DBT) scheme for nutritional support under the National Tuberculosis Elimination Program (NTEP) in India, offering monthly financial incentive of INR500, to meet additional nutrition requirements of patients with TB.

**Intervention or response:** We conducted this cross-sectional study under USAID funded TIFA project implemented through JSI Research & Training Institute Inc. among patients with TB notified under NTEP and completed treatment between May and October 2022. We selected nine states by random sampling from strata based on TB score.

We used probability-proportionate-to-size sampling, for selection of districts, Tuberculosis Unit (TU), Peripheral Health Institutions (PHI) in the subsequent stages. Eligible participants with TB were interviewed from each PHI. We used Open Data Kit for collecting data which was analysed using Stata Version.17.0.

**Results/Impact:** The mean (SD) age of the 2061 participants interviewed was 41.23 (16.07) years and 1301 (63.1%) of them were males.

Overall, 1355 (65.7%; 95%CI 63.7,67.8) reported having received at least one NPY benefit, of whom, 1141 (86.3%) had spent it on their own nutritional requirements and 217 (19%) had spent it on the nutritional requirements of their household.

Participants with higher educational attainment ( $p=0.003$ ) and favourable treatment outcomes ( $p<0.001$ ) were more likely to have received at least one NPY benefit. Only 147 (10.9%) were satisfied with the monthly

benefit amount of INR500 provided, as they had spent a median (IQR) amount of INR1500 (1000-2500) per month on additional nutritional requirements due to TB.

Variables	Category	Received at least One NPY Benefit		p-value †
		Yes n (%)	No n (%)	
	<b>Total</b>	1355 (65.7)	706 (34.3)	
Age (in Years)	18 to 59	1102 (65.6)	578 (34.4)	0.764
	>= 60	253 (66.4)	128 (33.6)	
Gender	Male	861 (66.2)	440 (33.8)	0.614
	Female	494 (65.1)	265 (34.9)	
Education	Cannot read or write	275 (60.7)	178 (39.3)	0.003*
	Literate without formal schooling	151 (61.6)	94 (38.4)	
	Any formal schooling	737 (67.0)	363 (33.0)	
	Graduate	192 (73.0)	71 (27.0)	
Tuberculosis site <sup>§</sup>	Extra Pulmonary	294 (66.2)	150 (33.8)	0.959
	Pulmonary	1060 (66.1)	544 (33.9)	
	Not Reported	1 (7.7)	12 (92.3)	
Patient type	New	1168 (65.7)	609 (34.3)	0.269
	PMDT	98 (70.5)	41 (29.5)	
	Retreatment	89 (61.4)	56 (38.6)	
Treatment Outcome	Favourable	699 (70.5)	292 (29.5)	0.000*
	Unfavourable	656 (61.3)	414 (38.7)	
HIV Status <sup>§</sup>	Non-Reactive	1318 (66.0)	679 (34.0)	0.558
	Reactive	17 (60.7)	11 (39.3)	
	Unknown	20 (55.6)	16 (44.4)	
Diabetes <sup>§</sup>	Diabetic	166 (72.8)	62 (27.2)	0.031*
	Non-Diabetic	1160 (65.7)	607 (34.3)	
	Unknown	29 (43.9)	37 (56.1)	
Household Income based quintile	First	126 (62.1)	77 (37.9)	0.500
	Second	88 (61.5)	55 (38.5)	
	Third	112 (66.3)	57 (33.7)	
	Fourth	120 (65.9)	62 (34.1)	
	Fifth	91 (58.0)	66 (42.0)	
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PMDT- Programmatic Management of Drug-resistant TB  
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<sup>†</sup> Chi-square test/Fisher's Exact test used  
<sup>\*</sup> p value < 0.05

Table 1. NPY benefit receipt status among patients with TB from six states of India, 2022 (n=2061).

**Conclusions:** More than two-thirds of the notified patients with TB reported receipt of at least one NPY benefit. There is a need to accurately estimate the cost of additional nutrition required by patients with TB, in the light of which a revision of the current amount offered as benefit is recommended.

## EP20-1175-17 Good TB treatment success rates among the prison population in Malawi

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**Background and challenges to implementation:** Infectious diseases like tuberculosis (TB) pose serious threats in Malawian prisons and the world at large; and present significant challenges for prison and public health authorities. Prisoners, once released, bring communicable diseases contracted while in prison into the society. Prison health, therefore, must be the concern for all.

**Intervention or response:** The National Tuberculosis Elimination Programme (NTLEP) has been collaborating with the prison health services in Malawi for several years, and had put in place TB/HIV surveillance mechanism in all prisons. Among others, the collaboration includes referral of presumptive and confirmed TB patients from prisons to Ministry of Health facilities, supervision of prison TB services by NTLEP staff, provision of TB recording and reporting tools and provision of TB diagnostic tools and laboratory consumables. In 2019, the NTLEP revised the policy for integrated TB/HIV management in Malawian prisons. The policy advocates for Government's commitment for TB/HIV prevention and care in Malawian Prisons. We therefore, analysed the TB case notifications and TB treatment outcomes among prison population in Malawi from 2017 to 2022. Existing data for the general population reported at the national level for the same period was used as a control. **Results/Impact:** TB case notifications among prison population decreased from 424 in 2017 to 159 in 2022. A marked decrease was observed in 2020/2021 due to covid-19 pandemic. Similar trend was observed for general population notifications. TB treatment success rate (TSR) varied from 97% for 2019 cohort to 100% for 2021 cohort. This is in contrast to 82% and 90% TSTs among the general population for 2017 and 2021 cohorts.

**Conclusions:** TB case notification trends in Malawian prisons is similar to the general population, however, TSR is much better among prison population than the general population. The NTLEP needs to strengthen its collaboration with the prison health service to maintain the gains made.

## EP20-1176-17 Mass TB screening events with mobile diagnostic units in Malawi prisons: sufficient for TB control?

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**Background and challenges to implementation:** High burden of TB in prisons is a major public health problem in many low-middle income countries. In Malawi, measures have been put in place to ensure optimal TB diagnosis and treatment, but gaps remain as most prison facilities lack onsite diagnostic equipment, regular sample transport and adequate human resources for health.

**Intervention or response:** Partners in Hope (PIH), a Malawian NGO, collaborated with Ministry of Health (MoH), Malawi Prison Services and the National TB Program to conduct TB mass screening events in 6 district prisons. These events take place with mobile diagnostic unit (MDU) vans on a bi-annual basis with support from USAID. The MDUs are equipped with MTB Xpert and digital X-ray machines, including computer-aided-diagnostic software for chest X-ray image interpretation. TB screening took place using both the WHO standard 4-symptom screen and chest X-ray imaging for each individual.

Inmates identified as presumptive TB through screening and who were able to produce sputum, underwent MTB Xpert testing. Those who could not produce sputum were further evaluated by clinicians on site.

**Results/Impact:** From December 2021 to March 2023, three cycles of TB mass screening events were conducted in 6 prisons; 5,607 inmates were screened, 555 (10%) were identified with presumptive TB. 37 (0.7%) were diagnosed with active TB and all initiated treatment. Key enablers for successful TB mass screening in prisons were good collaboration among all stakeholders and availability of adequate resources (human, funding, time, equipment). Barriers included cost intensiveness and knowledge gaps among prison facility staff.

**Conclusions:** While mass screening with MDUs has potential to improve TB identification in prisons, the contribution to case notifications was moderate. Additional measures, including permanent availability of on-site TB diagnostic equipment and clinical staff, as well as institution of TB preventive treatment may be needed for optimal TB control in Malawi prisons.

## EP20-1177-17 Engaging community volunteers in ethnic minority communities in Viet Nam to detect TB

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**Background and challenges to implementation:** Ethnic minorities and remote communities in Viet Nam have long faced healthcare barriers related to travel distance, socioeconomic conditions, lack of access to localized information sources, and limited human resources to provide people-centered support.

These barriers were intensified during the COVID-19 pandemic, when movement in border regions was heavily restricted.

We aimed to enhance rights and access to high-quality care for vulnerable communities by filling programmatic gaps left by the pandemic.

**Intervention or response:** We engaged and trained 21 community advocacy volunteers from ethnic minority communities to conduct TB mobilization efforts within their communities. We co-created mobilization strategies for TB screening with these individuals.

Over three months, TB awareness and education sessions were conducted in 49 remote, mountainous villages of Viet Nam, using illustrated and video materials in four vernacular languages. The volunteers verbally screened people for TB symptoms and risk factors, and made referrals to health facilities for TB screening.

**Results/Impact:** 312 people (165 male, 147 female) were identified with symptoms of TB and referred for further evaluation. 248 (79.4%) referrals ultimately received a CXR, resulting in the detection of 11 people (7 males, 4 females) with TB.

An additional 64 sputum specimens were collected in the community by volunteers and transported to a laboratory due to insurmountable barriers in accessing facilities in certain communities. In total, 20 people (14 males, 6 females) were diagnosed with TB. This translates to

a detection rate of 8,065 per 100,000 people screened, which is 45x higher than the national TB incidence rate. All were linked to appropriate treatment.

	Males	Females	Total
People verbally screened in ACIS	165	147	312
People screened by chest X-ray (CXR)	121 (73.3%)	127 (86.4%)	248 (79.5%)
People with sputum test after abnormal CXR results	20 (16.5%)	17 (13.4%)	37 (14.9%)
Bac (+) TB detected after abnormal CXR results	7 (35.0%)	4 (23.5%)	11 (29.7%)
People with sputum testing without CXR	44	20	64
Bac (+) TB detected without CXR	6 (13.6%)	2 (10.0%)	8 (12.5%)
People clinically diagnosed with TB	1	0	1
All Forms of TB detected	14	6	20
All Forms of TB linked to treatment	14 (100%)	6 (100%)	20 (100%)

**Conclusions:** Engaging with ethnic minority populations in Viet Nam using locally-tailored, co-created approaches has the potential to improve TB treatment coverage and equity in healthcare provision.

### EP20-1178-17 Impact of doctor-hopping on monetary costs of TB care-seeking in a rural setting in Rajasthan, India

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**Background:** Doctor-hopping is a common phenomenon and a crucial barrier to tuberculosis (TB) care. Patients switch between providers which set back their treatment.

To assess why patients, switch among providers and the monetary impact, we surveyed TB patients residing in a rural and tribal block of the Udaipur district of Rajasthan.

**Design/Methods:** We surveyed 118 patients seeking TB care at AMRIT not-for-profit primary healthcare clinics (the focal care unit - FCU) from April to November 2020, the eliciting pathway of care-seeking, perception towards the providers, and cost incurred at each point of care.

Using descriptive data analysis, we assessed the hopping behavior of patients among five categories of Point of Care (POC) – public centers, private centers, informal care (quacks), traditional care (faith healer), and FCU.

**Results:** We recorded 39 pathways of care-seeking among five providers. Patients incurred significant expenses at other POC before consulting FCU.

We observed significant difference in charges already incurred by the patients with various providers when FCU was the third or later in the pathway as against first or second.

Further, patients report a positive perception towards certain private providers, poor quality of care in the public system, faith on the traditional healers, and a sense of indifference and apathy from the providers in the primary healthcare system.

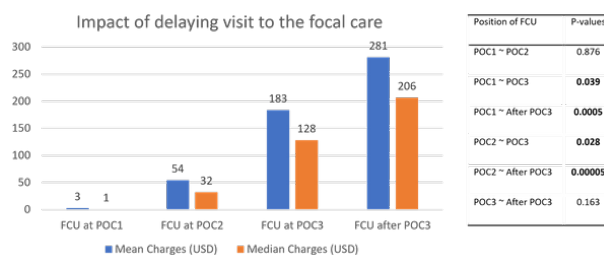


Figure 1. Mean and median expenses incurred (in USD) at healthcare providers when the FCU is the first, second, third, or later point of care (Left). Single factor ANOVA between groups (Right).

**Conclusions:** Our findings suggest that TB patients tend to try various expensive and ineffective options before arriving at the FCU. This highlights the need for targeted communication by affordable TB care providers such as the AMRIT among patients suspected of TB to initiate care seeking at the right provider at an early stage of TB care.

### EP20-1179-17 Piloting non-payment interventions in TB strategic health purchasing: Early experience from Indonesia

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**Background and challenges to implementation:** Presidential Decree No. 67 of 2021 on Tuberculosis (TB) Control was issued in 2021 and includes guidance on utilization of the National Health Insurance (JKN) resources in TB elimination.

However, the current payment structure of JKN does not incentivize primary-level TB service delivery. A 2022 study by O'Connell and colleagues showed that 81% of uncomplicated TB patients under JKN were up-referred unnecessarily to hospitals, which typically resulted in poorer treatment outcomes and increased health care costs.

**Intervention or response:** The proposed TB strategic health purchasing (SHP) pilot aims to better incentivize primary health facilities to provide quality TB services for people with drug-susceptible TB through non-pay-



ment and payment interventions. Non-payment interventions, which include health facility certification and modification to contracting process were successfully implemented in Medan and Denpasar districts in Indonesia from 2021-2022.

**Results/Impact:** Health facility certification which includes capacity building for health workers has improved the engagement, commitment and compliance with guidelines of private primary health care facilities to provide quality TB services. During the intervention, 94% (129/137) of JKN-empanelled private primary health facilities in Medan and 87% (78/89) of JKN-empanelled private primary health facilities in Denpasar were certified. These certificates contributed towards the JKN re-credentialing points for the facilities in 2022. During the certification process, the number of health facilities committed to provide comprehensive TB services (diagnosis, treatment, reporting) increased by 300% from 11.69% to 46.67% in Medan. While in Denpasar, 29% more facilities (32.33% vs 41.67%) committed to diagnose TB patients.

**Conclusions:** Non-payment interventions developed through modifications in the JKN credentialing process should be scaled-up to priority districts in Indonesia and TB capacity building through the credentialing process should be made compulsory to ensure quality of TB services. For maximum impact, payment reforms are also required to adequately incentivize primary health facilities for providing TB services.

## EP21 Is investing in TB knowledge a good idea?

### EP21-1180-17 TB coaching through professional organisations: An approach to improve TB care in health facilities

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**Background and challenges to implementation:** In Indonesia, only 54% of private hospitals reported TB cases in 2021, and adherence to national guidelines is sub-optimal according to the National TB Program (NTP).

In collaboration with the NTP and The National Coalition of Professional Organization for Tuberculosis (KOPI TB), USAID Tuberculosis Private Sector (TBPS) launched a TB coaching initiative in hospitals to increase numbers of presumptive TB cases reported and improve the adherence to national TB guidelines.

**Intervention or response:** The 4-month duration coaching initiative, implemented in 27 hospitals (22 private, 5 public), provided TB services and had the potential to improve their patient care/data reporting.

A trained 'TB Coach' engaged 'coachees' within each hospital in coaching cycles using standardized tools for doctors, pharmacists, lab technicians, and nurses. Each cycle consisted of four meetings:

1. An introduction and needs assessment,
2. Enhancing knowledge and skills
3. Monitoring the progress
4. Reviewing improvements and planning for any necessary follow-up.

Prospective coaches were identified and proposed by KOPI TB and district health offices and underwent a two-day online training to equip them with basic coaching skills and align their knowledge and understanding of the PPM approach and the national TB guidelines. They were remunerated for each coaching session they conducted.

**Results/Impact:** A comparison of the numbers of presumptive TB cases reported and the proportion of presumptive TB cases confirmed with GeneXpert was made prior to and during the intervention:

- 81% (22/27) of hospitals increased the number of presumptive cases reported.
- The proportion of hospitals testing all presumptive cases with GeneXpert increased from 44% (12/27) to 63% (17/27).

**Conclusions:** TB coaching through professional organisations in Indonesian private and public hospitals contributed to improved reporting and adherence to national guidelines.

Coaches perceived that their knowledge and skills in providing standardized TB care improved, and structural changes in infrastructure were observed, where hospital management participated.

### EP21-1181-17 TB knowledge and self-reported behaviour of primary healthcare nursing professionals regarding precautionary measures

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**Background:** Despite the access to standard precautions (SP) and specific precautions (EP) by nursing professionals in Primary Health Care (PHC) in Brazil, there has been a significant increase in the transmission and contamination of infectious diseases in this setting.

Therefore, the objective of this study is to identify the knowledge and self-reported behavior of nursing professionals regarding precautionary measures.

**Design/Methods:** This is a quantitative, cross-sectional, descriptive study conducted with 97 nursing professionals from 38 Family Health Units and five Health Teams at a municipality in the central-western region of the state of Minas Gerais, Brazil.

Data were collected through individual interviews using an instrument to assess knowledge and self-reported behavior regarding standard and specific precautions in PHC. Descriptive analysis of the data was performed using the Statistical Package for the Social Sciences.

**Results:** So far, 97 nursing professionals have participated. Preliminary analysis of variables related to precautions for suspected or confirmed tuberculosis (TB), in the “use of masks and cough etiquette” axis, showed that the majority of professionals answered correctly regarding the dispensing of mask use for users starting supervised TB treatment during short stays at the health unit (93.8%), the indication of minimum stay of these users in the unit for monitored dose (93.8%), and the need for respiratory protective mask (PFF2/N95) use by the professional during this type of care (66%). However, there was a low percentage of correct answers regard-

ing the use of surgical masks, cough etiquette, and preference for well-ventilated places by the health professional during home care for these individuals (24.7%).

**Conclusions:** Health professionals recognize the correct precautionary measures regarding TB cases, and the weaknesses can be overcome through the strengthening of systematic and active educational interventions on this topic.

### EP21-1182-17 USAID-supported eLearning platform to train frontline workers and promote active TB case-finding through contact investigations and screening of persons living with HIV

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**Background and challenges to implementation:** The EndTB Strategy has set ambitious targets for reducing TB cases and deaths by 2035, requiring sustained efforts to find persons with active disease and interrupt transmission. A highly trained workforce in TB contact investigation (TBCI) will be required to meet the EndTB goal.

**Intervention or response:** USAID, in collaboration with TB DIAH Project, developed a virtual eLearning platform ([www.https://training.tbdiiah.org/](https://training.tbdiiah.org/)) that currently hosts two self-paced online courses targeted to high TB burden countries to train front-line workers to:

1. Conduct TBCIs, and;
2. Find TB cases among PLHIV.

The courses are free and available on computer or mobile devices, are being translated into French, Portuguese, and Russian, and take approximately 4 hours to complete. Course modules include: Basics of TB; Steps in a TBCI; Communication Skills and Ethics; and TBCI M&E.

**Results/Impact:** Between April 2022 and March 2023, 698 persons from 45 countries enrolled in the TBCI course; 319 (46%) completed the course and received a

certificate; 72 enrolled in either the Portuguese or French versions of the course. 492 completed a pre-test with an average score of 51%; 319 (65%) completed the post-test with an average score of 90% for a +39% knowledge gain; 335 completed an end-of-course evaluation and 95% agreed or strongly agreed with the following statements: "I will apply what I learned in this course to my job," and "the online course was an effective way for me to learn this content and was a worthwhile investment of my time."

**Conclusions:** Virtual eLearning platforms are important for efficiently providing front-line workers with initial or refresher training to develop skills and capacity to perform critical public health disease intervention. Online TBCI training is acceptable to front-line workers and improves workplace performance.

### EP21-1183-17 Investing in building capacity of TB survivors to provide person-centred care: Lessons learnt from community-led interventions in 10 Indian states

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**Background and challenges to implementation:** Trained TB survivors are best positioned to be engaged as powerful peer counselors, having experienced the challenges and struggles associated with TB. Strengthening and building the capacity of TB survivors as Champions (TBCs) and peer counselors can amplify community access to TB prevention and care.

**Intervention or response:** Investing in training communities to provide person-centered care services to people with drug-sensitive TB (PwTB) is an intervention under the Unite to ACT (UTA) project being implemented in 10 states of India. TBCs were engaged under a mentorship program for six months in about 541 TB Units at the sub-national level. TBCs supported PwTB in their communities through gender-responsive peer counseling, treatment literacy, stigma mitigation, and by assessing vulnerabilities and challenges faced by people with TB during the entire treatment period.

**Results/Impact:** In all, 950 TBCs reached out to about 90,148 PwTB in 80 districts during the intensive phase. 40% of PwTB were female. TBCs emerged as a resilient pool at the community level, sharing their personal stories with PwTB and providing peer and family counseling on treatment adherence.

Literacy on cough hygiene, sputum disposal, and self-care was delivered by TBCs. The TBCs could reach out to 61% of all PwTB in the 15-44 age group and provide

real-time feedback to the TB program to resolve challenges or issues faced in the care cascade. Treatment outcomes have been declared for 35,701, of whom 91% have been declared cured or treatment completed. This is an increase of 6% from the previous year's treatment success rate, that roughly translates into the cohort of almost 150 thousand PwTBs.

Total PwTB Reached out		PwTB reached out as per site of disease			Age range of PwTB reached out		PwTB reached out through 3 services by TB Champions during mentorship period		
Male	Female	Trans-gender	Pul-monary	Extra Pul-monary	15-44	45 and above	Treatment literacy	Gender peer counseling	Sensitization of family members
54003	36112	33	67470	20678	60781	29367	90148	44509	41116

**Conclusions:** Investing in building community capacity to provide person-centered care and support can improve treatment outcomes for those affected. TB Champions are uniquely.

### EP21-1184-17 Trained peer counsellors identify and respond to key challenges to TB treatment completion in a high drug-resistant TB burden setting in Western Province, Papua New Guinea

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**Background and challenges to implementation:** Following an outbreak of Drug Resistant tuberculosis (DR-TB) in South Fly District (SFD), Western Province, Papua New Guinea (PNG) the rates of DR-TB remain among the highest documented globally, with enormous health, social and economic costs to the community. There is a multitude of challenges faced by people seeking to commence and complete their treatment. Peer support and counselling can play an essential role in identifying and overcoming these challenges to a successful treatment outcome.

**Intervention or response:** Most residents of SFD have first-hand experience with TB making it a highly unique context to explore the impact of peer-provided counselling from people affected by, living with, or having survived TB. In 2016, a peer education and counselling model was implemented to strengthen the programmatic response, focusing on education, social and emotional support exploring and addressing the various treatment challenges.

**Results/Impact:** Deidentified aggregate programmatic data from 16,234 counselling sessions (January 2017 to December 2022) was analysed retrospectively. Chal-

lenges to treatment adherence were raised in 7029 (43%) of these including: physical ailments (22%); treatment supply requests (15%); treatment interruption (14%); accommodation (10%); access to food (8%); lack of family support (5%); and gender-based violence (3%). Numerous surveys have found high satisfaction for the counselling services provided. Familiarity with context, shared language and peer status all contributed to positive therapeutic relationships. Loss to follow-up rates for drug-susceptible and drug-resistant TB have fallen from 2014 to 2022: 27.5% to 3.2% and 19.8% to 4.9% respectively.

**Conclusions:** The peer counselling intervention has been associated with improved treatment completion, highlighting the importance of comprehensive person-centred approaches to care that are inclusive of affected community members providing psychosocial and emotional support. The program remains fully integrated into the community and facility-based model of care in SFD and has been introduced in other PNG settings.

### EP21-1185-17 Strengthening community engagement via the Digital TB Champion module under India's National TB Elimination Programme

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**Background and challenges to implementation:** The National TB Elimination Programme (NTEP) in India prioritizes engaging TB Champions, who are TB survivors trained to work actively in the community towards TB elimination. A Comprehensive curriculum is designed for the TB Champions to enhance knowledge of TB and equip them with the necessary skills to effectively advocate, communicate, and provide peer support to persons with TB (PwTB).

**Intervention or response:** On March 24th, 2022, the TB Aarogya Sathi PwTB App (TAS) implemented a new feature aimed at enhancing engagement and tracking the progress of TB Champions.

This feature enables users of the app who have successfully completed TB treatment to access training modules to become TB Champions and mark their course completion on the Integrated Government Online Training (iGOT) Portal. Once all the required courses have been completed, TB Champions are provided with the ability to report the number of meetings conducted, PwTB visited, and upload pictures of the events they have conducted.

**Results/Impact:** A total of 1809 TB survivors (66% male, 82% public sector) who had completed TB treatment accessed the training content through TAS. Out of the total TB survivors, 53 (who had completed all the courses) registered as TB Champions and reported their activity through the app. As a result, 601 visits were conducted, and a total of 1220 PwTB on treatment were visited.

**Conclusions:** This feature has enabled a significant number of TB survivors to access training modules and become TB Champions, resulting in the mobilization of TB Champions to conduct visits and provide support to PwTB. These results signify the potential for community-led efforts to combat TB and achieve India's goal of ending TB by 2025. The implementation of innovative features like the one introduced by TAS is essential for sustained engagement and progress in TB elimination efforts.

### EP22 Comprehensive system impacting tobacco use: industry tactics and tobacco control

#### EP22-1186-17 Exposing tobacco industry tactics in the implementation of the e-cigarette ban in India

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**Background and challenges to implementation:** E-cigarettes pose significant health risks to users that are frighteningly similar to those of conventional cigarettes. They are being marketed as a harm reduction product which is contrary to the truth. In order to prevent the initiation of Electronic Nicotine Delivery Systems (ENDS) by non-smokers and youth, Government of India issued an advisory to ensure that E-cigarettes and the like devices that enable nicotine delivery are not sold (including online sale), manufactured, distributed, traded, imported and advertised in their jurisdictions. However the tobacco industry continuously kept pressure on the Government to withdraw this advisory.

**Intervention or response:** Using earned media to expose tobacco industry tactics on misleading the Government and the public that E-cigarettes is a harm reduction product. The strategy was to ensure that news items or stories come out to attract the attention of the government and the public. To do so, we decided to increase consumer awareness about the health issue of E-cigarettes in the news through a sustained strategy of media engagement. We increased our interactions with the media, both on a one-to-one basis and through press interactions.

**Results/Impact:** This strategy of media advocacy resulted in nearly over 500 earned media stories supporting for the E-cigarette ban. These stories created pressure and became a national debate.

As a result, the Government of India passed “*The Prohibition Of Electronic Cigarettes Ordinance, 2019*” prohibiting production, manufacture, import, export, transport, sale, distribution, storage and advertisement of electronic cigarettes in the interest of public health. This has been come into force from 18th September 2019.

**Conclusions:** The media was sensitized and in the process, a personal rapport began was developed with journalists. All these efforts helped to make the E-cigarette issue a Pan India campaign.

### EP22-1187-17 Illicit tobacco trade In India: What government reports tell us

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**Background and challenges to implementation:** In India, more than 1.3 million adults die prematurely from tobacco related disease. All tobacco products are cheap and affordable in India, despite of it there is still a massive underground economy which further pushes down the retail price of domestic and international brands.

**Intervention or response:** The publicly available government sources: The Comptroller and Auditor General of India (CAG); Directorate of Revenue Intelligence (DRI); Central Board of Indirect Taxes and Customs (CBIC); Parliament reports published online from 2005 to 2020 were referred for the study.

**Results/Impact:** We found that illicit trade by both registered and unregistered or unlicensed entities is widespread and they deal in legal, smuggled, counterfeit and fake tobacco products. Even tobacco industry admits to widespread smuggling, Federation of Indian Chambers of Commerce and Industry produced a report titled Activities Destroying the Economy states India is fourth largest illegal cigarette market in the world.

1. On 8th February 2021, the Indian finance minister shared in Parliament there are a total 25 cases of evasion of excise and customs duty on tobacco companies.

2. CAG reports have recorded a tax violation by tobacco companies INR 390.37 Cr (\$47.6 million).

3. DRI recovered illicit tobacco goods worth INR 130 crore (\$15.8 million), and several goods for which the value was not determined.

4. CBIC seized 2.35 million cigarettes that were being smuggled.

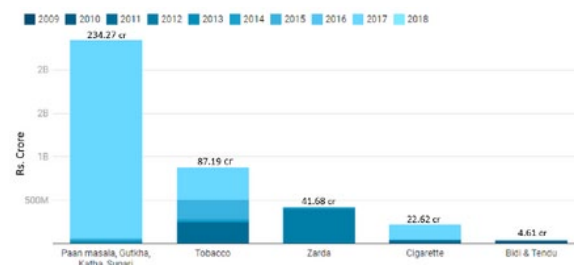


Figure. The most illegally traded tobacco products.

**Conclusions:** Government reports find that the tobacco industry in India employs a range of legal and illegal activities including stockpiling, manipulating prices, non-disclosure of revenues, and tax evasion. The proliferation of India's tobacco industry and trade needs a regulatory framework, and the current lifecycle of products is regulated by a piecemeal approach by multiple agencies. To meet the dual goals of revenue generation and reducing tobacco related disease, it is critical to reduce illicit trade of tobacco products.

### EP22-1188-17 A cross-country study of cigarette prices and affordability in eight sub-Saharan African countries: Evidence from the Global Adult Tobacco Survey

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**Background:** Economic growth can offset tobacco tax and price increases, thereby limiting their impact on tobacco use. The affordability of tobacco products, which is determined by the interplay of consumers' income levels and tobacco prices, has therefore become a key focus of tobacco tax policy. On the back of rapid population growth and aggressive marketing by the tobacco industry, tobacco consumption in Africa is expected to rise dramatically.

Yet, countries on the African continent have some of the lowest tobacco tax rates in the world and research on the interplay between tobacco prices, affordability and consumption in the region is limited.

**Design/Methods:** This research uses data from the Global Adult Tobacco Survey, conducted in eight African countries (2012–2018), to analyse cigarette prices

and affordability in the region. Prices are stratified by sociodemographic characteristics and smokers' purchasing styles. Within-country price variability is measured by the coefficient of variation. This paper also calculates country-specific Relative Income Prices and estimates their correlation with smoking prevalence and per capita cigarette consumption.

**Results:** Results show that prices range from 8.94 constant international dollars in Botswana to 2.01 constant international dollars in Cameroon. Single stick sales dominate all markets: between 61% and 93% of sample respondents report purchasing single sticks the last time they purchased cigarettes. The distribution of cigarette prices is tightest in Kenya and largest in Senegal. Cigarettes are most affordable in Nigeria, followed by Botswana. The correlation coefficient on RIP and smoking prevalence is  $-0.27$  ( $p < 0.001$ ), indicating that a decrease in affordability is associated with lower smoking prevalence. The correlation coefficient on affordability and consumption is  $-0.26$  ( $p < 0.001$ ).

**Conclusions:** Results point to the need for governments on the continent to increase excise taxes in a manner that renders them less affordable over time, and to enact and enforce legislation that prohibits the sale of single cigarettes.

### EP22-1189-17 Compliance monitoring of the hookah bar ban in the state of Rajasthan, India

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**Background and challenges to implementation:** Hookah bars have rapidly grown in urban and suburban pockets within the state of Rajasthan, India- just as it has in the rest of the nation. In 2019, the government of Rajasthan banned hookah bars by amending (Section 4a) the existing central Act, Cigarette and Other Tobacco Products Act (COTPA), 2003 (effective from January 2020).

**Intervention or response:** A compliance assessment for Hookah bar ban in Rajasthan, India was conducted using the "Near Me" feature of Google Maps/search engine. The search strategy involved 'hookah bar' as a keyword over the 'near me'- Google map. Functional hookah bar were located and identified, keeping major market locations of 33 major and 8 suburban (relatively smaller) cities as an epicenter .

**Results/Impact:** An initial list of 348 Hookah bars were listed and mapped. Despite the existing ban in the state of Rajasthan, a total of 82 Hookah Bars were found to be actively serving hookahs. The status quo report motivated relevant departments to strictly enforce the law and 238 Hookah Bars were fined during enforcement checks.

**Conclusions:** Despite a ban, 82 hookah bars were found to be functional within Rajasthan. Based on the study findings following recommendations were submitted to the government of Rajasthan:

1. Regular monitoring by all relevant departments/officials of opening and functioning of all eateries.
2. For implementation of act against the violation of Section 4a, allocation of enforcement power to the same set of officials exercising powers for enforcing section 5 and 7 under COTPA Act 2003.
3. Develop and display of signage of Section 4a at all eateries or Section 4 signage should be amended-to include all other tobacco products such as bidi, cigar and hookah.

### EP22-1190-17 Programmatic factors associated with tobacco use among medical students in Nepal: Effectiveness of the MPOWER strategy in reducing tobacco use

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**Background:** Smoking among healthcare personnel is a significant public health issue. As future healthcare providers, medical students have an important role in preventing and controlling tobacco-related burdens like cardiovascular diseases, cancer, etc in the general population. Thus, programmatic factors like knowledge regarding regulations on tobacco control are important among medical students.

**Design/Methods:** The total sample size was 398, with a response rate of 98%. A pre-tested structured questionnaire was used for data collection. Written informed consent was obtained from participants. The analysis of the data was done using SPSS v20 software. Chi-square test and odds ratio were calculated.

**Results:** The study revealed that tobacco use among medical students was 35.12%, including 22.8% cigarette smoking. The median age of smoking was 22 years old, and the prevalence was found high among male students (73%). Among the total participants, 78% had heard about any of the regulations on tobacco products and 72% had heard about graphical health warnings (GHW). Only 19.7% of the participants thought that the government's efforts were sufficient to control tobacco in Nepal.

The study showed that exposure to anti-smoking messages (OR 2.917, 95% CI 1.675-5.080) and family discussion about the harmful effects of tobacco (OR 0.500, 95% CI 0.300-0.835) were found significantly associated with smoking behavior.

**Conclusions:** The study revealed that the pervasiveness of tobacco use among medical students is a public health concern. This study suggests that measures to regulate tobacco use at the family and community level, along with policy changes are required for effective to-

bacco control. The policies regarding MPOWER, especially “warning on dangers of tobacco” should focus on individual/group discussion and mass awareness along with graphical warnings currently implemented. These evidences when turned into practice would lead to minimal tobacco use among medical students.

### EP22-1191-17 Health impact of tobacco use in Nepal and comparison with other South Asian countries

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**Background:** Tobacco use is having a significant and growing negative impact on the health and lives of Nepalese. This study systematically reviews the data extracted from the Global Burden of Disease Study and sets out to assess the age-specific and sex-specific mortality and disability attributable to different forms of tobacco from 1990 to 2019, in Nepal.

**Design/Methods:** This cross-sectional study extracted data from the Institute for Health Metrics and Evaluation's Global Burden of Disease database, then was quantitatively analyzed to show the trends and patterns of prevalence of tobacco use, deaths, and disability-adjusted life-years (DALYs) attributable to tobacco use from different diseases from the year 1990 to 2019 in Nepal.

**Results:** In 2019, tobacco was responsible for 19.4% of all deaths in Nepal, which is an increase from 10.5% in 1990. Tobacco has become the second biggest risk factor for death in Nepal, with only air pollution causing a bigger risk to life in 2019. In 1990, tobacco was the fourth biggest risk factor.

Overall, the incidence of tobacco-attributable deaths has increased by more than 60% over the past 30 years – it was less than 24,000 in 1990 and had increased to 37,529 by 2019. Nepal has the highest proportion of tobacco-caused deaths in South Asia.

In India, tobacco was responsible for 13.1% of deaths in 2019, which is significantly less than Nepal's 19.4% of tobacco-attributable deaths. Nepal is amongst the top 15% of countries in the world with the highest proportions of tobacco-attributable deaths – it is 29th out of 204 countries.

**Conclusions:** The consistently high smoking prevalence rates in Nepal indicate that tobacco will continue to be a major cause of premature death and ill health in the future, unless action is taken. Attention should be made to implementing a strong plan to control all forms of tobacco including secondhand exposure.

### EP23 Different pathways for accessing services

#### EP23-1192-17 Systematic TB screening among key TB risk groups at the primary healthcare level in four regions of Ukraine

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**Background and challenges to implementation:** Ukraine has the fourth highest TB disease prevalence in Europe, with one of the highest MDR-TB burdens globally. Healthcare reform, the COVID-19 pandemic, and the war have disrupted TB services. Efforts to increase TB active case-finding and access to timely, person-centered TB services and treatment are critical to combat TB in Ukraine.

**Intervention or response:** STBCEU is implementing systematic TB screening among key TB risk groups in primary health care services (PHCCs) by assessing symptoms, using chest radiography, molecular rapid diagnostic tests, and C-reactive protein. Fifteen PHCCs and four laboratories with GeneXpert were selected in Volynska, Vinnytska, Rivnenska and Kyivska regions, where the project and regional TB facility specialists conducted assessments and developed and got approval for the new algorithms. In February and March 2023, the STBCEU project team conducted 10 workshops for 260 PHC providers in selected facilities on systematic TB screening among key TB risk groups, with screening starting first in the Volynska region.

	Jan-Mar 2022	Apr-Jun 2022	Jul-Sep 2022	Oct-Dec 2022	Jan-Mar 2023
Total of diagnosed with TB	2	5	5	11	29
Age group: 1 – 5 years	-	-	-	2	3
6 – 18 years	-	-	1	1	9
19 – 60 years	2	4	3	8	17
> 60 years	-	1	1	-	0
Diagnosed with DS-TB	2	5	4	11	23
Diagnosed with DR-TB	0	0	1	0	6
Newly diagnosed with TB	2	4	1	8	25
Contacts identified	4	15	1	103	65

*Acceleration of active TB case finding in Horokhivskyi PHCC in Volynska oblast within STBCEU pilot implementation of systematic TB screening among the prioritizing TB key risk groups.*

**Results/Impact:** During three months of implementation, Horokhivskiy PHCC family doctors in Volynska examined 80 TB high-risk persons using GeneXpert, detecting 29 (36,3%) TB cases. They also identified 65 contacts from 29 index patients. Notably, all persons with confirmed TB started ambulatory treatment under their family doctor's observation- a huge success. Concurrently, regional TB facility specialists supported PHCC providers, and contact investigation continues with TB specialist coordination.

**Conclusions:** Systematic TB screening among the key TB risk groups through PHC providers is highly effective in improving active TB case-finding, identification of TB cases, and provision of timely, person-centered TB services treatment. Close collaboration among PHC providers and regional TB facility specialists is critical. STBCEU project will continue to support and scale-up systematic TB screening in PHCCs in Ukraine.

### EP23-1193-17 The engagement of National Army and Police health facilities in the TB programme in Indonesia

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**Background and challenges to implementation:** Tuberculosis remains the main health problem in Indonesia. The Indonesia Presidential decree of 2021 mandates all facilities to provide standardized Tuberculosis care. In 2021, however, only 77.8% of public hospitals and 36.7% of public clinics were engaged. Military-Police healthcare providers account for 171 (15%) of hospitals and 301 (57%) of clinics among all registered public providers. Despite the status of government-owned health facilities, only 127 (74%) Military and Police hospitals and 2 (1%) clinics engaged in the national TB program in 2021.

**Intervention or response:** Advocacy meetings with high-level positions (Colonel and Inspector) and online workshops for primary and secondary health facilities under the Indonesia Military and Police have been implemented. The Ministry of Health issued a circular letter in July 2022, requesting the head of the Health Department in the National Military and Police to strengthen the TB program in their health facilities. 520 clinics and 50 hospitals under the National Police and 528 clinics and 103 hospitals under the National Military (87% of all registered Military-Police HFs) are targeted to be engaged in the TB program.

**Results/Impact:** Six months after the implementation, number of Military-Police HFs reporting TB cases increased from 127 to 141 hospitals and 2 to 23 clinics,

respectively. TB case notifications also increased from 7.849 cases in 2021 to 13.166 cases in 2022. Access to molecular WHO-recommended Rapid Diagnostic (mWRD) tests increased from 64% in 2021 to 71% of patients tested in 2022. Challenges were faced in the implementation, such as not all HFs under Military/Police had engaged with the TB program at the end of 2022.

**Conclusions:** Central coordination between the Indonesia Military and Police Department and the Ministry of Health, as well as an official circular letter from the headquarters, are required to increase the engagement of Military-Police (public non-NTP) healthcare facilities.

### EP23-1194-17 Continuity of essential health services during the ebola Sudan outbreak in Uganda, 2022

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**Background:** Public health emergencies, such as the COVID-19 epidemic and Ebola Virus Disease (EVD) outbreaks, have put immense pressure on health systems globally, leading to the compromise of essential healthcare services. In Uganda, the Ugandan Ministry of Health created the Continuity of Essential Health Services (CEHS) pillar to strengthen coordination mechanisms, maintain access to essential quality health services, and enhance capacity for emergency medical services.

We present the results of an assessment of the continuity of essential health services in the context of the Ebola outbreak in Uganda.

**Design/Methods:** A cross-sectional survey was conducted in health facilities (HFs) nationwide in December 2022. HFs were selected using a stratified random sampling method. We used a World Health Organization (WHO) continuity of essential health services structured questionnaire. The questionnaire included; Service delivery and utilization, infection prevention and control and personal protective equipment, availability of selected tracer Medicines and supplies, and Vaccine readiness.

**Results:** A total of 325 HFs were visited. 81% of HFs reported that 41 tracer basket medicines were available, 83% of HFs provided PPE to health workers, 23% of HFs reported a decrease in all outpatient services, 36%



of HFs reported a decline in inpatient attendance, and 20% of HFs reported a reduction in emergency services during EVD outbreak. 69% of HFs had Infection Prevention and Control (IPC) guidelines for EVD and COVID-19. Of those HFs offering outreach services, 32% (28/120) suspended outreach immunization services.

Almost half of the selected HFs reported that diabetes, hypertension, HIV, and TB screening, diagnosis, and management were unavailable.

**Conclusions:** Although the government of Uganda responded swiftly to control the EVD outbreak, findings from this study reveal that essential services were partially disrupted, highlighting the importance of balancing emergency response measures with efforts to maintain essential services.

### EP23-1195-17 The final evaluation of “Bridge TB Care”, a 3-year trial cross-border TB patient referral programme

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**Background and challenges to implementation:** Japan reached low tuberculosis (TB) notification rate of 9.2 per 100,000 with 11,519 patients in 2021. While the proportion of foreign-born TB patients has constantly increased, reaching 11.4%. The proportion of transfer-out TB patients among foreign-born is relatively high compared with that among Japanese-born, and about half of them are estimated to move out of Japan.

There has yet to be a systematic cross-border TB patient referral programme in Japan to assist them in continuing to receive TB medical services across the border.

**Intervention or response:** The Research Institute of Tuberculosis introduced a cross-border TB patient referral programme, “Bridge TB Care” (BTBC), in 2019 to refer TB patients moving out of Japan to TB medical services in the destination country and follow them up until they complete the treatment course.

**Results/Impact:** BTBC received requests for cross-border referrals of 130 patients by the end of December 2022. We enrolled 112 patients, excluding those who had cancelled their travel or finished their treatment before departure. The median age was 27 years old, 65.4% (85/112) were males, 68.5% (89/112) were diagnosed with pulmonary TB, and 9.8% (11/112) were multi-drug resistant patients. The major destination countries were Vietnam (27.7%), the Philippines (22.3%), and Indonesia (18.8%). 87.5% (98/112) were confirmed to have access to medical facilities (Table 1). 92.8% (13/14) of the lost-to-follow-up patients were not confirmed to have access to medical facilities. The treatment success rate among those who were scheduled to complete treatment was 83.5% (66/79 as of February 28, 2023) (Table 1).

Access to TB medical services	N	% ([95% Confidence Intervals])
Access confirmed	98	87.5 ([80.1 – 92.4%])
Treatment status	N	% ([95% Confidence Intervals])
- Those due for treatment completion before February 28, 2023	79	100
Treatment success confirmed <sup>*1</sup>	66	83.5 ([73.9 – 90.1%])
Lost to follow-up confirmed <sup>*2</sup>	13	16.5 ([9.9 – 26.1%])
- Still on treatment <sup>*3</sup>	33	

TB: Tuberculosis

<sup>\*1</sup> One multi-drug resistant tuberculosis (MDR-TB) patient was included.

<sup>\*2</sup> Three MDR-TB patients were included.

<sup>\*3</sup> Seven MDR-TB patients were included.

*Table 1. Access to TB medical services and the treatment status of 112 TB patients who were referred from Japan via the Bridge TB Care programme from September 2019 to December 2022*

**Conclusions:** The access to TB medical services and treatment success of this programme indicated promising results. One of the critical steps to achieving a high treatment success rate was to ensure access to a medical facility in the destination country.

### EP23-1196-17 Optimising TB active case-finding at high-volume health facilities with the support of lay linkage assistants in Kenya

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**Background and challenges to implementation:** Kenya is among 30 high-burden countries for Tuberculosis (TB) and TB/HIV. TB is the 4th leading cause of death in the country. Kenya TB prevalence survey showed that 40% of people with TB are missed annually. Contributing factors include; suboptimal TB screening for people seeking care and weak linkages to different service delivery points (SDPs) among others.

To bridge these gaps, linkage assistants (LAs) (lay people with minimal training/mentorship on TB) were engaged to strengthen TB screening and link patients to different SDPs.

**Intervention or response:** Amref, the non-state Principal Recipient for Global Fund TB, in collaboration with county teams identified and supported 580 LAs strategically stationed at different SDPs in 580 high-volume health facilities in the country.

Working closely with healthcare workers, the LAs provided health education on TB, fast-tracked people with cough, ensured TB screening, registration in presumptive registers, and subsequent linkage of presumptive persons to different SDPs including; outpatient, laboratory, radiography and TB clinic for those diagnosed for treatment initiation and proper documentation. Data for the period January to December 2021 and 2022 respectively was analyzed using Excel.

**Results/Impact:** In 2022 a total of 19,347,847 clients seeking services at health facilities were screened out of whom 841,655 (4%) were presumed to have TB, 622,524 (74%) accessed diagnostic services (sputum test and chest x-ray) where 28,431 (7%) were diagnosed with TB and initiated on treatment.

This was an improvement from 2021 where 4,896,176 were screened, 126,655 (3%) were presumptive, all tested and evaluated and 9,372(7.4%) were diagnosed with TB and initiated treatment. The facilities recorded a 33% increase in case notification.

**Conclusions:** Linkage assistants stationed at designated SDPs in health facilities are key in finding missing people with TB through screening and linking presumed clients to clinicians, laboratory, radiography, and chest clinic for treatment.

### EP23-1198-17 Use of symptom screening and digital chest X-ray to increase TB case detection in Nelson Mandela Bay, Eastern Cape, South Africa

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**Background and challenges to implementation:** Systematic TB screening in high-burden areas is recommended as a strategy for early detection of TB disease<sup>1</sup>.

Advances in Digital Chest X-Rays have resulted in much higher sensitivity in screen compared to symptom based screening<sup>2</sup>.

The project included the use of Digital Chest X-Ray in order to understand its feasibility in improving TB case identification at community level.

<sup>1</sup>WHO consolidated guidelines on Tuberculosis, 2021

<sup>2</sup>World Health Organization. Chest radiology in tuberculosis detection. Summary of current WHO recommendations and guidance on programmatic approaches. 2016 [cited 2019 Nov 29].

**Intervention or response:** High-burden areas within the Nelson Mandela Bay District in the Eastern Cape were identified by geographic hotspot mapping using data from active TB case finding activities. A mobile DCXR machine and intervention team of Community Healthcare Workers, Data officers, and Professional Nurse conducted household visits offering TB symptom screening and as well as referring them to mobile DCXR services in the area (within 1km radius). All presumptive patients had sputum collected for Xpert testing as per South African guidelines.

**Results/Impact:** From July 2022 to March 2023 (9 months), a total of 19,137 clients were screened with both symptom-based questionnaire and DCXR, 1,203 (6%) were presumptive with a total of 115(10%) patients being diagnosed with TB.

Of these 3,208 clients were screened using the mobile DCXR service, with 556 being clients presumptive for TB and 85 testing positive for TB. The yield from the integrated screening project was 0.6%, compared to DCXR at 2.6%.

**Conclusions:** The inclusion of the DCXR detected 42% additional active TB cases who would otherwise have been missed with symptom screening. Therefore, the investment on making DCXR accessible in community and primary healthcare can improve case detection and assist in achieving the 2030 End TB Strategy global plan.

### EP23-1199-17 Evaluating the performance of 11 computer-aided detection products for the detection of TB compared with radiologists from four regions in a high TB-HIV setting

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**Background:** Computer Aided Detection (CAD) software uses artificial intelligence (AI) to read chest X-rays for signs of tuberculosis (TB). The World Health Organization (WHO) has recommended the use of CAD for TB screening and triage as an alternative to human readers.

However, there is a lack of impartial evidence on how different CAD products perform compared to radiologists.

We aimed to evaluate 11 commercially available products' performance in a high HIV/TB setting against the performance of radiologists from four WHO regions: AFRO, AMRO, EURO, and SEARO.

**Design/Methods:** Using a case-control sample of 774 participants from a recent TB prevalence survey in South Africa, we compared the performance of 11 CAD products with radiologists from WHO regions.

We matched the sensitivity of the radiologists with each product and compared the corresponding specificity and did the same process vice versa. Statistical difference was determined using the McNemar test for paired proportions.

**Results:** Many CAD products performed similarly to or better than radiologists. Using a classification when X-rays with only TB-related abnormalities were categorised as "TB", Lunit outperformed radiologists from all regions, Xvision outperformed all regions except EURO, and CAD4TB performed better than AFRO in terms of specificity.

For sensitivity, Lunit again outperformed all regions' radiologists, Xvision performed better than SEARO and AFRO.

When categorising X-rays with any abnormalities as "TB", Lunit outperformed all regions and InferRead outperformed all regions but SEARO in specificity.

A further three products outperformed AMRO radiologists and an additional product outperformed AFRO. In sensitivity, Lunit outperformed all regions, JF CXR, ChestEye and qXR outperformed AMRO and AFRO, and Genki also outperformed AMRO. Radify and XRayAME always performed worse than radiologists.

**Conclusions:** Our results show that several CAD products perform better than or on-par with radiologists. These could be useful tools for screening and triaging in settings with human resource constraints.

### EP24 Local and global policies and politics

#### EP24-1200-17 Designing a TB elimination framework through participatory processes in Ethiopia: results from stakeholders' discussions

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**Background:** There is limited understanding of multi-pronged interventions that should be designed and implemented to eliminate TB.

To develop a model for TB elimination, we developed multipronged intervention which was guided by the Medical Research Council (MRC) Framework complex interventions.

Our aim was to explore the feasibility of applying the proposed package of interventions.

**Design/Methods:** As part of the pilot phase of MRC, we explored the reflections of TB program managers on the proposed interventions.

We held participatory discussions with mid-level TB program managers in three regions about the feasibility of the study and operational procedures as part of the study launching in February 2023.

Two senior researchers have taken note to document reflections from the participants. Thematic analysis was carried out to summarize the reflections.

**Results:** A total of 108 participants attended the launching session of the study. The participatory discussions

were articulated in four sub-themes under the main theme of “Looking for local evidence compulsory for TB elimination.”

Sub-themes include:

1. The importance of community engagement which describes the need to include health extension workers, the health development army, and other community structures to support the study and,
2. Government interest toward local evidence, which describes how local evidence is essential to support the TB program and address challenges.
3. In homogeneity of officials’ commitment across the regions, they showed their immense support to undertake the study yet suggested working together for the study follow-up.
4. In considering multiple factors, issues, such as nutrition, sociocultural factors, livelihood, and housing, were considered.

**Conclusions:** The results suggest a need to engage the community, ensure the commitment of TB program managers, and the need to consider a multifaceted intervention to prepare the TB elimination framework. These factors should be considered during the main phase of the study and for wider adoption.

### EP24-1201-17 Factors influencing the scale-up of TB interventions: Insights from TB REACH-funded projects in Nigeria and Kenya

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**Background:** TB REACH-funded projects test and evaluate innovative short-term interventions for TB prevention, detection, and care. The challenge of scaling-up small but effective interventions is a well-known phenomenon in global health, including TB programs. There is insufficient understanding regarding the process, and the multiple agents and factors involved in sustaining and expanding such interventions. Our aim was to improve the understanding of barriers and enablers that influence scale-up.

**Design/Methods:** We adopted an embedded multiple case study design and purposively selected eight TB REACH funded projects: four in Nigeria, four in Kenya. A desk study was performed reviewing both project reports and quantitative data analyzed using the TB REACH monitoring and evaluation framework.

Primary qualitative data was collected via 14 semi-structured interviews guided by the WHO/ExpandNet framework for scaling-up, and was analyzed thematically.

Case studies were initially analyzed independently. Subsequently, all were compared to draw cross-case conclusions.

**Results:** Four of the eight cases had their activities partially or fully scaled-up. Although five projects demonstrated quantitative effectiveness using trends in TB notifications and the yield of interventions, two were not funded for scale up.

One project that showed negative trends in notifications was however taken to scale. The qualitative analysis revealed that the process of scaling-up TB REACH funded interventions is context-sensitive and not based on results and impact alone.

Demonstrating quantitative success from empiric results seemed to be less important than having the right relations, both with the TB programs and donors, as well as the larger community.

In addition, dedicated funding, the compatibility of the interventions with the local TB program structures, sufficient time, and longer-term vision for scaling-up played key roles.

**Conclusions:** Scaling-up small-scale public health interventions is a difficult and not fully comprehended process. To optimize opportunities for scale-up, projects must leverage on contextual opportunities and mitigate potential barriers.

### EP24-1202-17 Assistance actions and health surveillance for the detection of TB and HIV in people deprived of liberty in prisons in Mozambique

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**Background:** In Mozambique there are 184 prisons, with a total capacity of 8,498 places. Prisons are overcrowded, and in 2020 around 20,000 people were deprived of their liberty, that is, 135.34% above their total capacity. People Deprived of Liberty (PDL) is classified as a group at high risk of contracting and transmitting infectious diseases, such as the human immunodeficiency virus, tuberculosis, viral hepatitis, syphilis, COVID-19, among others.

The objective is to identify health care and surveillance actions for the detection of TB and HIV in People Deprived of Liberty in prisons in Mozambique

**Design/Methods:** Descriptive cross-sectional quantitative study carried in the province of Gaza, Mozambique in the districts of Xai-xai, Chongoene and Mabalane with health professionals (HP) and penitentiary agents (PA) using a questionnaire for interview in which descriptive and univariate analyzes were carried out regarding the infrastructure and flow network.

**Results:** 100 health and safety professionals were invited to participate in the study, of which 81 answered the survey form, 52 (64.2%) HP and 29 (35.8%) PA. As for access to the specialized service for the treatment of TB and HIV, 72.42% of the PA do not know, all the PA and HS understand that there is no transfer flowchart for PDL in treatment for TB and HIV, and the testing is not carried out entry point for TB and HIV upon admission to the penal institution

**Conclusions:** The study demonstrated the need to qualify PDL transfer flows in treatment for TB and HIV and the implementation of screening for infectious and contagious diseases at the prison gates. In this way, the study contributes with subsidies for managers linked to penitentiaries to make efforts to reduce, monitor and control TB and HIV in prisons.

### EP24-1203-17 The local promotion of the rights of people affected by TB among health service providers, local authorities and community health workers

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**Background and challenges to implementation:** The lack of human rights protections makes people more vulnerable to developing TB disease, negatively affects their ability to access effective treatment and exposes them to stigma and discrimination by the very fact of having TB. TB-related human rights violations include failures to diagnose or treat people properly, restricted access to health information by people living with TB and shackling prisoners accessing TB treatment in hospital.

**Intervention or response:** In collaboration with TBpeople Global, KHANA implemented the local promotions of the Declaration of the Rights of people affected by TB in selected operational health districts in Cambodia.

Initially, KHANA translated the declaration into local language and then convened several workshops to sensitize the health service providers, local authorities, and community health workers (CHW). Also, KHANA introduced and trained to leaders of peer support group (PSG) of people affected by TB on Rights to Breathe: TB and Human Rights using the regional manual developed by ACT!AP.

KHANA additionally run the TB and human rights community scorecard amongst people affected by TB for producing a strong evidence-based on the human rights-related barriers in TB service access and then inform the advocacy agenda for the TB programs development and reprogramming.

**Results/Impact:** 180 participants who are health service providers, local authorities were sensitized on the Declaration of the Rights of people affected by TB, 20 PSG leaders were trained on Right to Breathe, and TB and human rights community scorecard was implemented amongst CHWs. They have equipped with knowledge, skills and experiences on the rights of people affected by TB.

**Conclusions:** The declaration, rights to breathe and TB and human right scorecard are the tools to promote the right-based and people-centered in TB programming. Importantly, the results from the community scorecard were used to inform the TB prevention, diagnosis, treatment and support services at health facility and community levels.

### EP24-1204-17 The impact of TB stigma along the TB service cascade in Nigeria

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**Background:** Tuberculosis continues to be a public health challenge around the world. TB-related stigma has the power to frustrate or impeded the effective prevention and management of TB from the local to the global levels. We evaluated the impact of TB stigma along the TB service cascade.

**Design/Methods:** The study utilized a cross-sectional research design to elicit information from persons with TB (PWTB) using interviewer administered questionnaires. The level of self-stigma among PWTB was measured by using a set of 12 statements describing the impact of TB stigma along TB service cascade. Data was analyzed using descriptive statistics and stigma radar.

**Results:** A total of 3,252 PWTB were interviewed across the eighteen states. The majority of PWTB (59%) were men between the ages of 25 and 44 (50%).

Overall, about two-fifths of PWTB (37%) reported to have ever experienced TB stigma and stigma occurred the most within community (53%).

High levels of self-stigma among PWTB were reported, especially relating to disclosure of TB status (80%), feeling alone (50%), feeling hurt and feeling guilty for themselves (50%).

By place of residence, high stigma was slightly higher among those in urban slum (55%) compared to rural dwellers (53%). The impact of TB stigma along the TB service cascade showed that inhibited them from accessing care 50%; recognizing symptoms (63%), getting accurate diagnosis (42%), beginning treatment (40%), getting treatment adherence support (39%), completing treatment (35%) and getting post-treatment follow-up (35%).

**Conclusions:** TB stigma levels are high and pervasive with stigma occurring across multiple settings. TB stigma has negative psychosocial and socioeconomic impact and thus evidence-based strategies which are urgently needed, must be multifaceted in their approach and implementation to mitigate the impact of TB stigma on uptake of TB services.

### EP24-1205-17 Mid-media to overcome hard-to-reach areas: generating TB awareness among tribal communities in Odisha, India

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**Background and challenges to implementation:** Around 59% of the 25 lakh total population in Mayurbhanj district, Odisha belong to the tribal community, living in media-dark and hard-to-reach areas where there is lack of proper connectivity and conveyance.

Its challenging for people with TB (PwTB) to access health facilities and notify their diagnosis. Service providers are unable to effectively reach out to them for awareness generation and treatment follow-ups. Special health camps and active case finding campaigns are focused upon but a larger need was felt for increasing TB-related awareness.

**Intervention or response:** The Accountability Leadership by Local communities for Inclusive, Enabling Services (ALLIES) Project implemented by REACH, supported by of USAID, focuses on community engagement and training TB survivors as TB Champions who work with PwTB and the health system to improve quality of care and services.

To reach out to the tribal communities of Mayurbhanj, TB Champions, who belong to the community, became the biggest asset and mid-media became the best tool. TB Champions started doing wall-paintings (over 160 across 100 villages) with messages in local languages and disseminated IEC materials to generate awareness on TB. They created WhatsApp groups to share regular information, directly.

Awareness was built on symptoms of TB, myths and health facilities offering TB treatment. They also engaged local leaders, elected representatives and community influencers in activities to address self and social stigma associated with TB.

**Results/Impact:** The mid-media campaign proved to be one of the factors that contributed to an increase in TB related awareness. This was reflected in the significant

increase in sputum examination and notification rate per 100000 population in the district. The table below shows the rate of increase (data source: Nikshay).

Indicator	2020	2021	2022
Sputum examination rate per 100000 population	1212	2186	2629
Notification rate per 100000 population	181	208	227

**Conclusions:** There has been significant improvement in TB awareness and TB response from the tribal population with the active involvement of TB champions using mid-media tools.

### EP24-1206-17 Youth engagement to end TB through the Red Ribbon Clubs in Kangra, India - dispelling stigma and breaking the ice

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**Background and challenges to implementation:** Red Ribbon Clubs (RRCs) were created in educational institutions under National AIDS Control Programme, which led to a cadre of youth peer educators for seeking & encouraging positive health behavior.

These were primarily focused on HIV/AIDS & sexuality, drug abuse prevention, blood donation awareness. These have evolved into platforms for life-skills education, personality development in Kangra, a hill district in North India. NTP initiated the engagement of these key stakeholders to make TB Elimination into a public movement.

**Intervention or response:** We leveraged the power & innovation of youth of RRCs to expand the Kangra EndTB Dialogue for the last 5 years. We conducted Red Arrow Contests for youth to engage them through play-way approach. With a series of annual workshops for the Nodal Officer Teachers & peer educators. Over 500 persons were sensitized on basics of TB, social media. We had a core team of best 10 clubs interact with TB Survivors & rural self-help groups, to help them understand challenges like stigma. Club members are also supporting program in providing psychosocial support to TB patients to complete their treatment.

**Results/Impact:** The intervention led to innovative creatives from youth on TB, increased presence of TB Messages on social media which intensified during the World TB month. We have succeeded in making TB part of the discourse for youth among our 50 RRCs to some extent. 220 events on TB month were held in various RRCs.

**Conclusions:** To achieve EndTB targets, services of RRCs should be expanded across all educational institutions in the State and country.

However, there still exists a need to build capacity of the club members further, polishing their communication and leadership skills and empower youth and change agents to take the dialogue to village panchayat (local government) and facilitate adopting the concept of TB Free village.

### EP24-1207-17 Factors associated with multidrug-resistant TB treatment outcomes in Indonesia

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**Background:** Multi-drug resistant tuberculosis (MDR-TB) is a serious problem in Indonesia, this study aims to identify factors that contribute to its treatment outcomes.

**Design/Methods:** This study utilizes 2,499 MDR-TB patient data with treatment outcomes reported in TB Community Information System, managed by the Global Fund Principle Recipient TB Community, using ordinal regression and Cox regression to explore the associations between treatment outcomes and sex, age, geographical region, community support, and treatment regimen.

**Results:** Poorer treatment outcomes among people treated for MDR-TB were associated with Long Term Regimen (LTR) (OR 1.7; CI 95%: 1.4-2.2), and not receiving community support (OR 1.6; CI 95%: 1.2-2.2). Cox regression showed that living outside Java/Bali/Sumatera (HR 1.4; CI 95%: 1.0-1.9), not having community supports (HR 1.6; CI 95%: 1.2-2.0), receiving LTR (HR 1.8; CI 95%: 1.4-2.3), and older age (HR 1.02; CI 95%: 1.01-1.03) increased the risk of death from MDR-TB. In the first six months of treatment, living outside Java/Bali/Sumatera, receiving LTR, and older age increased the risk of death from MDR-TB. Those without community support were more likely to die (OR: 1.8; CI 95%: 1.3-2.4). However, community support did not reduce the risk of loss to follow-up (LTFU) or shorten the delay between diagnosis and treatment. Those living outside Java/Bali/Sumatera (CI 95%: 1.3-2.4) had a higher risk for LTFU. By contrast, receiving LTR was associated with a lower risk of LTFU (OR 0.5; CI 95%: 0.4-0.7).

**Conclusions:** In Indonesia, MDR-TB treatment outcomes are associated with geographical area of living,

age, and prescribed regimen. While community support lowered the risk of death, it did not lower the risk for LTFU. Further investigation on how STR increases LTFU risk and improvement of MDR-TB services are needed.

### EP24-1208-17 Community engagement, an effective mechanism to support people with tuberculosis: experience on survivor led networks from India

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**Background and challenges to implementation:** Various studies suggest that the TB survivors have strong self-stigma leading non declaration of their status. This was major a challenge in the formation of the TB survivors led networks, which are strong advocacy groups, in Delhi and four North Eastern states in India.

**Intervention or response:** Under The Accountability Leadership by Local communities for Inclusive, Enabling Services (ALLIES) project supported by REACH, an intervention was launched to raise awareness and bust the myths about TB. Social and mid media campaigns were launched engaging TB Survivors, NTEP officials and prominent personalities. Post, campaign 60 TB Survivors carried out 4860 house visits and counselled 5040 people. In addition, 748 community meetings were also organised by the TB survivors and 2720 downloads of Arogya Saathi app were facilitated. These efforts were made between October 2020 to March 2023.

**Results/Impact:** The intervention led to formation of 10 district level networks, 3 State level networks and 1 National level TB Survivors' led network.

Currently there are 515 TB Survivors associated with the network working in close coordination with the affected community and the NTEP to provide the support to people with TB.

**Conclusions:** It may be concluded from the intervention that, sensitization of the community in breaking the myths is critical in empowering the affected community to play an active role in the fight against TB. Once empowered the TB Champions become a critical link between the program and people seeking care.

## EP24-1209-17 Estimating the prevalence and risk factors of catastrophic costs among people with TB in semi-rural Mozambique

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**Background:** Catastrophic costs (CC) due to tuberculosis (TB), defined as total costs exceeding 20% of the annual pre-TB household income, lead to household impoverishment and negatively affect TB treatment adherence and outcomes. Mozambique, a high TB burden country, has achieved the WHO End TB milestone of 35% reduction of TB deaths.

However, the prevalence of CC is still unknown, which is necessary to achieve the milestone of zero households incurring CC. We estimated the proportion of people incurring CC due to TB and determined its risk factors in Mozambique.

**Design/Methods:** This was a multi-centre cross-sectional survey conducted in health facilities with TB treatment in Inhambane province, Mozambique. Adults with drug-susceptible or drug-resistant TB undergoing treatment for at least two weeks were enrolled. Based on the WHO Patient Cost Survey, information on direct and indirect costs of TB treatment among patients, household income, clinical and socioeconomic background data were collected.

**Results:** 200 people with TB (58.5% women, median age 52 years old IQR 38-62, 56% breadwinner) were included. Monthly individual income before TB was mean USD71.95, which decreased by 29.7%, to USD50.56 during TB treatment. Of 200 participants, only 74 (37%) had full data available to allow CC calculation, of whom 50% (37/74) incurred CC.

The overall mean total cost was USD29.4, which corresponded to 58.1% of the mean individual income. The incurrance of CC was higher amongst participants with primary educational level, unemployed, and men.

**Conclusions:** The individual and the household's income considerably decreased after the initiation of TB treatment, and half of the participants with available data incurred CC, suggesting that TB has a negative impact on the household's finances.

Those with primary educational levels, men or unemployed were more susceptible to incurring CC. Further large-scale research on CC in Mozambique is needed for the development of policies that can support TB-affected households.

	Care Seeking Costs (US dollars)		Estimated Catastrophic costs			
	mean	sd	n (%)			
Mean individual income before TB	71.95	163.45	WHO Catastrophic Costs Threshold (medical and non-medical costs plus lost income exceeding 20% of household's annual pre-TB income).			
Mean individual income now	50.56	55.20				
Mean household income before TB	89.49	166.41				
Mean household income now	60.36	64.78				
Total medical costs	15.05	89.66				
Total non-medical costs	14.34	43.26				
Total medical and non-medical costs	29.40	108.11				
Total income loss	22.58	168.57			37/74 (50%)	
<b>RISK FACTORS</b>						
Determinant	Univariable Logistic Regression				Multivariable Logistic Regression	
	cOR (95% CI)	p-Value	aOR (95% CI)	p-Value		
Sex	Female	Ref.	Ref.	0.978		
	Male	1.44 (0.55-3.79)	1.02 (0.22-4.56)			
Educational level (%)	No education	Ref.	Ref.	0.035		
	Primary	0.41 (0.13-1.32)	0.18 (0.36-0.88)			
	Secondary	0.11 (0.20-0.63)	0.013 (0.007-0.38)			
	Vocational training	0.20 (0.50-0.81)	0.025 (0.13-0.65)			
Occupation (%)	Employed	Ref.	Ref.	0.131		
	Unemployed	1.65 (0.61-4.40)	2.66 (0.74-9.45)			

Table. Costs.



## ABSTRACT PRESENTATIONS SATURDAY 18 NOVEMBER 2023

### ORAL ABSTRACT SESSION (OA)

#### OA54 NTM infection a new challenges

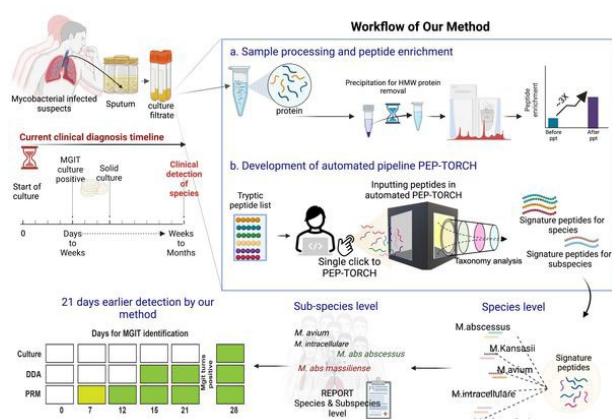
##### OA54-623-18 Rapid differentiation of mycobacteria at sub-species resolution by an antigen-peptidome algorithm

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**Background:** Mycobacterial infections are a major and growing public health concern worldwide. Further, non-tuberculosis mycobacteria (NTM) infections caused by common clinical NTM species and subspecies isolates produce symptoms similar to tuberculosis (TB) symptoms, but can require individual drug regimens. Polymerase chain reaction (PCR)-based tests widely adopted for TB diagnosis are not as effective for NTM diagnoses and may not distinguish related taxa. Thus, accurate species or subspecies identifications are critical for their effective treatment.

**Design/Methods:** As shown in Figure 1, we employed a streamlined procedure to fractionate and digest culture filtrate protein (CFP) samples of early-growth mycobacterial growth indicator tube (MGIT) cultures (Fig 1a) and then analyzed the MS data of these samples with a novel and automated peptidomic pipeline approach, Peptide Taxonomy/Organism Checking (PEP-TORCH) to identify species/subspecies-specific NTM peptide signatures.



**Results:** This approach facilitated selection of species-specific peptides for targeted mass spectrometry assays suitable for use in clinical laboratories, including peptides that distinguished drug-sensitive and drug-resistant *Mycobacterium abscessus* strains difficult to discriminate by conventional means. Longitudinal analysis found that species-specific peptide signatures could be detected by 7-days culture, but not until 28-days culture when using the gold-standard diagnostic approach.

**Conclusions:** We found that this rapid streamlined identification procedure could distinguish common clinical isolates and their subspecies, including NTM subspecies with differential drug resistance, to provide diagnoses well before conventional methods using MS instruments suitable for use in clinical laboratories.

##### OA54-624-18 Determining automatous quantitative minimum inhibitory concentrations mycobacteria using a reducing chromogenic reagent, WST-1

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**Background:** WST-1, a tetrazolium salt, is reduced by viable cells to produce yellow formazan dyes. Our objective was to quantitatively determine the minimum inhibitory concentration (MICs) of antibiotics against the major Mycobacterial species by absorbance measurement using WST-1 solution.

**Design/Methods:** We tested a total of 150 clinical isolates for 14 drugs, including *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Mycobacterium intracellulare*, *Mycobacterium abscessus* subsp. *massiliense*, *Mycobacterium fortuitum* subsp. *fortuitum*, *Mycobacterium chelonae*, and *Mycobacterium peregrinum*, as well as each type-strain. WST-1 solution was added to the culture medium, and the drug susceptibility testing (DST) was performed according to CLSI M24 3<sup>rd</sup> ed.

We established determination criteria by comparing absorbance with visual MICs and evaluated the accuracy of determination by calculating the concordance rate between automatous and visual MIC determinations.

**Results:** Automatous MICs determination showed more than 80% agreement with visual MICs in the strains tested; 11 drugs for *M. abscessus* and *M. chelonae*, 12 drugs for *M. fortuitum*, and 10 drugs for *M. peregrinum*.

In all four species, automatous MICs determination of AMK, TOB, DOXY, LVFX, CLF, MFLX, and CAM (Day 14) showed high agreement with visual MICs. For *M. avium*, 12 out of 14 drugs matched more than 90%, and for *M. intracellulare*, 9 out of 14 drugs matched

more than 80%. Among these two, automatic MICs determination of CAM, MFLX, STFX, KM, DOXY, INH, LZD, and EB showed more than 80% concordance with visual MICs.

However, for *Mycobacterium tuberculosis*, only 2 out of 8 drugs showed high accuracy, suggesting that the indicator reagent requires modification.

**Conclusions:** MICs detection with WST-1 showed high concordance with MICs based on visual observation.

We hope that this automated method will be a great help in DST, because it never requires addition of reagent after the growth of bacteria. It is technically easy and safe.

### OA54-625-18 Prevalence, incidence and antibiotic resistance testing frequency of non-tuberculous mycobacteria isolated in German microbiology laboratories, 2016-2020

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**Background:** Reports on non-tuberculous mycobacteria (NTM) and NTM-pulmonary disease (PD) have increased over the last 10 years. There is a paucity of information regarding NTM prevalence and incidence in Central Europe. Our study-objectives were to:

1. Estimate prevalence and incidence of NTM detection in German microbiological laboratories over a 5 year period (2016-2020);
2. Determine which NTM are most commonly encountered and whether they show regional particularities, and;
3. Determine the proportion of NTM samples that are tested for antibiotic susceptibility (DST).

**Design/Methods:** Complete microbiology laboratory data on NTM and tuberculosis (TB) from pulmonary samples was submitted from 22 laboratories across Germany for the years 2016 to 2020. Laboratory incidence and prevalence of TB were calculated (using the German surveillance databank) and estimated for NTM using TB as reference. The proportions of NTM-isolates with DST results of the first were compared to those of the last study year.

**Results:** Our study databank comprises >30% of all German TB and NTM cases detected during the study period. Prevalence (5.1-5.8/100,000) and incidence (4.5-4.9/100,000) of NTM in German laboratories did not change over the 5 year period, also not when stratifying for facultative pathogenic NTM, the *M. avium/intracellulare* (MAIC) or the *M. abscessus* complexes (MAB-SC). *M. xenopi* was far more frequent in the German South.

The proportion of NTM isolates with DST and of drugs tested specifically for MAIC following the most recent NTM guidelines increased from the first to the last study year.

**Conclusions:** Incidence and prevalence rates were stable over the five year study period and may represent the ceiling of the frequency of NTM-PD in the population. Recent testing guidelines appear to have had a positive effect on the proportion of NTM isolates that are tested for drug resistance. DST is however still insufficiently performed.

### OA54-626-18 Prevalence of non-tuberculous mycobacteria among sputum samples of presumed and diagnosed drug-resistant people with TB in Ghana, a 10-year retrospective laboratory analysis

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**Background:** The awareness about nontuberculous mycobacterial pulmonary disease (NTM-PD) is rising worldwide with increasing isolation of NTM in sputum samples. In 2009, Ghana disseminated use of mycobacteria growth indicator tube (MGIT) for diagnosing and monitoring people with presumed or diagnosed drug-resistant tuberculosis (DR-TB), also resulting in increasing isolation of NTM species. Our study aimed to establish the proportion of NTM-positive culture-tested sputum samples per year and characterise the circulating species.

**Design/Methods:** This is a retrospective analysis of existing laboratory data from 2012-2021 from the Eastern Regional Hospital and Cape Coast Teaching Hospital in Ghana. All sputum samples submitted are taken through sputum smear microscopy (SSM), culture and drug-susceptibility testing (DST) using MGIT and Lowenstein-medium.

All positive NTMs were stored at -20°C. After regrowing on the MGIT 7H9 broth medium, NTM isolates were analysed using GenoType CM/AS (Bruker, Germany) to characterise the species.

**Results:** Of the 2492 sputum samples analysed, 1434/2492 (57.5%) were submitted for follow-up and 1004/2492 (40.5%) for diagnosis of DR-TB. 503 (20.2%) of these 2492 were smear, and 839 (33.7%) culture-positive.

Of the culture-positive isolates, one-third (257; 30.6%) were NTM-positive. Figure 1 presents the trend of culture-positive TB and NTM isolates.

Among 225 NTM isolates regrown and analysed, results showed predominance of the potential pathogenic *M. intracellulare* (15.1%) followed by probable contaminant *M. fortuitum* (4.9%) and few isolates of potential pathogens *M. abscessus* (0.9%), *M. malmoense* (0.9%), and *M. avium* (0.4%).

Remarkably 18/225 (8%) isolates initially classified as NTM were identified as MTB complex, while an important proportion (85/225) could not be species identified, and 43/225 (19.1%) were negative.

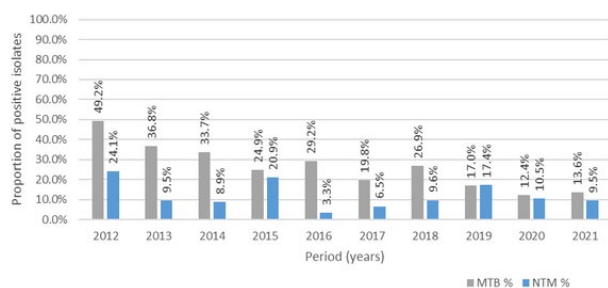


Figure. Trend of MTB and NTM positive culture results in samples of people with presumptive or diagnosed drug resistant TB.

**Conclusions:** NTM has been identified in one-third of the sputum samples of presumed and diagnosed people with DR-TB. It is crucial to implement genotype analysis for NTM as a first step in clinical decision-making in case of NTM isolation from sputum in Ghana.

### OA54-627-18 Emerging multidrug-resistant, rapid-growing non-tuberculous mycobacteria in a tertiary care institute in India

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**Background:** A significant number of resistant strains has been reported amongst various rapidly growing nontuberculous Mycobacterial (RGNTM) species. The aim of the study was to find out the resistance pattern in RGNTM isolated from clinically confirmed cases at the tertiary care referral institute in New Delhi, India.

**Design/Methods:** The study was conducted during January 2020 to December 2022. A total 42 rapid growing mycobacterial strains were subjected for antimycobacterial susceptibility testing in Sensititre™ RAPMYCO Susceptibility Testing Plate.

**Results:** Mycobacterial species identified were *M. chelonae* (22), *Mycobacterium fortuitum* (17), *M. abscessus* (02), and *M. boletti* (01). In the RAPMYCO susceptibility testing plate, 15 antimicrobial agents were tested by microdilution broth technique according to CLSI guidelines.

Resistance strains were categorised in 3 groups; high resistant strains (> 40% R strains), Moderate resistant strains (20-40% R strains) and minimally resistant strains (<20 R strains).

The drug susceptibility results showed high level of resistance to *cefepime* (53%), *ceftriaxone* (53%), *augmentin* (51%), *doxycycline* (51%), *minocycline* (49%), moderately resistant strains were; *tigecycline* (37%), *cefoxitin* (29%), *linezolid* (26%), *clarithromycin* (21%) and minimally resistant strains were *tobramycin* (21%), *ciprofloxacin* (19%), *moxifloxacin* (12%), *amikacin* (9%) and *imipenem* (7%).

The commonest RGNTM *M. chelonae* (22) strains were found high susceptibility to tobramycin (95%), amikacin (95%), moxifloxacin (88%), imipenem (87%), clarithromycin (77%) and ciprofloxacin (68%). The majority of *M. fortuitum* group isolates were susceptible to imipenem (100%), moxifloxacin (94%), amikacin (88%), and clarithromycin (77%).

**Conclusions:** The study shows that less frequently used antimicrobial agents like tobramycin, amikacin, moxifloxacin, and imipenem have shown high sensitivity among rapidly growing mycobacteria, whereas commonly used antibiotics like cefepime, ceftriaxone, augmentin, and doxycycline are having less invitro activity. The susceptibility/resistance pattern profile gives clinicians precise therapy and patient management options.

## OA54-628-18 A machine-learning algorithm for distinguishing non-tuberculosis mycobacteria from *M. tuberculosis* bloodstream infection in people living with HIV

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**Background:** Clinical features of mycobacteria bloodstream infection (MBI) with Non-tuberculosis mycobacteria (NTM) or *Mycobacterium tuberculosis* complex (MTB) may be difficult to distinguish, and culture results are delayed.

We developed a decision tree-based clinical model to differentiate NTM from MTB cases in people living with HIV (PLHIV) with MBI.

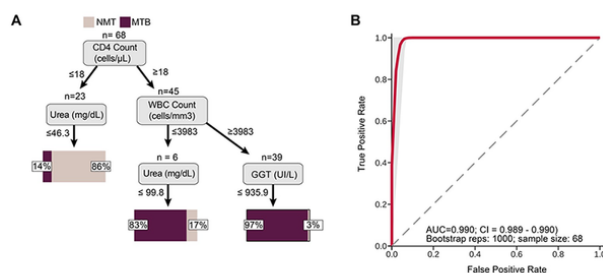
**Design/Methods:** We conducted a retrospective cohort study at a reference center for TB and HIV in Brazil. We defined MBI as a PLHIV hospitalized with systemic signs of infection and at least one mycobacteria identified from blood culture. *Mycobacterium sp.* was isolated from blood using the blood culture BACTEC 9240 system.

Data were obtained from electronic medical charts. We used the Mann-Whitney *U* test to compare continuous variables. Fisher's exact test was applied to evaluate categorical variables. Random Forest was used to obtaining the final decision-tree model. Statistical analyses were done using Stata/MP (14.0), Rstatix, Stats, Caret (6.0.86), R packages, and Phyton software.

**Results:** Of 68 PLHIV with MBI, 50 (74%) had MTB-MBI, and 18 (26%) had NTM-MBI. All isolates of NTM-MBI were identified as *Mycobacterium avium* complex.

Patients with NTM-MBI were younger (median age 29 (10–42) vs. 35 (11–67) years;  $p=0.011$ ) than MTB-MBI, more likely to have had previous anti-TB treatment (56% vs. 16%;  $p=0.002$ ), less frequent tobacco use (22% vs. 52%;  $p=0.027$ ), lower CD4 counts (88% vs. 60%  $\leq 50$  cells/ $\mu$ L;  $p=0.042$ ), normal blood urea level (78% vs 46%  $< 40$  mg/dL;  $p=0.020$ ), normal lactate dehydroge-

nase level (72% vs 0  $\leq 211$  UI/L;  $p=0.000$ ), and higher gamma-glutamyl transferase (100% vs 42%  $\geq 220$  UI/L;  $p=0.000$ ). The decision tree model resulted in a three-level structure, with overall high accuracy (AUC: 0.990).



**Figure.** Machine learning decision tree model to predict non-tuberculosis mycobacteria (NTM) tests on peripheral blood. (A) The random forest technique with 1000x bootstrap was applied. A Box plot of the distribution according to levels of markers was used. (B) The receiver Operator Characteristics (ROC) curve was employed to assess the accuracy of the model including the markers selected in the random forest algorithm discriminating MTB from NTM cases  $p<0.001$ . MTB: *Mycobacterium tuberculosis* complex; NTM: Nontuberculosis mycobacteria; WBC: White blood cell; GGT: Gamma-glutamyl transferase;  $\mu$ L: microliter; IU/L: International units per liter; mg/mL: Milligrams per deciliter; CI: confidence interval.

**Conclusions:** A combination of clinical laboratory variables was able to differentiate NTM from MTB with high accuracy that could prompt specific treatment before culture results. Those results are promising and warrant further validation in larger cohorts.

## OA54-629-18 Genotypic characterisation of non-tuberculous mycobacteria among presumptive TB patients in parts of Kaduna State, Nigeria

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**Background:** Non-tuberculous mycobacteria (NTM) infection is an emerging problem of public health significance with increasing cases from different countries. The distribution of species isolated from clinical samples varies significantly by region. In Nigeria where Tuberculosis (TB) burden is high, information on NTM is lacking due to limitations in tools for identification and characterization.

Hence, this study aimed to genotypically identify NTM among TB patients in Parts of Kaduna State, Nigeria.

**Design/Methods:** A total of 2,212 sputum samples from presumptive TB patients were screened for Acid Fast Bacilli (AFB) between April 2021 to March 2022. Mycobacteria were isolated from smear-positive culture using Lowenstein Jensen's (LJ) media and further analyzed with a rapid TB antigen assay to differentiate Mycobacterium tuberculosis complex (MTBC) and NTM.

The DNA of the isolates suggestive of NTM was extracted for detection of the genotypes species using Hain's Genotype® Common Mycobacteria(CM) and Additional Species(AS) assay.

The one not characterized by both assays was selected for sequencing of their 16S rRNA genes and the Basic Local Alignment Search Tool (BLAST) analysis of the sequences was done.

**Results:** Out of the 42 (15.4%) NTM phenotypically isolated, the most common species identified were: *M. intracellulare* 15(35.7), *M. abscessus* 7(16.7), *M. malmoense* 4(9.5), *M. kansasii* 3(7.1), *M. fortuitum* 3(7.1), *M. gordonae* 2(4.8), *M. scrofulaceum* 2(4.8), *M. smegmatis* 1(2.4), *M. avium* 1(2.4), *M. simiae* 1(2.4), *M. xenopi* 1(2.4), *M. interjectum* 1(2.4) and the 1(2.4) species that was not characterized by GenoType assay was confirmed to be *M. chitae* which has not been a predominant NTM species isolated from humans in Africa.

**Conclusions:** The presence of NTM in these patients has might have a significant impact on clinical diagnosis and patient management. The likely role of inadequate laboratory infrastructure in its occurrence presents a novel challenge in diagnosis and classification for an effective treatment plan.

## OA55 The impact of bacterial zoonotic diseases in animal and human health

### OA55-630-18 *M. orygis* and *M. tuberculosis* but not *M. bovis* are recovered from cattle at a slaughterhouse in Chennai, India

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**Background:** Bovine tuberculosis (bTB), a significant cause of cattle mortality and economic losses and endemic in many parts of the world, results from infection with *Mycobacterium bovis* and other members of the *Mycobacterium tuberculosis* complex (MTBC).

This study reports the presence and recovery of *M. tuberculosis* and *M. orygis* from the lymph node samples of slaughtered cattle in Chennai, India.

**Design/Methods:** A total of 534 tissue samples (271 bronchial Lymphnode (LN) and 168 mediastinal LN, 95 other tissues) collected from 500 animals were used in this study. Culture, molecular (PCR and spoligotyping) and whole genome sequencing methods (WGS) (Illumina) were used for species identification from these samples. WGS results were assessed with Galaxy/vSNP. Phylogenies were constructed with RAxML. RD Analyser and RDScan were used to localize the regions of difference (RD) within the sequences. Histopathology of tissue samples were performed using H&E staining.

**Results:** Sixteen out of 500 (3.2%) animals were positive for MTBC by culture, of which of which fifteen were *M. orygis* and one represented a mixed infection with both *M. orygis* and *M. tuberculosis sensu stricto* lineage 1. Strikingly, no *M. bovis* was found. RD analysis identified the animal-adapted MTBC clade-specific deletions in the regions RD 7 – RD10 in all the *M. orygis* isolates. Whole genome sequencing and phylogenetic analyses show that *M. orygis* isolates recovered from southern India have relatively restricted genetic diversity, There were also 108 Non-tuberculous mycobacteria (NTM) isolated from this study. Histopathology analysis revealed different stages of tuberculoid granulomas in the culture positive tissue samples.

**Conclusions:** Our studies suggest that bTB in India is likely to be different than elsewhere and highlight an urgent unmet need to better understand the epidemiology of bTB and develop rational strategies to accelerate the control of bTB in India and other regions where the disease remains endemic.

### OA55-631-18 Estimation of risk associated with zoonotic TB in India (ERAZTB)

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**Background:** Members of the *Mycobacterium tuberculosis* complex (MTBC) cause tuberculosis (TB) in humans and animals. India has a high burden of TB in humans, and also the largest population of cattle and buffalo in the world with endemic bovine TB.

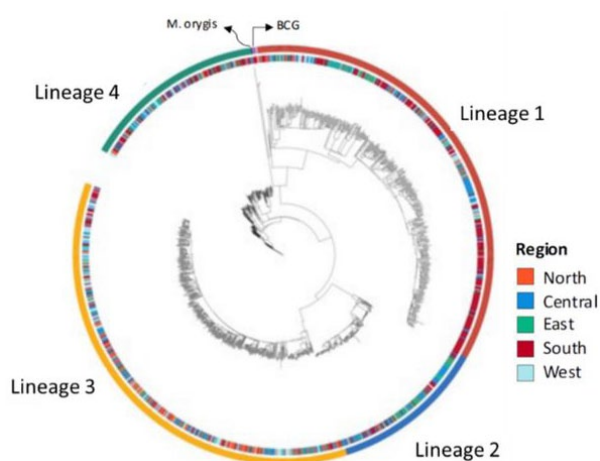
However, the burden and risk of zTB in India is poorly understood. To begin to address this knowledge gap, a consortium of major government research and academic institutions from India, UK, and Canada, performed a molecular epidemiologic investigation to identify MTBC lineages in routinely collected human TB specimens across India.

**Design/Methods:** A prospective study over 2 years was performed with MTBC cultures/specimens from pulmonary and extrapulmonary TB patients across India. Isolates were geographically stratified with a regionally

representative sampling approach based on overall burden of TB. Samples were submitted to CMC Vellore for DNA extraction and PCR; Whole Genome Sequencing (WGS) of MTBC was performed and analysed with vSNP.

**Results:** Of the 4,378 isolates collected from 44 sites, 3,852 were cultures and 506 were clinical specimens. DNA was extracted for 3,454 MTBC isolates of which WGS data is available for 1,958 isolates.

The results reveal a striking non-random distribution of MTBC lineages- Lineage 1 predominant in the South, Lineage 3 in the North and West and Lineages 1 through 4 evenly distributed in the Central and Eastern zones. No *M. bovis* was identified other than BCG, while *M. orygis* was represented by <1% of the samples.



**Conclusions:** Our findings reveal spatial heterogeneity in circulating MTBC lineages and provides strong evidence of a surprising paucity of *M. bovis* in humans in India.

Given recent reports of the recovery of *M. orygis* and *M. tuberculosis* sensu stricto from cattle in India, ongoing efforts seek to better assess the burden of zTB and to identify associated risk factors of disease.

### OA55-632-18 Zoonotic tuberculosis in high bovine tuberculosis burden area of Ethiopia

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**Background:** Zoonotic transmission of TB (zTB) to humans is frequent particularly where TB prevalence is high in cattle. In this study, we explored the prevalence of zTB in central Ethiopia, an area highly affected by bovine TB (bTB) in cattle.

**Design/Methods:** A total of 385 patients with pulmonary tuberculosis (PTB) and tuberculous lymphadenitis (TBLN) were included in this cross-sectional study in central Ethiopia. Sputum and fine needle aspirate (FNA) samples were obtained from patients with PTB and TBLN, respectively, and cultures were performed using BACTEC™ MGIT™ 960. All culture positive samples were subjected to quantitative PCR (qPCR) assays, targeting IS1081, RD9 and RD4 genomic regions for detection of MTBC, *M. tuberculosis* and *M. bovis*, respectively.

**Results:** Two hundred and fifty-five out of 385 sampled patients were culture positive and all were isolates identified as MTBC by being positive for the IS1081 assay. Among them, 249 (97.6%) samples had also a positive RD9 result (intact RD9 locus) and were consequently classified as *M. tuberculosis*. The remaining six (2.4%) isolates were RD4 deficient and thereby classified as *M. bovis*. Five out of these six *M. bovis* strains originated from PTB patients whereas one was isolated from a TBLN patient.

Occupational risk and the widespread consumption of raw animal products were identified as potential sources of *M. bovis* infection in humans, and the isolation of *M. bovis* from PTB patients suggests the possibility of human-to-human transmission, particularly in patients with no known contact history with animals.

**Conclusions:** The detected proportion of culture positive cases of 2.4% being *M. bovis* from this region was higher zTB rate than previously reported for the general population of Ethiopia.

Patients with *M. bovis* infection are more likely to get less efficient TB treatment because *M. bovis* is inherently resistant to pyrazinamide.

### OA55-633-18 Genetic characteristics of *M. bovis* isolates from cattle and humans in Madagascar

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**Background:** Bovine tuberculosis (bTB) remains endemic in many areas around the world and is still highly prevalent in Madagascar. It mainly affects cattle, which are the most important animal reservoir, although it can be transmitted to humans as zebu meat is a major Malagasy food.

In this study, we aimed to compare whole genome sequences between *Mycobacterium bovis* (*M. bovis*) isolates from humans and cattle collected in Madagascar from 1994 to 2001.

**Design/Methods:** A retrospective epidemiological study based on genotyping of *M. bovis* and its transmission to humans was carried out. About 200 *M. bovis* strains from cattle and human patients were sub-cultured and sequenced to assess the strains genetic diversity. Phylogenetic trees were generated by using the multi-FASTA file obtained by the pipeline MTBseq 1.0.3. The SNPs pairwise distance matrix was inferred using snp-dists 0.8.2 to define clusters of bovine and human strains in the same phylogenetic node. A total of 18 *M. bovis* samples (10 from humans and 8 from cattle) were successfully sub-cultured and sequenced using Illumina technology.

**Results:** Of the 18 samples, 17 samples were identified as *M. bovis* and one sample as *M. tuberculosis*. All the 17 *M. bovis* isolates sequenced belonged to one cluster: the *Mbovis*-29 group. This *Mbovis* group 29 corresponds to a clonal complex newly named La1.8.21. This group mainly includes isolates from Western Europe. Matrix distance calculations between the genome sequences of *M. bovis* from cattle and humans had from 52 to 104 SNPs differences.

**Conclusions:** *M. bovis* isolates from Madagascar belonged to the same cluster. Human and cattle isolates had relatively similar genomes (<104 SNPs distance suggesting active transmission of this cluster of mycobacteria in cattle as well as humans). Eradication of TB in humans cannot be fully addressed without controlling bovine TB and improving food safety.

### OA55-634-18 Genomic analysis of *M. bovis* isolates to determine zoonotic TB infection patterns in Mexico

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**Background:** Previous studies have shown that *Mycobacterium bovis* has been found in Mexico in both cattle and humans, however, the transmission dynamics at the livestock-human interface and the respective transmission rates between both host species are still not well understood.

**Design/Methods:** To investigate the *M. bovis* infection patterns and to quantify the role of cattle in *M. bovis* transmission to humans, we applied Bayesian phylogenetic approaches to 209 publicly available *M. bovis* whole-genome sequences collected from Mexico (cattle and human) and the US (cattle) with associated metadata (year of collection, host-species, and geographical location) from the NCBI database.

**Results:** The 209 *M. bovis* isolates were sampled between 2002 and 2015 from cattle and humans identified and variant calling analysis identified 3,473 Single Nu-

cleotide Polymorphisms (SNPs). The mean evolutionary rate of *M. bovis* was estimated to be 0.44 substitutions per genome per year (95% HPD: 0.24–0.51), being consistent with previous evolutionary studies. The time-measured phylogeny showed five major clades, three of them belonging solely to cattle, however, two of them have both cattle and human isolates indicative of inter-species transmission events. Discrete Trait Analyses showed strong statistical support for *M. bovis* transition from cattle to humans.

**Conclusions:** Further analyses are ongoing to determine specific rates of pathogen transition between hosts and locations. However, these data already demonstrate the high value of using genomic tools and Bayesian approaches to study *M. bovis* transmission dynamics in animals and humans, which emphasizes the requirement of a coordinated One Health approach.

### OA55-635-18 Genomic profiling of *M. orygis* isolated from wild ungulates in Chennai, India

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**Background:** Wildlife tuberculosis in India likely hinders tuberculosis elimination. This study reports the isolation of *Mycobacterium orygis* from postmortem tissue samples (PMTS) and presence of drug-resistant *Mycobacterium tuberculosis* complex organisms (MTBC) from excreted feces of wild ungulates namely black bucks (BB) (*Antelope cervicapra*), spotted deer (SPD) (*Axis axis*), and sambar deer (SD) (*Rusa unicolor*) at Guindy National Park, Chennai, India.

**Design/Methods:** PMTS (natural death) showing pale-yellow lesions in lungs and lymph nodes were harvested from two BBs, two SPDs, and one SD. Culture, PCR, spoligotyping, and whole genome sequencing (WGS) (Illumina) were used for speciation. Galaxy/vSNP facilitated WGS analysis. Phylogenies were constructed using RAxML. RDAAnalyser and RDScan located regions of difference (RD) between sequences. Histopathological analysis was performed on tissue sections (hematoxylin and eosin (H&E) staining).

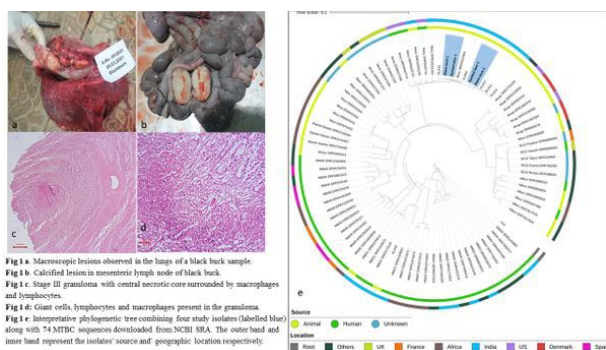
Calcified mesenteric lymph nodes observed in PMTS prompted collection of fecal samples from live animals (six SD, four BB, four SPD). Line probe assay (LPA), GeneXpert-Ultra (GXU) and PCR were performed to test MTBC presence and drug resistance.

**Results:** The isolates cultured from PMTS were drug-sensitive and confirmed as *M. orygis* by PCR, spoligotyping (ST587), WGS and RD analysis (de-

letion of RD7 to RD10, RD<sub>Oryx\_1</sub>, RD<sub>Oryx\_4</sub>, RD12<sub>Oryx</sub>, RD301, RD315). The isolates clustered well amongst *M.orygis* isolates worldwide in the phylogenetic tree.

The SNP difference between isolates ranged from 40-110 SNPs ruling out in-herd transmission (cut-off: 3-14). The H&E staining revealed Stage-III granuloma formation in all tissue samples.

For fecal samples, GXU and LPA confirmed the presence of MTBC in 7/14 samples. LPA further confirmed presence of one isoniazid-resistant isolate and one rifampicin as well as isoniazid-resistant isolate (both from cohabiting BBs).



**Conclusions:** Though the source of infection in these animals is an enigma presently, the presence of drug-resistant MTBC organisms and increased human-animal interaction in the area hints transmission from humans. Since the pathogen is known for traversing the host barrier, systematic surveillance and screening of humans and animals are essential for successful implementation of the One Health approach.

### OA55-636-18 The prevalence and distribution of insertion sequence 6110 among *M. orygis*, a member of *M. tuberculosis* complex causing TB in multiple hosts

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**Background:** *Mycobacterium orygis* (*M.orygis*), a subspecies of *Mycobacterium tuberculosis* complex (MTBC) is receiving increasing attention in the realm of one-health, as it is believed to cause zoonotic tuberculosis. MTBC contains the unique insertion element IS6110 which acts as a diagnostic marker.

The transposition of IS6110 encourages various genetic modifications in MTBC strains, resulting in genome plasticity and significant biological implication. Our laboratory recently isolated *M. orygis* from cattle and wild ungulates.

This study investigates the distribution of IS6110 in *M.orygis* strains worldwide as well as its effect on the genes involved in its adaptation to various hosts.

**Design/Methods:** IS6110 analysis was conducted using the sequence of 68 strains, comprising of 57 strains downloaded from the National Centre for Biotechnology Information (NCBI) and 11 strains from our lab. The ISMapper 2.0 pipeline was employed to locate IS6110 on the sequences, with *Mycobacterium tuberculosis* (*M.tb*) H37Rv (NC000962) and *M. orygis* (CP063804) serving as reference genomes.

The identified gene protein sequences underwent orthology analysis with eggNOG 5.0. Phylogenetic tree was constructed using vSNP, and annotated using iTOL.

**Results:** The analysis of IS6110 localization among the 68 sequences showed that 7.3% (5/68) had no copies, 4.4% (3/68) had low copies, and 88.3% (60/68) had high copies.

Among the sequences, a total of 228 novel insertion sites were identified, with 95 being intergenic and 133 being intragenic. Using 285 protein sequences, eggNOG analysis revealed almost 180 genes to be involved in various metabolic processes, including biological processes, cellular components, and molecular functions. KEGG pathway analysis identified 40 genes involved in various pathways, including Arginine and proline metabolism, tuberculosis, and Pyrimidine metabolism.

**Conclusions:** The results of this study offer new insights into the insertion of IS6110, the regions where it is more likely to be inserted, and its impact on various metabolic processes and pathways that contribute to its adaptation.

### OA55-637-18 Study of spondylodiscitis in the Moba Territory, Democratic Republic of the Congo

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**Background and challenges to implementation:** Usually, not more than 5% of all forms of tuberculosis (TB) present as TB spondylodiscitis. In this study, we investigated whether brucellosis contributed to the high proportion



of TB spondylodiscitis among patients diagnosed with TB in the Moba Territory, Democratic Republic of the Congo.



**Intervention or response:** Methods: Cross-sectional descriptive study of patients who presented with clinical signs of spondylodiscitis between 2018-2019. Laboratory diagnosis of brucellosis was done in Moba and Sciensano (patients -114- and control -93-).

Control patients were persons without fever or symptoms of spondylodiscitis from whom blood was drawn for another reason, sharing similar epidemiological context as targeted patients. Awaiting complete *Brucella* serology results, patients were treated for TB.

**Results/Impact:** Of 138 patients with spondylodiscitis, 81 (58.7%) presented with a spinal deformity, 18(13%) showed neurological signs, such as paraesthesia, paresis or paralysis, and five had urinary retention.

Among 114 patients tested for the presence of antibodies against *Brucella* by the Rose Bengal test (RBT), two were positive (1,7%); this prevalence was similar in the control group. All 138 patients were treated for extrapulmonary tuberculosis (EPTB). One patient was lost to follow-up before starting TB treatment. The treatment success was 88% (121/137).

**Conclusions:** This study investigated patients with spondylodiscitis in the Moba Territory. Albeit two patients showed positive RBT results, a definitive diagnosis of chronic brucellosis could not be established. Patients responded well to TB treatment.

## OA56 Tobacco interference: monitoring tool and countering strategy

### OA56-638-18 Government Pension Schemes and tobacco investment in India: an investigative research

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**Background:** ESG (Environmental, Social and Governance) investing is a way of investing sustainably with focus on environment, human wellbeing and economy and thus have traditionally grouped the Tobacco business with environmentally harmful industries. Tobacco business are ethically and morally questionable, stranded assets with high litigation and regulatory risk.

In 2017, the UNPRI decided that tobacco was fundamentally inconsistent with the UN Global Compact and launched the Tobacco Free Finance Pledge. Global examples of pension funds divesting from tobacco includes Australia, Dutch, Netherlands, UK and France.

With this background, the aim of the study was to assess Tobacco industry investment by the Govt. Pension Funds (National Pension Scheme/NPS) in India.

**Design/Methods:** The current study was a desk review of the Govt. Pension Schemes and their investment in Indian Tobacco Companies. The List of Tobacco companies listed on National Stock Exchange (NSE) was obtained. Four companies viz. ITC Ltd., VST Ltd., Godfrey Phillips and Golden Tobacco were included in the study. All seven Govt. Pension Schemes (available on GoI website) were analyzed and data (number of Units, amount & percent of portfolio invested) from portfolio reports for the month of March 2022 were assessed.

**Results:** The pension funds only invested one Tobacco business (ITC ltd). Overall percent portfolio invested in ITC Ltd. Ranged from 2.4% to 3% for 6 pension funds. Overall, 192 million USD invested by Govt. Pension Funds under NPS. Life Insurance Corporation (LIC) of India Pension fund comprised 53% of the total amount invested in the tobacco business followed by HDFC (21%), SBI (14%) and ICICI (8%).

**Conclusions:** The results of the current study reports that there is evident investment of the Govt. Pension Funds into Tobacco Companies in India. Therefore, the pension funds in India should sensitized about global practices of ESG investments and thus avoid investing in business like Tobacco.

## OA56-639-18 Lost government revenues due to illicit cigarettes in South Africa

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**Background:** Since 2010 the illicit cigarette market has burgeoned in South Africa. Cheap cigarettes undermine tobacco control policies, specifically excise tax increases. The government also losses much-needed revenue.

**Design/Methods:** Our analysis covers the period 2002 to 2022. First, using gap analysis, we estimate the size of the illicit market as the difference between the number of self-reported cigarettes and the number of legal (tax-paid) cigarettes.

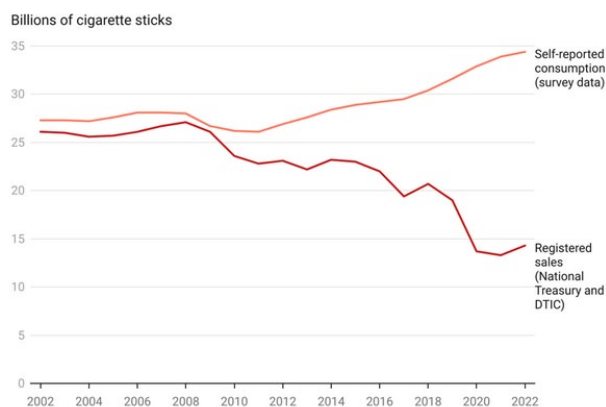
Self-reported consumption is estimated using several nationally representative surveys. Legal consumption is estimated using government sources.

Second, we calculate the revenue the government lost due to illicit trade, taking into account that some people would have quit or reduced their consumption if cigarette prices were higher (i.e., tax paid). We estimate this reduced consumption using the arc formula for the price elasticity of demand.

**Results:** The illicit cigarette market in South Africa was negligibly small until 2009, after which it increased sharply. It comprised around 30-35% of the market in 2017, breached 50% in 2020, and remained above that threshold in 2021 and 2022.

If excise tax and Value Added Tax had been paid on all cigarettes (i.e., no illicit market), about 76% of previously-illicit cigarettes would become part of the legal market, while 24% of previously-illicit cigarettes would disappear, because they would be too expensive.

Accounting for this decrease in demand, the amount of tax revenue (excise and VAT combined) lost by the South African government exceeded R16 billion (nearly 1 billion USD) in each of the years 2020 through 2022.



Source: Self-reported consumption is calculated from: the All Media and Products Survey, the National Income Dynamics Study, and the Global Adult Tobacco Survey, weighted using population data from the United Nations. Registered sales is calculated using excise revenue data from National Treasury, and imported cigarettes data from the Department of Trade, Industry and Competition. • Created with Datawrapper

Figure 1. The widening gap.

**Conclusions:** The South African government is losing much revenues from illicit cigarettes. The government should secure the supply chain to monitor cigarettes from point of production to point of sale. If the revenue authority does not do this, the government will continue to bleed revenue. Aside from the lost revenues, the public health costs are substantial.

## OA56-640-18 Monitoring and counter strategy to stop tobacco industry interference in Bangladesh

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**Background:** Bangladesh ratified the WHO Framework Convention on Tobacco Control (FCTC) in 2004, passed the Smoking and Tobacco Products Usage (Control) Act 2005, and amended this act in 2013. However, there is no guidance on how to implement FCTC Article 5.3.

As a result, tobacco industry interference (TII) increases against public health intervention including tobacco control. TI also violating the TC Law and hinder the national and local level policy-making initiatives. WBB Trust, with technical support from The Union, monitor TII by which data was collected. Then and address these TII and inform and sensitized concerned officials to stop this.

**Design/Methods:** WBB Trust collected TII information published in the newspaper, magazines, website and social media from January to December 2022. Collected data analysed, segregated categorized, and countered those initiatives to stop the interferences.

**Results:** Total 370 TII incidents were found by which tobacco industries interfere the policy makers, media and government officials. Some of these include TI's planting trees in different areas in the name of social forestation (Samajik Bonayan), setting up safe drinking water projects 'Probaho', and solar plants. The tobacco industry also sponsored Women's Day, Water Day observation and sports and cultural events. Tobacco industry also engaged Members of Parliament in different programs.

WBB Trust team undertook various initiatives to counter the interferences, including removing tobacco advertisements from several websites by sending letters and face-to-face communications with the officials to stop facilitating the tobacco industry's programs. Also sent letters to the University Grant Commission (UGC) to stop Battle of Mind programs all over Bangladesh.

**Background and challenges to implementation:** Bangladesh ratified the WHO Framework Convention on Tobacco Control (FCTC) in 2004, passed the Smoking and Tobacco Products Usage (Control) Act 2005, and

amended this act in 2013. However, there is no guidance on how to implement FCTC Article 5.3. As a result, tobacco control, public health intervention, and other government programs are unprotected from tobacco industry interference (TII).

Violation of the Tobacco Control Law by industries is widespread in Bangladesh. It is noted that TII hinder the national and local level policy-making and decision-making initiatives in Bangladesh.

**Intervention or response:** This is action research by which data collected on TII incidents. Then and address these TII and inform and sensitized concerned officials to stop this. WBB Trust collected TII information published in the newspaper, magazines, website and social media from January to December 2022. Collected data analysed, segregated category, and countered those initiatives to stop the interferences.

**Results/Impact:** WBB Trust found that 370 TII incidents happened between January-December 2022. The significant interferences include planting trees in different areas of Bangladesh in the name of social forestation (Samajik Bonayan), setting up safe drinking water projects 'Probaho', and solar plants. The tobacco industry also sponsored Women's Day, sports, and water day observation. Tobacco industry also engaged Members of Parliament in different programs.

WBB Trust team undertook various initiatives to counter the interferences, including removing tobacco advertisements from several websites by sending letters and face-to-face communications with the officials to stop facilitating the tobacco industry's programs. Also sent letters to the University Grant Commission (UGC) to stop Battle of Mind programs all over Bangladesh.

**Conclusions:** To stop TII, a national guideline on FCTC Article 5.3 implementation is necessary. To strengthen the existing TC Law enforcement, a Code of Conduct for Government employees should also developed to accelerate anti-tobacco movements.

## OA56-641-18 Use of information and communication technology in enforcing tobacco control laws and reducing interferences of the tobacco industry in Bangladesh

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**Background:** In Bangladesh, 35.3% adults currently use tobacco and tobacco killed nearly 126,000 people in Bangladesh in 2018. The total economic cost of tobacco-related death and disease was USD 3.6 billion. In Bangladesh, there is progress in reducing tobacco use but this progress is threatened by tobacco industry tactics and existing weak regulatory environments.

**Design/Methods:** Grambangla Unnayan Committee (GUC) conducted two censuses in 2019 and in 2022 on POS. For this census GUC used a android based software and mobile phone (online surveillance system) to record incidences of TAPS ban violation at POS, GPS location of POS etc. During 2019-2022, a set of tobacco control activities were implemented by GUC in all project towns.

**Results:** Comparative analysis between first round census data collected in 2019 from 6820 POS of 12 towns and second round census data collected in 2022 from 9990 POS of 18 towns found that an average of 3.2 advertisements were found per POS in 2019 and an average of 1.42 advertisements were found per POS in 2022. Thus the rate of incidences of violations of TAPS ban reduced by 55.63 percent in project areas. In 2019, at 2.6% POS there was no advertisements for tobacco products. But in 2022, at 31.3% POS no advertisements were found. GUC facilitated implementation of tobacco control laws through various activities in all the 18 towns during 2019-2022. Findings show the positive impact of GUC strategies in reducing incidences of TAPS violations at POS.

**Conclusions:** Use of Information and Communication Technology (ICT) is helping the law enforcing agencies to act at the specific POS where incidences of TAPS ban violations are occurred and recorded in the online databases. The database shows address and GPS locations of POS and information on types of TAPS ban violations. Use of ICT in tobacco control program has positive impact.

### OA56-642-18 Piloting alternative livelihood for beedi rollers: an intervention study in the Jamui District of Bihar, India

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**Background and challenges to implementation:** Beedi is most common smoking form (7.7%) in India. Beedi industry is widely home based and therefore women and children are commonly get engaged. India has more than 3.6 million beedi workers and work under extremely hazardous conditions.

Jamui district of Bihar is home of largest registered beedi workers (1,15,815) in the state. Beedi workers are highly underpaid and face abuse alongside varied range of occupational health hazards. Beedi workers and their dependents thus emphasize the need for an alternative livelihood.

As mandated in WHO FCTC Article 17 which recommends Parties to promote economically viable alternatives for tobacco workers, growers and sellers, BRPL, Government of Bihar in association with SEEDS and WHO piloted a project for beedi rollers in Jamui.

**Intervention or response:** Existing government schemes on skill development (PMSDY), rural livelihood (MN-REGA) were examined in consultation with Labour Welfare Commissioner, Bihar and project started well in coordination with district administration.

Aspirational Surveys were conducted through 14 Focus Group Discussions (FGD) in three pockets of Beedi rollers and beedi rolling groups sensitized about legal rights and entitlements; health hazards and importance of safer, more economically viable alternative options.

**Results/Impact:** Approx. 90% of the participants of higher age group have complaint of irritant eyes, sore fingers, lower back pain and some of their family members were also suffered from Tuberculosis. 47 beedi workers and their dependents get themselves enrolled in various skill development programs such as tailoring, data entry and computer hardware training based on educational backgrounds and interests.

**Conclusions:** Findings of this piloting indicated that beedi workers are willing to change their profession but it can only be accomplished if the right opportunities are provided. To be compliant with article 17 of FCTC, it is recommended that countries should develop alternative livelihood options other than beedi rolling to tackle the deplorable condition of these workers.

### OA56-643-18 Big tobacco, tiny targets - study highlighting tobacco advertisements, product displays, sales and promotions around educational institutions in India

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**Background and challenges to implementation:** As per Section 6 of the Cigarettes and other Tobacco Products Act, 2003 (COTPA), there is a ban on the sale of tobacco to and by minors and sale of tobacco products is prohibited in an area within a radius of 100 yards of any educational institutions and mandatory signage in this regard should be displayed prominently near the main gate and on the boundary wall of the school/institute. Under COTPA Rules, tobacco advertising, promotion and product display is banned at the point of sale.

**Intervention or response:** Voluntary Health Association of India & Consumer Voice conducted a Tiny Targets study across India - 243 schools, 487 points of sale, and 20 cities across 6 states of India to assess COTPA compliance near educational institutions and to expose tobacco industry tactics which target children. Field investigators were trained and equipped with a mobile reporting form to document instances of tobacco companies advertising, selling, displaying, or incentivizing the sale of tobacco products within a 100-meter radius on their smart phones.

**Results/Impact:** 225 points of sale were selling tobacco products out of the 487 surveyed around schools. The most common and popular types of points of sale in these areas were street vendors (56.6%), followed by mobile vendors (17.5%) and small grocery stores (13.7%). Tobacco products are displayed in ways that are appealing to children and youth.

**Conclusions:** This has helped civil society to effectively strategize and mount a stringent campaign on tobacco control across the country, garner political support from select leaders, sensitize the media and seek general public support for compliance & implementation of Section 6 of COTPA.

## OA56-645-18 Challenges for tobacco control in a north Indian state: a qualitative analysis

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**Background:** Himachal Pradesh, a north Indian hilly state has been a front-runner in Tobacco Control efforts and has reported reduction in prevalence of any tobacco use from 21.1% (GATS 1) to 16.1% (GATS 2). The objective of the study was to identify the challenges for Tobacco Control in the state and suggest ways to overcome them so that the goal of reduction in prevalence of tobacco use to less than 5 % by 2030 is achieved.

**Design/Methods:** A qualitative research design was adopted, 85 Key Informant Interviews (KIIs) and 20 Focused Group Discussions (FGDs) were conducted among executors, implementors and frequent visitors involving 285 respondents at community settings, educational institutions, and points of sale.

**Results:** The major challenges identified are lack of inter-departmental collaboration on Tobacco Control, limited percolation of government guidelines to all departments, lack of clarity regarding personnel authorized to levy penalties and nonavailability of challan books. Challans are being done mostly by Police and Health department officials. Most of the respondents opined that the amount of ₹200 as fine was a non-deterrent and that there are limited designated smoking places.

There is a lack of awareness about Quitline numbers and tobacco cessation facilities. Tobacco Free Educational Institutions (ToFEI) guidelines are not available across all institutions. Indirect advertising, smoking scenes on TV, movies and OTT platforms, illegal sale of smoked and banned smokeless products and emerging newer tobacco varieties and flavours are the other identified challenges.

**Conclusions:** Improved inter-departmental collaboration by developing a strong interface to steer Tobacco Control implementation further in a coordinated manner, stricter penalties, Tobacco free educational institutions, increased designated smoking areas, curbing indirect advertising, strengthening cessation facilities and strict Tobacco vendor licensing can facilitate achievement of the 2030 goal.

## OA57 TB Diagnosis for all and MWD for all

### OA57-646-18 Upgrading TB specimen transport system using existing infrastructure of Department of Posts, Telangana, India

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**Background and challenges to implementation:** Specimen transportation system from the peripheral health facilities to centralized district or state laboratories is a challenge for National TB Elimination Program (NTEP) in Telangana, leading to delayed TB diagnosis. Private courier services are scarce and expensive.

**Intervention or response:** NTEP Department under the Directorate of Public Health, Ministry of Health and Family Welfare (MoHFW) took an initiative to work in collaboration with Department of Posts (DoP), Ministry of Communication to address this issue.

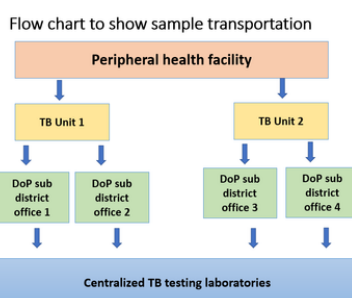
Book Now Pay Later (BNPL) options are offered to few stakeholders, and the associated costs are reasonable, in accordance with departmental rules. The DoP has about 789 sub district post offices across the state.

The 14 Tuberculosis Units (TB Units), specimen collecting hubs were linked to the 48 DoP offices in the 2 pilot districts with a population of 27.67laks (2.76 millions) as shown in the figure below including the increase in number of TB samples transported from 2019 to 2022. Health personnel from the TB Units dropped samples at the linked DoP offices. These were then transported via speed-post delivery mechanism to the designated laboratories.

**Results/Impact:** Interdepartmental cooperation has helped the program in improving the TB specimen transport services as under-

1. Number of samples transported on an average increased by 43 % from the year 2019 to 2022.
2. The specimen testing time came down from an average of 7 days to 3 days.
3. The cost of specimen transportation reduced by 40% from 100 INR to 60 INR/ box.

Number of TB samples transported via speed post		
Year	Kamareddy	Nizamabad
2019	353	380
2020	440	488
2021	581	500
2022	560	521



**Conclusions:** Leveraging on existing resources through effective interdepartmental collaboration can improve the efficiency of specimen transportation systems.

### OA57-647-18 Implementation of alternative specimen transportation to access GeneXpert services in health facilities found in post-conflict areas of Amhara Region, Ethiopia

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**Background and challenges to implementation:** In Ethiopia, access to drug susceptibility testing (DST) has remained a persistent challenge in health facilities located far from GeneXpert sites. In the past two years, access to DST was further compromised as services were interrupted during the conflict in Amhara region. This led to the need for rapid restoration of specimen transport by deploying alternative mechanisms.

We evaluated of this rapid alternative specimen transportation (AST) system in conflict-affected health facilities.

**Intervention or response:** The USAID Eliminate TB Project collaborated with the Amhara regional health bureau to implement AST in selected Zones, Woredas and health facilities. Rapid assessment and orientation were done with stakeholders. Regional specimen referral network map was used to link referring facilities (RFs) with Xpert sites.

Administrative staff from RFs were trained and used as couriers to pick up specimens twice per week from high-load facilities, and once per week from low-patient-load facilities transport the specimens and return test results in the same way. Performance was reviewed for the period of September 2022-January 2023.

**Results/Impact:** Alternate sample transport using administrative staff was implemented in 64 health facilities found in 9 zones and 24 Woredas. A total of 4060

samples were transported of whom 4038 of the samples were tested for GeneXpert which shows 99.5% processing rate. A total 157 samples (4%) were positive for TB.

Variables	Performance (#)	Remark
# of participating Zones	9	
# of participating Woredas	24	
# of health facilities linked by alternate specimen transport	64	
# of Samples transported	4060	
# of Sample processed (GXP)	4038	99.5% processed
# of MTB positive tests detected	157	4% yield

*Table: Performance of alternative sample transport, Amhara region, Ethiopia, September 2022-January 2023.*

**Conclusions:** Implementation and scale-up of Alternative specimen transportation for all inaccessible health facilities ensured rapid access to GeneXpert and DST service in conflict-affected areas. The involvement of government counterparts was pivotal for the successful implementation.

### OA57-648-18 Better outcomes in TB diagnosis through TB transportation system and digital health solutions in Kyrgyzstan

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**Background and challenges to implementation:** Rapid detection and early initiation of treatment with adequate treatment regimens are essential to reduce the spread of tuberculosis (TB) infection. However, in Kyrgyzstan, sputum-to-laboratory time could take up to five days, posing a risk of delayed detection. This was due to the lack of transportation system services at the rayon level resulting in failure to meet the delivery time from primary health facilities to GeneXpert and reference laboratories for testing.

Also, due to the paper-based workflow, the lab-to-clinician turn-around time (TAT) could take up to 90 days resulting in delayed initiation of treatment.

**Intervention or response:** The USAID Cure Tuberculosis project, led by JSI, mapped facilities and developed clear transportation routes so that samples could be received and tested faster by laboratories. We developed standard operating procedures and trained primary health workers to ensure on-time dispatch and safe delivery of samples to labs.

We helped the Mandatory Health Insurance Fund develop a system of reimbursement for transportation expenses borne by healthcare workers. New digital health

solutions enabled online tracking of deliveries controlling for time of collection, dispatch, and delivery of patient samples. Digital health solutions also enabled electronic patient data management and immediate sharing of test results with clinicians.

**Results/Impact:** The delivery of patients' sputum from collection to laboratories aligns with the 72-hour requirement in three regions – Naryn, Talas, and Chui. Prompt and safe delivery of sputum samples reduced the number of rejections to zero.

Thanks to clear routing, updated procedures, and a switch from paper referrals to a digital lab test result management system, the lab-to-clinician TAT decreased for Xpert and phenotypic drug susceptibility tests three times and for HAIN – six times.

**Conclusions:** The Cure Tuberculosis interventions helped ensure the prompt delivery of biomaterials for rapid TB diagnostic testing. The Ministry of Health will expand the project solutions to the entire healthcare system.

### OA57-649-18 Role of logistics in TB laboratory network optimisation: case of Uzbekistan

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**Background and challenges to implementation:** Tuberculosis remains a significant factor contributing to poor health outcomes globally. Although the new molecular diagnostics methods are hugely used in the disease detection, preanalytical and post-analytical stages of tuberculosis diagnostics have clear regional differences and affecting patient's access, timeliness and accuracy of diagnostics. TB laboratory network of Uzbekistan underwent reorganization and expansion by additional 42 GeneXpert labs in 2022. All specimen logistic routes were established from the scratch and implemented in late 2022.

**Intervention or response:** This work aims to analyse the changes in logistics component as a crucial stage in the diagnostics of Tuberculosis in Uzbekistan with specific focus on comparison of the differences in logistics of samples: test turnaround time (TAT), total number of diagnostic samples and diagnostic load before and after intervention.

**Results/Impact:** Around 70 specialists were taught to operate and support new delivery system. The retrospective and current data of sample delivery was collected and analysed for 6 laboratories in Fergana, Jizzak and

Syrdarya oblast' for period of year quarter. As a first results we observed 1,5-2 times increase in the number of delivered samples from primary suspects. Strikingly, TAT time for Jizzak laboratories improved from 2 weeks to 3 days representing biggest impact among the labs.

**Conclusions:** The introduction of “on schedule” and regular transportation system leads to increase in number of transported diagnostic samples as well as well in number of TB detection and to great improvement of TAT.

### OA57-650-18 Promoting quality TB diagnosis through the implementation of an intervention package to strengthen the Zimbabwean TB diagnostic network

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**Background and challenges to implementation:** In 2017, Zimbabwe adopted GeneXpert as the initial test for tuberculosis (TB) and by 2019, had installed 140 GeneXpert instruments. However, in 2019, the capacity to continue using GeneXpert was threatened by a lapse in service and maintenance of the instruments, resulting in 120 of the 560 modules breaking down. This delayed the return of laboratory results, causing delays in patient care. The USAID-funded Infectious Disease Detection and Surveillance (IDDS) project implemented an intervention package at all GeneXpert sites. We present the trends in TB notifications resulting from this intervention package.

**Intervention or response:** The IDDS supported a three-pronged intervention package consisting of revision and development of key TB diagnostic network documents, which are the national TB algorithm, TB diagnostic network supportive supervision guide, and checklist, as well as the GeneXpert multiplexing module. The second component of the package comprised of training a team of national supervisors on these documents and supporting them to conduct mentorship sessions at the diagnostic sites. The last component provided a platform for collaboration between the equipment service provider and connectivity solution provider to monitor the number of non-functional modules and their immediate repair within set indicators. The intervention package was implemented from April 2020 to April 2022.

**Results/Impact:** The country recorded an increase in the proportion of pulmonary TB patients with bacteriological confirmation from 56% (11,760/21,000) in 2019 to approximately 61.5% (10,043/16,320) in 2021.

This increase can be attributed in no small part to the increased access to functional GeneXpert instruments, because the number of functional modules increased along with the ability of health care workers to provide quality TB testing services.

**Conclusions:** A holistic model for diagnostic strengthening - supporting development of key documents, training of health workers and prompt response to equipment breakdown - resulted in greater system improvements than any individual intervention.

### OA57-651-18 A multi-stakeholder, diagnostic network-informed, roll-out of TrueNat MTB RIF assay: the Kenyan experience

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**Background:** The rollout process of novel Tuberculosis diagnostic assays is a complex multi-staged process, requiring collaboration of multiple stakeholders. The Division of National Tuberculosis, Leprosy and Lung Disease Program (DNTPD-P) collaborated with United States Agency for International Development and Stop-TB Partnership to roll out the new TB diagnostic tools project. DNTPD-P, Center for Health Solution-Kenya, and other partners collaborated to oversee implementation. We document the processes and lessons learned in Kenya's Truenat MTB/RIF assay rollout.

**Design/Methods:** A joint implementation work plan was co-created with DNTPD-P and stakeholders in 2022. Identification of Health facilities to place the 38 devices was conducted riding on the diagnostic network optimization model. Capacity assessments for identified sites followed. Training materials were reviewed and a cascaded training model from program managers to end-users conducted. The Truenat devices were installed, a super-user and end user were paired for ownership and mentorship, and routine monthly superuser mentorships conducted.

Other support included technical assistance, rollout of an online data reporting system, quarterly equipment service by the in-country Molbio agent, and implementation monitoring.

**Results:** For 38 machines, 3.4% (146/4263) sites were identified through a deterministic optimization model, 55% (80/146) identified labs were assessed for capacity, 75% (60/80) met the criteria, and 37 were prioritized for placement. One device was placed at the NTRL. Trainings were conducted using a cascaded model: 40 national officers for buy-in, 47 Laboratory Coordinators as Trainers, 33 superusers for technical support, and 77 end-users for testing. Over the period July 2022 to February 2023, 21,350 valid tests have been conducted, 2230 (10%) MTB detected, 49/2230 (2.2%) Rifampicin Resistant cases, Truelab error rate 293/21,350 (1.4%), Rif detection error rate 22/2230 (1%), and indeterminate results 515/2230 (23%).

**Conclusions:** Meaningful partner collaboration and informed assessments are critical to the successful implementation and rollout of novel TB molecular diagnostic tools.

### OA57-652-18 Impact of using WHO-recommended rapid molecular diagnostics in a mobile fashion for community active case-finding interventions: the KNCV Nigeria experience

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**Background and challenges to implementation:** WHO recommends that Tuberculosis Program transition from microscopy as the initial TB diagnostic test to rapid molecular diagnostics because such tools have the potential to provide accurate and quick results. Nigeria is known for facility-based TB testing where samples from communities are moved to stationary laboratories in the facilities for testing.

Sample transportation challenges and delays in result retrieval prompted KNCV Nigeria to initiate mobile TB testing for active case finding in communities using rapid molecular diagnostics such as TB LAMP and Truenat. We sought to evaluate the impact of the intervention on TB case finding.

**Intervention or response:** A total of 2 Truenat and 2 TB LAMP platforms were deployed for mobile TB testing in hard-to-reach communities between September 2022 and March 2023. Communities visited were selected using TB hot spot analytics. Same-day testing was done after screening with a WHO symptom checklist and portable digital X-ray (PDX) with artificial intelligence.

**Results/Impact:** A total of 2285 (8%) presumptive were identified from 28,263 individuals screened. The number of TB cases detected after evaluating 2275 presumptive clients was 556 (24%). Fifty-eight percent of the cases



(324) were bacteriologically diagnosed while 42% (232) were diagnosed clinically. From the bacteriologically diagnosed cases, TB LAMP detected 204 TB cases out of 1164 samples tested with the platforms while Truenat detected 120 cases out of 1111 samples tested with truenat machines. TB yield recorded with TB LAMP and Truenat were 18% and 11% respectively.

**Conclusions:** The high proportion of bacteriologically diagnosed cases recorded in this intervention demonstrated the ability of the rapid molecular platforms to perform optimally even outside the laboratory setting. The high TB yield showed the usefulness of combining PDX and rapid diagnostics for TB screening and testing in communities.

### OA57-653-18 "I need not had to loss my wage to get tested for TB": an experience from a pilot project implemented in an industrial population in Telangana, India

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**Background and challenges to implementation:** Innovations which reach to TB vulnerable population are key to strengthen India's fight for TB Elimination. Industrial workers are one of the vulnerable groups to whom access to information, testing & treatment are difficult due to their work timings (long working hours, same as health facilities), nature of work, and poor health seeking behavior.

In order to make innovation access to them TB Alert India (TBAI) with funding support from Stop TB Partnership in coordination with NTEP (National TB Elimination Program) District TB Officer (DTO) piloted chest x-ray camps using an Artificial Intelligence (AI) enabled hand held portable X-ray machine.

**Intervention or response:** Two Blocks of Sangareddy district in Telangana are industrial belts with people from nearby villages as work force. X-ray camps were organized at time (early morning or late evening) and places (centre point) where maximum industrial worker can get benefited. People attending the camp were sensitized about TB and purpose of the camp before subjecting to the X-ray. AI segregated the X-rays with presumptive TB persons immediately. These people were counseled and further testing and treatment initiation was facilitated within 2 days.

**Results/Impact:** 32 X Ray Camps conducted in 6 months period. 2021 individuals were screened and undergone chest x ray, 598 were found suggestive of TB and 140 were bacteriologically confirmed. This resulted in reaching an additional notification of 199 new TB patients in the year 2021-22. One of the industrial workers

who benefitted from the project said "Complete diagnosis was completed and treatment was initiated in just 2 days. I had to take only one day leave"

**Conclusions:** Scaling up X Ray services as a primary tool for TB testing can be considered for industrial workers considering the challenges and constraints they have in access

### OA58 Progress in TB case finding

#### OA58-654-18 Adapting active case-finding using "hybrid" approaches in Vietnam: outreach and linkage to facilities increases TB screening

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**Background and challenges to implementation:** In Vietnam, active case finding (ACF) campaigns target household contacts (HHCs) of people living with TB and other vulnerable groups, prioritizing high-burden districts for ACF once per year. Additional strategies are needed to screen HHCs and key and vulnerable populations (KVPs) year-round.

**Intervention or response:** We developed hybrid ACF approaches to actively reach HHCs and KVPs, integrating screening at health facilities. To reach HHCs, TB staff conduct systematic, timely contact investigation for each new TB diagnosis and people diagnosed in the last 24 months, constituting another avenue to reach people missed by ACF campaigns. Other KVPs are reached actively through promotion of an online screening tool that provides referrals. Criteria for referral include having a chronic disease,  $\geq 60$  years, smoker, alcohol use disorder, undernourishment, history of TB treatment and/or having TB symptoms.

**Results/Impact:** In 2022, eight community campaigns were held in four provinces; hybrid approaches were rolled out in 36 facilities in seven provinces. Community campaigns screened 3,879 HHCs with CXR while hybrid ACF screened 7,113 HHCs with higher TB detection yield (1293 versus 696/100,000 CXR). Campaigns screened 24,542 KVPs with CXR, resulting in 438 diagnosed with TB (yield: 1785/100,000 CXR). Out of 2,553 online screening users who completed hybrid screening, 227 were diagnosed with TB (yield: 8892/100,000 CXR). Rates of TB-presumptive CXR and Xpert positivity among KVPs were significantly higher for hybrid ACF compared to community campaigns.

Setting	Population	Outreach	Screened with CXR	# TB-presumptive CXR	% TB presumptive CXR/Screened with CXR	Tested with Xpert	TB Diagnosed (All forms)	% TB Positive	Yield per 100,000 CXR
Community ACF (8 campaigns)	Household contacts*	Contact investigation and direct invitation	3,879	266	6.9%	358	27	7.0%	696
	TB key and vulnerable populations†	Mass media communication, listing and direct invitation for people with chronic disease	24,542	3,936	16.0%	4,023	438	9.6%	1,785
		Total		28,421	4,202	14.8%	4,381	465	9.4%
Facility/Hybrid ACF (36 district health facilities)	Household contacts	Contact investigation and direct invitation	7,113	1,358	19.1%	1,416	92	6.1%	1,293
	TB key and vulnerable populations	Online screening promoted by QR code	2,553	1,061	41.6%	1,047	227	20.6%	8,892
		Total		9,666	2,419	25.0%	2,463	319	12.3%

\* Defined as living at the same house with the index patient or living for the preceding 3 months (either slept in the same house at least one night per week or spent more than 1 hour in the house at least 5 days per week). Index patients have pulmonary DS or DR-TB with or without bacteriological confirmation within 2 years prior to campaign

† Criteria for referral include having a chronic disease, ≤60 years, smoker, alcohol use disorder, undernourishment, history of TB treatment and/or having TB symptoms

OA58-654-18 Table Case finding results from ACF and hybrid ACF approaches in 7 provinces of Vietnam, Jan-Dec 2022.

**Conclusions:** Traditional ACF and hybrid approaches complement each other, while expanding ACF contributes to a more resilient TB system. Community campaigns bring TB screening closer to people, but hybrid approaches diagnosed an additional 319 people with TB using existing resources. While fewer KVPs are screened through hybrid ACF, yield among KVPs who completed a referral from online screening is five times ACF yield among KVPs and 51 times the national incidence rate of 173/100,000.

### OA58-655-18 Active TB screening in transgender populations

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**Background and challenges to implementation:** Transgender women are a vulnerable population due to difficulties in accessing health services, stigmatization, and the presence of other comorbidities. Socios En Salud has added strategies to its active TB screening program to offer TB screening to the transgender population in Lima.

**Intervention or response:** In July 2022, we implemented two strategies for active TB screening in Lima's transgender population. Urban mobile brigades included

transgender individuals who visited sex venues and collected sputum samples for molecular testing with Xpert MTB/RIF Ultra. We also brought a portable X-ray machine equipped with automated screening software (Cad4TB) to areas where the transgender population lived and requested a sputum sample for molecular testing from people with abnormal x-ray results. Individuals diagnosed with TB were linked to treatment at public health facilities.

**Results/Impact:** During the first 8 months of implementation, we carried out 33 mobile brigades and 11 portable X-ray interventions. Of the 361 transgender persons approached by mobile brigades, 342 (95%) left a sputum sample, among whom 10 (2.9%) persons affected by TB were diagnosed. Among 111 transgender women approached by the portable X-ray team, 110 (99%) were evaluated. Abnormal x-rays results were detected for 34 (30%) individuals, of whom 33 (99%) were evaluated with sputum testing. Four individuals (3.6% of those screened by radiography) were diagnosed with TB. In total, 12 (86%) of the 14 individuals diagnosed with TB started treatment.

**Conclusions:** Both screening strategies diagnosed TB in about 3% of the transgender people evaluated, which is more than 10 times the estimated incidence in Peru (130 per 100,000). It is important to implement active TB case-finding in this population using strategies adapted to this vulnerable population.

**OA58-656-18 Evaluation of active TB case-finding among special populations in Bauchi State, Nigeria**

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**Background and challenges to implementation:** Migrating populations such as Nomads usually have difficulties accessing health care due to travelling from place to place in search of healthy pasture for their cattle. Studies have shown increased morbidity and mortality among these groups and interventions to actively find TB cases among such is strongly recommended.

**Intervention or response:** KNCV TB LON 1 and 2 has continued to implement active TB case-finding among special populations in Bauchi state. The Jana Foundation, which is a community Based organization (CBO) has been contracted to Screen, identify presumptive and link them to health centers where they are further evaluated for TB using trained ad hoc staff. These ad hoc staff are also saddled with the responsibility of identifying where these special populations reside within a given period since they are a migrating population.

This intervention kicked-off in 2020 and has been ongoing to date. For the purpose of this intervention data was extracted from the KNCV DHIS and analyzed using excel from January to December 2022.

**Results/Impact:** From January – December 2022 a total of 12,322 clients screened for TB of which 419 (33%) were presumed to have signs and symptoms of TB. Presumptive TB cases who were successfully evaluated were 3,895 (95%) while clinically diagnosed patients were 58 (27%).

Total number of TB cases diagnosed were 212 (5%) among those diagnosed, Childhood TB cases were 11 (5%) while those started on treatment and notified were 208(13%).

Due to the unstable nature of the nomadic settings and changing seasons, TB case notification fluctuates.

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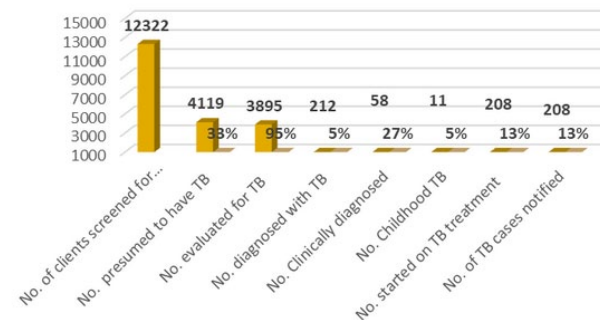


Fig 1. Showing TB yield among Nomadic group in Bauchi state - Jan-Dec 2022.

**Conclusions:** Since large-scale interventions in vulnerable populations can improve TB case detection, it is advised to expand such innovations to achieve higher yield in TB case-findings.

**OA58-657-18 Local TB Response Project in Mozambique: great progress in TB case-finding and treatment initiation**

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**Background and challenges to implementation:** Mozambique is one of the high-burden countries for drug susceptible (DS) TB, drug resistant (DR) TB and HIV/TB. People to People Development Agency (ADPP) is implementing United States Agency for International Development (USAID) Local TB Response (LTBR) Project in 50 districts across 4 provinces: Nampula, Zambezia, Sofala and Tete, covering 13 million people. Despite progress, challenges remaining include limited access to TB information, TB diagnosis and treatment services, long distances to health facilities, poor roads and climate changes with several floods and storms.

These challenges along with stigma, discrimination, human rights issues and related social and economic barriers lead to missed opportunities to find people with TB, contact screening and treatment completion.

**Intervention or response:** LTBR engaged 800 well trained and equipped community activists to deliver a comprehensive TB package of services under Community Based (CB) DOT and DOTS Plus that includes TB education, TB screening, referrals to health facilities for diagnosis, treatment follow up, contact screening and provision of Tuberculosis Preventive Therapy (TPT) within the community through implementation of home visits, monthly mobile clinics, screening in prisons and FAST strategy in primary health facilities.

**Results/Impact:** From January to December 2022, LTBR reached 1.846.554 people with TB messages and screening activities. 9% (162.671/1.846.554) were people with signs or symptoms consistent with TB and 96% of them were tested for TB (141.169/147.368). 19% (27,492) had TB all forms (AF); of these 47% were bacteriologically confirmed (BC) TB. Among people with bacteriologically confirmed TB, 52% had GeneXpert positive results and 99% started treatment under CB DOTS.

**Conclusions:** In 2022, LTBR community activities contributed 55% of all TB cases notified in the 50 districts, 46% across the four targeted provinces and 25% of all cases notified nationally. This highlights the high-impact role of community interventions in strengthening national TB response.

### OA58-658-18 Targeted community TB active case-finding through self-screening using automated machines for TB screening in Nairobi, Kenya

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**Background and challenges to implementation:** The Kenya National Tuberculosis (TB) Prevalence survey (2016) found that 40% of the country's estimated people with TB are missed and 67% of the people with TB symptoms in the community did not seek care. TB burden was higher in urban areas where a huge population lives in informal settlements. These findings called for investment in innovative community TB activities that encourage early care seeking for symptoms. Amref under the Global Fund TB project supported community initiatives dubbed Kenya Innovation Challenge Fund (KIC-TB) where organizations developed and implemented innovative ways to find missing people with TB. **Intervention or response:** Sema limited implemented interventions using Automated TB Self-Screening Machines (ATSM) in 4 TB zones in Nairobi from July 2019 to date. The project targeted the urban poor with sites conveniently located in places with high human traffic to enable the public screen for TB. The ATSM manned by Community Health Volunteers (CHV), offers guided symptom screening for TB. Those found presumptive for TB provided sputum samples onsite or were further evaluated by a clinician. Individuals diagnosed with TB were linked to care and managed as per the national TB guidelines.

Year	2020		2021		2022	
Subcounty	Subcounty Case Notification	Sema Case Contribution	Subcounty Case Notification	Sema Case Contribution	Subcounty Case Notification	Sema Case Contribution
Makadara	329	22	355	19	458	29
Starehe	697	57	695	75	841	160
Kibra	237	46	182	38	288	68
Kamukunji	336	16	384	24	565	38
Total	1599	141	1616	156	2152	295
Annual % Contribution	9%		10%		14%	

**Results/Impact:** A total of 161,930 clients were screened and 32,047 (20%) identified as presumptive for TB. 13,262 people were investigated for TB and 657 TB cases (541(82%) bacteriologically confirmed and 116 (18%) clinically diagnosed) were identified. The Number Needed to Screen (NNS) was 246. The annual percentage contribution to TB case finding in the four TB zones 2020 to 2022 was 9%, 10% and 14% respectively.

**Conclusions:** ATSM has improved community TB case identification through self-screening and diagnosis at clients' convenience. This demonstrates that bringing health services closer to the people is a key strategy to finding the missing TB cases.

### OA58-659-18 Expanded contact investigation into household contacts of non-bacteriologically confirmed cases in Yogyakarta Province, Indonesia

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**Background and challenges to implementation:** The World Health Organization (WHO) recommends contact investigation of household contacts (HHC) of bacteriologically confirmed tuberculosis (TB) cases. Non-bacteriologically confirmed TB patients are also potential to transmit the disease.

We compared the yield of TB disease between HHC of bacteriologically confirmed TB cases and non-bacteriologically confirmed.

**Intervention or response:** We investigated HHC of all ages of bacteriologically and non-bacteriologically confirmed cases registered in 2018-2022 in three districts in Yogyakarta province. A TB nurse conducted home visits, screened for symptoms and performed tuberculin skin tests (TST) for symptomatic children and referred all contacts aged over five years and symptomatic children under five years for chest X-ray screening. Sputum was collected for Xpert MTB/RIF examination if the contact had TB symptoms or the CXR suggestive TB. TB diagnosis was made by doctors in health facilities and reviewed with a pulmonologist.

**Results/Impact:** Of 2738 total index cases with 8132 HHC registered, We conducted symptom screening on 3160 HHC of 1243 index cases with non-bacteriologically confirmed cases. 2564(81%) contacts were screened with CXR, 385(12%) had presumptive TB, and 24 (0.8%) were diagnosed with TB.

There were 8 (0,3%) bacteriologically confirmed diagnoses, including one case of DR-TB. Of 1495 bacteriologically confirmed index cases, We screened symptoms

to 4541 contacts and 3823 (83%) were screened with CXR, 801(18%) had presumptive TB and 124 (2.7%) were diagnosed with TB. Among contacts of non-bacteriologically confirmed cases, the number needed to screen (NNS) was 132 for all forms of TB and 395 for bacteriologically-confirmed TB. The equivalent NNS for contacts of bacteriologically-confirmed cases is 37 and 227.

**Conclusions:** Despite, lower yield, TB cases were still found among contacts of non-bacteriologically confirmed cases, and importantly this included one DR-TB case. It is therefore important to investigate all index cases as resources permit.

**OA58-660-18 Scaling up innovative and integrated mobile TB screening services to improve active case-finding among key and vulnerable populations: programme implementation experience in Malawi**

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**Background and challenges to implementation:** The COVID-19 pandemic has reversed years of progress in providing essential TB services and reducing the TB disease burden (Global TB report, 2022). Global TB targets are mostly off-track, although there are some countries and regional success stories like the case of Malawi. This informed the program to go beyond passive TB case finding, rather embarking on systematic TB screening by use of Mobile Diagnostic units (MDUs) as a key strategy in finding missing TB cases among the key and vulnerable populations(KPs).

**Intervention or response:** In the year 2022, urban poor communities, healthcare workers, ART clients, outpatient department attendees(OPD), internally displaced people, refugees, prison staff and inmates were reached by seven MDUs equipped with GeneXpert and digital X-rays.

In particular, the MDUs targeted healthcare facilities that do not have X-rays and GeneXpert for screening and diagnosis.

All mentioned groups were screened using symptoms and chest X-ray (CXR), those found with one or more cardinal sign(s) of TB and abnormal CXR had to undergo a GeneXpert test to confirm the diagnosis.

**Results/Impact:** Intervention data shows that a total of 105,008(Table 1) clients were screened for active TB, of which 7.5% (7,917) were identified as TB presumptive. Among the presumptive, 1,438 TB cases were notified presenting a significant overall yield of 1369/100K. All notified TB cases were referred and initiated on treatment (100%). A significantly high yield was among the OPD attendees (2,370/100,000) and has the low number needed to screen (NNS 42) to get one case.

Furthermore, results have revealed low yield among prison staff regardless of prison inmates having some form of TB(523/100K).

Target Group	Total Screened	Screening contribution	Presumptive TB cases	TB cases	Yield/100K	NNS
ART Clients	6,094	6%	743	84	1,378	73
Urban poor Communities	40,271	37%	2,574	517	1,284	78
Health care workers	2,939	3%	199	15	510	196
Internally Displaced People(IDP)	7,412	7%	410	42	567	176
OPD Clients	28,351	29%	2,605	672	2,370	42
Prison staff	67	0.10%	2	0	0	0
Prison Inmates	18,934	17%	1,344	99	523	191
Refugees	940	1%	40	9	957	104
<b>Total</b>	<b>105,008</b>	<b>100</b>	<b>7,917</b>	<b>1,438</b>	<b>1,369</b>	<b>73</b>

Table 1. Screening outcomes among high-risk populations.

**Conclusions:** The targeted intervention of systematic TB screening using a combination of symptoms and CXR screening is an effective supplementary strategy to find people with active TB, and scaling up will significantly improve case notification among the key and vulnerable populations.

**OA58-661-18 Comprehensive counselling of TB patients is the key to high-quality TB case management in the Kyrgyz Republic**

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**Background:** A national health facility survey using Quality of TB Services Assessment (QTSA) methodology was implemented January-April 2021 in Kyrgyzstan. Findings show low treatment adherence leads to suboptimal outcomes; high proportions of lost-to-follow-up, death and treatment failure.

Provider and patient data triangulation provided insights into the content and quality of patient counseling and demonstrated the need for strengthened patient-centered case management including targeting of messages to specific patient barriers to care.

**Design/Methods:** A total 350 provider and 740 TB patient interviews were conducted in 258 facilities randomly selected using cluster sampling in seven Kyrgyzstan regions, assessing provider-patient interaction; patient counseling; attitudes, concerns, and patient experience during case management.

Statistical analysis was conducted by facility type/level and location (region, rural/urban).

**Results:** Healthcare workers mostly discuss general TB messages without identifying and addressing specific barriers most likely to impact individual treatment adherence. Only one-third of providers discuss treatment status or progress (32%), the need for a treatment supporter (30%), or treatment support options (36%). Slightly more discuss individual barriers (transportation, facility distance, treatment cost, family situation, disability, etc.) (41%); sources of support (family, social, financial) (45%); ability to follow treatment plan (49%); or patient's beliefs about curability (51%).

Discrepancies between the information providers report they cover during counseling versus what patients confirm was covered include precisely those messages most likely to impact treatment adherence: the importance of adherence and completing treatment, curability, length of treatment, and side effects.

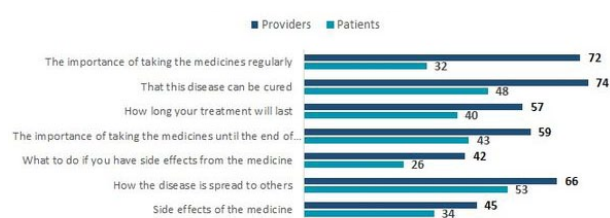


Figure. Comparison of provider and patient reports (unprompted) on information covered during counseling, from largest difference to lowest (N=350 providers; N=740 patients) (%).

**Conclusions:** TB patient counseling must promote patient-centered case management by addressing individual barriers most likely to impact treatment adherence. Patients more involved in the treatment process have a better understanding and ownership of the treatment process; thus, options for community-based treatment support should be improved. Health providers' interpersonal counseling skills should be improved, and counseling should be paired with better provision of informational materials for patients.

## OA58-662-18 Factors associated with non-completion of TB examination through contact person investigation in Kyrgyzstan

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**Background and challenges to implementation:** The Kyrgyz Republic has a high TB burden, with an estimated TB incidence of 130 per 100,000 people according to the WHO. The incidence of active TB among contact persons is 1.6%, which is suboptimal.

**Intervention or response:** In 2021-2022, the USAID Cure Tuberculosis project, JSI led in partnership with URC, conducted a pilot to enhance TB contact investigation (CI). The pilot was implemented in 12 primary health care (PHC) facilities in Naryn, Batken, and Chui oblasts.

Interventions included updating CI protocols to require in-person visits, revising TB screening at PHC level, and developing reporting forms. TB contact persons were defined as household and close contacts (8+ hours indoors) and diagnosed TB testing (clinical exam, x-ray, sputum analysis with cough manifestation for adults; Tuberculin skin test for children <14 years).

**Results/Impact:** Over 24 months, 2,947 TB contact persons were notified. The mean age was 27.8 years; 53.1% females; 10.2% had cough; 0.7% had TB previously; 0.4% had fever; 0.2% had noticeable weight loss; 2.5% had comorbidities; and 4.5% were active smokers.

Among TB contact persons, 1,275 (43.3%) underwent diagnostic testing with 5.2% diagnosed with active TB, three-fold over the national coverage rate. Univariable logistic regression analysis determined factors associated with TB diagnostic exam completion among contact persons.

Multivariable logistic regression estimated the adjusted associations by selecting the variables purposefully in the model. Variables in the model were selected based on statistical and epidemiological significance.

Factors significantly associated with non-completion of TB diagnostic examination included younger age (adjusted OR [aOR] 1.042, 95% CI 1.038–1.046), being male (aOR 1.244, 95% CI 1.054–1.467), and lack of cough (aOR 2.235, 95% CI 1.710–2.921).

**Conclusions:** Non-completion of TB diagnostic examination is common among TB contact persons, highlighting a need to enhance targeted interventions at PHC level, particularly among younger people, males, and/or without cough.

## OA59 TB control: from diagnosis to treatment outcome

### OA59-663-18 Creating a global individual patient data platform for TB treatment, TB-IPD

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**Background:** In 2021, the WHO Global TB programme partnered with UCL to set up a new platform for aggregating and sharing individual patient data (IPD) on tuberculosis (TB-IPD). By providing open access to researchers worldwide, the aim is to stimulate TB research by encouraging and facilitating scientists to develop novel research proposals that make use of the data, expanding the knowledge and understanding of TB globally, including informing future treatment guidelines. Here we describe the platform, our experience in beginning this process of building the TB-IPD platform and our plans for onward data sharing.

**Design/Methods:** This project builds on two previous drug-resistant TB-IPD meta-analyses (Ahuja *et al.*, PloS Med 2012, Ahmad *et al.*, Lancet 2018) and data submitted in 2021 to the latest WHO Guideline Development Group (GDG) meeting. New data will be gathered following WHO calls for data as well as direct offers from researchers.

The governance of this project encompasses ethical and data protection requirements, legal agreements, procedures for review and oversight, and the secure storage and handling of data.

The IPD is set up within the UCL Data Safe Haven computing environment, which is designed for the secure storage, handling, and analysis of identifiable data.

Summaries of each contributing dataset will be added to UCL's Repository providing visibility for researchers planning to make data requests for analyses. Summaries of data within the TB-IPD are also available on the TB-IPD website.

**Results:** We currently have 15000 records of participant data from 35 datasets. Data collected includes information on demographics, TB disease, treatment and outcomes, drug resistance.

**Conclusions:** Curating data from many different sources in an ethical, user-friendly, and secure way is not a trivial undertaking but will facilitate evidence-based studies of larger datasets than would otherwise be available.

### OA59-664-18 Factors predicting mortality risk in adults with drug-susceptible TB on treatment in Ethiopia

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**Background:** Tuberculosis (TB) remains a global health problem with high morbidity and mortality rate. Evaluating the period of TB treatment initiation and identifying risk factors for mortality could help formulate targeted interventions to improve TB care continuum which support the global End TB strategy.

We analysed data from a cluster-randomised trial of digital adherence technologies and differentiated care in Ethiopia to assess risk factors for mortality during TB treatment.

**Design/Methods:** Data were obtained from a cohort of adult trial participants with drug-sensitive pulmonary TB, starting treatment between December 2020 and July 2022. Using Poisson regression, we examined the mortality rate and its association with socio-demographic, clinical variables, calendar period and time since treatment start, based on lexis expansion.

**Results:** Among 4320 participants, the median age was 30 years (interquartile range 24-40), 1744 (40.3%) were female and 541 (12.5%) were living with HIV of whom 97% were on ART. 138/4320 (3.19%) died during TB treatment giving a mortality rate 7.1/100 person-years.

The risk factors for TB mortality included: age  $\geq$  50 years (adjusted rate ratio (aRR): 7.13, 95% confidence interval (CI): 3.77–13.48) compared with age  $<$ 25 years; living with HIV (aRR: 1.57, 95% CI: 1.03–2.38); clinical (aRR: 1.50, 95% CI: 1.07–2.11) versus bacteriological diagnosis; treatment started in July-September 2021 (aRR: 2.16, 95% CI: 1.14–4.11) compared with July 2022-February 2023; and the intensive (aRR: 2.25, 95% CI: 1.59–3.19) versus continuation phase of TB treatment (Table).

		N (%)	Deaths	Rate/100 person-year	Unadjusted RR (95% CI) <sup>1</sup>	Adjusted RR (95% CI) <sup>2</sup>
<b>Sex</b>	- Male	2576 (59.63%)	89	7.7	1	1
	- Female	1744 (40.37%)	49	6.2	0.81 (0.57-1.15)	0.93 (0.66-1.33)
<b>Age, years</b>	- < 25	1258 (28.89%)	12	2.1	1	1
	- 25-29	877 (10.30%)	19	4.7	2.26 (1.10-4.66)	2.21 (1.07-4.56)
	- 30-39	961 (22.25%)	27	6.2	2.97 (1.50-5.86)	2.69 (1.35-5.35)
	- 40-49	557 (12.89%)	28	11.2	5.35 (2.72-10.52)	4.50 (2.24-9.03)
	- ≥ 50	677 (15.67%)	52	17.5	8.34 (4.45-15.61)	7.13 (3.77-13.48)
<b>HIV Status<sup>3</sup></b>	- Negative	3772 (87.46%)	107	6.3	1	1
	- Positive	541 (12.54%)	31	12.9	2.06 (1.38-3.07)	1.57 (1.03-2.38)
<b>TB Diagnosis</b>	- Bacteriological	2825 (65.39%)	71	5.5	1	1
	- Clinical	1495 (34.61%)	67	9.9	1.80 (1.29-2.51)	1.50 (1.07-2.11)
<b>Calendar period</b>	- Dec 2020 - Jun 2021		7	5.1	1.36 (0.55-3.33)	0.91 (0.36-2.27)
	- Jul 2021 - Sep 2021		28	10.0	2.63 (1.41-4.93)	2.16 (1.14-4.11)
	- Oct 2021 - Dec 2021		32	8.9	2.29 (1.24-4.23)	1.98 (1.06-3.68)
	- Jan 2022 - Mar 2022	NA <sup>4</sup>	35	9.0	2.39 (1.30-4.37)	2.03 (1.10-3.75)
	- Apr 2022 - Jun 2022		21	5.5	1.5 (0.75-2.81)	1.24 (0.63-2.42)
	- Jul 2022 - Feb 2023		15	3.8	1	1
<b>Time since starting treatment</b>	- intensive phase		80	11.2	2.40 (1.71-3.47)	2.25 (1.59-3.19)
	- continuation phase	NA <sup>4</sup>	58	4.7	1	1

Notes: (1) Unadjusted rate ratio (RR) and 95% confidence intervals (CI) calculated using Poisson regression. (2) Adjusted rate ratio (aRR) and 95% confidence intervals (CI) calculated using Poisson regression. (3) HIV status at baseline, 97% of those persons with HIV were on ART and 3 participants had unknown HIV status. (4) Not applicable (NA). TB: Tuberculosis

Table.

**Conclusions:** Older age, HIV co-infection, clinical TB diagnosis, and being in intensive phase predicted higher mortality rates among adults with drug-sensitive pulmonary TB suggesting the need to pay particular attention to those with these risk factors. The association between calendar period and mortality warrants further examination of additional external factors such as COVID-19 associated deaths.

### OA59-665-18 Assessing the efficacy of TB regimens in the presence of treatment non-adherence: are intention-to-treat and per-protocol analyses fit for purpose?

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**Background:** Non-inferiority trials assessing novel tuberculosis (TB) regimens are often subject to treatment non-adherence, which has been associated with unfavourable outcomes and can result in misleading estimates of efficacy.

The use of both intention-to-treat (ITT) and per-protocol (PP) analyses has been advocated in such studies, yet these approaches are not guaranteed to be unbiased in the presence of differential non-adherence between trial arms.

**Design/Methods:** The REMoxTB trial evaluated two 4-month experimental regimens (one isoniazid- and one ethambutol-based) compared with a standard 6-month control regimen for drug-susceptible TB.

We conducted a simulation study based on REMoxTB to assess the performance of statistical methods that account for treatment non-adherence in non-inferiority trials.

Statistical methods included: ITT, PP, adjustment for observed adherence, multiple imputation (imputing the outcomes of non-adherent participants as if they had been fully adherent), inverse-probability-of-treatment weighting (IPTW; upweighting the outcomes of fully adherent participants), and a doubly-robust estimator (combining properties of the imputation and IPTW methods).

**Results:** When non-adherence differed between trial arms, ITT and PP analyses often resulted in non-trivial bias in the estimated treatment effect, which consequently under- or over-inflated the type I error rate.

Adjustment for observed adherence led to similar issues, whereas the multiple imputation, IPTW and doubly-robust approaches were able to correct bias in the estimated treatment effect under most non-adherence scenarios; these methods did not perform as well in the presence of unobserved confounding. The IPTW and doubly-robust methods were generally unbiased and maintained the desired type I error rate.

**Conclusions:** When the quantity or mechanism of non-adherence differs between trial arms, ITT and PP analyses can produce biased estimates of efficacy, potentially leading to the acceptance of inferior treatments or efficacious regimens being missed. The doubly robust estimator is a relatively straightforward method to supplement ITT and PP approaches.

### OA59-666-18 Programmatic implementation of the bedaquiline, pretomanid and linezolid (BPAL) regimen in Georgia

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**Background:** Clinical trials have demonstrated high treatment success of BPAL regimens for the treatment of drug-resistant tuberculosis (DR-TB), although data from programmatic settings are scarce. The Georgian National TB Program (NTP) implemented BPAL regimens in January 2021. We sought to evaluate the efficacy and safety of BPAL schemes in programmatic settings in Georgia.

**Design/Methods:** We conducted a retrospective cohort study among individuals with pulmonary pre-XDR-TB receiving BPAL regimens within the Georgian NTP following WHO recommendations. The dose of linezolid until June 2022 was 1200 mg, then - 600 mg.



**Results:** Twenty-nine HIV (-) negative patients were enrolled in BPAL regimens during the study period. Twenty-two (81%) were male, the median (IQR) age was 40 (31-49) years, and the median (IQR) BMI was 21 (19.8-23.3) kg/m<sup>2</sup>. Nine (33%) participants were excluded from the study within a median (IQR) of 41 (23-62) days due to revealed baseline resistance. In 7 (24%) cases was detected resistance to bedaquiline, in 2 (7%) cases to delamanid, and in 1 (3%) case to linezolid. The median (IQR) time from BPAL initiation to receiving drug susceptibility test results and switching to another regimen was 38 (22-60) days. Of the remaining 20 patients, 2 (10%) participants with 1200 mg linezolid, experienced linezolid-related adverse events, which were resolved by dose reduction to 600 mg, and 2 (10%) persons developed hepatotoxicity requiring temporary treatment discontinuation. All 20 (100%) patients achieved sputum culture conversion (SCC). The median (IQR) time to SCC was 36 (31-60) days. Seventeen (85%) patients completed their treatment within 6 months with a successful outcome, and 3 (15%) persons were lost to follow-up.

**Conclusions:** BPAL regimens showed excellent efficacy and good safety in programmatic settings in Georgia. The emerging resistance to new anti-TB drugs highlights the urgent need to develop rapid tests for the timely initiation of adequate treatment.

### OA59-667-18 Does the choice of fluoroquinolone affect treatment outcomes in rifampicin-resistant TB?

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**Background:** WHO guidance recommends either moxifloxacin or levofloxacin be used in a nine-month regimen for rifampicin-resistant TB. It is not known whether there is any difference in safety or efficacy between the two drugs. In STREAM Stage 2 the fluoroquinolone used in the control regimen was changed part-way through the trial from moxifloxacin to levofloxacin. We investigated whether the change affected the efficacy or safety of the regimen.

**Design/Methods:** A marginal structural modelling approach was used to balance differences in the baseline characteristics of participants receiving the control regimen containing moxifloxacin (Bmox) and participants receiving the control regimen containing levofloxacin (Blev) as this is not a randomised comparison. The difference in proportions between regimens (Bmox-Blev) was estimated for unfavourable outcome, grade 3/4 AEs and QTcF>500ms up to week 76 of follow-up, using a weighted analysis. Weights were generated using sex, age, BMI, HIV status, QTcF interval, culture status, and extent of opacity at trial start.

**Results:** The Control arm included 140 (127) Bmox and 62 (60) Blev participants in the safety (modified intention-to-treat) population. At baseline, participants starting Blev were heavier than those receiving Bmox (76.7% vs 59.8% were >50kg) and had more extensive disease (41.7% vs 30.7% had sputum culture 3+). Unfavourable outcomes occurred in 23.3% on Blev and 31.5% on Bmox. The weighted difference in proportion with an unfavourable outcome was -2.3% (95% CI: -17.1%, 12.5%). The proportion of participants reporting at least one AE during follow-up was 55.0% on Blev and 58.3% on Bmox, a weighted difference of 1.9% (-14.4%, 18.2%). A QTcF>500ms was recorded in 6.7% on Blev and 5.5% on Bmox, a weighted difference of -5.1% (-22.2%, 12.0%).

**Conclusions:** There is no suggestion of a difference in key efficacy or safety outcomes between regimens including moxifloxacin or levofloxacin from these data.

### OA59-668-18 Socio-economic burden of TB and its impact on child contacts in The Gambia

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**Background:** Child contacts experience social, educational and economic consequences when their caregivers are diagnosed and receive tuberculosis (TB) treatment. Given the dearth of data in this field, this study aimed to examine the impact of adult TB on child household contacts in the Greater Banjul Area, The Gambia.

**Design/Methods:** Prospective observational cohort study among adults (≥18 years) starting treatment for drug-susceptible pulmonary TB between 06/2019 and 07/2021 reported having at least one child household contact. Data on school attendance and school performance was extracted from school report cards. At the start of TB treatment and at 6 months of treatment, participants were asked about expenses for school fees, healthcare, festivities, and food security of child contacts.

We compare expenses, school attendance, school performance, and food security before and after 6 months of TB treatment.

**Results:** 51 participants with 180 child contacts (an average of 3.5 child contacts per participant) were enrolled in the study. While school attendance of the child contacts remained unaffected, there was significant drop in school performance, from 92% achieving good or very good performance when participants started TB treatment to 53.6% 6 months later ( $p < 0.001$ ).

Participants reported spending less on school fees, school uniforms, shoes, and transport costs at 6 months than at the start of TB treatment ( $p < 0.05$ ). Furthermore, child contacts faced significant food insecurity over time in terms of food quantity and variety, with increases by at least four-fold ( $p < 0.001$ ).

**Conclusions:** Despite free TB treatment and care at public facilities in The Gambia, child contacts face a potential decline in school performance and decreased spending on school supplies. While a plethora of work is being undertaken to alleviate costs of care for TB patients, further emphasis is needed to ensure educational and social prosperity for child contacts, as caregiver TB has socio-economic implications for the wider household.

### OA59-669-18 Verbal autopsy as a tool for exploration of TB deaths in Tamil Nadu, India

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**Background and challenges to implementation:** The death rate among notified drug-susceptible tuberculosis in Tamil Nadu showed an increasing trend from 2017 to 2022. Systematic verbal autopsy of deaths among known TB patients to identify the causes and factors leading to death using standardized tools and reporting mechanisms was lacking. We implemented a system for verbal autopsy in the state starting from May 2020.

**Intervention or response:** A standardized format for verbal autopsy was devised, consisting of the detailed medical history, events leading up to death and a narrative section. Cascade training of all medical officers and TB-related health workers was conducted over one month. Field-level health workers or medical doctors visited the household of each notified TB death and

conducted the verbal autopsy with the primary caregiver as the respondent. The collected data was verified and given an ICD code based on International Classification of Diseases, Tenth Revision by a medical doctor, before being aggregated at the state level. Monthly reconciliation of number of notified TB deaths for which verbal autopsies were conducted was done. Quality improvement measures included field visits for identification of challenges and hands-on training.

**Results/Impact:** The data from the verbal autopsies collected from May 2020 to February 2022 was analyzed.



The proportion of reported TB deaths for which verbal autopsies were completed improved consistently from around 35% in the first 10 months to 59% over the first 21 months. We found that tuberculosis was identified as a cause of death in around 65% of the deaths. More than two-thirds of the deaths happened at the residence of the person affected with TB.

**Conclusions:** The findings of the intervention triggered the following actions:

- Formulation of TB Death Surveillance and Response guidelines which stressed on an integrated health system response to TB deaths, and;
- Launch of a differentiated TB care model.

### OA59-670-18 TB disease burden among people who smoke illicit drugs: a respondent-driven sample, Western Cape, South Africa

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**Background:** To find individuals with tuberculosis (TB) disease, we need to identify high risk groups. People who smoke drugs (PWSD) may have increased TB risk from

increased opportunity for infection and vulnerability to disease progression. Before we can design TB transmission interventions, we must first understand disease burden heterogeneity and drivers, including among those not accessing clinic.

**Design/Methods:** We recruited 604 PWSD in the community using respondent-driven sampling from 2021-2023 in Worcester, South Africa. All participants were ≥15 years old, self-reported and screened urine positive for methamphetamine and/or methaqualone, received microbiologic TB testing, and completed biobehavioral surveys and a medical history. We defined TB disease as culturable TB, currently on TB treatment, GeneXpert Ultra MTB detected and no prior TB, or Ultra trace and living with HIV. We used the RDS-II estimator to estimate TB prevalence overall and prevalence stratified by HIV. We compared our estimate to Worcester community-wide prevalence estimates from CORTIS (NCT02735590), 2016-2018. We identified disease risk factors using logistic regression.

**Results:** Overall, 71.5% were male, median age was 34 years (IQR 28, 39), 91% used methamphetamines and 91% used methaqualone. Sixty (9.9%) participants had TB disease. Adjusted TB prevalence was 10.7% (95%CI: 5.9%, 15.4%). TB prevalence among people without HIV was 7.9% (95%CI: 3.7%, 12.2%), ~3 times greater than prevalence estimated by CORTIS (2.4%; 95%CI: 1.6%, 3.5%). PWSD with TB were more likely to be living with HIV (OR:2.8, 95%CI: 1.5, 5.2) and more likely to be of mixed ancestry (OR: 2.7, 95%CI: 1.1, 8.0), after adjusting for other risk factors (Table 1).

	Unadjusted OR (95% CI)	Adjusted OR* (95% CI) *adjusted for all other variables in table
Age	1.15 (1.0, 1.3)	1.1 (0.9, 1.3)
Male sex	1.2 (0.7, 2.3)	1.3 (0.6, 2.7)
Mixed Ancestry	2.6 (1.1, 7.7)	2.7 (1.1, 8.0)
Living with HIV	2.8 (1.5, 4.9)	2.8 (1.5, 5.2)
History of incarceration	1.9 (1.0, 3.5)	1.5 (0.8, 3.1)
History of TB	1.8 (1.0, 3.1)	1.4 (0.8, 2.5)
BMI, Normal	0.6 (0.4, 1.1)	0.8 (0.4, 1.4)
BMI, Overweight or obese	0.3 (0.4, 0.9)	0.3 (0.1, 1.2)

Table 1. Logistic regression predicting tuberculosis disease among people who smoke illicit drugs.

**Conclusions:** We found very high TB disease prevalence among PWSD, ~3 times greater compared to a community-wide survey. PWSD may be more efficient transmitters, have increased close contact, and/or faster rates of disease progression and are an important group to consider when designing interventions.

## OA60 Information Systems for TB

### OA60-671-18 Empowering citizens with a TB self-assessment mobile tool for ending TB in India

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**Background and challenges to implementation:** National TB Elimination Programme (NTEP), India identifies population screening for TB as one of the key interventions to address the missing persons and impact reduction in incidence.

Specific emphasis has been laid on Community engagement for person with TB (PwTB)-centred and community led response to TB.

**Intervention or response:** A TB Screening tool has been rolled out in May 2021, integrated with the Citizen and PwTB app of NTEP - TB Aarogya Sathi. This tool empowers citizens to assess if the presenting symptoms require them to be tested for Tuberculosis (TB) or not. In addition, the citizens can enroll in NTEP MIS (Ni-ksay) and get linked to the nearest health facility where they can undergo testing.

To support tracking and follow up of PwTB registered using this screening tool an escalation matrix has been setup to ensure that they visit the allocated facility for further management.

**Results/Impact:** Following the implementation of this tool, nearly 71,943 beneficiaries have been screened for TB, >5389 presumptive TB cases have been registered for testing and nearly 500 PwTB have been additionally diagnosed with TB.

**Conclusions:** This tool is expected to increase in the number of presumptive TB cases being identified, which is then expected to address the issues of missing cases. In order to encourage the wide usage of this tool, it is planned to be positioned in various portals and websites of the Ministry of Health and line Ministries, encouraging a multi-sectoral engagement to Ending TB.

## OA60-672-18 Digital support to bi-directional TB and COVID-19 testing in communities: improving linkage to care and follow-up in Mozambique

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**Background and challenges to implementation:** During the second and third waves of the COVID-19 pandemic, the National Health System in Mozambique faced the risk of overload and collapse. To mitigate the risk of community transmission of other respiratory diseases such as TB, innovative screening and testing approaches were implemented in community posts. However, there were challenges in linking people to appropriate healthcare.

Hence, many individuals did not receive the necessary care and treatment, leading to missed positive cases and increased disease spread in the communities. Using a UNITAID-funded grant, we designed an intervention to address the observed gap in linkage to care in community settings

**Intervention or response:** In March 2022, we developed TrackerApp, based on the DHIS2 platform. The TrackerApp was installed on smartphones used by community health workers in community posts and clinicians at selected referral health facilities.

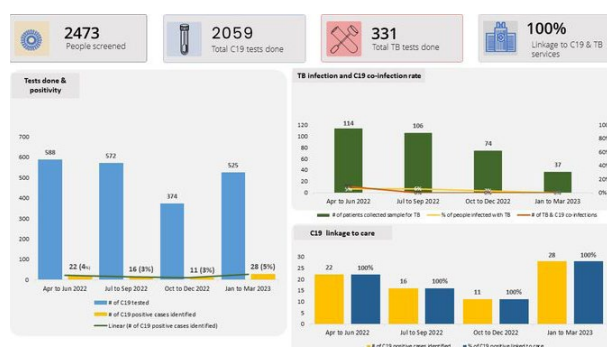
The TrackerApp allowed community workers to capture demographic and screening data and refer individuals needing healthcare. Clinicians at health facilities received notifications and data collected at the community post via the app. Data entry was completed by clinicians on person arrival, and follow-up was closed when applicable.

In addition, the TrackerApp allowed for active case finding using captured phone numbers if a person did not show up. The system also synchronized daily all information collected at the community posts and health facilities.

**Results/Impact:** Since we started using the app, 100% of people referred from community posts were linked to care.

**Conclusions:** The TrackerApp allows integration of TB and COVID-19 screening, testing, linkage to care and reporting results in one digital tool; reduces the need for data capture at health facilities; ensures the continuity of essential services for TB and helps break the trans-

mission chain of these diseases, strengthening the public health response. Further evaluation of the TrackerApp is planned to assess provider and client acceptability.



## OA60-673-18 Implementing the Data-to-Action Continuum Toolkit in Ghana, Nigeria, the Kyrgyz Republic and Bangladesh

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**Background:** Strong tuberculosis (TB) monitoring and evaluation (M&E) and surveillance systems are vital to track progress made in fighting the TB epidemic. The TB Data-to-Action Continuum (D2AC) Toolkit assesses countries' TB M&E and surveillance systems current capabilities and gaps and helps transform evidence into practice by identifying barriers to data use, areas of improvement, and priority actions. The Toolkit is implemented in a workshop setting.

**Design/Methods:** The D2AC Toolkit was field tested in Ghana and Nigeria and implemented in the Kyrgyz Republic and Bangladesh using a mixed methods approach. In total, 132 participants were involved (26 to 41 per country) representing all levels of the health system and other TB stakeholder groups.

Participants completed the D2AC Toolkit's data collection instrument individually and in groups. Then, they identified priority actions for post-workshop implementation. Quantitative data was automatically generated into visuals and tables using the D2AC Analysis Tool.

**Results:** The overall D2AC assessment score from the aggregate group responses was 3.18 (out of 5) for Ghana, 3.45 for Nigeria, 3.06 for the Kyrgyz Republic, and 3.26 for Bangladesh. All countries were at an "established" level according to the continuum. Once the highest- and lowest-performing domains were reviewed for each country, the priority subdomains for recommended follow-up actions were identified.

**Background and challenges to implementation:** Strong tuberculosis (TB) monitoring and evaluation (M&E) and surveillance systems are vital to track progress made in fighting the TB epidemic. The TB Data-to-Action Continuum (D2AC) Toolkit assesses countries' TB M&E and surveillance systems current capabilities and gaps and helps transform evidence into practice by identifying barriers to data use, areas of improvement, and priority actions. The Toolkit is implemented in a workshop setting.

**Intervention or response:** The D2AC Toolkit was field tested in Ghana and Nigeria and implemented in the Kyrgyz

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**Results/Impact:** The overall D2AC assessment score from the aggregate group responses was 3.18 (out of 5) for Ghana, 3.45 for Nigeria, 3.06 for the Kyrgyz Republic, and 3.26 for Bangladesh. All countries were at an "established" level according to the continuum. Once the highest- and lowest-performing domains were reviewed for each country, the priority subdomains for recommended follow-up actions were identified.

**Conclusions:** Despite progress to end TB worldwide, significant challenges remain. Country-specific recommendations articulated during the D2AC workshops include: integrate data quality metrics in program review, develop TB data management standards and advanced data analytics training, orient staff on new tools and forms, improve the harmonization of data collection and reporting while moving toward electronic tools, create standard operating procedures and build data collection and reporting capacity, increase supportive supervisions and peer-to-peer mentoring, implement data quality assessments and a hardware needs assessment, and allocate funds for hardware and essential TB diagnosis and screening equipment.

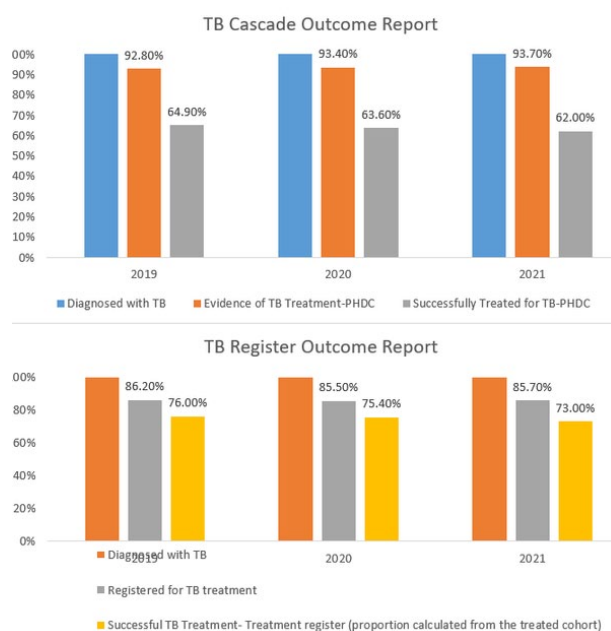
## OA60-674-18 Rethinking reporting on TB outcomes: an urgent need to refine programmatic monitoring and evaluation

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**Background and challenges to implementation:** Routine TB programmatic monitoring and evaluation (M&E) used to identify gaps in care only tracks the treated cohort and fails to report on outcomes relative to the diagnosed cohort, missing those who die before treatment initiation or never link to care.

We report on TB outcomes for the diagnosed and treated cohorts, among those diagnosed in 2019, 2020, and 2021 in the City of Cape Town, to highlight the disparity in reported outcomes.

**Intervention or response:** Aggregate data on TB outcomes for persons diagnosed with TB and persons treated for TB (registered for treatment) were obtained from the Provincial Health Data Centre (PHDC), an integrated data system which collates data from routine health information sources into one patient record. TB episodes are assigned on the basis of laboratory data, other clinical investigations (i.e. chest X-rays), and treatment records.



**Results/Impact:** In 2019, 2020, and 2021 28,189, 22,208 and 24,736, persons were diagnosed with TB, with 92.8% (n=26,170), 93.4% (n=20,752), 93.7% (n=23,187) starting treatment and 64.9% (n=18,295), 63.6% (n=14,134), and 62.0% (n=15,325) successfully treated, respectively.

According to the TB register, in 2019, 2020, and 2021, 24,310, 18,991, and 21,207 persons started treatment, which represents 92.9%, 91.5%, and 91.5% of those who actually started treatment in the respective years. The reported rates of treatment success among those notified on treatment according to the register were 76.0% (n=18,481), 75.4% (n=14,316), and 73.0% (n=15,490), which overestimates the success rates by 117%, 118%, and 118% each year, respectively.

**Conclusions:** Reporting on the full TB cascade allows for better programmatic insights and planning. It is recommended that the World Health Organization and TB programmes redefine the calculation of TB outcomes to be reported out of the diagnosed cohort to accurately reflect patient prognosis, and improve programmatic response to the gaps in the TB care cascade.

### OA60-675-18 Whose case is it? Enabling a continuum of TB care for nationally migrating persons suffering from TB

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**Background and challenges to implementation:** Programmatic services has to follow the person, where ever he chooses to go, especially in a large country like India, where people migrate frequently for economic and personal reasons. For patients that migrate temporarily or permanently, it is important that the responsibility of continuing public health care is reliably handed over by program units.

Traditional practices of paper based transfers in and out, while providing a basic framework it is wrought with a range of practical challenges that prevent effective patient handover and result in double counting of the case in various reporting units.

**Intervention or response:** Leveraging the unified online patient management and notification system Ni-kshay, India implemented a process to reliably hand over patients from one reporting unit to another. Nationally unique patient identifiers were made agnostic to geography, and individuals were informed of the ID physically/electronically. Individuals could use either these identifiers to access care from any health facility in India.

The system was designed to follow the patient; with reporting units requesting to push or pull patient records from others based on where the patient requested to go, or where the person eventually landed up. Using the, "Notifying Unit" and "Current Unit", and Nikshay could generate counts/ registers, using both geographic attributions. The "Current Unit" was designated as responsible for providing any pending services.

**Results/Impact:** The new patient transfer system was successfully implemented in Nikshay in early 2019. Nearly 13% (N=0.31 million cases) of all notified cases in 2019 accessed the transfer facility and moved between district boundaries between stages of diagnosis and treatment. Nearly of the 17% (N~55000) of all transfers were between state boundaries.

**Conclusions:** The national patient transfer system enabled patient centric service delivery across the nation. The reporting method of "Diagnosis" and "Current" ensured better assignment of responsibility of patient care continuum.

### OA60-676-18 Feasibility study on application-based therapy support for TB patients with "TB Companion" in cross-border care between Romania and Germany

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**Background:** The World Health Organization recommends the use of digital adherence technologies (DATs), especially under the conditions of the current SARS-Cov2 pandemic. In tuberculosis (TB) care, a number of solutions are aimed at therapy monitoring in addition to directly observed therapy (DOT). Further, DATs are needed that not only record adherence, but also have the potential to improve it. The application "TBCompanion" was developed as an interactive DAT intended to keep TB patients motivated throughout their treatment.

**Design/Methods:** The TBCompanion provides information tailored to the individual disease profile, gives daily reminders to take TB medication and also monitors possible adverse drug reactions (ADRs). Through dialogues and interactive games, it encourages patient adherence and visualizes treatment progress, complementing ongoing medical guidance. Within a project by the German Federal Ministry of Health to improve cross-border TB care between Romania and Germany (RoGer-TB), a prototype of the application "TBCompanion" was introduced to Romanian patients in Germany via health care providers from 2021-2022. The acceptability of the DAT was studied through an analysis of usage data and through qualitative interviews in Romanian language.

**Results:** Altogether, 23 Romanian patients from 95 contacted health care institutions across Germany agreed to study participation. The population was predominantly

male (71%) and aged 15-50 years (91%). In five qualitative interviews, patients indicated a strengthened sense of commitment to TB therapy, with the greatest benefits seen at therapy initiation and in support of interactions with their health care practitioners.

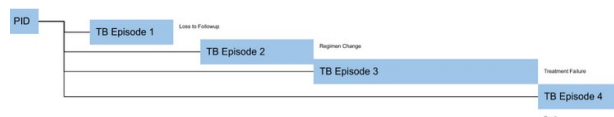
**Conclusions:** The TBCompanion was only used by a small proportion within the mobile group of Romanian TB patients in Germany and is therefore currently not a suitable DAT for this target group. Among all participants with sufficient use, the DAT was rated positively. An expansion of the target group to include TB patients from Ukraine is planned and can enable a comparison of individual experiences.

### OA60-677-18 Implementing the concept of life cycle approach in TB programme information systems of India

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**Background and challenges to implementation:** The global standard of case based digital/ online TB notification systems does not take into account the individual person, who may have important TB epidemiological properties beyond the case. This is especially true when one person may become a case of TB again and get notified within/ after the reporting year, or from alternate geographies. In such cases, it is important to retain links to the previous case notified.

**Intervention or response:** Based on the felt need, the concept of a case was divided into the concept of “Person” and “Episodes”. Two case notifications/ Episodes could be linked with each under a person. A person would be identified using a unique identifier (PersonID) and all episodes linked to him/her would be identified by a unique Episode identifier (EpisodeID). Related features were built into the National TB information system (Ni-kshay).



**Results/Impact:** The concept of episodes were successfully built into the TB Information system in early 2019. Field level actors notifying cases could search through the previously notified cases using these identifiers and other proxy identifiers such as mobile numbers and create additional episodes.

Further features to promote creation of episodes and prevent duplicate PersonID creation were also implemented. Using these features in the year, 2019 2.40 mil-

lion episodes were notified linked to 2.32 individuals. Of those who got notified again (~80000 notifications), about 50% had an existing notification within the same year and the rest had prior notification in previous years. The results of this feature would get amplified in further years as the pool of existing notifications in the system increases and utilization/ coverage of the feature reaches 100%.

**Conclusions:** The episode concept used in TB information system enable both patient centric approaches in recording information and service delivery, while also enabling the next level of epidemiological analyses in terms of probability/ risk of TB recurrence.

### OA60-678-18 Mitigating the impact of integrated TB-COVID-19 testing using GeneXpert equipment on TB testing and detection in Kaduna State, Nigeria

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**Background and challenges to implementation:** The COVID-19 pandemic has no doubt affected the progress made in TB prevention and care globally and Nigeria is not left out. At the onset of the pandemic, Kaduna State had limited capacity for COVID-19 testing. As such, the Kaduna State Government (KDSG) in its quest to build capacity for COVID-19 testing and diagnosis, the available Gene Xpert machines used for TB diagnosis situated in public Health facilities were identified for integrated TB/COVID-19 testing.

**Intervention or response:** The State identified Eight (8) Gene Xpert laboratories and released ₦98 million counterpart funds to optimize the sites for integrated testing. A needs analysis was conducted and gaps were prioritized. Structural modifications, backup solar power systems, and level II biosafety cabinets were installed. The capacity of laboratory staff built on TB/COVID-19 testing using the machines and additional staff posted to run shifts. Tracking of daily and weekly workload for both TB and COVID-19 was instituted and an efficient sample referral system was instituted.

**Results/Impact:** A range of 12% - 728% (average of 197%) increase in the number of samples tested was noted across the eight facilities where integrated TB/ COVID-19 testing was piloted when compared with the

pre-integration period. This enabled increased COVID-19 testing capacity at a time that really matters without affecting TB diagnosis and it made a huge difference in the effort to stem the spread of the infection.

**Conclusions:** This result has demonstrated that the Gene Xpert machines and laboratory network when fully optimized have the potential for integrated testing and increased testing capacity without adversely affecting TB diagnosis. This approach should be implemented in similar settings to optimize the capacity of the Gene Xpert machines.

## OA61 Health education and capacity building

### OA61-679-18 Unravelling the significance of health literacy for ending TB: a global systematic review and meta-analysis

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**Background:** Health literacy (HL) plays an important role in the acquisition of skills to navigate the health-care system, understand and apply health information to prevent, control and cure chronic disease, particularly Tuberculosis (TB). TB with a need for ongoing management presents a steep learning curve about risks, treatment and self-care and constitutes a complex, long-term challenge for patients, providers and healthcare system. Successful integration of HL into TB policy and practice rests on the availability of the evidence related to its contribution to health outcomes. With this background, this review aims to synthesize existing HL levels and their association with treatment adherence, outcomes, and the potential underlying mechanisms for studied association.

**Design/Methods:** We searched MEDLINE, EMBASE, CINAHL, PsycINFO, Scopus and ScienceDirect to find studies published between January,2000-December,2022, reporting HL levels and TB. Two authors independently extracted data and assessed the bias using JBI critical appraisal tool. A random-effect model was used to derive the pooled prevalence of limited HL, testing for heterogeneity with Cochrane's-Q and I<sup>2</sup> statistics.

**Results:** Out of 4281 records, 22 studies (14 quantitative, 5 qualitative and 3 mixed method study) were included. The pooled prevalence of limited HL was found to be 55%.

For the studies (n=4) showing association with odds ratio to assess HL, a statistically significant association was observed between low HL and poor TB treatment adherence [Pooled-OR:1.95 (95%CI:1.37,2.78)] HL acted as a mediator between TB knowledge and social support. TB-knowledge, self-care, self-efficacy, patient-provider engagement, and provider's skills influenced the levels of HL among TB patients.

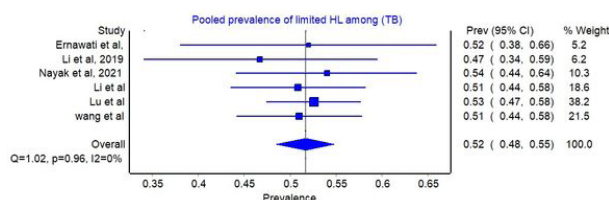


Figure. Pooled prevalence of limited HL among (TB).

**Conclusions:** This review underlines the importance of HL in TB care with consistent association between the two. Specifically, TB patients with lower HL levels are more likely to have poor treatment adherence. There is a clear need to develop and implement effective HL interventions to improve treatment outcomes and document the lessons.

### OA61-680-18 Leveraging behavioural change communication models to increase uptake TB preventive treatment among healthy contacts of TB patients in India

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**Background and challenges to implementation:** India's National Strategic Plan for ending Tuberculosis (TB) proposes scaling up TB preventive treatment (TPT) to hasten the rate of decline in incidence from 2.5% at present to 10% annually. Expansion of TPT to all eligible household contacts (HHCs) of TB patients requires fostering disease prevention behaviour amongst patients and healthy HHCs. Global Fund supported JEET project, implements TPT for HHCs of drug sensitive PTB (DSPTB) patients (65 districts, 11 provinces).

**Intervention or response:** JEET adopted a communication strategy leveraging Transtheoretical & Spheres of Influence models of behaviour change. Communication touch-points, audio-visual & printed tools were designed for sustained pursuance to drive uptake of TPT. Patients and HHCs were educated about the disease, transmission and prevention. There was sustained interaction with HHCs from first counselling until TPT initiation and completion. NTP teams, doctors (public



& private) and community health workers were trained on TPT and engaged to optimize social influence in decision making.

Stages of TTM	HHC behaviour status	JEET touch-point/ communication strategy	Tools (developed under JEET)	Escalation to social influencers in case of denial to JEET staff
Precontemplation	low/no awareness about TB disease, transmission, risk of infection and disease, possibility of prevention, availability of preventive treatment	1. Telephonic conversation with patient/HHC	printed IEC collateral (picto-graphic and text) with information on TB disease, do's & don't's for patients, infection transmission and likely progression to disease, prevention measures (available in 5 languages) (explained in person and left behind for later reference by HHCs)	local NTP team, community health workers, treating doctor (public & private)
		2. Home visit for meeting with patient + HHCs for counselling		
Contemplation	Aware of TB patient in the family and risks of infection & disease progression amongst HHCs	3. Treating doctors' prescription for TBi/CXR for HHCs	standardized prescription template for screening & test of HHCs, designed to be appended to index patient prescription	
		4. Informing about free availability, easy access to test facilities	video detailing the simple steps for HHCs to take tests and treatment (available in 5 languages) (shown in person and shared on mobile phone for later reference)	
Preparation	Aware of needful tests to be done; their availability and accessibility	5. Facilitating home collection of samples for IGRA	e-vouchers for free test at a JEET- contracted private facility	
		6. Mobilizing to nearest public/private facility for CXR		
Action	Aware of their test results and available preventive treatment	7. Mobilizing to nearest health facility for prescription of TPT after medical consultation & provision of drugs	prescription template for listing all HHCs of an index patient, documenting individual body weights, treatment regime, dosage, duration and date of initiation	
		Initiated on TPT	8. Regular follow-up until completion of treatment for checking adherence, counselling in case of any missed doses; checking for any adverse drug reactions, TB symptoms	
9. Follow-up for drug refills, symptoms of TB; adverse drug reactions				

Table 1. JEET HHC communication-cum-engagement strategy summary.

**Results/Impact:** From Jan-Dec'2022, JEET covered 0.23 million DSPTB patients. Initial telephonic interaction happened with 90%, followed by home visits for 0.15 million patients. 0.56 million HHCs were screened and counselled about TB disease and prevention, 74% of the eligible HHCs received test for TB infection. 0.29 million underwent chest X-ray for TB screening (95.8% of them were asymptomatic). 0.32 million HHCs were initiated on TPT (93% of the eligible HHCs on TPT got CXR) and 84.5% completed treatment successfully. NTP team and community health workers across 677 sub-districts and >4000 doctors were engaged.

**Conclusions:** Sustained, multi-pronged communication-cum-engagement strategy for patients and HHCs is essential to educate and convince people to choose TB prevention measures and comply to the treatment protocols. Adoption and implementation of Transtheoretical and Spheres of Influence models can yield significant gains in TB education for patient families, cultivating preventive health-seeking behaviour and adherence to recommended treatment algorithm.

### OA61-681-18 The effectiveness of two different nurse training models for managing multidrug-resistant TB in South Africa

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**Background and challenges to implementation:** Prior to 2011, National Guidelines mandated that patients with drug-resistant (DR) TB be hospitalized for treatment. With a few specialized TB hospitals, a shortage of doctors, and numbers surpassed the available bed capacity, a decentralized approach to manage DR-TB, including Nurse Initiated Management of Drug Resistant TB (NIMDRTB) were implemented.

Regenerate response

**Intervention or response:** Previously, NIMDRTB training programs consisted of an 8-week curriculum, which comprised one-week didactic training, one-week ancillary training, and six weeks of practical training in an MDRTB unit. Nurses were certified upon completion of the 8-week training program. In 2019, a new training model was introduced, which consisted of a shorter, 2-week curriculum - one week of didactic training, followed by 4 days of ancillary training and an Objective Structured Clinical Examination (OSCE) on the fifth day. Nurses were certified as competent upon passing the OSCE.

**Results/Impact:** A comparative analysis of the two training models were conducted, using a survey that was randomly distributed to 100 students who completed NIMDRTB training.

The response rate was 30%, (53% trained on the 8-week model and 47% on the 2-week model). Rating the quality of their training (on a scale of 1 to 5), respondents who received the 8-week training had an average rating of 4.5 and those received the 2-week training a rating of 4.7.

The average rating for both groups on the knowledge they gained was 4.6. The confidence rate for initiating MDR TB treatment was 4.5 for the 8-week and 4.6 for the 2-week training. 91% trained on the 8-week and 94% trained on the 2-week model reported improvement in patient outcomes. 91% trained on the 8-week model and 94% trained on the 2-week model reported feeling comfortable handling challenges in the management of MDRTB.

**Conclusions:** There were no significant differences observed between the eight-week training and the two-week training.

### OA61-682-18 Continuous quality improvement: an approach to increasing contact investigation coverage in three multidrug-resistant TB treatment centres, the Philippines

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**Background and challenges to implementation:** Contact investigation (CI) involves systematically assessing MDR-TB patients' contact persons to identify active TB disease and interrupt transmission. In 2021, the National Capital Region in the Philippines reported 1% CI coverage, significantly lower than the target of 65%. Multiple factors account for low uptake, including unclear healthcare worker roles, utilization of radiology as the sole screening tool, and weak mechanisms to track MDR-TB patients' contact persons.

**Intervention or response:** In collaboration with three MDR-TB treatment centers in Caloocan and Quezon Cities, USAID's TB Platforms Project implemented Continuous Quality Improvement (CQI) to enhance CI processes and structures, improving patient outcomes, healthcare systems, and organizations.

Following CQI training, the treatment centers developed and implemented an intervention package including a designated CI point-person, a screening algorithm process redesign, and a register to monitor DR-TB contacts. The Activity conducted biweekly coaching meetings and monthly cross-validation of records to assess implementation fidelity.

**Results/Impact:** From October to December 2022, 196 contact persons of 74 index MDR-TB patients were screened and tested; 2 TB cases (1 drug-sensitive, 1 drug-resistant) were diagnosed and enrolled in treatment. The 3 treatment centers achieved a CI coverage of 91% from an average baseline of 43%.

The CQI teams screened MDR-TB contact persons using chest x-rays or Xpert MTB/RIF assay. The new screening algorithm allowed contact persons to choose a screening tool that was acceptable and accessible, promoting person-centered care.

Additionally, CQI teams utilized the register to track outcomes, ensuring that every contact person was screened for TB and diagnosed contacts initiated treatment.

**Conclusions:** CQI is an effective approach to improving processes and providing the best possible health care for all. CQI facilitates the implementation of small, fast,

and impactful changes, improving service delivery and patient outcomes. The approach could be applied in various situations, ensuring a standardized, structured, and systematic way of solving health problems.

### OA61-683-18 Reported behaviour on the use of personal protective equipment: development and validation of a tool

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**Background:** Despite the extensive scientific and official literature on the use of personal protective equipment (PPE) by nursing professionals, there is still low adherence, and knowledge about their reported behavior could guide the development of effective interventions. Therefore, the objective of this study is to develop and validate an instrument on the reported behavior of nursing professionals regarding the use of PPE.

**Design/Methods:** This is a methodological study for the development and content validation of an instrument on reported behavior regarding the use of PPE. The instrument was developed based on an extensive literature review and validated by a committee of ten nursing experts in the thematic area, selected by convenience. Data were collected using the Google Forms<sup>®</sup> electronic platform. The content validity of the items and the instrument as a whole were assessed by calculating the Content Validity Index (CVI), with a reference value of  $\geq 0.8$  for validation. Data were analyzed using the Statistical Package for the Social Sciences.

**Results:** The instrument contains 55 items organized into five domains:

1. Use of gloves;
2. Use of masks;
3. Use of protective goggles/face shield;
4. Use of cap/hat; and
5. Use of gown/coat.

All items of the instrument were validated (CVI > 0.8). However, the experts indicated minor adjustments in spelling, formatting, and wording of some items. Some suggestions for more substantial modifications, such as specifying tuberculosis and meningitis, were discussed and analyzed by the research team in light of the literature.

**Conclusions:** The development of a tool that allows standardized measurement of the reported behavior of nursing professionals regarding the use of PPE enables situational diagnosis, as well as the proposal of more appropriate interventions for identified gaps.

### OA61-684-18 Using quality improvement, a strategy to improve TB screening and notification in Buffalo City Metro, Eastern Cape Province, South Africa

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**Background and challenges to implementation:** BCM is a high Tuberculosis (TB) burden District in Eastern Cape, South Africa. According to Kweza et.al, BCM had an estimated TB incidence of 823/100 000, higher than the national rate of 593/100 000 between 2014 and 2015, However between April 2019 and March 2020, the district has consistently reported low TB notifications and screening rate below 90%.

**Intervention or response:** Between September 2021 and March 2022, three QI officers, 27 nurses and 23 data captures were deployed in (27/85) of the BCM health facilities to form a learning collaboration with the department of health staff to improve facility TB services.

The team used the Model for Improvement as the methodological framework to identify the health facility system weakness and optimized the workflow. The plan-do-study-act (PDSA) cycle was used as a guiding framework to test and gather knowledge on all change ideas proposed by the team.

The change ideas were recorded, data was collected and monitored for any unintended negative impacts on the facility system. Annotated run charts were used to track performance and reviewed every 4 weeks, and the team will then decide on adapting, adopting, or abandoning the change idea until a perfect change idea is agreed up and implemented.

The change interventions generated by the team included, patient flow restructuring, data checks using Routine Data Quality Assessment tools, learning sessions, coaching, mentoring and provision of TB stationeries.

**Results/Impact:** Three learning sessions, 10 RDQAs and 10 mentoring/coaching sessions per quarter were conducted and 85 TB ID registers were distributed. The district TB screening improved from 83% in April 2021 to 97% by March 2022. All DS-TB treatment start/notification rate improved from 59% in Quarter 4 2019 to 90% in quarter 1 2022.

**Conclusions:** Three learning sessions, 10 RDQAs and 10 mentoring/coaching sessions per quarter were conducted and 85 TB ID registers were distributed.

### OA61-685-18 Sustained capacity-building for active monitoring of the safety of new TB medicines in Kazakhstan

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**Background and challenges to implementation:** Over the past seven years, Kazakhstan's National TB Program (NTP) introduced new all-oral treatment regimens for drug resistant (DR) TB through several operational studies and then scaled them up. This has led to a need to develop knowledge and skills on the use of new medicine and for active drug safety monitoring (aDSM). The country's national TB plan prioritizes aDSM of new TB drugs and new treatment regimens as an important part of the programmatic management of DR-TB.

**Intervention or response:** To build health worker capacity in aDSM for new TB drugs, the NTP, with support of the medical university, Global Fund and the USAID Eliminating TB in Central Asia activity, created an aDSM web-based learning module.

The e-course is adapted from an in-person course that has trained about 900 physicians over seven years. The NTP introduced the 24-hour course as part of its online TB management training platform, available to doctors through the official NTP website.

The online module meets health care workers' desire to have course access when and where is convenient for them and allows for rapidly training up newly placed health staff.

**Results/Impact:** The aDSM online module enables the NTP to build the capacity of a larger group of TB service and primary care specialists on active monitoring the safety of new TB drugs more quickly and at lower cost. Since the launch of the platform in June 2021, an initial 85 participants have used the aDSM module, without the need to leave their place of work for training. Incremental cost for e-training is about \$15/person vs. \$508/person through the in-person aDSM course.

**Conclusions:** The aDSM web module leverages online learning capability to rapidly train newly assigned health workers and build health workforce knowledge on a broader scale. This approach could be replicated for other TB topics.

## OA61-686-18 Shared and reflected experiences of Kagabays as partners in drug-resistant TB treatment in the Philippines

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**Background:** Through the government-funded CoACH-DRTB project, we trained community health care workers (CHWs), called them ‘Kagabays’, who combined paperback documentation and mHealth application ConnecTB for DR-TB community-based care. We share the Kagabays’ experiences as partners in DR-TB treatment, who had 89.4% treatment success rate and 96% monthly drug adherence in Cavite Province, Philippines. **Design/Methods:** In 2018, 57 Kagabays selected from a set of criteria prescribed by the National TB Program were trained in 4 batches. We organized four focus group discussions (FGD) who monitored 171 people during their DR-TB treatment and 2-year post treatment follow-ups; and 153 people with LTBI from 2019 to 2022. We audiotaped, transcribed verbatim the FGDs, coded inductively, and deductively identified themes via thematic analysis.

**Results:** In the FGD sessions, 32 out of 57 trained Kagabays participated, with an average age of 43 years and majority being female (94.59%). We identified four themes, similar to the healthy behavior conceptual model (Figure 1).

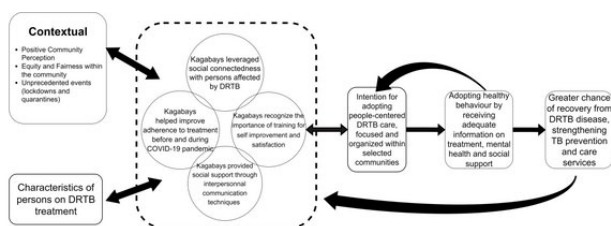


Figure 1. Conceptual framework of CHWs/Kagabays' adopting healthy behaviours for DRTB care (Katigbak et al, 2025).

Improving adherence to treatment before and during COVID-19 pandemic: Kagabays helped partners maintain healthy behaviour of daily DOT, adapted mobile phone applications even during lockdowns, and used their own resources to provide immediate aid to partners. Leveraging social connectedness: Residing in the same area as their partners, some had received “stigma” in their communities. Kagabays shared unique strategies to ensure continuity of care.

Provision of social support through interpersonal communication techniques: Kagabays integrated self-care and health maintenance into traditional values, eventually becoming resource persons in DR-TB health awareness campaigns.

Recognition of importance of training: Kagabays recognized adverse events from several trainings and demonstrated counseling competence as they recall their experiences when partners would likely to give up treatment. **Conclusions:** Trained ‘Kagabays’ or CHWs should be considered as crucial component of the psycho-social support package of community-based TB-/DR-TB patient-centered care programs throughout their long journey to treatment success.

## OA62 Access to care and services

### OA62-687-18 Barriers and facilitators to TB diagnosis among presumptive patients in selected health facilities of Uganda

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**Background:** Loss to follow-up of presumptive tuberculosis (TB) patients before completing diagnosis is a major gap in the TB care cascade likely to hamper achievement of the 2030 End TB strategy. This study explored facilitators and barriers to completing TB diagnosis among presumptive TB patients in selected rural and semi-urban health facilities of Uganda.

**Design/Methods:** We conducted a qualitative study involving; 25 in-depths interviews with presumptive TB patients, 20 key informants with health workers providing TB services and 8 focus group discussions with TB patients who had recently initiated treatment.

In-depth interviews and focus group discussions were conducted in the local language and key informant interviews in English using interview guides. Focus group discussions were sex specific with an average of 7 participants lasting between 50 minutes and 1 hour.

All interviews were audio recorded, transcribed verbatim in their original language of recording and back-translated to English. Data were organized into themes and subthemes using Atlas.ti V9.0.

**Results:** Facilitators for completing TB diagnosis included; need to be pain-free, family and community support, caring health workers and short turn-around time for results.

Key barriers included lack of transport to health facilities, anticipated TB stigma coupled with misconceptions that every TB patient has HIV, fear of positive HIV results which requires taking medication the rest of ones’ life and the misconception that TB does not cure hence would rather not know the diagnosis.

**Conclusions:** Facilitators and barriers to completing TB diagnosis cut across patient, social and health system factors. Key strategies to address these barriers include social protection, health system strengthening and increased awareness on TB.

### OA62-688-18 Outcomes of differentiated TB treatment service delivery models in Nairobi, Kenya, 2020-2022

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**Background and challenges to implementation:** Differentiated service delivery models (DSD) are not widely adopted in TB settings. COVID-19 containment measures necessitated reimagining of service delivery for continuity of TB care. Pre-COVID-19, Ministry of Health (MOH) standard of care (SOC) for drug-sensitive TB treatment recommended weekly and fortnightly anti-TB drug collection during the intensive and continuation phases, respectively.

During the COVID-19 pandemic, the MOH provided guidance for a DSD model allowing collection of medicine fortnightly (intensive phase) and monthly (continuation phase).

We describe TB treatment outcomes in DSD and SOC models in 14 Eastern Deanery AIDS Relief Program (EDARP) sites in Nairobi slums.

**Intervention or response:** In this study, clients were counselled and offered DSD. SOC was provided to those who opted out of DSD and the severely ill (based on clinician assessment). Clients on DSD models received adherence counselling, initiated treatment, and based on preference, subsequently followed-up weekly using text messages, telephone calls or home visits. EDARP adapted their electronic medical records for documentation.

We calculated frequencies, proportions, and Crude-odds-ratios (COR) with 95% confidence intervals (CI) to describe clients on TB DSD and SOC models from October 2020–September 2022.

**Results/Impact:** Overall, 2,522 people were initiated on TB treatment. Of these 1,049(41.6%) clients received care in DSD and 1,473(58.4%) received care in SOC models.

Among clients receiving DSD, 876(83.5%) had treatment success (TS), 33(3.1%) died and 78(7.4%) were lost to follow-up (LTFU). Of those receiving SOC, 1,119(76.0%) had TS, 96(6.5%) died and 128(8.7%) were LTFU.

Compared to those on SOC, clients on DSD models were more likely to be treated successfully, [OR,1.6, 95%CI:(1.3-2.0)] and less likely to die [OR,0.5, 95%CI:(0.3-0.7)]. There was no difference in LTFU, [OR,0.8, 95%CI:(0.6-1.1)].

**Conclusions:** TB DSD models are feasible and could improve outcomes while reducing clinic visits. The apparent lower TS among clients on SOC may be due to selection of severely ill clients.

### OA62-689-18 A comprehensive approach to respiratory disease screening at a primary healthcare facility in Vietnam

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**Background and challenges to implementation:** TB and other respiratory diseases such as COVID-19, RSV, and influenza A and B have some same symptoms like cough, fever, and sharing high-risk groups including HIV people, elders, diabetes, and children.

A programmatic screening has been implemented at 40 communes of 2 districts in Ha Noi since November 2022 with the aim of screening TB and the common respiratory diseases (COVID19, RSV, Influenza A and B) using POC testings and GeneXpert test.

**Intervention or response:** At Commun Health Stations (CHSs), people with COVID-19, Influenza A&B, or RSV, TB symptoms will be tested for COVID-19, Influenza A&B, or RSV by antigen RDTs, and people with TB symptoms will have their sputum specimens collected and sent to District health center (DHCs) TB units for TB testing.

If COVID-19 testing results are positive, CHSs will manage the patients as per National guidelines, if TB testing results received from DHCs are positive, CHSs will inform the patients to come back for TB treatment initiation.

**Results/Impact:** Over 6 months, 16,456 people who reached health services at primary health care facilities were screened. Of those 15,665, 15,567, 2,481 and 2,476 tests have been done for COVID-19, Influenza A&B, RSV, and TB, respectively.

The total number of diagnosed COVID-19 cases was 92, and influenza A,B, RSV were 89,32,24 cases respectively. Around 2.5% of those who had at least one on the symptoms list have bacteriologically confirmed with TB.

All cases then either received a treatment regimen right after diagnosis for COVID-19, Influenza A&B, or RSV at PHC or refer to the District health center for further clinical assessment before registering for TB treatment.

**Conclusions:** The comprehensive package screening for respiratory diseases should be included in the primary healthcare package which will get reimbursement from National Health Insurance Scheme.

### OA62-690-18 TB prevalence and associated factors among persons enrolling for HIV care in the pre- and post- test-and-treat era, East African Region, 2012-2020

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**Background:** In 2015, the World Health Organization (WHO) recommended the global adoption of Test and Treat (TT) strategy for HIV care. Increased access to antiretroviral therapy (ART) has improved viral suppression and decreased mortality.

However, the impact of TT on tuberculosis (TB) prevalence, the leading cause of morbidity and mortality in persons-living-with-HIV (PLHIV), is unclear. So, we sought to compare TB prevalence and associated factors before and after TT strategy in East Africa.

**Design/Methods:** In a cohort of PLHIV, aged  $\geq 18$  years, enrolling in HIV care between 2012-2020 at HIV primary care sites affiliated with the East Africa International epidemiology Databases to Evaluate AIDS consortium, prevalence and factors associated with TB before (2012-2015) and after (2016-2020) TT were analyzed.

Prevalent TB was defined based on bacteriological diagnosis or empiric TB treatment initiation within 60-days of enrollment. TB prevalence with 95% CIs and adjusted effects of TT were determined using multi-level Poisson regression models fitted with sites as random intercepts to account for variation in HIV care.

**Results:** Among 142,268 PLHIV studied, median age was 32(26-41) years, 37% were male, and 62% enrolled before TT. PLHIV enrolled after TT roll-out were more likely to start ART on day of receiving a positive HIV-test result (81% vs. 24%) than before.

The prevalence of TB was 8.8% (7,766) (95% CI: 8.2, 9.4) before versus 6.0% (3,254) (95% CI: 5.2, 6.8) after TT-adoption.

Adjusted for sex and age, TT strategy was associated with a lower prevalence of TB [aPR: 0.68 (95% CI: 0.65 – 0.71),  $p < 0.001$ ] than before, but males were twice as likely to have TB [aPR: 2.04 (1.96 – 2.12),  $p < 0.001$ ] than females, and ages  $\geq 25$  years associated with higher prevalence of TB than 18–24 years.

Characteristic		Total N=142,268 N (Column%)	TB prevalence n (row %)	Unadjusted		Adjusted	
				Prevalence ratio 95% CI	P-value	Prevalence ratio 95% CI	P-value
Enrollment period	Pre-TTS	88,308 (62)	7,766 (8.8)	Reference		Reference	
	Post-TTS	53,960 (38)	3,254 (6.0)	0.69 (0.66 – 0.72)	<0.001	0.68 (0.65 – 0.71)	<0.001
Sex	Female	89,757 (63)	4,801 (5.3)	Reference		Reference	
	Male	52,511 (37)	6,219 (11.8)	2.22 (2.14 – 2.31)	<0.001	2.04 (1.96 – 2.12)	<0.001
Age groups	18-24	25,734 (18)	908 (3.5)	Reference		Reference	
	25-34	54,960 (39)	4,020 (7.3)	1.96 (1.83 – 2.11)	<0.001	1.69 (1.57 – 1.82)	<0.001
	35-44	36,982 (26)	3,745 (10.1)	2.60 (2.42 – 2.80)	<0.001	2.03 (1.88 – 2.18)	<0.001
	45+	24,592 (17)	2,347 (9.5)	2.37 (2.20 – 2.56)	<0.001	1.82 (1.69 – 1.97)	<0.001

**Conclusions:** TT-adoption was associated with a reduced burden of prevalent TB; however, TB remains high among males and 25+year-old PLHIV enrolling into care.

### OA62-691-18 Increasing TB case detection by engaging informal healthcare providers in north-eastern Nigeria

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**Background and challenges to implementation:** Patient Medicine Vendors (PMVs) and Traditional Healers (THs) are informal healthcare providers with a significant presence in Northeast Nigeria and many parts of Africa. They have established partnerships and trust with stakeholders in communities and are typically the first point of contact for health seeking, especially in rural communities.

Despite their high potential for partnership in health care delivery, PMV and TH remained largely ignored by TB programs.

**Intervention or response:** We conducted a private sector engagement initiative in four Local Government Areas (LGAs) in Adamawa and Yobe States from October 2020 to September 2021 and used 4 comparable LGAs as control areas. PMVs and THs leadership was engaged and sites were mapped.

Community Volunteers (CVs) were linked to PMVs and THs to support the intervention. TB screening was conducted among clients of PMVs and THs, and people with presumptive TB had sputum samples collected and transported to GeneXpert sites. Results were retrieved and people with Bac+ TB were linked to treatment while those with Bac- results were referred for further management.

**Results/Impact:** Overall, 120 PMVs and 60 THs were mapped and engaged. They identified 7,553 people with presumptive TB and 92% (6,920) were tested. In total,

996 people with all forms of TB were notified; 923 were Bac+ including 12 with rifampicin-resistant TB. PMVs identified 4,503 (60%) of people with presumptive TB and 630 (63%) people with TB. TB notifications for all forms and Bac+ increased by 104%, and 114% in the evaluation population respectively, compared to an increase of 32% and 20% in the control population.

**Conclusions:** Despite the focus of private sector engagement in Asia, many people with TB seek care from informal providers like PMVs and THs in Nigeria.

Engaging these providers in Nigeria and beyond can lead to improvements in TB notifications and could be scaled.

### OA62-692-18 Enhancing delivery of TB services for newly diagnosed patients in the Western Cape, South Africa: a telehealth intervention

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**Background and challenges to implementation:** During the Covid-19 pandemic, the Western Cape Government (WCG) Contact Centre's "Track and Trace Programme" emerged as an innovative Health Information and Communication Technology (ICT). By contacting citizens telephonically, agents informed them of their positive test result, provided information on quarantine and isolation and linked them to care pathways.

This intervention aims to expand this innovation to improve initiation of Tuberculosis (TB) treatment, provide TB symptom screening of household contacts and promote uptake of COVID-19 vaccination with support from the Government to Government (G2G) programme between WCG and USAID.

**Intervention or response:** The intervention is being piloted in the Cape Metropolitan municipality since December 2022. The Provincial Health Data Centre (PHDC) enables access to patient information linked to Xpert MTB/RIF test results. Agents call patients 14 days after the test date. A patient-friendly script is followed to provide results and information. Patients are screened for signs of clinical deterioration and referred to community-based teams if indicated. They are encouraged to go to a clinic to start treatment if they have not already done so. Household contacts are screened for symptoms of TB and COVID-19 vaccination is promoted.

**Results/Impact:** Out of a total of 1 323 clients, nearly 90% had a linked cellphone number. Of these, 38.5% were successfully reached. 51 patients required linkage

to care, 21 of whom had signs of clinical deterioration. Another 50 clients who were hospitalised were offered follow up calls.

Most clients reached were very appreciative of the call. Poor quality of contact detail recording and reluctance of clients to answer calls have contributed to unsuccessful calls.

**Conclusions:** COVID-19 telehealth interventions can be expanded to enhance TB service delivery. Optimisation of the service may be achieved by improving quality of contact detail collation and building trust with citizens through communication campaigns.

### OA62-693-18 Multidisciplinary teams contribute to active screening and detection of TB cases among risk groups in Uzbekistan

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**Background and challenges to implementation:** According to WHO Global TB Database 2015–2020 data, 26% of the estimated new and relapse cases in Uzbekistan were missed (not diagnosed) in 2019. This statistic rose to 45% in 2020 linked with the effects of the COVID-19 pandemic.

Many of those who do get diagnosed do so late: in a 2021 USAID Eliminating TB in Central Asia (ETICA) activity study, 26% of surveyed TB patients consulted a doctor within 14-30 days of symptom onset.

**Intervention or response:** To best reach the people in TB risk groups (people in contact with TB patients, people living with HIV and migrant workers), in 2021, USAID ETICA and Uzbekistan's NTP activated MDTs in three oblasts. Each MDT is based at a health facility and includes a doctor, nurse, psychologist, and outreach workers.

MDTs screen people in risk groups and refer those with presumptive TB symptoms for testing using a voucher system that ensures confidentiality and proper registration of individuals with TB symptoms.

MDTs use gender-differentiated approaches to improve access to services by screening for gender barriers, providing psychological support and tackling issues of stigma and discrimination.

**Results/Impact:** From May 2021 to March 2023, MDT outreach workers in the USAID ETICA pilot regions screened 32,363 beneficiaries for TB symptoms; 12,460 of them were tested for TB; 382 received a diagnosis of active TB disease.

This represents 25.6% of the total number of TB cases registered in the pilot regions during this time (Figure 1).

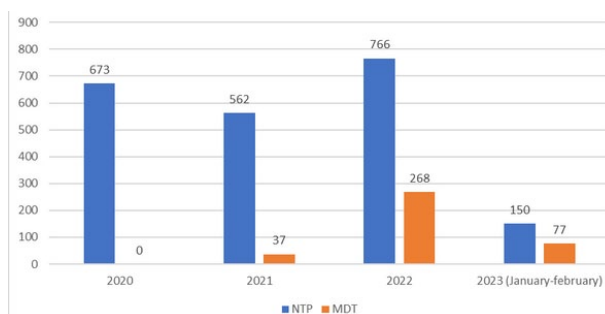


Figure. The number of identified by MDT and NTP.

**Conclusions:** MDTs have demonstrated their high effectiveness in contributing to case finding. They contribute to shifting TB screening from the TB service to PHC, help strengthen linkages between the NTP and PHC, and bolster reach to vulnerable populations which will improve timely detection. The demonstrated MDT approach can be expanded to other regions and countries.

### OA62-694-18 Addressing the social determinants and consequences of TB in Nepal: results from a four-arm randomised-controlled pilot trial of socio-economic support for TB-affected households

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**Background:** WHO policy advocates reducing stigma and eradicating catastrophic costs of people with TB but practical evidence on socioeconomic interventions is scarce. We conducted a pilot randomised-controlled trial (RCT) to evaluate the feasibility and acceptability of socioeconomic support for TB-affected households in four districts of Nepal.

**Design/Methods:** A total of 128 TB people with drug-sensitive pulmonary TB notified to the Nepal National TB Program were recruited and randomly assigned 1:1:1:1 to: control, social, economic, and combined socioeconomic support arms.

Social support consisted of:

Enhanced TB education (IEC) at household visits with an illustrated wall-calendar to increase knowledge; And TB-Champions/Survivor-led TB Clubs, which used group-counselling and a locally-made animated-video to reduce stigma.

Economic support consisted of six unconditional monthly cash transfers of 3000 Nepalese Rupees (~30USD). Process evaluation assessed acceptability and feasibility.

**Results:** Participant recruitment was 100%, retention was  $\geq 94\%$ , and fidelity to support package activities was high for cash transfers (62/62, 100%), Home visits and IEC (59/62, 95%) but slightly lower for TB Clubs (56/62, 90%, Table). Participant satisfaction with support packages was generally high for cash transfers and TB Clubs. Notable differences between study arms included lower satisfaction with home visits and IEC (23/30 [77%] vs 29/29 [100%] good/very good rating) and lower attendance at TB Club (25/30 [83%] vs 31/32 [97%]) in social vs socioeconomic arm participants.

Participants' qualitative survey feedback suggested: cash transfers were timely and used for nutrition and travel; Home Visits and IEC provided good information, motivation, and counselling (including about drug side effects); and TB Clubs were valued to share experience and reduce stigma (Table).

Recruitment, follow-up, study activity completion and participant survey feedback		Control	Economic	Social	Socio-economic	Participants qualitative survey feedback on support package activities received
Recruitment and follow-up	Recruited (%)	32/32 (100%)	32/32 (100%)	32/32 (100%)	32/32 (100%)	-
	Completed all study follow-up (%)	30/32 (94%)	30/32 (94%)	30/32 (94%)	32/32 (100%)	-
Six monthly unconditional cash transfers	Completed (%)	-	30/32 (94%)	-	32/32 (100%)	"Timely financial support"
	Rated Good or Very Good (%)	-	26/30 (87%)	-	29/32 (91%)	"My family was able to buy fruit and meat" "Cash transfers helped to reduce out-of-pocket costs"
Home visits and IEC with illustrated wall calendar	Completed (%)	-	-	30/30 (100%)	29/32 (91%)	"Good counselling and motivation"
	Rated Good or Very Good (%)	-	-	23/30 (77%)	29/29 (100%)	"We had the opportunity to ask about drug side effects" "The wall calendar gave useful information on TB symptoms and treatment"
TB clubs with mutually support and locally made animated TB-stigma reduction video	Completed (%)	-	-	25/30 (83%)	31/32 (97%)	"TB clubs and TB video provided new knowledge and were educational"
	Rated Good or Very Good (%)	-	-	24/25 (96%)	26/27 (96%)	"I liked sharing experiences with other people with TB at the TB clubs" "TB clubs will help reduce TB stigma"

Table 1: Fidelity to ASCOT pilot RCT recruitment, follow-up, study activity completion and participant survey feedback.

Legend: 128/128 (100%) of people invited subsequently agreed to participate, gave informed consent, and were recruited.

Intervention activities marked with a hyphen (-) indicate intervention activities that, as per protocol, were not applicable to particular study arms. \*n=4 participants in the socioeconomic arm who completed a TB club did not give feedback.



**Conclusions:** The ASCOT pilot trial showed that integrated socioeconomic support had optimal feasibility and acceptability to TB-affected households in Nepal and is suitable for large-scale trial evaluation. Cash transfers appeared to incentivize participation in social support activities.

## OA63 Perspective in person-centred care

### OA63-695-18 Psychosocial consequences of TB among people diagnosed through active vs. passive case-finding in Nepal: a longitudinal, prospective cohort study

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**Background:** The psychosocial consequences of tuberculosis (TB) are recognized as a key barrier to ending TB globally. We evaluated stigma, depression, and quality of life (QoL) among people with TB (PTB) diagnosed through active case finding (ACF) and passive case finding (PCF) in Nepal.

**Design/Methods:** We prospectively recruited consecutive adult PTB diagnosed through ACF and PCF strategies in four districts of Nepal between August-2018 and April-2019. We assessed stigma, depression, and QoL at 2-3 months (baseline) and 5.5-6.5 months (follow-up) post-treatment initiation.

Stigma was measured using an adapted VanRie Stigma Scale (VRSS). Depression was measured using a locally-validated Patient Health Questionnaire (PHQ-9) with scores  $\geq 10$  indicating depression. QoL was measured using EQ-5D-5L tool from 0 to 1 (optimal QoL), and a self-rating tool from 0% to 100% (optimal self-rated health).

**Results:** We recruited 221 PTB with mean age 48 years (Standard Deviation  $\pm 16$ ), of whom 147/221 (67%) were men, 111 diagnosed through ACF and 110 PCF. Reported stigma was common but decreased across all VRSS domains for ACF participants and only some

domains for PCF participants between baseline and follow-up (Figure). Levels of depression appeared higher amongst ACF than PCF participants and decreased between baseline and follow-up (14% ACF vs 6% PCF at baseline; 6% vs 3% at follow-up). Self-rated health (68% vs 71%; 79% vs 82%) and EQ-5D-5L scores (0.907 vs 0.938; 0.963 vs 0.978) appeared lower amongst ACF than PCF participants and increased between baseline and follow-up.

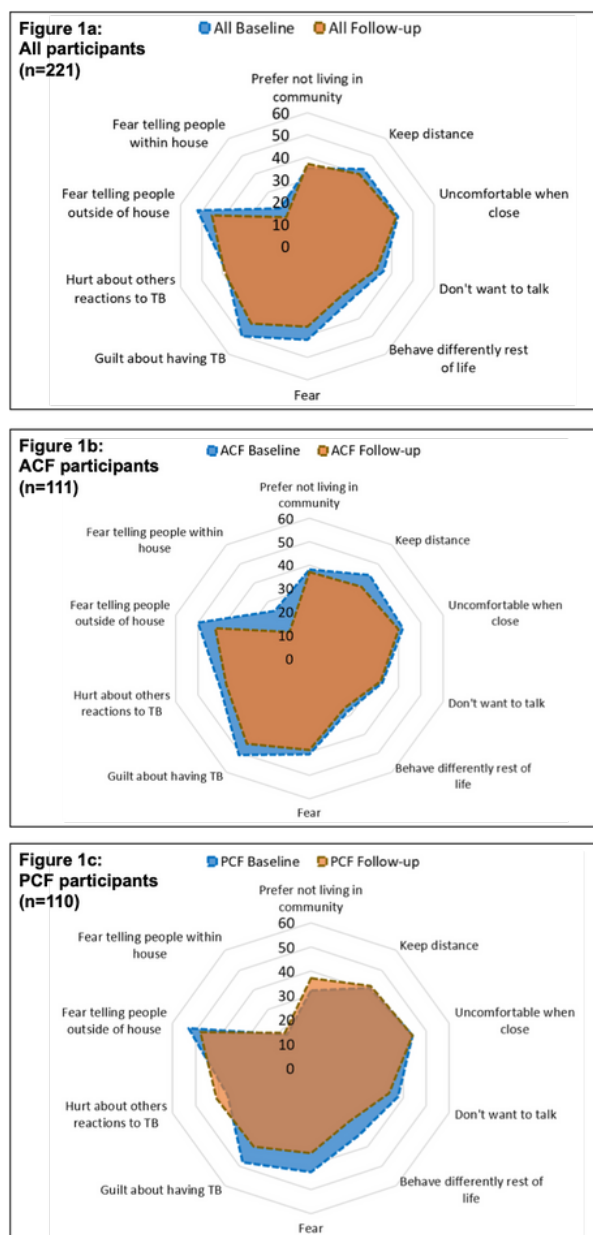


Figure 1. Percentage of all participants (a) and participants diagnosed by ACF (b) and PCF (c) agreeing with items of the Van Rie Stigma Scale at baseline and follow-up.

**Conclusions:** These findings suggest a substantial psychosocial impact of TB in Nepal, which wanes during treatment but is not eradicated, and affects people diagnosed through both ACF and PCF. ACF represents

a point of contact with TB-affected people that is a missed opportunity to provide additional holistic care. Evaluation of psychosocial support interventions, including those integrated with existing ACF activities, is warranted.

### OA63-696-18 Patient preferences for improving TB care in Chitwan District, Nepal: a discrete choice experiment

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**Background:** Understanding patient's preferences for tuberculosis (TB) care is crucial to develop patient-centred TB care.

However, there is a paucity of published literature to determine patient preferences for managing drug-sensitive TB in Nepal.

**Design/Methods:** Using the results of a review of published literature and conducting qualitative patient interviews, we designed a discrete choice experiment (DCE). The choice experiment was completed by 133 participants aged 18 years or above with pulmonary TB. Participants were recruited from 20 public TB treatment centres in Chitwan between December 2022 and February 2023.

The DCE study included six characteristics (attributes) of TB care (patient card, sex of healthcare provider, provision of transportation incentives, provision of psychosocial support, waiting time, and types of TB care provider).

In 24 choice tasks, participants selected their preferred option from 2 hypothetical care models. As part of the study, participants' socio-demographic characteristics including their health status, such as smoking and HIV status, were also collected.

The analysis used a conditional logit regression model to quantify the individual preference utility associated with each attribute.

**Results:** Among 133 patients who participated in DCE (97% response rate, mean age of 47 years, 71% male), 83% had pulmonary bacteriologically confirmed (PBC) TB, and 32% were in the intensive phase of treatment. Patient card with instructions, provision of psychosocial support, and waiting time were the significant attributes associated with TB care.

Patients highly valued TB care services that have the provision of psychosocial support ( $\beta=0.62$ ,  $p<0.001$ ), followed by improved patient card ( $\beta=0.50$ ,  $p<0.001$ ), and the waiting time for TB care within half an hour ( $\beta=0.25$ ,  $p=0.002$ ).

**Conclusions:** People with TB preferred to be supported by psychosocial interventions, improved patient card, and reduced waiting time. This study provides evidence for current/future TB control programme package to align with the patient's preferences.

### OA63-697-18 The Stigma-Free Healthcare Facility Initiative as a tool for patient-centred TB cure and care advancement

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**Background and challenges to implementation:** The Baseline Stigma Assessment conducted in Ukraine in 2021 revealed substantial reserve for reducing stigma and discrimination against people living with TB (PLWTB) by fostering tolerant attitudes among primary healthcare providers, whose role in TB detection and management has increased dramatically due to health-care reform.

The demand for patient-friendly environments has increased due to the COVID-19 pandemic and Russia's military invasion of Ukraine, which have negatively impacted accessibility of services and changed behavioral patterns of both patients and providers.

**Intervention or response:** Aiming at consistent and sustainable long-term intervention into patient-provider trustworthy relationship-building, the USAID-funded project "Support TB Control Efforts in Ukraine" together with Charitable Organizations TB People Ukraine and 100%LIFE launched the Stigma-Free Healthcare Facility initiative comprising medical personnel training on origins of stigma and ways to reduce it, developing, promoting, and evaluating the stigma-free policy (SFP) for healthcare institutions (HCI).

Following the development of training manual on stigma prevention, learning sessions were offered to family physicians and TB specialists throughout the country. The training module and certified on-line course on building tolerant attitudes were integrated into pre/postgraduate medical training curricula.

Responding to advocacy efforts, the National Health Service defined the adoption of SFP by HCI as an accreditation criterion that enabled dissemination of the Framework SFP to individual facilities. A pilot on introduction of SFP implementation monitoring and evaluation is underway.

**Results/Impact:** As on April 2023, despite COVID-19 pandemic and Russia's brutal military invasion, 80 trainers delivered 170 learning sessions on prevention of stigma and discrimination in primary healthcare facilities;

4000 medical professionals from 21 regions of Ukraine strengthened their skills in patient-friendly communication with PLW/TB; 4500 physicians completed certified on-line course; 300 healthcare facilities institutionalized SFP.

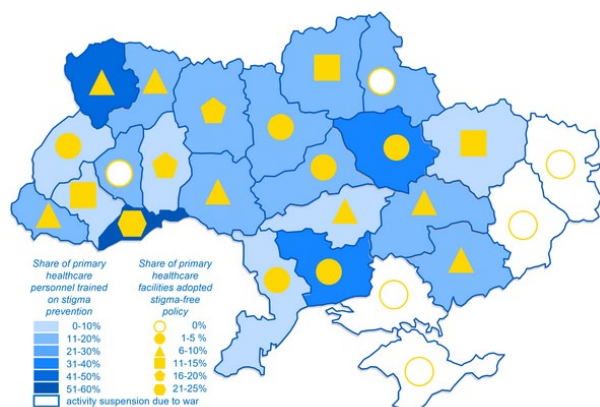


Figure. Status of stigma-free healthcare facility initiative rollout in Ukraine, 2023.

**Conclusions:** Combined effect of capacity-building, education and advocacy efforts is building a critical mass of SFP supporters, thereby transforming the culture of care delivery.

### OA63-698-18 The pivotal role of Kagabays in improving treatment outcomes among people with drug-resistant TB and household contact case-finding at the height of COVID-19 pandemic

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**Background:** Successful treatment outcome rate of drug resistant-tuberculosis (DR-TB) is often relatively low in the Philippines. Following WHO guidelines, the National TB Program (NTP) promotes community-based DOT for DR-TB. We implemented the Community Approach to Control and Halt DRTB (CoACH-DRTB) Project by training volunteers called ‘Kagabays’ (community health workers/CHWs). Kagabays served as DOT providers, Educators and Counselors of persons with DRTB with primary aim of improving treatment outcome.

**Design/Methods:** We conducted a prospective single cohort study in Cavite Province, Philippines. Kagabays followed-up study participants through daily home visits for drug adherence and program retention, with post-treatment follow-up every 6 months for 2 years. At each monthly scheduled visit, a nurse/physician assessed the Kagabays’ outputs during their daily monitoring. Household contacts were followed-up for symptoms screening to assess TB activation within 2 years.

**Results:** From 2019-2022, 57 trained Kagabays monitored 171 study participants in the community. Average monthly adherence was reported at 96% even during COVID-19 pandemic. The Kagabays used mobile app ConnectTB to monitor daily drug intake. 153/171 (89.4%) study participants achieved treatment success, 12 died (7.0%), and 6 (3.5%) were lost to follow-up. Successful treatment outcome is higher “compared” to 73% of those started second-line treatment in 2019 as reported by WHO in 2021, and 65% from a systematic review. Case holding was notably successful: 3% lost to follow-up as compared to 20.3% in 2018 national data. Among household contacts, 10% (8/77) developed active TB within 2-year monitoring. To date, 65% (37/57) Kagabays are currently active community volunteers and majority (81%, 30/37) are now employed by their local government unit.

**Conclusions:** The CoACH-DRTB is an effective program for treatment adherence improvement, loss to follow-up reduction and successful treatment outcome that may be adapted nationwide. Training and deployment of Kagabays should be adapted as an important component of NTP’s patient-centered community-based DR-TB treatment guidelines.

### OA63-699-18 Early results from the community-based, person-centred model of TB care by trained TB survivors in India

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**Background and challenges to implementation:** In India, to contribute to the unmet needs of community-based psychosocial needs of people with TB (PWTB), Unite to ACT- is being implemented in 10 states, with support of India National TB Elimination Programme (NTEP) since August 2021. The project focuses on providing continued psychosocial support to PWTB by trained TB survivors. This document describes the achievements during the first year of project implementation.

**Intervention or response:** Under the project, trained TB survivors provided door-step patient centered services to PWTB including treatment literacy, vulnerability assessment, gender peer counseling, gender family counseling besides others. The objective of the services is to ensure treatment adherence and favourable treatment outcomes. The project data is stored in hard copy (registers) and electronic version (project MIS). A dedicated

monitoring and evaluation team has been appointed to ensure completeness and accuracy of project data.

**Results/Impact:** A total of 1,423 TB survivors (Male-582, Female-841) received training and of these 950 were enrolled in the project (Male-409, Female-541). During January-September 2022, the trained TB survivors provided psychosocial support to 90,117 PWTBs and their families in 80 districts across 10 states. The psychosocial support was appreciated by PWTB and family members. Of the 35,701 PWTB that initiated TB treatment during Jan-Mar22 and reported TB outcomes, 91% (n=32,387) have successfully completed the TB treatment which is ~6% higher than the NTEP reported successful outcomes for 2021 in the same states (Figure 1).

States	Project reported Successful TB outcome, Jan-Mar 2022 (%)	National programme reported Successful TB outcomes, Year 2021 (%)
Bihar	89%	82%
Delhi	86%	74%
Gujarat	91%	89%
Haryana	92%	84%
Madhya Pradesh	91%	85%
Punjab	91%	84%
Rajasthan	92%	85%
Uttar Pradesh	91%	86%
Uttarakhand	92%	87%
West Bengal	89%	83%

\*Proportion of Successful TB Outcomes: Proportion of people with TB who have been reported either as cured or completed, of those who initiated TB treatment

*Figure 1. Proportion of successful TB outcomes\* (cured and completed) reported under the Unite to ACT project, compared to national programme in 10 states of India.*

**Conclusions:** The trained TB survivors, under the project, worked as an extended arm of National TB Programme in community, for successfully providing door-step psychosocial support resulting in higher favourable outcomes amongst TB patients. The project findings show the need for trained TB survivors in the community, to support the TB programmes in their efforts to end TB.

### **OA63-700-18 Nuances, complexities and opportunities of TB preventive therapy delivery in cross-border communities: the case of Beitbridge District Hospital, Zimbabwe**

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**Background and challenges to implementation:** The high-frequency of mobility within cross-border communities increases the risk of vulnerabilities to TB. A twenty-four-month observational study among PLHIV in Zimbabwe, Ethiopia, and South Africa attending routine HIV care is underway to understand TPT uptake, completion, and optimal service delivery models. We describe our implementation experience and outcomes of the retention strategies among highly mobile patients in Zimbabwe.

**Intervention or response:** The BBDH cohort in Zimbabwe is characterised by a mix of urban/rural, mostly self-employed, and highly mobile community with poor mobile network connectivity. HIV care is decanted for ART stable patients through differentiated service delivery (DSD) model. Over 12 months, 221 PLHIV above the age of 18 years were enrolled and followed-up at BBDH to collect information on TPT initiation, adherence, side effects and completion. During the first two months, participants were followed-up telephonically. The subsequent visits (3-, 6- and 12-months) included community visits supported by community health workers and research staff exploring TB care for TB investigation, diagnosis, TPT delivery, uptake and completions.

**Results/Impact:** Telephonically 49% and 47% of study participants at one- and two-months post enrolment respectively were reached due to network challenges and migration into South Africa. During the third month visit (baseline), 74% of study participants returned to the clinics for HIV care. Those not attending clinic visits cited being in DSD models. After implementing community visits (post intervention), 91% and 94% of participants returned to the facilities for HIV care 6- and 12-months post enrolment. 100% of clients in DSD models were reached in the community and 2% migrants were missed.

**Conclusions:** There is strong evidence for Zimbabwe to prioritize integrating TPT delivery with patient centered initiatives such as telehealth, DSD models and outreach programs for highly mobile population. Cross border collaborations between South Africa and Zimbabwe will allow for continuity of care for migrants on TPT.

**OA63-701-18 Early experience of digitally supporting drug-resistant TB patients at a MSF Clinic, Mumbai, India**

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**Background and challenges to implementation:** Persons living with drug-resistant tuberculosis (DRTB) struggle with multiple drugs and toxicities. challenges to adhere and unsuccessful treatment outcomes are caused by lack of knowledge about TB and its treatment, stigma, isolation, negative self-perception, and importantly, lack of timely care and support. Scalable digital solutions may help patients through their treatment journey in the context of limited support lines

**Intervention or response:** From November 2021 to January 2022, the Médecins Sans Frontières (MSF) Mumbai DRTB project piloted a digitally supported treatment (DOST) platform in collaboration with the Sweden Innovation Unit (SIU). Through a specially designed digital application, we provided treatment literacy, adherence support, and increased access to care for 26 patients, as part of this pilot intervention. The platform aimed to decentralize patient management, ultimately improving treatment adherence and psychological well-being

**Results/Impact:**

Features	Type of support provided
Push Notification	Reminders for taking medication
	Motivational messages
	Health promotion messages
Mood reporting	Follow up of psychological well being
	Counselling support and referral to psychologist as per the need
Confidence reporting	Gauge patient's general motivation
	Counselling support in case of lack of motivation
Adherence reporting	Monitor adherence
	Gather information on missed doses in non judgemental way
Side Effect reporting	Side effect follow up
	Referral to the doctor
Posters	TB education
	Test knowledge
	Test improvement knowledge
TB IEC videos	General education on TB
	Health promotion
Patient testimonial videos	Experience sharing by post TB patients – challengs faced during TB treatment

Table 1: Features of Digitally Supported Treatment (DOST) Application.

We observed that the application assisted patients in adjusting their attitudes toward the disease and its treatment. The medicine reminder feature reduced patients'

reliance on family members to take their medications on time. Patients were able to overcome their fear of the disease thanks to the TB information provided in the form of quizzes and testimonial videos. Through the application, patients communicated their mood and side effects to counsellors.

As a result, counsellors were able to assist patients as needed. We faced technical challenges such as the requirement to enter the password multiple times, the app's unavailability on non-Android phones, and glitches in medicine reminders.

**Conclusions:** The DOST app demonstrated several features of person-centeredness and the ability to act as a robust interface between the health care delivery system and the person living with DR-TB during the initial experience. The platform was well received by users, but technical issues remain to be addressed

**OA63-702-18 Risk factors associated with TB disease in patients attending health facilities in Rwanda**

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**Background and challenges to implementation:** Conducting a risk factor study in Rwanda is crucial to identify the factors contributing to the disease burden. Understanding the risk factors associated with TB can help in target screening and early detection, reducing transmission, and improving patient outcomes. Rwanda has 28% of TB missing cases according to the WHO global TB report in 2021 The aim of the study was to identifying risk factors of pulmonary TB to inform policy and public health strategies to reduce the incidence of TB in the country.

**Intervention or response:** This is a case-control study conducted in centers for diagnosis and treatment of TB in Rwanda. Three control participants matched for one case. Descriptive and logistic regression analysis were computed.

**Results/Impact:** This study included 2293 participants, with 676 cases and 1617 controls. Descriptive analysis showed that cases were more likely to have a history of smoking, alcohol consumption, being underweight, HIV-positive status, and contact with TB cases. Multivariate logistic regression analysis revealed that factors such as being male (aOR=1.4[95% CI: 1.01-1.87]), hav-

ing a BMI less than 18.5 (aOR=2.4[95% CI: 1.50-3.87]), a history of imprisonment (aOR=1.80[95% CI: 1.04-3.02]), and contact with TB cases (aOR=1.6[95% CI: 1.08-2.46]), and not being aware of such contact were associated with high odds of contracting pulmonary TB.

Conversely, living in a union (aOR=0.7[95% CI: 0.49-0.90]) and having a BMI greater than or equal to 30 (aOR=0.1[95% CI: 0.02-0.54) were associated with low odds of developing PTB.

**Conclusions:** The study highlights that Males, individuals with a BMI less than 18.5, those with a history of imprisonment or contact with TB cases, and those who are unaware of their family's TB status were identified as high risk groups for TB. These findings underscore the importance of healthcare providers considering these risk factors during the screening of TB presumptive cases in Rwanda. Effective screening and early detection can lead to timely treatment, reducing transmission and improving outcomes.

## OA64 Sustainability of accessing services translated into quality care

### OA64-703-18 Improving TB cure rate at private not-for-profit diagnostic treatment units in Busoga Sub-region, Uganda

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**Background and challenges to implementation:** The Ministry of Health of Uganda requires that 90% of all Tuberculosis (TB) cases receiving treatment get cured. Busoga is among the TB high burden regions. Between January and March 2022, 20 Private not for profit (PNFP) Tuberculosis (TB) diagnostic treatment units diagnosed 74 new and relapse Pulmonary Bacteriologically Confirmed (PBC) cases and were initiated on TB treatment and only 42 (54%) got cured.

The Uganda Protestant Medical Bureau's USAID funded project; Local Service Delivery for HIV and AIDS Activity (USAID/LSDA) sought to increase the TB cure rate in Busoga region.

**Intervention or response:** USAID/LSDA supported 20 diagnostic and treatment Units in Busoga to build capacity of Health workers through trainings and mentorships

on Integrated Comprehensive Tuberculosis and management guideline. Started a TB clinic day, instituted the use of TB appointment registers, aligned appointments with the date for sputum smear follow up, follow up of patients and community delivery of anti TB medicines. Performance reviews were conducted. Documentation gaps were addressed through data triangulation.

**Results/Impact:** From January- March 2022 to January-March 2023, TB cure rate improved from 57% to 94%

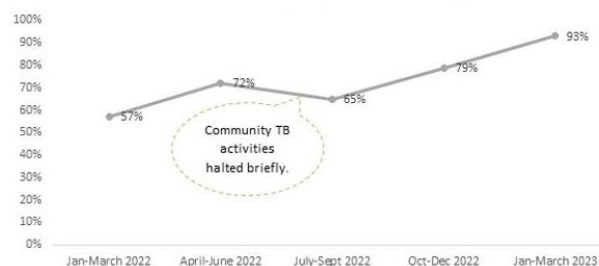


Figure. Cure rate among TB patients in Busoga.

**Conclusions:** Addressing TB community stock challenges, instituting TB clinic days, utilizing TB appointment register, proper documentation and delivery of community services coupled with capacity building of health workers improved TB Cure rate among TB patients. Provision of tailored TB community services such as community drug distribution and sputum follow ups improves TB treatment outcomes.

### OA64-704-18 Ensuring sustainable TB case detection and active case-finding in the context of war and COVID-19

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**Background and challenges to implementation:** Previously in Ukraine, TB contact investigation and active case-finding in Ukraine was difficult due to healthcare system challenges and ongoing reform, and unclear policies and definitions, for example, for index cases. Contact tracing was also deprioritized. Data from 2019 revealed that 10.9 TB cases were identified per 1,000 contacts.

**Intervention or response:** In response, STBCEU project, funded by USAID and implemented by PATH, invested in policy strengthening, creation of contact investigation algorithms and SOPs, and involved TB family doctors and epidemiologists in contact tracing. Training curricula were developed on a range of topics, with training and mentoring being provided through TB Training Hubs and in clinical settings. This assistance also included monitoring visits to remote areas to organize screenings for TB contacts.

**Results/Impact:** Between January 2020 to December 2022, 17,753 Index Patients (IPs) were investigated, and 45,843 contacts identified (2.6 contacts per IP). Of these, 39,727 contacts (86.7%) were screened for TB, of which 1,087 were identified with active TB (27.4 per 1,000 contacts). Between 2020 and 2022, active TB detection among contacts has steadily increased, despite the war.

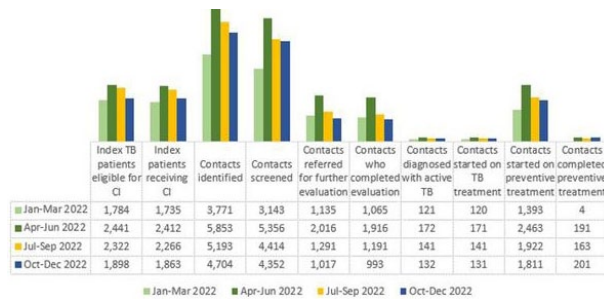


Figure. STBCEU CI cascade January-December 2022.

**Conclusions:** The investments in systematic TB contact investigation policies, procedures, training and monitoring and evaluation have led to important improvements in identifying active TB among contacts, with the numbers of TB cases being identified through contact investigation steadily increasing, even in the context of COVID-19 and the war.

We conclude that these higher rates are due to improved clinical and case management capacity and clarified policies and algorithms, resulting in improved detection (and faster links to treatment), as well as higher actual rates of TB due to living conditions resulting from war, although this requires more investigation. This approach has proven robust in the most difficult circumstances and has been recommended for national expansion.

**OA64-705-18 Feasibility and effectiveness of mobile clinics in increasing access to TB services in conflict-related settings: examples from Syria**

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**Background and challenges to implementation:** Since 2011, conflict in Syria has resulted in displacement, destruction of health facilities, and loss of skilled staff. This has led to breakdown in TB diagnostic and treatment networks and 30% decrease in annual case notification.

While the Global Fund’s Middle East Response grant through IOM and WHO has supported drug and diagnostic procurement, it does not address crucial gaps such as renovating peripheral health facilities. TB patients have to travel far leading to delayed diagnosis and lower notification rates. MOH collaborated with partners to extend primary care services closer to people.

**Intervention or response:** Three mobile clinics, each with an x-ray technician and nurse, were strategically deployed in Aleppo, Rural-Damascus, and Deir-Ezour governorates. The vans were linked to the governorate TB clinic and announced their arrival through local health facilities before visiting a town.

Symptomatic patients underwent simultaneous digital X-ray and sputum collection, and the digital film was shared with the chest physician at the governorate clinic through WhatsApp. Sputum samples were transported to the TB lab and results given to patients within two days via the local health facility. Local health workers supported TB patients in starting and completing treatment, and updating records regularly.

**Results/Impact:** Annual case notification rates increased by about 20% in 2021 in the three governorates, despite COVID-19. By end 2022, 50,717 patients were evaluated, 6,417 chest x-rays performed, 4,941 symptomatic individuals identified, 3,822 sputum samples collected, and 562 (11%) TB patients notified and treated; 6,258 household contacts were provided TB preventive therapy.

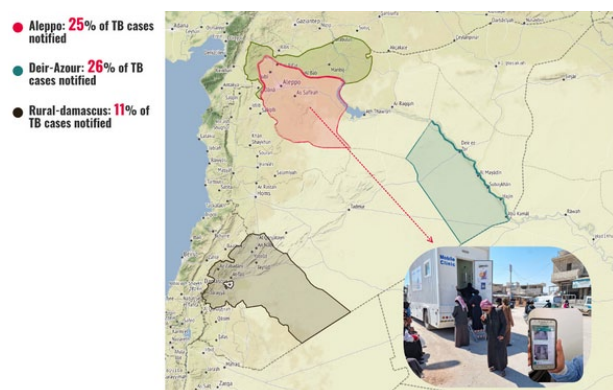


Figure 1. Additional TB cases notified in Syria through mobile units in 2021 and 2022.

**Conclusions:** Mobile clinics are a highly effective intervention in reaching underserved communities in conflict-affected settings like Syria, facilitating early diagnosis of TB and with significant potential to increase case finding. Additional analysis around cost-effectiveness will strengthen the case to scale up mobile clinics in humanitarian crises.

#### OA64-706-18 Impact of innovative strategies and multisectoral collaboration on TB screening, diagnosis and treatment during active case-finding activities among informal settlers in Parola, Manila City, the Philippines

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**Background and challenges to implementation:** Implementation bottlenecks such as inadequate social preparation during Active Case Finding (ACF) activities create testing and diagnosis delays, increasing early lost-to-follow-up especially among hard-to-reach communities. Innovative strategies are needed to address these challenges and enable effective and efficient ACF implementation.

**Intervention or response:** The USAID's TB Platforms Project collaborated with the Manila City Health Department, Parola village leaders, civil society organizations, and other development partners to conduct ACF activities using a "one-stop-shop" health and social services caravan approach for informal settlers. Community Health Workers (CHWs) conducted community and social preparation activities.

The one-stop-shop caravan approach provided onsite chest x-ray screening and TB testing using TrueNat, COVID-19 vaccinations, deworming, family planning and counseling services, access to child feeding pro-

gram, issuance of identification documents, and dance classes. The one-stop-shop caravan provided TB screening services along with other health and social services to increase participation. Contact Investigation (CI) was implemented for newly diagnosed cases.

**Results/Impact:** This intervention reached 4,193 community members by providing multiple health and social services leading to 1,039 individuals screened for TB, 207 (20%) presumed to have TB, 175 (85%) tested with 45 bacteriologically confirmed (BC) TB cases, and 23 clinically diagnosed TB cases. Of the 45 BC cases, 35 (78%) were enrolled in treatment. To find one BC case, 47 individuals must be screened. The overall yield from the activities was 4%. CI of 73 TB contact persons resulted in 13 children (18%) diagnosed with active TB and 2 (3%) with latent TB. All 15 were enrolled into treatment.

**Conclusions:** Implementing innovative strategies, supported by multisectoral collaboration, are key to raising community uptake of TB services and completing the TB cascade of care. Using evidence to identify target sites and populations to cover during ACF activities is instrumental in increasing case-finding efficiency and yield.

#### OA64-707-18 Outcomes of differentiated TB preventive therapy service delivery models in Nairobi slums, Kenya

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**Background:** COVID-19 pandemic containment measures necessitated restructuring tuberculosis (TB) Preventive Treatment (TPT) service delivery models for continuity of care. Pre-COVID-19, Ministry of Health (MOH) standard of care (SOC) for TPT recommended bi-weekly drug collection in the first month and monthly thereafter.

During the COVID-19 pandemic, the MOH provided guidance allowing alignment of TPT with ARV refills as a differentiated service delivery (DSD) model.

We evaluate the implementation and outcomes of TPT DSD and SOC models in 14 Eastern Deanery Aids Relief Program (EDARP) clinics in Nairobi slums.

**Design/Methods:** In this evaluation, clients were allocated to DSD or SOC based on their preference, appointment keeping history, and available support systems. Clients on DSD models received adherence counseling, initiated on treatment, and subsequently



followed up weekly using text messages, telephone calls, or home visits. Based on stock availability, clients were provided either three months of weekly rifapentine and Isoniazid (3HP) or six months of daily Isoniazid(6H). EDARP adapted its electronic medical record systems to support DSD documentation. Using MS-Excel® and Epi-info®, we calculated frequencies, proportions, and odds-ratios (OR) with 95% confidence intervals (CI) to describe PLHIV on TPT DSD and SOC models from October 2020–September 2022.

**Results:** Overall, 3,002 PLHIV including 2,502(83.3%) on 3HP and 500(16.7%) on 6H were initiated on TPT. Among those on 3HP, 2,316(92.6%) completed treatment (TC) while 368(73.6%) completed 6H.

PLHIV on 3HP DSD (n=1,684) were more likely than those on SOC (n=818) to complete treatment [OR,6.9, 95% CI:(5.1-9.2)] and less likely to be lost to follow-up (LTFU) [OR,0.06, 95% CI:(0.02-0.20)].

Of PLHIV on 6H, (n=196) in DSD there was no difference in TC and LTFU among those on DSD and SOC [OR,0.8, 95% CI:(0.6-1.2)] and [OR,1.4, 95% CI:(0.7-2.8)], respectively.

**Conclusions:** Scaling-up TPT DSD models may improve treatment outcomes in combination with 3HP. Client self-selection into DSD models could have contributed to better outcomes

### OA64-708-18 Implementation of differentiated service delivery models for TB treatment in North Central Nigeria

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**Background:** COVID-19 catalyzed piloting differentiated service delivery (DSD) models by Nigeria's National Tuberculosis (TB) Program, which include multi-month dispensing (MMD and remote monitoring. These models are adapted from successful client-centered approaches of Nigeria's HIV program.

To assess feasibility and effectiveness of DSD for TB treatment, we implemented a MMD model with remote monitoring from September 2021 to September 2022 across thirty facilities in Benue and Plateau States.

**Design/Methods:** We prospectively enrolled 1000 patients with drug-susceptible, pulmonary TB into a 2,3,1 MMD model, to align with sputum sample collection for follow-up examination after months 2, 5, and 6 of TB treatment.

We remotely monitored patients' adherence and treatment progress via biweekly phone calls during the intensive phase and monthly thereafter and documented treatment outcomes.

For comparison, we collected baseline data from similar patients enrolled in TB treatment at the same facilities from September 2018 to February 2019 (the "baseline cohort"). We used descriptive statistics to summarize patient characteristics and a chi-square test to compare treatment outcomes between cohorts.

**Results:** One thousand patients enrolled in the DSD model: 38.3% female, 36.0% aged 30–44 years, 31.4% HIV-positive, and 64.5% had bacteriologically-confirmed TB. Among 8194 adherence assessments, self-reported adherence was "good" (>80% of pills taken) at 8081 (98.6%) assessments.

Treatment outcomes were: 44.8% cured, 38.8% completed, 9.1% died, 4.3% lost to follow-up, 0.2% treatment failure, 1.4% removed from register (e.g., drug-resistant TB), 0.6% stopped treatment, and 0.8% not evaluated.

After excluding four facilities without baseline data, 862 DSD patients were compared to 465 patients in the baseline cohort. Treatment success rates were not significantly different (82.5% vs. 81.5%, p=0.41) for the DSD and baseline cohorts.

**Conclusions:** The DSD model showed promise in achieving successful TB treatment outcomes under project conditions. Capacity for remote monitoring is a consideration for scale-up plans.

### OA64-709-18 Drone (unmanned aerial vehicle) - a new vehicle for TB drugs and sputum sample transportation in Himachal Pradesh, India

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**Background and challenges to implementation:** The mountainous terrain of district Mandi in Himachal Pradesh, India has several hard-to-reach areas where timely transportation of sputum samples and TB drugs remains a challenging task.

The present study was conducted to assess the impact of use of drone (Unmanned Aerial Vehicle) services in ensuring early case detection in hard-to-reach areas of Himachal Pradesh.

**Intervention or response:** Based on the recommendations of a feasibility study, Himachal Pradesh government deployed drones (UAV) for transportation of sputum samples and TB drugs. In January 2023, five peripheral health institutions (PHIs) in hard-to-reach areas of district Mandi were identified for drone services. Use of drones in service delivery was analyzed in terms of early diagnosis of TB cases, reduction in transportation distance and operational cost.

**Results/Impact:** Total 32 transportations were completed by the drone from February 2023-March 2023 across five most hard-to-reach PHIs of district Mandi. Drones transported 53 drug boxes from district store to these PHIs and 169 sputum samples in a return flight to NAAT site. Flights were conducted daily on a rotation basis. Prior to deployment of drones, sputum samples were transported once a fortnight to NAAT site and TB drug boxes once a month. This led to delays in TB diagnosis and treatment initiation in hard-to-reach areas. With drones in operation, early case finding, and treatment initiation was made possible.

During the study period, drones travelled cumulative aerial distance of 318 Kilometer (km) (average distance of 10 Km/flight) in comparison to road transportation distance of 835 Km (average distance of 26 Km/travel), thus reducing transportation distance by 2.8 times and reducing operational cost of transportation by 2.4 times.



*Drone (UAV) transporting sputum sample in District Mandi in Himachal Pradesh, India.*

**Conclusions:** Deployment of drones (UAV) ensured early detection of TB cases in high-altitude hard-to-reach areas. The study strongly recommends scaling-up of drone services in similar hard-to-reach geographies.

### OA64-710-18 Taking DOTS services out of health facilities to traditional rehabilitation homes in hard-to-reach rural community: a conceptualised community-based TB care model for improving TB case-holding

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**Background and challenges to implementation:** TB case holding is as essential as TB case finding in the global fight towards ending tuberculosis. Diagnosed TB cases not placed on treatment continues to be a source of transmission of TB disease, consequently increasing the burden of TB disease. Treatment initiation for TB patients who may have difficulty accessing TB services in health facilities can be done in the community to ensure they are in care.

With the support of the USAID-funded TB-LON 3 project, 33 DS-TB patients were diagnosed through symptomatic TB screening done in 2 traditional rehabilitation homes located in a hard-to-reach community in Ogun state. The nearest health facility DOTs center to the homes is several kilometers away, making access

to facility care difficult and constituting a potential risk for catastrophic cost to patients which can cause pre-treatment or treatment LTFU.

**Intervention or response:** Two carers were selected in each rehabilitation home as treatment supporters and DOTs officers. They were both trained on DOTs services provision, including documentation of patient treatment cards and collection of follow-up samples. Daily DOTs are observed for patients with proper documentation of the recording and reporting tools.

The local government supervisor carries out a monthly mentorship and supervisory visit to the homes for quality assurance. Follow-up samples were transported to the AFB site by a sputum transporter.

**Results/Impact:** All the 33 patients who were commenced on treatment had their first follow-up sputum samples AFB test converted to negative accounting for 100% sputum-conversion rate, which suggests that the innovative community-based DOTs services could be as efficient as the health facility-based DOTs services when appropriately monitored.

**Conclusions:** When accessibility to facility-based TB care poses a programmatic challenge with a potential risk of LTFU, adopting an innovative patient-centered, community-based DOTs services model can stand as a reliable alternative to mitigate against LTFU and therefore improve TB case holding.

## OA65 Improving TB Diagnosis and Care

### OA65-711-18 Childhood TB case finding among PLHIV in USAID/PEPFAR supported countries: achievement and gaps data analysis

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**Background and challenges to implementation:** TB remains the most common cause of death among children living with HIV (CLHIV), with an estimated 20,570 (9.5%) of 216,570 CLHIV deaths attributable to TB in 2021. CLHIV are more likely to develop active TB disease after TB infection than HIV-negative children. We reviewed USAID/PEPFAR data on pediatric TB case finding, assessed data in supported countries, and evaluated strategies to reduce gaps in TB case finding among CLHIV.

**Intervention or response:** A retrospective analysis of TB cases among CLHIV (<15 year-old) in USAID-supported countries was conducted using PEPFAR data for fiscal years 2019-2022.

We calculated the TB screening yield and treatment initiation for children living with HIV over time and compared results to adults.

**Results/Impact:** In 2022, TB screening positivity yield among CLHIV was 3.3 % in quarter two (Q2) and 2.9% in quarter four (Q4) for all PEPFAR countries. While for USAID supported sites it was 2.5% and 2.8% for Q4 and Q2 respectively. These data follow the same trend as for adults' patients with 2.5% at Q4 and 2.8% for Q2 overall in PEPFAR supported countries. This achievement is still well below an expected 5% positivity yield for all CLHIV. In that same year, USAID/PEPFAR-supported sites initiated TB treatment for 2,499 (35.3%) CLHIV out of 7,078 children diagnosed with TB in PEPFAR supported countries. The number of CLHIV diagnosed with TB decreased from 13,724 in 2021 to 7,078 in 2022 (48.42%) overall.

**Conclusions:** Low TB screening yield among children and adults living with HIV warrants the use of more sensitive and innovative tools such as stool based diagnostics and digital chest Xray with CAD-AI to find the missing TB cases.

This should be supported with routine screening at every clinical encounter and systematic screening at all entry points.

### OA65-712-18 TB diagnosis among symptomatic and asymptomatic household contacts of PTB patients: significance of chest X-ray screening

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**Background and challenges to implementation:** Systematic treatment of latent TB infection is part of the End TB Strategy and achieving  $\geq 90\%$  coverage among close contacts with pulmonary TB is global priority. Active TB is to be ruled out before initiation of TB preventive treatment (TPT).

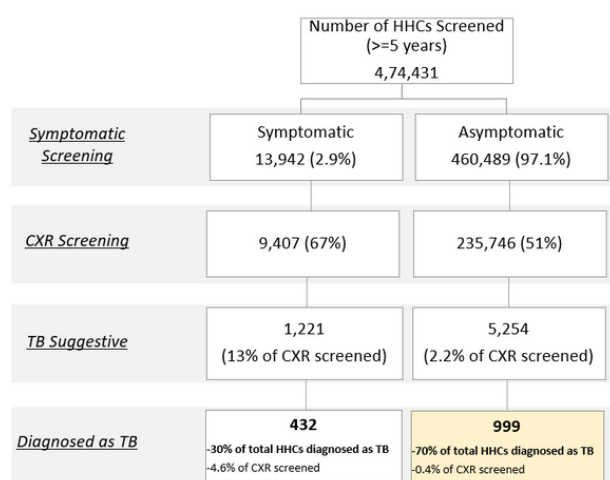
India's TPT guidelines recommend screening eligible HHCs using chest X-rays (CXR). National TB prevalence survey of India (2019-2021) reported 'only' X-ray abnormalities of 42.6% compared to 20.3% with 'symptoms and X-ray abnormality'.

This indicates the importance of using CXR examination in TB screening activities.

**Intervention or response:** Joint Effort for Elimination of TB (JEET 2.0) project, funded by the Global Fund is being implemented with an aim to initiate TPT among HHCs of pulmonary TB patients in 65 districts across 11 provinces of India.

CXR screening of all eligible HHCs ( $\geq 5$  years) is mandatory to rule out active TB, regardless of TB symptoms. HHCs identified as TB suggestive are referred to District TB Centre for confirmation of TB diagnosis.

**Results/Impact:** Around half million HHCs were screened for symptoms in one year (2022), of which 2.9% were identified as symptomatic. Project conducted CXR for more than half of the listed HHCs (~245K). Overall, 2.6% (6,475 HHCs) of CXR screened HHCs were identified as 'TB suggestive', this proportion is significantly higher (13%) among symptomatic than asymptomatic (2.2%). Furthermore, 4.6% (432 out of 9,407) of all symptomatic, CXR screened are diagnosed with TB while in the case of asymptomatic, it is ~0.4% (999 out of 235,746). 70% (999) of TB-diagnosed HHCs (1431) were asymptomatic during symptom screening.



**Conclusions:** The use of CXR screening among all eligible HHCs can help identify people with TB who otherwise will be missed if only screened for TB symptoms. Outcome is consistent with the findings of TB prevalence survey (2019-2021) that high proportion of TB cases would go undiagnosed without chest X-ray.

### OA65-713-18 The role of artificial intelligence in community active TB case-finding: a review of portable digital X-ray with computer-aided detection activities in Delta State, Nigeria

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**Background and challenges to implementation:** The organization of population screening with artificial intelligence (AI), particularly for socially important diseases, is one of the promising areas in the era of digitalization of medicine. In endemic areas, the prevalence of undiagnosed TB may rise as a result of insufficient

community-based case detection. For efficient and effective approach, there are a variety of screening methods that can be used in a mobile device with various technologies, such as Potable Digital X-Ray with Computer-Aided Detection (PDX-CAD). Hence, this study is aimed at determining the role of AI in community active TB case finding.

**Intervention or response:** KNCV Nigeria have is implementing community active case search in Delta state Nigeria using PDX-CAD. In 2022, clients were screened, and presumptive clients were identified using PDX-CAD. Identified presumptive TB clients are further evaluated using molecular WHO recommended rapid diagnostic tests (mWRD).

Data from KNCV Nigeria intervention data base was obtained. Information on number of Persons screened, number Presumptive identified, number of presumptive evaluated and number of diagnosed TB cases was extracted and used for this study. Analysis was done using descriptive statistics.

**Results/Impact:** A total of 14280 clients were screened for TB using PDX-CAD. Presumptive clients identified were 1426 (10%) and all were evaluated. The total Clients that were confirmed to have TB were 19% (n=1426; 270), of which 76% (n=268; 204) were confirmed by expert evaluation of X-Ray film, 1% (n=268; 2) were diagnosed by Trunat MTB-RIF assay and 23% (n=268; 62) were diagnosed using Xpert MTB-RIF assay.

**Conclusions:** In the result, a 19% TB yield out of 1426 presumptive yield using PDX-CAD shows a substantial potential of the PDX-CAD to detect TB if more number of the machine is deployed. Targeted ACF and support services improve health by promoting early, effective detection, enhancing therapy, and preventing the spread of TB and disease.

### OA65-714-18 Is public-private mix the way to end the TB epidemic? A case study of patent medicine vendors in five high-burden local government areas in Kano, Nigeria

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**Background and challenges to implementation:** Public-private mix (PPM) is a widely recognized strategy to improve tuberculosis (TB) prevention and care. The private health sector contributes as high as 70% to the health care delivery system in Nigeria (Health, March 2021) [1]. In Nigeria, 66% - 92% of all cases of respiratory diseases including those with symptoms suggestive of

tuberculosis, utilize the Patent medicine vendors as the first point of contact in the communities due to provision of easily accessible and affordable care. (Obioma Chijioke-Akaniro<sup>1\*</sup>, September 2022)[2]

**Intervention or response:** KNCV Nigeria with support from USAID is implementing the TB LON 1 & 2 project in Kano state, the PPM negotiated model was implemented in 5 LGA's. KNCV Nigeria partnered with patent medicine vendors association to identify, map and mentor 150 PMVs on TB Screening, presumptive identification, and linkages to treatment facilities. Based on their performance KNCV scaled up by additional 130 PMVs. Performance based Incentives was provided as a motivation, and the cascade data for October 2020 to June 2021 was compared with October 2021 to June 2022 and analyzed.

**Results/Impact:** Between Oct 2020 and June 2021, of the 5112 TB cases diagnosed and notified in the five high burden LGA's, PMV's contributed 36% of the total TB notification. Again, between October 2021 and June 2022; of the 8105 TB cases diagnosed and notified in the five burden LGA's PMV's contributed 43%. There was an observed increase of 59% in TB cases diagnosed and notified and a 92% increase in PMV contribution between the periods compared.

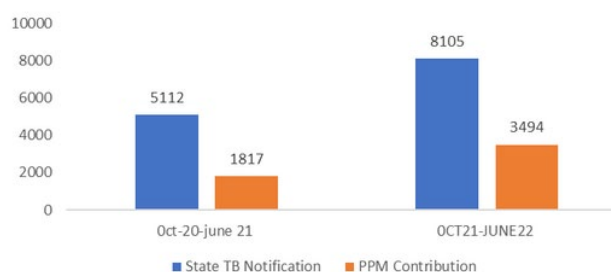


Figure. PMVs contribution to overall TB case finding in 5 high burden LGAs in Kano State.

**Conclusions:** Results demonstrates scalability potential of the intervention as a linear correlation exists with added PMVs and TB cases detected. We recommend further studies brought to scale in similar settings of high private sector healthcare contributions as this might well be a veritable roadmap to END TB.

### OA65-715-18 Private sector engagement in the TB cascade of care: a meta-analysis of TB REACH projects

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**Background:** In many high tuberculosis (TB) burden countries, individuals with TB often first seek care from a variety of private healthcare providers working outside of national TB programs (NTP). Effective links between

the NTP and private providers are essential to retain individuals in the cascade of TB care. We collated results from TB REACH projects implementing private sector engagement (PSE) strategies to understand yield of different PSE models and how these affect loss to follow-up across key junctures of the cascade of care.

**Design/Methods:** We retrospectively analyzed process indicators from 44 TB REACH projects from Waves 1-6. We calculated the number needed to screen (NNS) to identify a person with bacteriologically positive TB, and pooled proportions of individuals retained across several junctures of the TB cascade: screening, presumption for TB, testing, bacteriological confirmation, and initiating treatment.

These pooled proportions were disaggregated across different project characteristics and retention interventions (e.g., PSE model, training of providers, incentives, facilitating referral) to compute a random effects meta-analysis of proportions.

**Results:**

		Presumptive (n = 62)	Tested (n = 59)	Bact+ (n = 61)	Treatment (n = 40)	Pooled estimate as % (95% CI)	
						Tested / presumptive (n = 55)	Treatment / bact+ (n = 35)
<b>PSE model</b>	Private screening only (n = 20)	117,319	90,876	8,178	4,347	75.14 [68.36-81.92]	83.20 [73.26-93.14]
	Public notification only (n = 11)	202,705	185,057	16,393	11,321	86.92 [82.60-91.24]	81.31 [75.91-86.71]
	Follow NTP guidelines only (n = 15)	91,339	72,050	9,146	2,549	70.09 [57.57-82.61]	79.53 [56.57-102.48]
	Multiple (n = 8)	48,177	43,408	5,057	4,913	63.44 [24.50-102.37]	86.88 [74.47-99.28]
<b>Screening-diagnosis referral</b>	Patient determined (n = 17)	171,064	150,437	17,643	10,137	74.42 [66.59-82.25]	
	Provider monitored (n = 6)	40,095	35,218	3,048	2,857	81.20 [74.90-87.50]	
	Provider incentivized (n = 7)	15,771	5,749	754	71	43.03 [10.77-75.29]	
	Provider mediated (n = 26)	214,303	182,784	17,244	10,277	83.16 [80.53-85.79]	

Table. Cumulative persons presumptive for TB, bacteriologically tested, bacteriologically confirmed as TB positive and initiated on treatment across PSE model and referral mediation, as well as pooled proportions for each these two junctures of the TB care cascade.

The NNS was lower for Asian (189 [172-213]) compared to African projects (476 [400-556]). Private pharmacies and drug stores (n=11) had the highest NNS of 500 [417-667], while the formal private providers (n=10) had the lowest of 217 [172-294]. Interventions where providers mediated referral between screening and testing resulted in a higher proportion of presumptive individuals being

tested (83.2%; 95% CI: 80.5-85.8) compared to interventions where people were left to seek diagnostic services at another provider or for themselves (74.4%; 95% CI: 66.6-82.3).

**Conclusions:** This study shows the wide variation in the design and yield of PSE projects, with some evidence that mediating referral across different providers can decrease loss between junctures of the cascade of care. Further study into the design of PSE models and referral mediation could help judge their importance for TB case finding, diagnosis and treatment.

### OA65-716-18 Patient-provider interface model for TB care in Delhi, India

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**Background:** In India with one-fourth of global TB burden, where more than half of patients seek care in private sector, it is imperative to effectively engage the private sector to counter the delay in diagnosis, improve the quality of care (QoC) and treatment adherence.

The Patient Provider Support Agency (PPSA) implementation model was launched in 2018 in Delhi to enhance private sector engagement, promote standard TB care practices and access to microbiological confirmation. This cross-sectional study was conducted with the objective of assessing the impact of PPSA on improving the program indicators among private patients seeking care in Delhi.

**Design/Methods:** A secondary analysis was done by comparing various parameters of all private TB patients notified in Delhi on online database (Ni-kshay) in 2017 (before PPSA launch) with 2018. Program parameters analyzed were i) delay in diagnosis, ii) indirect indicators for QoC such as HIV/diabetes status to tackle co-morbidities, available bank details to enable cash benefit transfer, contact tracing for provision of preventive therapy and iii) treatment adherence. Univariate analysis and binomial logistic regression were performed to analyze the impact of the intervention on program parameters

**Results:** There was a fivefold increase in TB notification in the private sector from 1667 in 2017 to 9731 in 2018. The private health facilities actively engaged in notifying patients increased six-fold, from 173 in 2017 to 595 in 2018. Statistical analysis revealed a strong association between PPSA intervention and parameters of QoC (p-value:<0.001). The regression model showed that private patients with known status of HIV (aOR:2.59,95% CI: 1.17-5.72), known status of diabetes (aOR:3.11,95% CI:1.36-7.08), available bank details (aOR:11.6,95% CI:6.19-21.7) and contact traced (aOR:7.2,95% CI:2.29-22.9) were significantly associated with PPSA as an intervention.

**Background and challenges to implementation:** In India with one-fourth of global TB burden, where more than half of patients seek care in private sector, it is imperative to effectively engage the private sector to counter the delay in diagnosis, improve the quality of care (QoC) and treatment adherence.

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**Intervention or response:** A secondary analysis was done by comparing various parameters of all private TB patients notified in Delhi on online database (Ni-kshay) in 2017 (before PPSA launch) with 2018. Program parameters analysed were i) delay in diagnosis, ii) indirect indicators for QoC such as HIV/diabetes status to tackle co-morbidities, available bank details to enable cash benefit transfer, contact tracing for provision of preventive therapy and iii) treatment adherence. Univariate analysis and binomial logistic regression were performed to analyze the impact of the intervention on program parameters

**Results/Impact:** There was a fivefold increase in TB notification in the private sector from 1667 in 2017 to 9731 in 2018. The private health facilities actively engaged in notifying patients increased six-fold, from 173 in 2017 to 595 in 2018. Statistical analysis revealed a strong association between PPSA intervention and parameters of QoC (p-value:<0.001). The regression model showed that private patients with known status of HIV (aOR:2.59,95% CI: 1.17-5.72), known status of diabetes (aOR:3.11,95% CI:1.36-7.08), available bank details (aOR:11.6,95% CI:6.19-21.7) and contact traced (aOR:7.2,95% CI:2.29-22.9) were significantly associated with PPSA as an intervention.

**Conclusions:** In a country with vast and fragmented private sector across diverse settings, private sector engagement for TB care is the game changer for ending TB.

### OA65-717-18 Comparative analysis of informal and formal private sector provider channels in screening individuals with presumptive TB and referrals for TB diagnosis

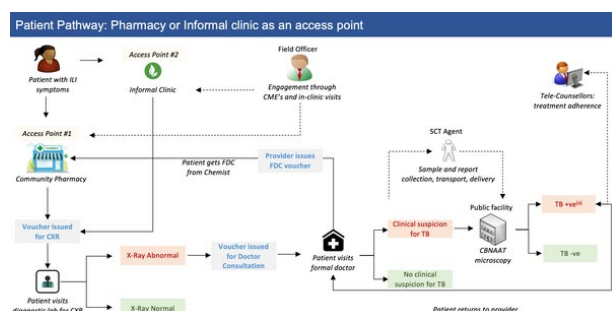
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**Background and challenges to implementation:** Private sector engagement in India is centred around formal providers and has successfully increased private sector notifications from 406,689 in 2018 to 735,784 in 2022.

However, the initial touch points of patients are generally pharmacies, AYUSH and informal providers who are not prioritised due to low TB load and higher cost of engagement.

**Intervention or response:** In a pilot project, pharmacies, informal and formal providers were engaged to disburse free chest X-ray (CXR) vouchers to presumptive individuals who screen positive on TB symptoms. Presumptive individuals' care-seeking journey was analysed for each channel, important metrics and leakages at different stages of the service delivery funnel was studied including voucher redemption ratios, CXR abnormality, NAAT positivity and TB diagnosis rates. The project got implemented in urban and rural pockets of Durg district in Chhattisgarh between Jan'21-Sep'22. 5,463 individuals got free x-rays through the project which were disbursed by 590 active service providers and redeemed by 17 empanelled x-ray labs.



**Results/Impact:** CXR voucher redemption rates were 69% for pharmacies, 82% for informal providers, and 83% for formal doctors, indicating that patients are as likely to get a diagnostic test performed when prescribed by informal providers as formal doctors. CXR abnormality suggestive of TB was 15% for individuals referred by pharmacies, 14% for formal doctors and 11% for informal providers, indicating that pharmacies outperformed both informal & formal doctors in their ability to target symptomatic individuals for CXR. Confirmed TB diagnosis rates were observed to be 11% for pharmacies, 7% for informal providers, and 13% for formal providers.

**Conclusions:** Engagement with private sector entities: pharmacies, informal providers, who are the initial touch points for TB patients, helped in improving screening

coverage. Pharmacies performed well in screening and targeting symptomatic individuals for CXR, their case diagnosis yield of 11% similar to that of formal providers.

### OA66 Moving forward with MPOWER for tobacco control

#### OA66-719-18 Exposure to secondhand smoke at workplaces and public places among adults aged 15 and older in Cambodia: National Adult Tobacco Survey, 2014 and 2021

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**Background:** To see effect of a six-year Cambodia efforts (2014-2021) to address SHS exposures inside work places and public places. In 2014 and 2021, Cambodia conducted third and fourth round of the NATS to gather comprehensive information on tobacco use and key tobacco control indicators.

**Design/Methods:** NATS in Cambodia is a nationally representative household survey of adults aged 15 and older.

NATS data in 2014 and 2021 were used to examine differences in secondhand smoke (SHS) exposure (adults who were exposed to SHS in enclosed public places in the past 30 days) among all adults and by gender. It was a face-to-face interview by using tablets. Sample sizes were 17,642 in 2015 and 5,416 in 2021.

Overall response rates were 93.48% in 2014 and 92.27% in 2021. Data analysis was conducted with SUDAAN to account for the complex sampling design; statistically significant differences ( $p < 0.05$ ) were determined using a two-sample z-test.

**Results:** Overall exposure to SHS inside my workplace decreased significantly from 48.0% in 2014 to 24.50% in 2021 (from 50.3% to 29.88% among males; from 44.3% to 16.62% among females).

Government buildings decreased from 49.4% in 2014 to 17.75% in 2021 (from 53.2% to 20.50% among males; and from 43.90% to 14.28% among females).

Health care facilities decreased significantly from 21.6% in 2014 to 11.54% in 2021 (from 23.2% to 9.78% among males; from 20.10% to 13.12% among females).

Restaurants decreased from 75.80% to 50.95% (from 78.30% among males to 54.80%; and from 73.0% to 46.11% among females).

**Conclusions:** Between 2014 and 2021, significant decreases occurred among Cambodian adults aged 15 and older SHS exposure in enclosed workplaces and public places.

Comprehensive, evidence-based tobacco control interventions can help further reduce exposure to SHS in Cambodia.

Keywords: Cambodia, NATS, Secondhand smoke, Adults.

### OA66-720-18 Engaging concerned stakeholders for removing designated smoking areas from public places and transport: a case study from Bangladesh

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**Background and challenges to implementation:** The first amendment of tobacco control law titled ‘Smoking and Tobacco Products Usage (Control) Act 2005’ passed in 2013 that ban smoking in various public places and all motorized transports.

Several public place and transports were declared 100% smoke free including one room restaurant, hospital, education institutes and Children Park and bus. This law allowed designated smoking area (DSA) in public place and transport that has more than one room or compartment. Around fifty thousand restaurants are serving across the country.

However, GATS 2017 data shows that about 50% visitors were exposed to second-hand smoke (SHS) in the restaurants. VOICE, an NGO discovered that Tobacco Industry is promoting DSA in major restaurants and 73% DSA display tobacco advertisement that violate section 5 (ban on tobacco advertisement and promotion) of the TC law. The air also moves from DSA to smoke-free area while anyone enter to/exit DSA.

**Intervention or response:** The Health Services Division, Ministry of Health and Family Welfare have taken initiative to amend the TC law. Dhaka Ahsania Mission (DAM) is sensitizing concerned government officials & drafting committee members to remove DSA from all public places/transports including restaurant.

DAM also engages policy makers (such as members of parliament), government officials, media and other stakeholders to support the removal of DSA from restaurants. DAM engaged restaurant owners and employees as they are first victim. DAM organized meetings, seminars and workshops at central and regional level with all concerned stakeholders.

**Results/Impact:** Both restaurant owners and workers sent request letter to government to remove DSA from public places.

Through various sensitization meetings, government developed draft law with the proposal to remove DSA from public place and public transports.

**Conclusions:** Tobacco industry put pressure to government against removing DSA. That is why DAM also countering the TIs and support the government on TC law amendment.

### OA66-721-18 Assessing compliance of Tobacco Control Law in broadcast television in Bangladesh, 2019

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**Background and challenges to implementation:** The tobacco control law of Bangladesh bans television from broadcasting any scene depicting smoking or any tobacco use in any cinema, drama or documentary produced or available in Bangladesh. In cinema, if the story necessitates, scenes of tobacco use are permissible provided that written warning about the harmful effects of tobacco shall be displayed on the screen as per the 2015 Rules. The study assesses the compliance with these provisions.

**Intervention or response:** All the drama and cinema contents broadcast in the 19 TV media channels in the total span of 24 hours were captured. Monitoring was done on two separate occasions, during Eid festival period (5 June - 11 June 2019) and regular period (5 July - 11 July 2019) to identify any deviation in the frequency of scenes associated with tobacco use. The length of such scenes, purpose of depiction, health warnings (if any) were recorded in a table for evaluation.

**Results/Impact:** Although the law bans and penalizes scenes depicting tobacco use, most (59 percent) TV media were found to be in violation. Regarding broadcasting cinemas depicting such scenes, the study did not find any TV media complying with proper warning messages. Instances of violation spikes during festival-centered special programs.

In drama, tobacco use appears most frequently in scenes with leisure (40 percent of such scenes), anxiety (23 percent), criminal activities (21 percent). In 56 percent of cases, the smoker is the male protagonist. In case of cinema, tobacco use appears more frequently in scenes depicting criminal activities (62 percent), leisure (19 percent), and anxiety (14 percent).

**Conclusions:** The findings of the study underscore the need to ensure compliance in TV media through strict monitoring. It also suggests that allowing scenes depicting tobacco use “if the story necessitates” also weakens the law and thus, should be eliminated.



### OA66-722-18 Upscaling the implementation of tobacco-free educational institutions in India through mobile-based adherence monitoring and certification

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**Background and challenges to implementation:** Schools represent a critical setting for inculcating health practices and lifestyles among the youth. In India, the National Tobacco Control Program includes focused interventions to promote “Tobacco Free Educational Institution” for which a detailed guideline with nine indicators were issued in 2019.

However, implementation of these guidelines at grass-root level faces challenges in the form of low HR under State NTCP, varying number of schools and size of the districts posing challenges in implementation and enforcement.

The objective of the current study was to explore use of mobile app to make the process of monitoring compliance in schools with TOFEI guidelines more transparent and easier.

**Intervention or response:** We developed a Mobile based Application (Android App) which is used by the district level staff under NTCP or Education Dept, who are designated enforcement officials under COTPA section 6, to facilitate and expedite the process of TOFEI implementation. The app has all the nine criteria used for assessment of TOFEI and also supports real time capture of the signages/ violations in the schools.

The app also generates automated certification for school that complies with at least the first eight indicators and scores the minimum 93 points.

Further, a real time dashboard shows the TOFEI status of the schools assessed to the State Cells for better monitoring and evaluation.

**Results/Impact:** The app has been pilot tested in 4 States (Uttar Pradesh, Karnataka Bihar and Jharkhand) covering more than 150 districts for its feasibility and further implementation challenges and will be soon rolled out in other states on full scale and full experience from this exercise will be presented at the conference. Result will be published within 1 months after pilot testing is completed.

**Conclusions:** Mobile based monitoring system is a feasible option to upscale the implementation of the TOFEI guidelines and facilitating educational institutions go tobacco free.

### OA66-723-18 Setting up a hospital for tobacco prevention using the health promotion approach: an experience from a hospital in Sri Lanka

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**Background and challenges to implementation:** Healthcare professionals play an important role in guiding and supporting people to promote healthy behaviours. The Base Hospital Galgamuwa in Sri Lanka initiated a health promotion approach in collaboration with the Ministry of Health, the Presidential Task Force on Drug Prevention and the Rajarata University.

The project's main objective was to curb tobacco use among hospitalised patients, their relatives, hospital staff, and the local community through comprehensive tobacco use prevention programs.

**Intervention or response:** A selected group of hospital staff underwent a train-the-trainer program that enabled them with substance use prevention knowledge, attitudes, and skills. Tobacco prevention discussions were conducted with the patients, their caregivers and family members who visited them. A “health promotion tool room” was established to give patients and hospital staff a better understanding of tobacco prevention. The hospital infrastructure and atmosphere were changed using simple health promotional tools to promote tobacco prevention strategies.

These included- installing mirrors in the lifts so that people could self-assess their faces, displaying motivational messages on Bed-head tickets (BHTs) and common areas, and establishing tobacco prevention rooms inwards to educate people on company strategies, expenditure and the negative impact of tobacco use.

**Results/Impact:** The effectiveness of the intervention was measured after three months using questionnaire-based pre and post-tests and a telephone-based survey with 310 participants who engaged in the project throughout.

Findings show a reduction in tobacco consumption among 65% of the participants, and 15% quit smoking. The Base Hospital Galgamuwa was successfully transformed into a tobacco prevention centre and became the first “tobacco prevention model hospital” in Sri Lanka.

**Conclusions:** The study highlights the importance of using health promotion approach in tobacco control and the role of healthcare professionals in smoking cessation and tobacco use prevention.

### OA66-724-18 Results from a randomised controlled trial on behavioural intervention for tobacco cessation in tertiary healthcare settings of North India

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**Background:** Tobacco is a significant health problem in public health. Behavioral change intervention is considered one of the most cost-effective interventions; however, changes produced by counseling tend not to persist over time, so it is necessary to implement enforcement mechanisms. Tertiary care settings provide the opportunity to use the treatment for nicotine dependence with intervention for other chronic conditions.

To obtain the evidence, we aimed to evaluate the multicomponent behavioral intervention for tobacco cessation delivered in a tertiary care setting in the current study.

**Design/Methods:** A total of 366 patients who met the inclusion criteria: being motivated, aged over 18 years, having a mobile phone, and being able to read and send messages were included in the trial. Patients were randomized to two groups of intensive and brief interventions, including cessation advice through face-to-face counseling, motivation videos, information leaflet, text messaging, and telephone counseling.

The primary endpoint was the biochemically confirmed patients who stopped using tobacco by six months and confirmed by urinary cotinine assessment. Data were entered in MS Excel and analyzed using SPSS v.22. Trial registration: The study was registered in the clinical trial registry of India and ethically approved.

**Results:** Abstinence rates at the end of six months were 19% with intensive intervention and 13% with brief intervention; however, the difference between the two was not significant for 7-day point prevalence abstinence reported biochemically. Besides, the participant's quality of life, knowledge attitude, and practices were all found to improve with the intervention.

**Conclusions:** The in-person interaction for changing the behavior towards tobacco use was more effective. While the addition of text messages and interaction through telephone for bringing the change was not of much help for the current population.

### OA66-725-18 Availability of smoking cessation support in primary care facilities and communities - analysis by WHO Region

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**Background:** There are 1.3 billion tobacco users globally with over 80% of them in developing countries. This epidemic has annual mortality of over 7 million, with 1.2 million additional deaths from second-hand smoke exposure. The WHO Framework Convention on Tobacco Control (FCTC) obliges member countries to implement tobacco cessation measures to counter the globalization of this epidemic.

This analysis highlights gaps in the availability of health facility- and community-based smoking cessation support across the WHO regions, while also supporting the rationale for a paradigm shift in tobacco cessation strategies.

**Design/Methods:** We accessed the Global Health Observatory portal of the WHO and extracted data on the availability of smoking cessation support in "health clinics and primary care" and "communities". We calculated the frequencies and proportions of smoking cessation support mechanisms.

**Results:** Overall, only 60% of countries globally have smoking cessation support in some health clinics and primary care facilities. The proportion was lowest in the African region – 24% of countries, followed by the Americas (57%), South-East Asia (64%), Eastern Mediterranean (68%), Western Pacific (74%), and Europe (81%).

Community-based support was present in only 41% of all countries, and distributed as follows: Africa (32%), Americas (34%), Eastern Mediterranean (41%), Europe (45%), Western Pacific (48%), and South-East Asia (64%).

**Conclusions:** Forty percent of all countries have no smoking cessation support systems in health clinics or primary care facilities, whilst within communities the gap is as high as 60%. The Africa region has a disproportionately lower availability of support systems, with the European region contrasting sharply across the two domains – 81% versus 45%.

While these figures reflect a low availability of support systems in general, they also signal under-utilization of community support mechanisms which have been shown in some settings to be superior to facility-based measures. Smoking cessation support should be increased to promote tobacco control targets.

### OA66-726-18 Period effect of nicotine replacement therapy inclusion in National Essential Medicine List: evidence from two waves of global adult tobacco survey in four countries

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**Background and challenges to implementation:** The inclusion of NRT (Nicotine Replacement Therapy) in NEML (National Essential Medicine List) is considered as an important enabling policy environment for tobacco cessation.

This study explores the period effect of NRT inclusion in NEML by analyzing GATS (Global Adult Tobacco Survey) data from four countries.

**Intervention or response:** The GATS data from Russian Federation (wave1 2009, wave2 2016 & NRT in NEML 2014), Turkey (wave1 2012, wave2 2016 & NRT in NEML 2014), Mexico (wave1 2009, wave2 2015 & NRT in NEML 2010), and Uruguay (wave1 2011, wave2 2017 & NRT in NEML 2010), were considered for analysis. NRT use among current smokers while making quit attempts in the past year and among former smokers who had quit in the past year was estimated.

Additionally, the policy environment in these countries prevalent before the second wave was analysed.

**Results/Impact:** The NRT use among current and former smokers increased by 4.7% and 17.1% respectively from the first to the second wave of GATS. Decreased use (by 0.7% to 3.6%) of NRT among current smokers, was observed in Turkey, Mexico, and Uruguay. Marginally increased use among former smokers was seen in Turkey, and Mexico but decreased use was observed in Uruguay. NRT was legally sold in all four countries and was available in pharmacies without a prescription (Over The Counter-OTC). NRT cost was fully covered in Turkey and Uruguay in 2010 and 2007, respectively, while NRT cost in Mexico was partially covered since 2014 and not covered in Russian Federation.

**Conclusions:** Increased NRT use among former smokers for quitting following inclusion in NLEM is a positive sign for tobacco control, however decreased use among current smokers while making quit attempts despite its availability as an OTC product is a concern. Awareness about and access to NRT may be explored to increase its use in smoking cessation.

### OA67 Tax measures, tobacco control capacity building and tobacco related epidemiology

#### OA67-727-18 New indicators of global progress on tobacco taxation: statutory cigarette tax rate increases

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**Background:** Statutory excise tax rates are the key policy tools that affect tobacco tax shares and prices. The frequency and magnitude of these rate increases are not widely studied globally but are crucial to how quickly countries raise their taxes to reduce consumption

**Design/Methods:** Data on statutory tax rates on cigarette collected by the World Health Organization over 7 editions of the Report on the Global Tobacco Epidemic between 2008 and 2020 for 195 countries were analyzed. Differences in frequency and size of tax rate increases were examined by WHO region and income group.

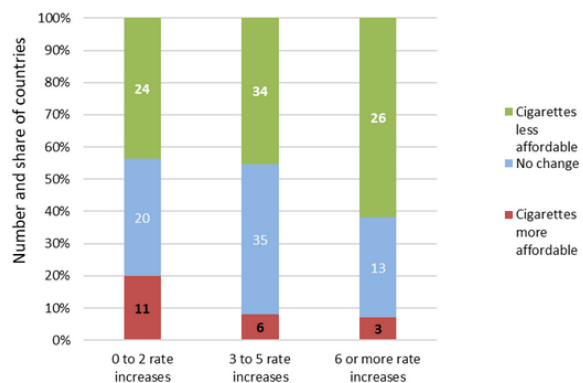


Figure. Countries with more frequent statutory tax rate increases were more successful at reducing cigarette affordability between 2008 and 2020.

**Results:** For 181 countries with complete data, specific excise tax rate increases were nearly 3 times as frequent (mean 2.75 increases, standard deviation 2.18, 64 reporting countries with exclusive specific taxes) than ad valorem rate increases (mean 1.16, SD 1.16, 40 reporting countries with exclusive ad valorem taxes).

Mean specific tax rate increases over 2018-20 were 20% (median increase 8.35%) and typically matched or exceeded inflation rates between those two years in countries that raised rates. The EURO region (mean 4.3 increases) and high-income countries (mean 3.1 increases) had the most frequent tax increases.

Within the European Union, minimum excise duties and the requirement for the excise tax to be at least EUR 90 per 1000 cigarettes and 60% of weighted average price are a framework that obligate countries to adjust rates

more often. More frequent statutory tax rate increases correlated favorably with both total tax share improvements and reductions in cigarette affordability relative to income.

**Conclusions:** Frequent and large statutory tobacco excise tax rate increases are key to insuring countries raise their tax and price and reduce affordability. Lower income countries with large smoker populations have had the fewest tax increases between 2008-20 but have the most to gain in using taxes to reduce consumption.

### OA67-729-18 The Asia Pacific Cities Alliance for Health and Development: building strong leadership for tobacco control

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**Background and challenges to implementation:** Tobacco control is a complex issue that requires a coordinated effort across sectors, and Mayors are key decision-makers in the fight against tobacco use. The Asia Pacific Cities Alliance for Health and Development (APCAT) was established in 2016. APCAT believes that the role of subnational leaders is the key to bring change through good city-level governance.

The objectives of APCAT are to reinforce leadership, build accountability and ensure sustainability.

**Intervention or response:** APCAT's success can be attributed to its emphasis on a comprehensive government approach that enhances political leadership, forges new partnerships, and promotes the efficient utilization of resources to enhance health system performance and outcomes. By bringing together city leaders and stakeholders from different sectors (high level national and regional meetings, trainings, workshops, webinars) APCAT has been able support the development and implementation of effective tobacco control strategies.

**Results/Impact:** Since its inception, the APCAT alliance has grown from 12 cities to 121 cities from 12 countries in 2022 (Bangladesh, Cambodia, India, Indonesia, Lao PDR, Malaysia, Myanmar, Nepal, Philippines, Singapore, Timor-Leste, and Vietnam). The majority of these 121 cities have adopted smokefree local policies. National Mayor alliances have been established in 4 Countries. (Bangladesh, Myanmar, Cambodia and Vietnam). Bogor City, Indonesia, became the first in the country to implement a point-of-sale tobacco display ban, which has since been replicated in 17 other Indonesian cities. 7 Regional Summits have been conducted. Philippines conducted is first national APCAT summit in 2022. The 1<sup>st</sup> APCAT Youth Summit was conducted at the 8<sup>th</sup> APCAT Summit in 2022.

**Conclusions:** APCAT has played a vital role in supporting subnational leaders in the Asia Pacific region to address the significant public health challenge of tobacco use. Its efforts have led to the adoption of new policies,

the replication of successful practices, and the promotion of a comprehensive government approach towards health solutions.

### OA67-730-18 Building capacity at national and sub-national level to strengthen implementation of National Tobacco Control Programme in India

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**Background and challenges to implementation:** Building strong national tobacco control capacity is essential for the sustainability of the National Tobacco Control Programme in India. India's National Tobacco Control Programme faces various challenges, like sub-optimal priority for tobacco control, lack of institutional framework, insufficient human-resources, and limited multi-stakeholder engagement and public awareness.

**Intervention or response:** The data on the program's capacity-building from 2011 to 2022 have been gathered and reviewed. We analysed the effectiveness of various capacity building programmes on the implementation of the programme. In all 213 trainings/workshops at national and sub-national level were conducted by The Union wherein more than 7700 stakeholders across India have been trained and sensitised.

**Results/Impact:** Capacity building involved enhancing the skills, knowledge, and resources of stakeholders and organizations to effectively implement and sustain the programme.

As a result, all states and districts institutionalised a tobacco control implementation mechanism. This led to 106 jurisdictions (districts/cities) that have been declared smoke-free, 15 districts achieved high compliance to various provisions of COTPA.

Tobacco cessation has been scaled up in 3 states which resulting 60,000 health workers trained on providing basic tips of quitting to tobacco users. FCTC Article 5.3 policy notified in 13 states and many districts in few states.

Stakeholders also took initiative and notified ENDS ban, tobacco vendor licensing, ban on loose cigarette in 15 jurisdictions. NTCP Management Information System strengthened across NTCP states. 7 states developed the various resource materials including Health Worker Guide COPTA implementation guidelines and also established networks and multi stakeholder engagement at national and sub-national level.

**Conclusions:** Capacity building is crucial for the long-term sustainability of the National Tobacco Control Programme in India. Through capacity building, stakeholders have been equipped with the necessary skills and resources to effectively implement and maintain tobacco control measures, which will ultimately lead to a healthier and tobacco-free India.

### OA67-731-18 Determinants of smoking and smoking frequency among women of reproductive age in West Africa

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**Background:** Not much is known about the social determinants of cigarette smoking in sub-Saharan Africa. We assessed the determinants of smoking and smoking frequency among women of reproductive age in West Africa. **Design/Methods:** We analysed data from the most recent Demographic and Health Surveys in seven West African countries (n = 114,646). The data were adjusted for sampling weight, stratification, and cluster sampling design. The outcome variables were smoking status and smoking frequency (daily smoking and occasional smoking). The predictor variables included women's socio-demographic and household characteristics. Pearson's chi-squared test and complex sample logistics regression were used to evaluate the relationship between outcome and predictor variables. Statistical significance was set at a p-value < 0.05.

**Results:** The prevalence of smoking was 0.9%. The frequency of daily and occasional smoking was 0.4% and 0.6%. Age 25-34 (AOR:1.97, 95%CI:1.55-2.51, p < 0.001), age 35-49 (AOR:2.46, 95%CI:1.97-3.07, p=0.021), owning a mobile phone (AOR:1.33, 95%CI: 1.08-1.64, p=0.008), and ownership of health insurance (AOR:1.76, 95%CI:1.05-2.98, p=0.033) increased the likelihood of smoking among women.

The odds of daily smoking were associated with age 25-34 (AOR:4.64, 95%CI:2.39-9.02, p<0.001), age 35-49 (AOR: 6.78, 95%CI:3.75-12.28, p=0.008), being poorer (AOR:1.86, 95%CI:1.24-2.79, p=0.003), middle quintile (AOR:1.72, 95%CI: 1.07-2.76, p = 0.026), widowed/divorced/separated (AOR:1.68, 95%CI:1.04-2.71, p =0.033), employment (AOR:2.50, 95%CI:1.15-5.42, p=0.020), working in clerical/sales/services (AOR:1.83, 95%CI:0.74-4.50, p=0.014) and agriculture (AOR:2.09, 95%CI:0.85-5.17, p=0.024).

While age 25-34 (AOR:1.54, 95%CI:1.03-2.39, p=0.007), owning a mobile phone (AOR:1.70, 95%CI:1.25-2.31, p = 0.001), being richer (AOR:1.56, 95%CI:1.11-2.20, p=0.011), and ownership of health insurance (AOR:2.79, 95%CI:1.43-5.48, p =0.003) increased the likelihood of occasional smoking, distance from health facility as a big problem (AOR:0.53, 95%CI:0.37-0.77, p=0.001) and poor gender attitude (AOR:0.51, 95%CI:0.38-0.68, p<0.001) decreased the likelihood of occasional smoking.

**Conclusions:** The study highlights factors that can be used to develop interventions to maintain the low prevalence of cigarette smoking among West African women.

### OA67-732-18 Consequences of tobacco expenditure on the nutrition, health and education in those living below the poverty line in India: a unit-level analysis of National Sample Survey Office data

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**Background:** Tobacco consumption has been found to be associated with increased poverty. Moreover, in the case of India, the problem is pronounced as according to Global Hunger Index 2022, 16% of the population is undernourished, and India ranks 107 out of 121 countries. Tobacco Use in India- absolute term, and it is estimated that approximately 15 million people dropped the poverty line after accounting for their tobacco use (John et al. 2011).

The study aims to quantify the opportunity costs of tobacco expenditure in terms of nutrition (i.e., food quantity/energy), education and health facility forgone if the money is diverted from tobacco towards these domains in the lower income/below poverty line class across the Indian states.

**Design/Methods:** The study is based on unit-level NSSO data corresponding to 2011-12 (68<sup>th</sup> Round). The quantity and value of food item, education and health consumption at the household level for the lower income/below poverty line class were obtained from 68<sup>th</sup> Round NSSO data.

The price of tobacco products and essential cereals, proteins, education and health are computed to analyse the household level nutrition, education and health foregone across the Indian states.

**Results:** The highest proportion of tobacco users was reported from North-East (NE) states of Tripura, Mizoram and Manipur. The average expenditure on tobacco consumption for India was calculated to be INR 497.7802 billion, which could well be translated to meeting the nutritional, education and health requirements of the undernourished/deprived population of India. This expenditure is equivalent to 43.22% of Government of India's total expenditure towards Food and Public Distribution in 2019-20. It is further equivalent to approximately 10% and 50% of current health and education expenditures.

**Conclusions:** The existing difference in the nutritional, education and health status of lower/below-income class households further validate the need for strong regulations for tobacco control in India.

### OA67-733-18 Economic implications and lost life-years averted: predictive estimates for the Indian cigarillos (*bidi*) industry

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**Background:** Indian cigarillos (*bidi*) are a low-cost alternative to cigarettes and treated as cottage industry. Only 22% tax is imposed in contrast to WHO recommendation of 75% while a massive production of less than 4 million per year is exempted from taxation.

Since bidis are just as harmful as cigarettes, this paper attempts to estimate the revenue implications and potential loss of life years (YLLs) averted, if the industry is subjected to increased regulations and taxation.

**Design/Methods:** In a two-fold methodology, revenue estimations after 10% increased regulation and at 100% regulation were done, followed by estimates at tax increase equivalent to cigarettes and WHO recommendation.

Price elasticity for the poorest tertile of consumers was considered to assess demand reduction, and two separate fractions of products (previously regulated - taxed and previously unregulated - untaxed) were used to calculate potential YLLs averted.

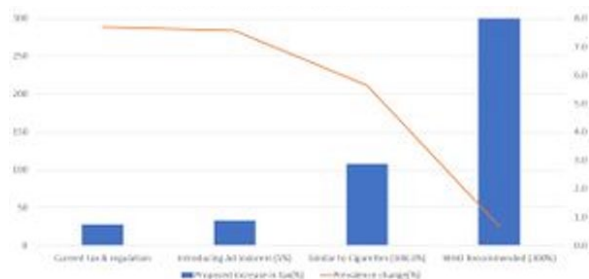


Figure 1. Trends in bidi prevalence as a result of change in taxes.

**Results:** Annual revenue of INR 4.74 billion is obtained by the government at current regulation (20.6%) and taxation (22%). Considering price elasticity of -0.43 and taxes equivalent to cigarettes, 10% increase in regulation will bring the revenue to INR 14.34 billion while averting 695,159 YLLs, and complete regulation (100%) will take the revenue to INR 51.07 billion, while saving 4,527,597 YLLs. At WHO recommended taxation, demand will decrease drastically, with revenue only from

previously regulated proportion of bidi, of INR 4.38 billion. at 10% increased regulation, 2,233,740 YLLs and complete regulation, 10,486,192 YLLs could be averted.

**Conclusions:** The proposed model is WHO recommended as it considers demand elasticity and suggests substantial increase in revenue, while averting potential YLLs due to bidi consumption in India.

Given the unorganised nature of bidi industry in India, there remains a need for national action to build on such innovations, drive the policy decisions for increased regulation and taxation including in revisions to India's tobacco control legislation.

### OA67-734-18 Annual estimates of tobacco product waste in India: a countrywide cross-sectional study

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**Background:** Apart from its health impact, the environmental burden posed by the indiscriminate disposal of tobacco product packaging need to be understood to quantify the exact proportion of hazard posed by the tobacco consumption.

This study was conducted to estimate the waste generated due to consumption of tobacco products in India and various Indian states/Union Territories.

**Design/Methods:** A cross-sectional survey was conducted by gathering samples of cigarettes, bidis and smokeless tobacco products from 33 districts of 17 Indian states. Segregated weights of plastic, paper, foil and filter components of the packaging were taken and data modelling was done using GATS-2 data to assess consumption and estimate the quantity of waste generated by the various products.

**Results:** After exclusion of duplicates, 70 cigarette, 94 bidi and 58 smokeless tobacco brands were included in the final analysis. A total waste of 1,70,331 ( $\pm$  29,332) tonnes was estimated (annually), out of which 43.2% was plastic, 3.6% was foil and 0.8% was filter, while two-thirds of this waste was contributed by smokeless products alone. Maximum waste was generated from the states of Uttar Pradesh (20.9%; 35,724  $\pm$  6,152 tonnes), Maharashtra (8.9%; 15,117  $\pm$  2,603 tonnes) and West Bengal (8.6%; 14,636  $\pm$  2,520 tonnes).

**Conclusions:** To our knowledge this is a first of kind national level figures/estimates on various types of tobacco product waste significantly contributing to the environmental burden from the context of a low- and middle-income country. These findings puts a spotlight on industry behaviour, may reinforce existing policies around regulation of tobacco product packaging and environmental compensation by the tobacco industry.

## OA68 Diagnosis for TB Diagnosis

### OA68-735-18 Whole-genome sequencing of drug-resistant TB strains

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**Background and challenges to implementation:** Drug-resistant tuberculosis (DR-TB) poses a significant threat to global public health and three countries India, China and Russia account for almost half of all cases. Whole genome sequencing (WGS) has emerged as a powerful tool for investigating the genetic basis and surveillance of DR-TB. FIND is supporting NTP in initiating WGS to evaluate prevalence and patterns of drug resistance in India.

**Intervention or response:** In this study we are planning analysis of nearly 2200 DR-TB clinical isolates from patients visiting public sector facilities in six WGS labs located in north, west and south India. All study sites are performing WGS on DR-TB isolates using MiSeq-Illumina platform.

Sequencing data are shared with NRL-NIRT Chennai through FTP server for analysis using NIRT in-house CAMSPRED pipeline. 184 (9%) samples have been tested since January 2023, and data analyzed to study drug resistant genetic variants and their phylogenetic relationships. Preliminary analysis on drug resistance and mutations were performed by using perl scripts.

**Results/Impact:** Preliminary results showed two predominant lineages, lineage3-CAS (49%) and lineage2-Beijing (38%), followed by lineage4-EA (11%) and lineage1-EAI (2%) among drug resistant isolates.

Lineage3 and lineage2 uniquely contributed to the maximum drug resistance with 34.7% and 27.3% respectively.

Data revealed known mutations [RIF\_S450L; INH\_S315T; STM\_K43R, STM\_K88R; FLQ\_D94G, FLQ\_A90V; EMB\_M306V, EMB\_Q497R; PZA\_H71R, PZA\_A3E, PZA\_G132A; ETH\_C-15T, LZD\_C154R] associ-

ated with drug resistance, as well as mutations not found in WHO catalogue. INH\_S315T, and FLQ\_D94G, these are two common mutations seen among all four lineages contributing to 4.1% drug resistance.

**Conclusions:** Preliminary WGS results provide important insights into the basis of drug resistance in TB and the prevalent resistant strains. Analysis of more DR-TB isolates on a regular basis is required to monitor the resistance patterns for surveillance. Development of new analysis pipelines and in-depth examination of mutations not listed in WHO catalogue would lead to valuable findings.

### OA68-736-18 Analysis of proficiency panel testing performance among Xpert TB testing facilities in Kenya: What has changed 5 years later?

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**Background and challenges to implementation:** Cepheid's Xpert tuberculosis (TB) assays enable a highly sensitive, specific, and timely diagnosis of *Mycobacterium TB* and the detection of rifampicin (RIF) resistance. To ensure quality in TB testing services, Kenya, through US President's Emergency Plan for AIDS Relief (PEPFAR), implemented Xpert TB proficiency testing (PT) in 2014. We sought to assess PT performance progress made by the National Xpert TB PT program.

**Intervention or response:** We retrospectively extracted data from the National Xpert TB PT database for health facilities (HF) with Xpert machines enrolled in the PT program in 2015 and 2020 in Kenya in PT round one (2015A and 2020A). In each PT round, each HF received five PT samples. The maximum score per PT sample when correctly reported was 20 marks (satisfactory performance (SP)), while incorrect, uninterpretable (error and indeterminate) PT results were scored zero, 5 and 10 marks respectively. We abstracted data on the number of HF enrolled, returned PT results, and performance. We assessed HF performance (satisfactory  $\geq 80$ ) trends over the two periods using Jonckheere-Terpstra test.

**Results/Impact:** The number of Xpert TB testing facilities enrolled in the National Xpert TB PT program increased more than threefold, from 56 in 2015 to 185 in 2020. Returned PT results decreased from 50/56 (89.3%) to 138/185 (74.6%), SP increased significantly from 45/50 (90%) to 136/138 (98.6%) in 2015 and 2020 respectively, p-value=0.003. PT samples with suboptimal

marks decreased from 21/250 (8.4%) in 2015A to 28/690 (4.1%) in 2020A,  $p$ -value $<0.001$ . Uninterpretable results dropped from 9/250 (3.6%) in 2015A to 17/690 (2.5%) in 2020A,  $p$ -value=0.008.

**Conclusions:** We observe that large expansion of enrolled facilities over the five-year period, increase in SP, decrease in results that were returned, incorrect and uninterpretable. The analysis demonstrates that it is possible to implement and scale up a successful national Xpert TB PT program.

### OA68-737-18 Introducing molecular technology (Truenat) below sub-districts for enhancing patient-centred TB diagnostic services

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**Background and challenges to implementation:** Bangladesh is still a high burden country for tuberculosis (TB). To heat the TB incidence in the country, it is crucial to identify more missing cases from the community and to treat them promptly. Currently TB diagnosis at the peripheral level relies heavily on smear microscopy. Based on World Health Organization's (WHO) conditional recommendation of using Truenat instead of microscopy, BRAC a development organization with the support of Infectious Disease Detection and Surveillance (IDDS) project and National TB Program has started implementation of Truenat in 20 microscopy centers since July 2022.

**Intervention or response:** A total of 20 microscopy centers were selected considering higher presumptive load in hard-to-reach areas, who were being missed from diagnosis because of long distance Xpert site. Twenty Truenat machines were introduced by refurbishment of the mentioned sites. Existing laboratory technicians were trained on Truenat testing and implementation. Total 570 community health workers/volunteers of BRAC, 211 graduate medical doctors and 430 other non-formal providers were sensitized for presumptive referral.

**Results/Impact:** From July 2022 to March 2023, a total of 28,221 samples were tested by Truenat and 1,966 were identified as MTB detected. All these MTB detected samples were tested to identify RIF resistance (RR) and 21 of them was found as RR. Positivity rate of Truenat Vs microscopy is 7.1% and 3% respectively in these centers. There was significant increase of presumptive tested by Truenat over the quarters (3,808; 11,315 and 13,098) of implementation.

Quarter	Total presumptive	Tested by Microscopy	Smear Positive by Microscopy	Positivity Rate	Tested by Truenat	MTB detected by Truenat	Positivity Rate	RR
Q3 2022	8768	4960	190	3.83	3808	284	7.46	3
Q4 2022	13511	2196	73	3.32	11315	836	7.39	10
Q1 2023	15521	2423	46	1.90	13098	846	6.46	8
Total	37800	9579	309	3.20	28221	1966	7.1	21

**Conclusions:** Considering the promising result for TB detection including DR-TB by testing with Truenat in remote peripheral laboratories, country has planned to scale up in another 112 sites for enhancing TB diagnostic services for underserved population. These machines are expected to play an important role in identifying TB and DR TB patients and preventing its spread that can support in reducing country's TB incidence.

### OA68-738-18 Poor adoption of TB lipoarabinomannan testing in national guidelines in 30 high TB-HIV burden countries

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**Background and challenges to implementation:** TB-LAM is the only point-of-care rapid test for diagnosing TB, the largest killer among people living with HIV/AIDS (PLWHA). It is a simple, non-invasive, affordable test aimed at bridging the diagnostic gap for PLWHA and has the potential to accelerate the start of TB treatment. Despite WHO recommending its use as of 2015, its adoption is lagging.

To assess the adoption status of TB-LAM, we evaluated the national HIV and TB guidelines of 30 high TB/HIV burden countries.

**Intervention or response:** We selected the countries based on the WHO list of 30-high burden countries for TB-HIV coinfection. To identify the adoption status of TB-LAM, we reviewed the most recent national documents from these 30 countries, inter alia, national strategic plans for HIV/TB, country-level guidelines, and updates. These documents were found via desktop reviews or the document repository of the HIV Policy Lab ([www.hivpolicylab.org](http://www.hivpolicylab.org)).

**Results/Impact:** Our results show that 14 out of the 30 countries have recognized the importance of this tool and have adopted it in their national guidelines or plans to diagnose TB/HIV coinfection. However, 13 of the 30 countries have not included TB-LAM in their national policies or guidelines. No guidelines were found in our desktop review for 3/30 countries: Gabon, Guinea,



Guinea Bissau. The 13 countries that have not adopted TB-LAM either depend on rapid molecular tests, sub-optimal modalities like symptomatic approach, or inefficient methods such as culture and microscopy.

**Conclusions:** These findings highlight the need for increased efforts to promote the use of TB-LAM, particularly in countries with high rates of HIV/TB co-infection.

TB-LAM can improve the diagnosis and treatment of TB in people living with HIV, ultimately reducing mortality and morbidity from TB.

**OA68-739-18 Early microbiologic surrogate markers of pulmonary TB treatment outcomes**

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**Background:** Early detection and prompt anti-tuberculosis treatment (ATT) are key components of the tuberculosis (TB) prevention and care strategies. Traditionally, clinical trials and national programs have used acid-fast bacilli (AFB) microscopy and mycobacterial culture conversion at the end of the intensive phase to predict cure. Earlier biomarkers of pulmonary tuberculosis (PTB) treatment outcomes are critical to define a primary endpoint for treatment-shortening trials and to monitor shortened ATT.

We evaluated all microbiologic markers assessed serially during the intensive phase of ATT.

**Design/Methods:** We analysed two large prospective TB cohort studies conducted from 2013-2019 in India. We included participants ≥18 years who initiated 6-month ATT for clinically or microbiologically diagnosed, drug-sensitive PTB and completed ≥ 1 follow-up visit.

Sputum specimens underwent baseline Xpert MTB/RIF, acid-fast bacilli (AFB) microscopy and liquid and solid cultures, and serial AFB microscopy and liquid/solid culture at week 2, 4 and 8. Poisson regression assessed the impact of available microbiologic markers (test positivity, smear grade, time-to-detection and time-to-conversion) on a composite outcome of failure, recurrence or

death by 18 months after the end of treatment; models were adjusted for age, sex, nutritional status, diabetes, smoking, alcohol consumption and regimen type.

**Results:** Among 1098 eligible cases, there were 251 (22%) primary outcomes; 127 treatment failures, 73 recurrences, and 51 deaths. The primary outcome was independently associated with: Xpert (medium-positive aIRR 1.91, 95% CI 1.07 – 3.40 and high-positive aIRR 2.51, 95% CI- 1.41 – 4.46), AFB smear (aIRR 1.48, 95% CI 1.06 – 2.06) and liquid culture (aIRR 1.98, 95% CI 1.21 – 3.23) at baseline; week 2 liquid culture (aIRR 1.47, 95% CI 1.04 – 2.09); and week 8 AFB smear (aIRR 1.61, 95% CI 1.05 – 2.46) and liquid culture (aIRR 1.54, 95% CI 1.07 – 2.22) (Figure 1).

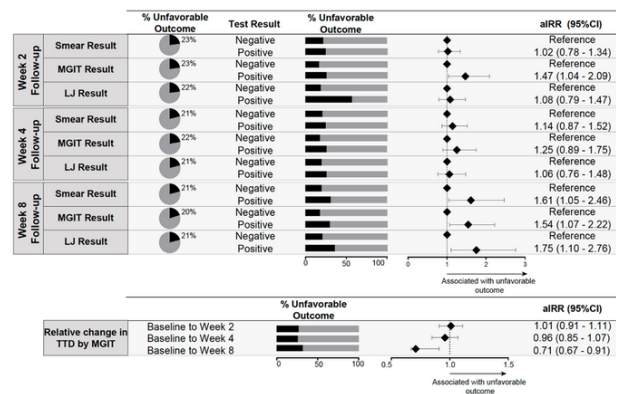


Figure 1. Forest plot summarizing associations between longitudinal respiratory microbiologic markers and the composite unfavourable tuberculosis treatment outcome.

**Conclusions:** Our analysis identified week 2 respiratory mycobacterial culture as the earliest microbiologic surrogate of unfavorable PTB treatment outcomes.

**OA68-740-18 Evaluation of the ESAT6-CFP10 skin test for M. tuberculosis infection among persons living with HIV in China**

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**Background:** Recent global guidelines recommend Mycobacterium tuberculosis antigen-based skin tests, such as the ESAT6-CFP10 (EC) skin test, as acceptable alternatives to the tuberculin skin test (TST) and QuantiFERON-TB Gold In-tube test (QFT). However, the diagnostic value of these tests among persons living with HIV (PLHIV) is unknown. We aimed to assess the diagnostic accuracy of the EC among a cohort of PLHIV in China.

**Design/Methods:** We recruited PLHIV in Jiangsu Province, China to assess the sensitivity and specificity of the EC. Participants were tested with the QFT, TST, and EC skin test. Results were stratified by age, BCG vaccina-

tion, and CD4 count. The sensitivity and specificity of the EC skin test were assessed using distinct cutoffs of the QFT and TST.

**Results:** Of 350 PLHIV enrolled in the study, 58 (16.6%), 89 (25.4%), and 59 (16.9%) tested positive for the EC, QFT, and TST, respectively. Positivity increased with CD4 count; however, these trends were similar across tests. At a 5mm cutoff, EC skin test specificity was high (99.6%, 95% CI, 97.7-100.0), however, sensitivity was moderate (81.4%; 95% CI, 66.6-91.6).

After stratifying by BCG, sensitivity and specificity were 86.4% (95% CI, 65.1-97.1) and 99.1% (95% CI: 95.0-100.0) among vaccinated and 76.2% (95% CI, 52.8-91.8) and 100.0% (95% CI, 97.2-100.0) among unvaccinated PLHIV.

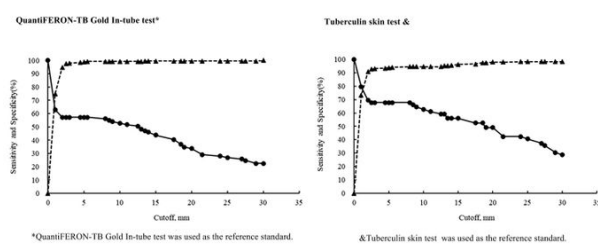


Figure 1. Sensitivity (circles) and specificity (triangles) of the ESAT6-CFP10 skin test with different cutoffs.

**Conclusions:** Among PLHIV, the diagnostic value of the EC skin test remained high, regardless of BCG vaccination or CD4 count. The EC skin test performed comparably to TST and may be a valid alternative diagnostic in settings or populations with high HIV prevalence and BCG vaccination.

### OA68-741-18 Clinical strains of *M. tuberculosis* exhibit differential lipid metabolism-associated transcriptome changes in *in vitro* cholesterol and infection models

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**Background:** Many studies have identified host-derived lipids, characterised by the abundance of cholesterol, as a major source of carbon nutrition for *Mycobacterium tuberculosis* during infection. Members of the *Mycobacterium tuberculosis* complex are biologically different with regards to degree of disease, host range, pathogenicity and transmission.

**Design/Methods:** Clinical strains of *M. tb* were used to infect pulmonary alveolar epithelial cells. Post 48-hour infection, *M. tb* RNA was extracted, reverse transcribed to generate complementary DNA and then used in quantitative real-time PCR (qRT-PCR) to quantify the expression of a selection of lipid-associated virulence genes (fadD28, hsaC, icl1, 430 choD, treS).

**Results:** The results revealed the upregulation of fadD28 and hsaC in both the KZN605 and Beijing strains. An *in vitro* lipid model was created to subject clinically diverse *M. tb* strains to a rich cholesterol environment, mimicking the metabolic state of the host.

Growth curve analyses revealed KZN605 and Beijing to be slow growers in this type of single carbon source assay. RNA was extracted using a standard Trizol protocol in conjunction with the Direct-zol™ 435 RNA Miniprep Kit. Next generation RNA sequencing was performed using the Illumina 2×150 436 HiSeq×10 platform.

Resulting sequences revealed variable changes of lipid-associated gene expression in several lipid-metabolic pathways, in the different clinical strains of *M. tb*. Four genes of interest (pks2, 439 accA3, mmpL8, kshB) were chosen, in a bid to perform functional confirmations of gene expression. All four genes corroborated with the RNA sequencing results.

**Conclusions:** Analysis of transcriptomic signatures provided better insight into the differences encountered by these strains and may prove to be useful in developing novel therapeutics to counteract the devastation caused by TB.

Therefore, genetic diversity needs to be accounted for and lipid metabolism in *M. tb* plays a key role in nutrient acquisition and energy.

### OA68-742-18 Lineage 7 of *M. tuberculosis* - a failing or host-adapted lineage?

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**Background:** Global molecular epidemiology of tuberculosis has revealed nine phylogenetic lineages among the human-adapted members of the *Mycobacterium tuberculosis* complex (MTBC). Exploring L7, which is geographically restricted to Ethiopia, aimed to provide

new insights into the evolution, diversity of MTBC lineages, boost our knowledge of the fundamental biology of host-MTBC interactions.

**Design/Methods:** To find genetic features that may underlie the geographic restriction of L7, its genome was compared to globally dispersed MTBC lineages. Bioinformatic analyses identified a conserved stop-gain mutation in *mmaA3* (*Rv0643c*) of L7. Complementation of L7 isolates with wildtype *Rv0643c* at the *attB* site allowed exploration of the phenotypic impact of this mutation, with subsequent analyses of lipid profiles, cell structure through transmission electron microscopy (TEM), colony morphology by culture on solid media, drug susceptibility, biofilm formation.

**Results:** Lipid analysis of L7 showed that the stop-gain mutation in the *mmaA3* gene caused a lack of methoxymycolates in L7, an important component of the mycobacterial cell wall. Deficiency of methoxy-mycolates also altered L7 cell structure and colony morphology. This was evidenced by abnormal colony morphology on modified 7H11 agar, and TEM imaging that showed a reduced cording phenotype, poor cell separation, secretion/shedding of material into the medium, suggesting an impaired cell envelope compared to well-defined cell-wall structures seen for a complemented L7 strain and for *M. tuberculosis* H37Rv. Reduced cording, considered a virulence factor, was demonstrated by changed biofilm growth. No effect of this mutation was observed on antimicrobial drug susceptibility or bacterial growth rate.

**Conclusions:** The inability of *M. tuberculosis* L7 to produce methoxy-mycolates impacts its cell-wall structure, cording phenotype, which may alter the host-pathogen dynamic for L7. Whether this can explain the limited geographical distribution of L7, e.g. by having a negative effect on disease progression and/or transmission, or by being adapted to a confined human population, will be discussed.

## OA69 TB stigma, discrimination and equity

### OA69-743-18 Stigma in households of children with rifampicin-resistant TB in South Africa, India and the Philippines

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**Background:** Stigma is a barrier to TB diagnosis, treatment initiation, adherence, and health outcomes. Little is known about TB stigma experiences in households with children with rifampicin-resistant TB (RR-TB).

In the CATALYST trial we explored direct and vicarious experiences of anticipated, internal, and enacted stigma from children receiving RR-TB treatment and their caregivers.

**Design/Methods:** We collected qualitative data from 26 child/caregiver dyads in South Africa, India, and the Philippines (Age: 0–14y). Children and/or their caregivers were interviewed 4 times over ~24 weeks. Interviews were recorded and detailed case descriptions written. Comparative thematic analysis was employed to explore household experiences of stigma and resilience using the health stigma discrimination framework.

**Results:** All children/caregivers reported experiencing stigma over the course of children's treatment. Children experienced physical markers of TB (e.g., weight loss, swollen nodes) and TB treatment (e.g., hyperpigmentation from clofazimine), which left them fearful of inadvertent disclosure.

Anticipated stigma was most noticeable in the Philippines and India where children/caregivers concealed the child's TB status for fear of mistreatment, opting to tell neighbours that children had asthma, pneumonia, or allergies. Internal stigma manifested in children's exacerbated fears of transmission, where some children avoided peers even after treatment completion (Philippines). Caregivers across contexts blamed themselves for exposing their children to RR-TB. Children experienced enacted stigma (isolation/blame) in school settings (South Africa), from neighbours, extended family (South Africa, India, Philippines), and peers (India, Philippines) through avoidance or gossip. Stigma experiences extended into the households where siblings of children with

RR-TB encountered associated stigma. Neighbours would avoid these children, fearing that they also had RR-TB. Participants with strong communal support reported more resilience against stigma.

**Conclusions:** Children with RR-TB and their households experience multiple domains of stigma, substantially impacting on their treatment experiences. Interventions to address TB stigma alongside improved RR-TB care are urgently needed.

### OA69-744-18 Using a mixed-methods approach to bringing stigma research measurement closer to clinical application in KwaZulu Natal, South Africa

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**Background:** Tuberculosis (TB) stigma is a major barrier to global TB elimination goals. Currently, *VanRie's Patient Perspectives Towards TB Stigma* is the most widely validated scale for measuring stigma among people with TB. Despite extensive psychometric interrogation, the literature does not describe quantitative stigma scores compared against descriptions of the lived experience in South Africa (SA).

**Design/Methods:** We used parallel mixed methods to explore level of TB stigma among a cohort of people living with both rifampicin-resistant (RR-TB) and HIV. The aim was to evaluate stigma throughout the TB care cascade in KwaZulu Natal, SA.

Participants were purposively selected to maximize variation. Each individual completed the stigma scale concurrent with qualitative interviews in their preferred language. We used cognitive interviewing techniques to explore how participants understood scale items.

**Results:** Among 30 participants, all were Black African, 63% (19/30) male, and 87% (26/30) Zulu. At baseline, average TB stigma score was 32.3/50 (IQR 27.8-42.8). Stigma scores skewed high, with a 10% ceiling effect. Triangulating the data, quantitative scores were often incongruent with lived qualitative experience. Confusion about item wording led many participants (80%) to endorse items that did not correspond to their stigma experience.

Most participants qualitatively endorsed anticipating gossip and loss of respect, which was not represented in the scale. TB-related disability was central to the male experience contributing to identity loss and reduced self-concept. Men who scored in the lowest quintile [0-10/50(n=3)], still qualitatively described high levels of stigma impacting their mental health.

**Conclusions:** Significant discordance across scale items was identified, findings not previously documented. This study reaffirms the need for culturally valid instruments to measure TB stigma highlighting the importance of mixed-methods stigma research. A robust evaluation of the *VanRie* TB Stigma scales in RR-TB is warranted for use in South Africa and other high-burden settings.

### OA69-745-18 TB-related stigma among TB survivors and their household contacts: an overlooked but major barrier to TB elimination in India

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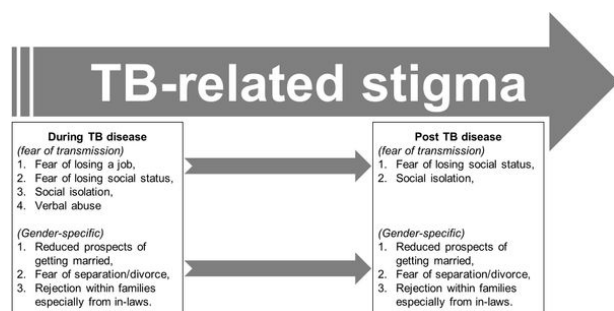
**Background:** India, globally ranked first in tuberculosis (TB) burden, must address the major barrier of TB-related stigma to achieve its TB elimination goal. Sagili et al., 2016, reported high (73%) stigmatizing and discriminating attitudes toward people with TB among the general population across 30 Indian districts, independent of prior TB knowledge. TB-related stigma affects people with TB and their household contacts (HHCs) for years beyond TB treatment completion (Figure).

Global and country-specific literature is scarce for post-TB stigma, hence this qualitative analysis explores TB-related stigma experienced by TB survivors and their HHCs enrolled in TB Aftermath, an ongoing post-TB active case finding (ACF) study.

**Design/Methods:** Adults (>18 years) who completed TB treatment were enrolled between February 2021 to March 2023 from six public TB units (TUs) in Pune, India. Enrolled participants and their HHCs were followed at months 6, 12, and 18 following TB treatment completion. Forty-two in-depth interviews (purposive sample of 21 TB survivors and 21 HHCs) were conducted in Marathi or Hindi language after their 12-month follow-up. In-depth interview transcripts translated into English were coded and analyzed thematically using MAXQDA Analytics Pro software.

**Results:** One year after TB treatment completion, 15 (71%) TB survivors and 11 (52%) HHCs reported perceived TB-related stigma. Experienced stigma was reported by one survivor and four HHCs. Respondents preferred to disclose TB history only to close family members compared to distant family members, neigh-

bors, peers, and colleagues. Respondents' primary concerns about disclosing TB history to neighbors or relatives were fear of losing social status and social isolation and discrimination.



**Conclusions:** We observed high TB-related perceived stigma among TB survivors and their HHCs. As this population is at increased risk of TB recurrence and new infections among HHCs, it is important to prioritize and address TB-related stigma by developing appropriate information education communication (IEC) strategies and patient-centered psychosocial interventions.

### OA69-746-18 Interventions to manage psychosocial distress associated with hospitalisation in children with TB

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**Background and challenges to implementation:** Long-term hospitalization has been part of TB care. New regimens in TB programmes led to a shift to out-patient care. However, many children experience hospitalization due to medical or social reasons. These children are often disproportionately vulnerable. Long-term hospitalization is psychologically distressing and includes social estrangement. We used participatory action research methods to co-develop ways to minimize hospitalization-associated distress in a paediatric ward of a provincial TB referral hospital in Cape Town, South Africa.

**Intervention or response:** We conducted semi-structured observations and in-depth interviews between August – November 2021 with healthcare workers, children, and caregivers (n=13). This informed the co-development of a story book about a caterpillar who goes to a TB hospital. The story included activities to facilitate the children's understanding of their hospital journeys. We piloted the story in the hospital-based primary school (n=6 learners aged 6-12-years) over 4 weeks and collected direct observations to refine its content and use.

**Results/Impact:** Children enjoyed co-creating the story. Teachers successfully used the activities to enable children to clearly describe their experiences in hospital, including their emotional challenges. For example, when a 7-year-old girl was asked why the story made her feel better, she said: "Because both of us miss our mom". The children initiated an extension of the activities where they developed and acted out the story, presenting it to their classmates. Teachers were able to use the structure of the story to keep the children's attention and to engage them in their school activities.

**Conclusions:** Simple, feasible and narrative-based strategies like these could be viable mechanisms to help children mitigate the distress associated with long-term hospitalizations for TB. Future research should expand the scope of such mitigation strategies beyond the school settings and evaluate the effectiveness of interventions to improve children's TB treatment journeys.

### OA69-747-18 Introducing psycho-social counselling for drug-resistant TB treatment – a paradigm shift for treatment adherence in India

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**Background and challenges to implementation:** The alarming increase of DRTB TB in India (Ref: TB India Report - 2013) and the long treatment duration called for moving away from a predominantly bio-medical model to a holistic psycho-social approach and addressing social determinants of TB. In 2015 the National TB Programme in India invited Saksham to introduce psycho-social counselling services for people with DR TB in 4 states of India.

**Intervention or response:** "Saksham" (which mean capable) is a project of the Tata Institute of Social Sciences (publicly funded Institution of Higher Learning) and is a model of public-public partnership for sustainable system strengthening of both the national HIV and TB. For the first time, professionally trained counsellors were introduced in the National Tuberculosis Programme. The counsellors are integrated within the District TB Centres and provide, person centric, priority-based home-bound counselling to people with DR TB, their family, caregivers for the entire treatment duration. Moving beyond the clinical aspects, the counsellors address a range of issues from stigma, discrimination, gender, and mental health. To reduce the catastrophic expenditure, the counsellors also link people with DR TB to various government social protection schemes and nutrition support services through private donors.

Results/Impact:

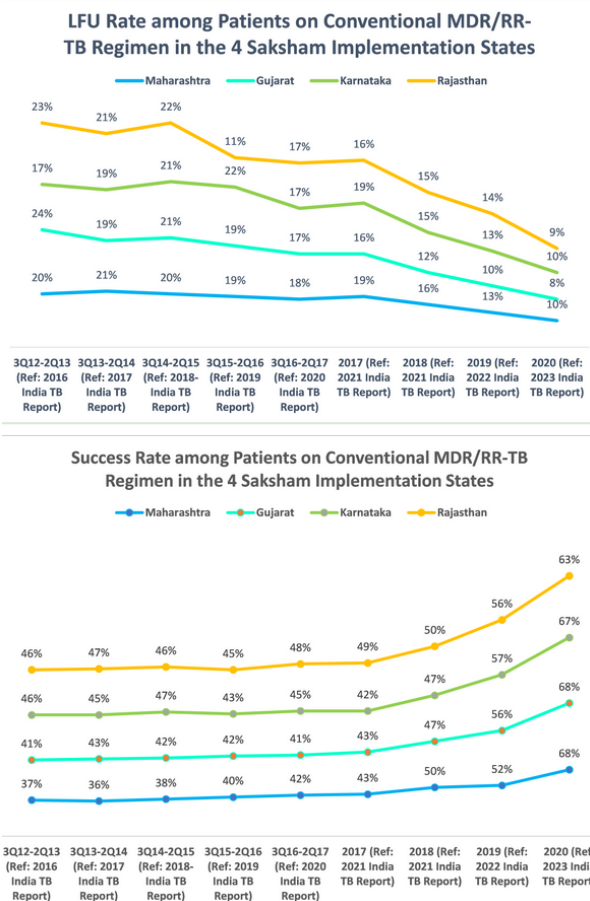


Fig.1: Lost to Follow Up and Success Rate among the Patients on Conventional MDR/ RR-TB regimen in the 4 Saksham Implementation States.(Ref: 2016-2023 India TB Report)

Between Sep.2016-Dec.2022 Saksham has counselled 103564 persons with DRTB (all types of drug resistance), retrieved 80% of treatment interruptions and linked 13143 families of persons with TB to social protection schemes and 22903 to nutrition support.

**Conclusions:** Integrating counselling and addressing social determinants of TB needs to be integrated within the treatment package for better treatment adherence. Acknowledging the success of this model, the national programme has entrusted Saksham to build capacities of national frontline TB staff on counselling which is unprecedented in India.

**OA69-748-18 "Once you tell them about your health, it will be like you have committed a crime": TB-related stigma among men and women in South Africa**

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**Background:** Although men face a higher burden of tuberculosis (TB) disease as compared to women in South Africa, both experience gender-specific barriers to care. However, there is limited understanding of the role of stigma in care access and support.

We aimed to understand gender differences in TB-related stigma and illness behaviors amongst patients and its impact on their lives during and after treatment in Eastern Cape.

**Design/Methods:** Qualitative interviews were conducted with men and women TB patients who were recruited from public health clinics. Participants were currently on treatment, completed treatment, or those who missed medication pick-up behaviors (> 2 weeks). Interviews explored TB treatment experiences, key supporters, and resource availability. All interviews were conducted in isiXhosa or English, audio-recorded, transcribed and translated for analysis.

A codebook was developed using inductive and deductive approaches. Guided by the Health Stigma and Discrimination Network model, data were analyzed using frequency analysis, code clustering, memo writing, and matrices with comparative analysis based on gender.

**Results:** There were 142 TB patients interviewed (93 men, 61 women). Both men and women expressed concerns about anticipated negative comments and mockery at the onset of TB symptoms. Patients described incidents of social isolation due to fear of infecting others and HIV associations. Women were concerned about gossip and community judgment, resulting in self-imposed isolation. Men described isolation as imposed by male peers and family members and discussed dating disruptions. Several male patients described a sense of loss and loneliness, showing the impact of illness on their social network, jeopardizing their resource accessibility.

**Conclusions:** Findings reveal two pathways in which isolation occurs for male and female TB patients. Male and female patients described the drivers and manifestations of TB-related stigma and the long-lasting effects of illness on their social networks. These gender differences give insight and highlight the need for gender-specific interventions.

**OA69-749-18 Creating-A-Hope: most preferred psycho-social intervention among adolescents and young adults with multidrug-resistant TB to improve programmatic outcomes in Pune, India**

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**Background:** Multidrug-resistant tuberculosis (MDR-TB) deeply impacts the biological, social, and mental well-being, of adolescents and young adults (AYA) resulting in poor treatment adherence and suboptimal outcomes in this most neglected but unique group. Exploring the psycho-social barriers to treatment adherence and retention and identifying the most preferred psycho-social intervention by AYA with MDR-TB is critical to mitigate these barriers and improve their engagement in care.

**Design/Methods:** This cross-sectional study adopted a mixed-method approach for data collection. We conducted 6 (4 females; 2 males) in-depth interviews and 30 semi-structured interviews (19 females; 11 males) with AYA with MDR-TB between April 2022 to March 2023 registered at public MDR-TB hospital. Qualitative data employed thematic analysis using MAXQDA-Pro-2022 software and STATA was utilized for quantitative analysis.

**Results:** Qualitative data identified, the individual-level psycho-social barriers such as mental stress suicidal thoughts, feeling of stopping medicines, perceived and experienced stigma, and socio-economic burden. Health system-related barriers included delayed diagnosis, drug stockout, and negative experiences with healthcare providers.

A quantitative questionnaire was administered to 30 participants. The majority (n=19/30) were females, single (n= 26/30), mean age of 20.5 years, and a median treatment duration of 8 months at the time of the interview. Our quantitative data supported the psycho-social barriers reported in in-depth interviews with 26/30 participants reporting psychological issues such as irritation, loneliness, anxiety, sleep disorder, suicidal thoughts, and stigma experiences. Fifteen participants were not satisfied with their health condition.

Individual-level intervention incorporating personalized self-care skills, emotional coping skills relaxation techniques, and informational counseling was identified by 18 (60%) participants as the most preferred intervention.

**Conclusions:** It is important to assess the psycho-social needs of AYA at the time of diagnosis of MDR-TB. Furthermore, to improve programmatic outcomes, individual-level psychosocial interventions with contextual adaptations should be designed and tested to address psychosocial barriers faced by AYA with MDR-TB.

**OA69-750-18 #TBFREEPH Online Patient Support Group: saving lives one posting at a time**

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**Background and challenges to implementation:** The COVID-19 pandemic in the Philippines restricted accessibility to diagnostic tests for people at risk for tuberculosis (TB) leading to a drop in national TB notifications by 35% from 2019 to 2020. The treatment success rate in 2021 was still less than 60%. To help improve this, the call for more gender-equitable TB programming has recently intensified.

**Intervention or response:** In March 2020, the Department of Health, USAID and TBIHSS implemented by FHI 360 launched an online patient support group on Facebook (FB) through the #TBFREEPH communication campaign. Moderated by a team of trained TB survivor-advocates called Treatment Buddies, the FB group receives TB-related posts and messages from members.

Moderators engage with members through group chats and emphasize seeking the help of primary care providers and completing treatment as prescribed. TBIHSS checks for accuracy of information and prepares educational social media cards based on commonly posted content.

	Female (n=435)	Male (n=315)	Total (n=750)	p-value
<b>Age</b>	31.5±7.7	29.6±9.4	30.6±8.6	0.0266
<b>Cascade of TB Care</b>				
Screening	7.4%	7.3%	7.33%	0.977
Diagnosis	26.2%	21.6%	24.27%	0.145
Treatment	34.9%	35.9%	35.33%	0.792
Management of adverse drug reactions	18.2%	22.5%	20.00%	0.139
Prevention	2.5%	1.0%	1.87%	0.115
Others	10.8%	1.8%	11.20%	0.687
<b>Types of Advice</b>				
Clinical	82.8%	85.4%	83.87%	0.332
Social	4.6%	5.1%	4.80%	0.761
Physical	3.9%	5.1%	4.40%	0.440
Mental	4.6%	1.9%	3.47%	0.047
Financial	3.0%	1.9%	2.53%	0.351
Emotional	1.2%	0.6%	0.93%	0.470

Table 1. Profile and Concerns of Tx support users

**Results/Impact:** Membership to the online patient support group reached 6,000 since its inception in March 2020. In January and February 2023 alone, treatment buddies engaged with 750 unique users. An analysis of gender differences shows that female users are statistically older than male users (p=0.0266).

Throughout the cascade of care, the support needed by males and females are similar and comparable. Regarding the type of advice sought, females need more support in terms of mental health concerns ( $p=0.047$ )

*I just want to share my happiness as a mom. My daughter finally graduated on her 6 months medication of primary complex. Thank you so much to this group. I learned a lot from the survivor advocates. – #TBFREEPH support ember:*

**Conclusions:** The #TBFREEPH online patient support group has given persons affected by TB a venue to seek critical information related to TB care and has contributed to identifying specific gender needs.

## OA70 Mental health, BMI, malnutrition

### OA70-751-18 Psychosocial needs of adolescents living with TB in Peru and South Africa

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**Background:** Adolescents (people 10-19-years-old) account for 11% of the global tuberculosis (TB) burden. Studies on chronic disease in adolescence have shown that psychosocial factors are key aspects in disease management and can impact treatment adherence and completion.

Yet, there is a paucity of data regarding psychosocial needs of adolescents living with TB. We examined the psychosocial profile of adolescents with TB to better understand their needs, to improve the care of this population.

**Design/Methods:** We analyzed data from two prospective cohort studies of adolescents on TB treatment, one in Peru ( $n=249$ ) and the other in South Africa ( $n=48$ ). Surveys were conducted between the third and fifth weeks of therapy in Peru and prior to treatment initiation in South Africa. We compared variables between the Peruvian and South African cohorts using Chi-squared and t-tests. (Table 1)

**Results:** There were no differences in age (median 17 years) between the cohorts. Males represented 63.9% of the sample in Peru compared to 39.6% in South Africa. 38.7% of adolescents reported being sexually active, though this is driven mainly by 18-19-year-olds

(51% sexually active). Adolescents at both sites had high scores on a depression screening tool, with most reporting moderate or severe scores. In both countries, but especially in South Africa, many participants reported experiencing TB-related stigma, low levels of family support and incomplete TB knowledge. In South Africa, there was some evidence of problematic alcohol use.

	Overall (n=297)	Peru (n=249)	South Africa (n=48)	p value
Male sex, n (%)	178 (59.9)	159 (63.9)	19 (39.6)	0.003
Age, median (IQR)	17 (15, 18)	17 (15, 18)	17 (15, 18)	0.379
Stigma score*, median (IQR)	23 (18, 30)	22 (18, 27)	29 (21, 33.3)	<0.001
Depression screening score** PHQ-9, median (IQR)	10 (6, 14)	9 (5, 13)	13 (11, 17)	<0.001
AUDIT score, median (IQR)	0 (0, 0)	0 (0, 0)	3.50 (0, 8.3]	<0.001
Sexually active, n (%)	106 (38.7)	86 (38.1)	20 (41.7)	0.761
Caregiver support score§, median (IQR)	42 (33, 49)	44 (39, 50)	22 (18, 28.5)	<0.001
TB knowledge score§§, median (IQR)	11 (9, 12)	12 (10, 12)	6 (5.8, 6)	<0.001
Illicit drug use within last 12 months, n (%)	55 (18.5)	35 (14.1)	20 (41.7)	

Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; IQR, interquartile range; PHQ-9, Patient Health Questionnaire-9; TB, tuberculosis.

\*Stigma score range 6-48; scale assessed for internal reliability in this population (Cronbach's alpha = 0.76).

\*\*PHQ-9 (depression screening) score range 0-28: 0-4, minimal depression; 5-9, mild depression; 10-14, moderate depression;  $\geq 15$  severe depression.

§ Caregiver support scale, 4 items, score range 4-20; scale assessed for internal reliability in this population (Cronbach's alpha = 0.95)

§§ TB knowledge scale, 3 items, score range 3-12; scale assessed for internal reliability in this population (Cronbach's alpha = 0.88)

Table 1. Adolescent demographic and psychosocial characteristics.

**Conclusions:** There is an urgent need for interventions aimed at reducing stigma, treating depression, and strengthening family and social support systems for adolescents with TB. The observed variation in psychosocial characters between sites further underscores the need for setting-specific evaluations of the psychosocial needs of this vulnerable population.

Further, rifampicin and other rifamycins diminish the effectiveness of hormonal contraceptives highlighting the need to improve sexual healthcare for this patient population.



### OA70-752-18 The mental health of TB-affected households in Zimbabwe

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**Background:** Tuberculosis (TB) has multiple and far-reaching impacts, including social, psychological and financial consequences. There is a significant burden of anxiety and depression among people with TB, however little is known about the mental health of their household members.

**Design/Methods:** As part of an integrated multi-component health check in Zimbabwe, we offered mental health screening to TB-affected households using a locally validated tool (Shona Symptom Questionnaire [SSQ]). Adults with pulmonary TB were invited within six months of TB treatment completion; their household members (HHM; ≥14 years) were invited at or within a year of the diagnosis of TB in their household. People with a positive screening result were referred to counselling through a local non-governmental organisation. Prevalence of mental health symptoms and univariable risk factors were described using logistic regression; adjusted for household level clustering.

**Results:** Overall, 419 HHM and 61 people with TB attended. No-one with TB and four HHM reported having anxiety or depression. Ninety four percent (n=453; 393 HHM and 60 people with TB) participated in mental health screening. The prevalence of mental health symptoms was 31% (95%CI 26–36%) among HHM and 41% (95%CI 29–54%) among people with TB.

Among members of TB-affected households without TB, risk factors for having mental health symptoms included older age, being HIV positive, food insecurity, drinking alcohol and smoking (Table). There was no association between time since TB diagnosis and mental health symptoms among people with TB or other household members.

**Conclusions:** There is a very high burden of mental health symptoms among both people with TB at time of treatment completion, and among other members of their households. Uptake of screening was high. Socio-economic factors may be contributing to poor mental health.

We suggest that interventions for TB-affected households should include strategies that identify and address mental wellbeing.

		SSQ+ / All HHM	OR (95%CI)	P value
<b>Total</b>		123 / 393 (31%)		
<b>Age (years)</b>	<b>Per year increase</b>	35 (23–47)	1.02 (1.01–1.04)	0.004
<b>Sex</b>	<b>Male</b>	35 / 128 (27%)	Ref.	0.2
	<b>Female</b>	88 / 265 (33%)	1.32 (0.83–2.10)	
<b>HIV status</b>	<b>HIV negative</b>	91 / 309 (29%)	Ref.	0.05
	<b>PLHIV</b>	32 / 78 (41%)	1.67 (0.99–2.78)	
<b>Drink alcohol</b>	<b>No</b>	75 / 264 (28%)	Ref.	0.03
	<b>Yes</b>	50 / 129 (39%)	1.66 (1.06–2.59)	
<b>Current smoker</b>	<b>No</b>	99 / 342 (29%)	Ref.	0.008
	<b>Yes</b>	24 / 50 (48%)	2.27 (1.24–4.14)	
<b>Days with insufficient food</b>	<b>No</b>	51 / 232 (22%)	Ref.	<0.001
	<b>Yes</b>	72 / 161 (45%)	2.87 (1.86–4.47)	
<b>Caring for the person with TB</b>	<b>No</b>	71 / 246 (29%)	Ref.	0.2
	<b>Yes</b>	52 / 147 (35%)	1.35 (0.87–2.09)	

Table: Univariable risk factors for presence of mental health symptoms among members of TB-affected households (N = 393).

\*Presented as n / N (%) other than age which is median (interquartile range). Abbreviations: HHM = household members; OR (95% CI) = odds ratio (95% confidence interval); PLHIV = people living with HIV; SSQ+ = positive result on Shona Symptom Questionnaire (mental health screening tool; either score of ≥8 or presence of ‘red flags’)

### OA70-753-18 Managers' views of barriers to and facilitators of mental health integration into primary healthcare and TB services in the Free State, South Africa: a qualitative assessment

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**Background:** This study sought to establish health managers' views of the barriers to and facilitators of integration of mental health (MH) into primary health care (PHC) and tuberculosis (TB) services in the Free State province, South Africa.

**Design/Methods:** This qualitative study used purposeful sampling involving two focus group discussions; one each with TB and HIV managers. Additionally, four semi-structured interviews were held with TB/HIV/MH managers. Audio-recorded data were transcribed and subjected to thematic analysis. Two researchers read the transcripts to familiarise themselves with the data. The World Health Organization's health systems building blocks (excluding essential medicines) were used as a priori data codes.

The codes were scrutinised to identify sub-themes; sub-coded as barriers and facilitators of TB/MH integration. A third researcher iteratively reviewed the sub-

themes and discussed these for consensus with the primary coders.

**Results:** In view of *health service delivery*, the managers noted the limited role of non-governmental organisations as a barrier and expansion of the “buddy system” as a facilitator.

Regarding *health workforce*, staff shortages and lack of MH training were perceived as barriers, while an expanded role for community health workers was thought to be a facilitator.

Considering *health information systems*, a lack of formal data elements to monitor MH integration was a perceived as a barrier, while an integrated (electronic) screening tool for TB/HIV/MH was seen as a facilitator. For *health financing*, insufficient resources and a lack of dedicated funding for MH were identified as barriers, and utilising community resources as a facilitator. Regarding *leadership/governance*, the slim MH management structure and the total lack of subdistrict MH managers were noted as barriers, and engendering positive perceptions of MH patients and care were noted as a facilitator.

**Conclusions:** From the perspectives of the managers, MH services remain poorly integrated into PHC and TB services in the Free State.

### OA70-754-18 Impact of providing comprehensive mental healthcare on depression and multidrug-resistant TB treatment outcomes in Lima, Peru

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**Background and challenges to implementation:** Depression is common among persons with multidrug-resistant TB (MDR-TB) and it is associated with poor treatment outcomes. Few studies have assessed the impact of mental health interventions on both mental health and MDR-TB treatment outcomes.

We report on the effects of providing comprehensive mental health care on mental health and TB treatment outcomes in a cohort of persons with MDR-TB and depressive symptoms.

**Intervention or response:** We enrolled 253 patients with MDR-TB, from Lima – Peru, of a multi-center cohort study. We used the PHQ-9 to screen depressive symptoms at enrolment and during three-month follow-up visits. We defined depressive symptoms as PHQ-9 scores  $\geq 5$ . Participants with PHQ-9 scores  $\geq 5$  received comprehensive mental health care, consisting of psychoeducation, emotional support groups, and/or occupational therapy.

We used the Wilcoxon Signed Rank Test to assess within-person change in median PHQ-9 scores. We used WHO definitions to define MDR-TB outcomes as poor (treatment failure, lost to follow-up, or death) or favorable (cured or treatment completion).

We used multivariable logistic regression to estimate the odds ratio (OR) for poor treatment outcome among participants with and without baseline depressive symptoms.

**Results/Impact:** Among 253 participants, 114 (45.1%) had PHQ-9 scores  $\geq 5$  at baseline. Thirty-one (12.7%) of 245 participants had poor treatment outcomes. We observed significant reductions in the median (IQR) PHQ-9 score between baseline (4 [2-7]) and the final visit (2 [0-4];  $p < 0.001$ ).

We did not observe a significant differences in the rates of poor treatment outcomes between participants with PHQ-9 scores 5 at baseline who then received comprehensive mental health care and those with PHQ-9 scores 0-4 (adjusted OR, 95% CI, 1.55, 0.66-3.64).

**Conclusions:** Providing comprehensive mental health care to persons with MDR-TB may improve depressive symptoms during MDR-TB treatment. Our findings provide indirect evidence that it may also improve rates of poor treatment outcomes.

**OA70-755-18 Body mass index as a predictor of progression from latent TB infection to active TB in people living with HIV: secondary data analysis of the WHIP3TB trial**

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**Background:** Low body mass index (BMI) is a globally important risk factor for tuberculosis disease progression. Little is known about this association in people living with HIV (PLHIV), the shape of the association, and its time dependency.

**Design/Methods:** Secondary data analysis of a randomized controlled trial of TB preventive therapy (WHIP3TB) among 3593 people living with HIV (PLHIV) receiving antiretroviral therapy. Participants received 3 months of high-dose rifapentine given once or annually for 2 years. Data were collected from November 2016-November 2017 in South Africa, Mozambique, and Ethiopia.

BMI was measured at baseline and 12 months after enrolment; participants were followed up for two years for incident TB. Fractional polynomials (FP) were used to investigate functional forms of BMI as a continuous variable.

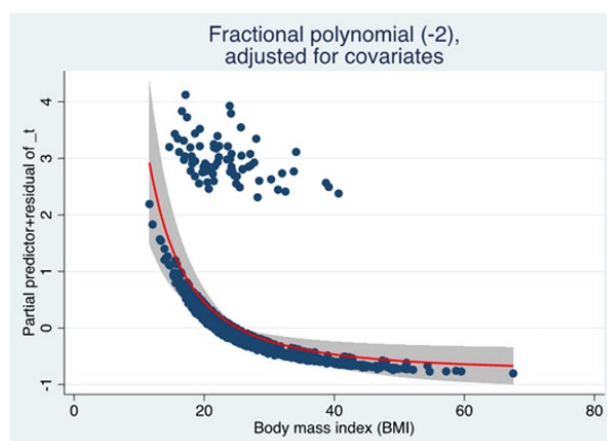
Time to incident TB was modeled using Cox's proportional hazard regression including BMI at enrolment (baseline) and as a time-updated variable.

**Results:** There were 76 TB events documented among 3593 HIV-positive individuals with a median follow-up time among participants with TB of 0.92 years. Base-

line BMI<18.5kg/m<sup>2</sup> was associated with a 2.5-fold increased risk of TB compared with BMI 18.5-24.9 kg/m<sup>2</sup> (hazard ratio [HR] 2.5, 95% CI 1.39-4.59) and showed strong evidence for linear trend (p<0.001).

This association was not affected by multivariate adjustment for gender and country of enrolment (adjusted HR 2.5, 95% CI 1.4-4.6, p=0.002). In FP analysis, low BMI was associated with incident TB (Deviance difference=3.959, p-value=0.047) with a sharp decrease in log(TB incidence) at BMI<24.9 kg/m<sup>2</sup> and a plateau in log(TB incidence) at BMI>24.9 kg/m<sup>2</sup>. Results for time-updated BMI will be presented at the conference.

Figure 1 shows the relationship between the probability of TB incidence as a function of BMI, and the 95% confidence interval.



**Conclusions:** In PLHIV, BMI is inversely associated with TB disease progression up to 25 kg/m<sup>2</sup>.

**OA70-756-18 Is nutritional supplementation with treatment sufficient to improve outcomes in persons with TB? The potential role of unresolved inflammation**

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**Background:** Malnutrition increases susceptibility, severity and mortality in tuberculosis (TB). Therefore, nutritional support is recommended for both preventing and improving outcomes in TB. However, human trials evaluating nutritional support along with TB treatment have yielded mixed outcomes, challenging the one-size-fit-all policy of nutritional support to persons with TB. Here we put-forth a biological hypothesis that explains the genesis of mixed outcomes from nutritional supplementation in TB with a distinct relevance to chronically malnourished persons.

**Design/Methods:** We reviewed published literature to identify possible biological mechanism(s) that may explain differences in the effectiveness of nutritional support-mediated disease outcomes. We reanalyzed publicly available blood gene expression and immune

response data set from TB study cohorts with BMI data by Gene Set Enrichment Analysis (GSEA) or principal component analysis (PCA) to verify the association of identified mechanism with patients' baseline nutritional status.

**Results:** The GSEA of TB patients' baseline expression data based on BMI showed that inflammatory responses and metabolism gene sets were significantly more enriched in severely undernourished TB patients than normal weight patients. PCA analysis of immune responses during treatment showed distinct inflammation resolution pattern in undernourished group. In parallel, literature review showed that inflammation and inflammatory mediators were correlated to nutrition intake and absorption potentially via disrupting metabolic hormones.

Further, TB and malnutrition were also shown to be associated with increased inflammatory responses and dysregulated metabolic hormones, which may impair nutritional absorption, likely exacerbated in comorbid TB-malnutrition.

**Conclusions:** We hypothesize that patients with very high inflammation (as in the malnourished population) may not resolve inflammation with treatment and continue to have impaired nutrition absorption leading to sub-optimal treatment outcomes.

We propose inflammation remediation via an anti-inflammatory diet or host-directed therapy *before* nutritional supplementation for better disease outcomes. Such strategies can improve the effectiveness of current nutrition supplementation policies for uniformly better control of TB disease.

## OA70-757-18 Radiologic damage and lung function at TB diagnosis in people with and without HIV: the INFIN-TB Pilot Study

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**Background:** Although post-TB lung disease is increasingly recognized as a major contributor to long-term morbidity and mortality among TB survivors, few studies have examined the association between lung function and imaging. To explore how HIV may impact the clinical presentation of PTLD, we examined spirometry and chest CT data for people with and without HIV with pulmonary TB in Johannesburg, South Africa.

**Design/Methods:** Adults with and without HIV who were recently diagnosed with a first episode of drug-susceptible pulmonary TB and who had moderate or severe disease on screening chest x-ray were enrolled into a cross-sectional cohort study during 2021 – 2022.

Participants underwent spirometry testing and had a chest CT scan performed which was semi-quantitatively scored (0 (0% involvement), 1 (<5%), 2 (5-25%), 3 (25-50%), 4 (50-75%), 5 (>75%)).

Participant characteristics were compared using chi-square or Wilcoxon rank-sum tests and correlations between spirometry and CT data were assessed using Spearman's coefficients.

**Results:** Among 30 participants, 5 (17%) were female, the median age was 32 (IQR 27-40), 16 (53%) reported ever smoking, and 11 (37%) had HIV coinfection. The median FEV1/FVC ratio was 73% (IQR 61-80%), FEV1 %predicted was 58% (IQR 50-65%), and FVC %predicted was 66% (IQR 62-91). The median overall chest CT score was 3 (IQR 2-4). Neither spirometry results nor CT scores differed by HIV status, but significantly fewer participants with HIV coinfection had cavitary disease ( $p=0.01$ ). Spirometry results were not significantly correlated with the overall CT score (FEV1  $\rho = -0.14$ ,  $p=0.52$ ).

**Conclusions:** Although impaired lung function was common among people newly diagnosed with pulmonary TB, the degree of impairment did not differ by HIV status, nor was it correlated with the extent of radiologic involvement. Longitudinal studies capturing the progression of lung damage during TB treatment will inform future interventions to reduce the burden of post-TB lung disease.

**OA70-758-18 Cardiac involvement in TB patients at the start of treatment: echocardiography results in an ongoing TB cohort in Zambia**

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**Background:** Tuberculosis (TB) primarily affects the lungs but can also involve cardiovascular structures such as the pericardium, the myocardium, and the aorta. Little is known about the type and frequency of cardiovascular involvement in people with TB. We established a TB cohort in Zambia to measure pulmonary and cardiovascular complications in HIV-positive and HIV-negative individuals with TB on treatment.

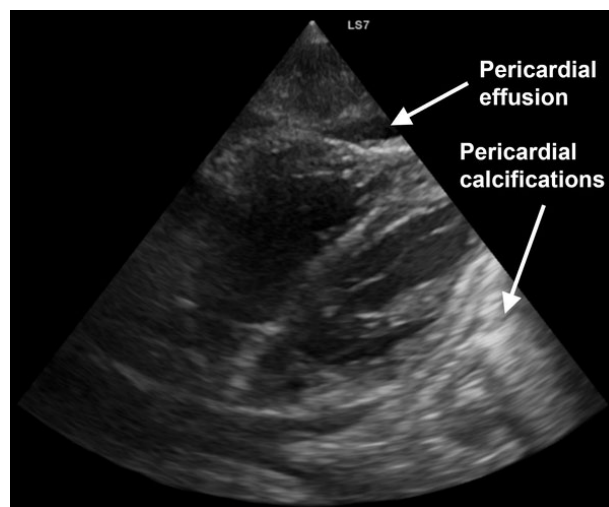
**Design/Methods:** As part of the ongoing TB cohort, we consecutively recruited clinically or microbiologically confirmed TB patients (>15 years old) between October 2022 and January 2023 in Lusaka/Zambia.

Clinical and laboratory data were collected electronically from all participants at recruitment (scheduled follow-up visits: month 6, 12, and 18). We performed standardized echocardiography imaging.

**Results:** So far, we have included 50 TB patients. The median age was 34 years (Interquartile range [IQR]: 29-39 years); 39 (78%) were men, and 21 (42%) were HIV-positive. Most frequent echocardiographic abnormalities were pericardial thickening (21 persons, 42%) and pericardial effusion (14, 28%), followed by diastolic dysfunction (6, 12%) and left atrial (LA) dilatation (6, 12%). Four individuals (8%) had pericardial calcifications (Figure).

Left ventricular (LV) systolic function was preserved in all patients, and right ventricular (RV) systolic dysfunction was observed only in one person. Four persons

(8%) had right atrial (RA) dilation. No RV/LV dilation and no relevant valvular heart disease were seen. The dimensions of the ascending aorta were normal in all persons. Recruitment, and study visits after completion of TB treatment, are ongoing.



**Conclusions:** Cardiac involvement of TB patients at the time of treatment start seems relatively frequent, particularly signs of pericarditis and diastolic dysfunction. Further investigations need to focus on the long-term outcomes, such as constrictive pericarditis and heart failure.

## SHORT ORAL ABSTRACT SESSION (OA)

### SOA22 Drug sensitive TB: Treatment and Care

#### SOA22-964-18 Long-term self-administered intravenous antibiotic therapy in outpatient treatment of drug-resistant TB

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**Background:** *Mycobacterium tuberculosis* drug resistance challenges a successful treatment of tuberculosis (TB). Latest WHO guidelines recommend treatment of multidrug-resistant/rifampicin-resistant-TB (MDR/RR-TB) and pre-extensively drug-resistant TB (preXDR-TB) with an all-oral drug regimen for six months. However, treatment of extensively drug-resistant TB (XDR-TB) still relies on 18-month drug regimens that often involve intravenously (i.v.-) administered drugs like meropenem, or amikacin. Maintaining daily i.v.-administration of anti-TB drugs in an outpatient setting is a logistical challenge that can be overcome by trained patient self-administration via a central venous catheter and special infusion systems. We evaluated self-administration of i.v. anti-TB medicines via a central venous catheter during the outpatient phase of treatment in patients with drug-resistant TB.

**Design/Methods:** We conducted a retrospective observational cohort study on consecutive data of patients with MDR/RR-, preXDR- and XDR-TB who were discharged from our hospital and finished their i.v.-therapy in an outpatient setting between 1<sup>st</sup> of January 2016 and 31<sup>st</sup> of December 2021. We analysed the duration of i.v.-treatment with meropenem, amikacin, PAS, and capreomycin, number of drug doses, dose changes, and changes of the port systems due to infections.

**Results:** Data on i.v. anti-TB drug treatment from 74 patients were included in the analysis, of which 47 self-administered daily treatment with one i.v.-drug, 24 with two, and three with three i.v.-drugs. The median outpatient treatment duration was 172 days (IQR 92-387), amounting to 25,105 outpatient treatment days

or 45,915 self-administered doses (31,215 doses of meropenem, 9,112 of capreomycin, 4,414 of PAS, and 1,174 of amikacin). Clinical or microbiological diagnosis of port infection necessitated seven port explantation in six patients. Hence, port infections occurred in less than 10% of patients or approximately once per 6,500 self-administered i.v.-doses.

**Conclusions:** With sufficient resources, long-term self-administered i.v.-therapy in outpatient treatment of drug-resistant TB is associated with a relatively low risk of port infection.

#### SOA22-965-18 The impact of fixed-dose combinations on TB treatment outcomes in Korea: a comparative study based on national data

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**Background:** The fixed-dose combination (FDC) for first-line anti-tuberculosis (TB) treatment has long been a standard practice. In the real-world, however, there is limited evidence on whether the use of FDC improves treatment outcomes. We identified the impact of FDC on treatment completion and TB recurrence.

**Design/Methods:** We designed a nested case-control study using national TB cohort database (2013 – 2018) that linked the national TB notification database and the national health insurance claims databases.

We identified 31,363 newly diagnosed drug-susceptible TB patients in 2015 and 2016 who had been prescribed FDC or non-FDC TB treatment. A 1:4 propensity score matching (PSM) using the nearest-neighbor algorithm was performed to match 4,045 TB patients treated with FDC with 16,180 TB patients treated with non-FDC.

Multi-variable logistic regression analyses were performed to assess for the factors influencing treatment outcomes between the two groups.

**Results:** In our PSM-matched cohorts, new DS-TB patients treated with FDC had higher unadjusted treatment completion rate (88.5% vs. 80.0%, p-value < 0.01) and lower death rates (4.7% vs. 8.6%, p-value < 0.01) with similar TB recurrence rate (2.2% versus 2.3%) compared to those treated with non-FDC. In multivariable analyses, use of FDC had higher odds treatment completion [adjusted odds ratio (aOR): 1.98; 95% con-

fidence interval (95% CI): 1.78–2.21]). TB patients with younger age (relative to 70+ age) and higher income level had higher odds for treatment completion. Use of FDC did not influence TB recurrence after treatment completion (adjusted hazard ratio [aHR] 0.98; 95% CI 0.76–1.25). The acquired drug resistance rate was similar between the two groups.

		FDC (n=4045)	Non-FDC (n=16180)	p-value
Treatment outcomes	Treatment completion, n (%)	3580 (88.5)	12944 (80.0)	<0.001
	Treatment incompleteness, n (%)	274 (6.8)	1841 (11.4)	
	Death, n (%)	191 (4.7)	1395 (8.6)	
The impact of FDC use on the treatment completion	Univariable, OR (95% CI)	1.93 (1.74 – 2.14)	Ref.	<0.001
	Multivariable, aOR <sup>a</sup> (95% CI)	1.98 (1.78 – 2.21)	Ref.	<0.001
The impact of FDC use on TB recurrence	Univariable, HR (95% CI)	0.94 (0.73 – 1.21)	Ref.	0.372
	Multivariable, aHR <sup>a</sup> (95% CI)	0.98 (0.76 – 1.25)	Ref.	0.584

Notes: FDC, Fixed-dose combination. CI, confidence interval. OR, odds ratio, aOR, adjusted odds ratio. HR, hazard ratio, aHR, adjusted hazard ratio. Ref, reference  
<sup>a</sup> Adjustments were made for subjects' sex, age group, region, income level, lesion of TB, acid-fast bacilli smear result, and Charlson comorbidity index

Table 1. State of the newly diagnosed TB patients according to the fixed-dose combination use.

**Conclusions:** FDC use was independently associated with treatment completion in patients with new DS TB patients. FDC use was not associated with TB recurrence or drug resistance. Thus, our study will promote the appropriate usage of FDC and better management of patients with TB.

### SOA22-966-18 Effectiveness of a comprehensive package based on electronic medication monitors at improving treatment outcomes among TB patients in Tibet: a randomised controlled trial

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**Background:** World Health Organisation recommends that electronic medication monitors (EMMs), a form of digital adherence technology, complement directly observed treatment for tuberculosis (TB). However, existing evidence about EMMs effectiveness is inconclusive. We evaluated the effectiveness of a comprehensive package based on EMMs among TB patients in Tibet.

**Design/Methods:** We conducted this pragmatic, unblinded, multi-centre, individually-randomised, controlled, superiority trial in six counties in rural Shigatse, Tibet. Eligible participants were drug-susceptible TB patients aged  $\geq 15$  years starting standard TB treat-

ment. TB doctors recruited patients from the public TB dispensary in each county and randomised them to intervention or control. Intervention patients received an EMM box. This included audio medication-adherence reminders and recorded box-opening data, which were transmitted to a cloud-based server accessible to healthcare providers to allow remote adherence monitoring. A linked smartphone app enabled communication between patients and healthcare providers. Control patients received usual care plus a deactivated EMM, no access to the app, and we did not train family treatment supporters.

Our primary outcome was a binary indicator of poor monthly adherence. We also conducted process evaluation to explore operational questions regarding acceptability, cultural appropriateness and burden of technology use.

**Results:** There were 143 to the intervention and 135 to the control. In the intervention arm 9.8% (84/854) of patient treatment months showed poor adherence compared to 36% (287/798) in the control arm. The corresponding intervention versus control adjusted risk difference was -28.7 percentage points ( $p \leq 0.001$ ). The process evaluation reported that the intervention package was acceptable by local providers and patients, and user-friendly. Ongoing training about TB and inclusion of community health workers were key factors to implement the interventions.

**Conclusions:** Our interventions were considerably effective at improving TB treatment adherence and outcomes, and our trial suggests that EMMs adapted to local context may positively impact TB programmes in high-burden and low-resource settings.

### SOA22-967-18 The use of bedaquiline in treatment of pre-extensively drug-resistant and extensively drug-resistant pulmonary TB patients in Limpopo Province, South Africa

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**Background:** In 2012, bedaquiline (BDQ) was approved for use by the Food and Drug Administration for combination therapy for multi-drug resistant tuberculosis (MDR-TB). The drug was adopted for use in Limpopo from 2016 to treat patients with MDR-TB (including pre-extensively drug resistant (pre-XDR) TB and extensively drug resistant (XDR) TB according to the National TB Programme treatment guidelines. However, the burden of pre-XDR and XDR TB in Limpopo remains high.

Thus, we have conducted this retrospective analysis to determine the effectiveness of this drug in treatment of pre-XDR and XDR patients in Limpopo.

**Design/Methods:** A retrospective analysis of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB) patients reported in the Limpopo province electronic drug-resistant TB register (EDRweb), 2016–2019 was conducted. Data which met the inclusion criteria were analyzed using SPSS v27.0.

**Results:** A total of 1580 patients were included in the analysis (mean age=39 years, interquartile range=17), and over half (57%) were male. Most patients had pulmonary TB (n=1559, 98.6%) and human immunodeficiency virus (HIV) (n=1062, 68%). The burden of Pre-XDR and XDR TB amongst patients with pulmonary TB was 100(6.4%) and 16(1.1%) respectively, while one (n=1/24, 4%) patient with extra pulmonary tuberculosis had XDR TB. 76% and 13% of patients with pre-XDR and XDR TB respectively were on BDQ combination therapy. Of patients on BDQ, 56% of those with pre-XDR pulmonary TB had treatment success while 4% of pre-XDR patients not on BDQ had treatment success. On patients with XDR pulmonary TB, there was 69.2% of treatment success among patients who were BDQ, while 50% of XDR patients not on BDQ had treatment success.

**Conclusions:** The study implies that an addition of BDQ in treatment of pre-XDR and XDR TB results in good clinical outcomes. There were better outcomes in patients who were on BDQ combination therapy in patients with pulmonary TB.

### SOA22-968-18 Investigating transmission of drug-resistant TB in Kaohsiung, Taiwan, using whole-genome sequencing

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**Background:** Drug-resistant tuberculosis (DRTB) is a remaining threat to global health. Knowing the local transmission dynamic can help develop DRTB control strategies. With the combination of genomic and epidemiological information, we aimed to investigate the transmission dynamic and identify potential risk factors for transmission of drug resistance.

**Design/Methods:** We conducted a population-based, prospective genomic study to include notified and culture-confirmed patients with tuberculosis between 2019 January and 2021 July in Kaohsiung, Taiwan. We per-

formed whole genome sequencing (WGS) of patients' isolates and measured the similarity of strains to classify genomic cluster, defined by a single nucleotide polymorphisms (SNPs) cutoff as 5. Epidemiological link, probable link, and genomic data were combined to illustrate transmission trees.

**Results:** We identified 246 (12%) of DRTB from 2,051 TB cases, and 13% of DRTB cases were attributed to recent transmission. Younger age was found to increase the risk of DR transmission (aOR=2.77) compared to people age over 65. 32 DRTB and 4 non-DRTB patients were grouped into 15 genomic clusters, in which we did not observe cumulation of DR resistance. Most of the clusters contained only two cases. Limited pairs of epidemiological and probable links were found in the genomic clusters. In most of the genomic clusters, no accumulation of drug resistance was found between hosts.

**Conclusions:** Our results demonstrate that age is associated with DRTB transmission, and the ongoing transmission of DRTB might be limited in Kaohsiung. Although no genetic mutations were accumulated between hosts, we cannot fully rule out the possibility of resistance accumulating during the transmission. Seldom epidemiological and possible geographical links were found in genomic clusters, it is worth a backward investigation to find the common source or place of transmission in the future. Future study should continue to surveil the transmission of DRTB occurred in Kaohsiung.

### SOA22-969-18 Spatial risk areas with temporal variations for TB in immigrants, Brazil, 2010-2021

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**Background:** Migration is a global social phenomenon that can have significant implications for health, particularly with regard to infectious diseases. In Latin America, where migration is a prevalent topic, there are various health-related implications. According to the International Organization for Migration (IOM) in its report "Global Migration: Challenges and Opportunities," immigrants represent about 3.5% of the global population, which means more than 270 million people worldwide (IOM, 2020). The aim of the study was to identify space-time risk areas for tuberculosis in immigrants in Brazil.



**Design/Methods:** Ecological study conducted in Brazil. The study population was composed of all TB cases in migrants available in DATASUS from 2010 to 2021. The technique called Spatial Variation in Temporal Trends (SVTT) was used, which does not aim to identify clusters with a high or low number of event occurrences (as in purely spatial scanning), but verifies whether the temporal trend of cases is increasing or decreasing over time.

**Results:** Figure 1 represents the scan analysis with spatial variation in temporal trend for the entire study period (2010-2021), in which a risk cluster was identified for the occurrence of TB in immigrants, presenting RR: 12.14, ITT: +52.01%, and ETT: +25.60%. This cluster was composed of 35 municipalities in the Northern region of Brazil, with a population of 4,723 immigrants, 44.18 expected cases, and 478 observed cases.



Figure 1 - Spatial risk area with temporal variation for the occurrence of tuberculosis in immigrants, Brazil (2010-2021).

**Conclusions:** The study revealed risk areas for the occurrence of tuberculosis in migrants. Based on the results, vigilance for TB should be intensified in these municipalities to prevent an increase in cases in this region, thus achieving the End TB Strategy goals.

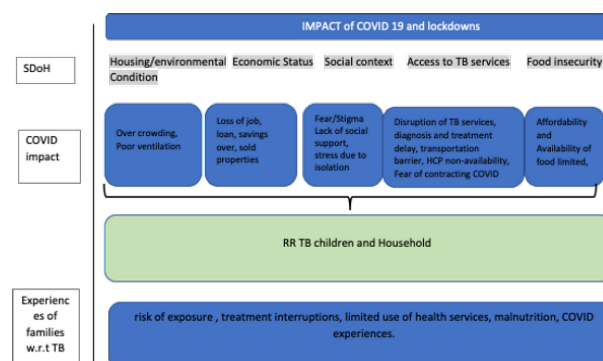
## SOA22-971-18 The socio-economic impact of the COVID-19 pandemic in households having children with rifampicin-resistant TB: A qualitative study from South Africa, India and the Philippines

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**Background:** The COVID-19 pandemic and state mandated lockdowns impacted people with tuberculosis (TB), including children. People with TB and their families faced severe consequences due to the COVID-19 response, including loss of income, challenges to accessing TB services, and psycho-social distress. However, there is little data on short- or long-term health implications for children with rifampicin-resistant TB (RR-TB) and their caregivers. We explore the socio-economic impact of the COVID-19 response on households of children with RR-TB in South Africa, India, and Philippines.

**Design/Methods:** Children enrolled in CATALYST treatment trial participated in four participatory interviews over ~24 weeks. We conducted 92 interviews with 26 child/caregiver dyads (SA: 13, India: 6, Philippines: 7).

In addition to treatment experiences, participants described how lockdown measures impacted their housing, economic and social circumstances, support structures, family life, and access to TB care. We conducted a comparative thematic analysis.



*Conceptual framework.*

**Results:** Our study demonstrated that lockdown-measures impacted households across all three countries in four ways:

1. COVID-19 lockdown measures forced family members, including adults and children with RR-TB, to live in crowded areas with poor ventilation, elevating risk of TB transmission;
2. Caregivers reported significant loss of income, increased spending of limited savings, and unplanned loans to meet daily needs, including buying nutritious food for children to take with RR-TB treatment;
3. Participants reported increased mental stress due to fear of contracting COVID-19 and anxiety related to the initial unknown impact of COVID-19 on children and people diagnosed with TB;
4. Delays in accessing TB care where health care staff were reassigned to COVID-19 efforts, lack of transport to facilities, and fear of contracting COVID-19 from hospitals/clinics.

**Conclusions:** Government programmes need to develop effective social protection measures to address underlying economic and social determinants for children with RR-TB and their household contacts for emergency preparedness in the post-COVID-19 era.

## SOA23 TB diagnosis by molecular lens

### SOA23-972-18 The use of next-generation sequencing to investigate the magnitude and patterns of drug resistance in Mozambique: results of the third national TB drug resistance survey

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**Background:** Mozambique is a high burden country for tuberculosis (TB), multidrug-resistant or rifampicin-resistant (MDR/RR)-TB and TB/HIV. Estimated MDR/RR-TB prevalence is 3.7% in new and 20% in previously treated cases.

As no recent nationally representative data on DR were available from the past 15 years, this third survey aimed to assess the current situation using also next-generation sequencing (NGS).

**Design/Methods:** A cross-sectional national survey was conducted in all 50 TB health facilities in the country. Enrolment of people with newly bacteriologically confirmed TB was conducted for 9 months, in 2019-2020. Sputum samples were tested using Xpert MTB/RIF assay, Line Probe Assay, Whole Genome Sequencing and/or targeted next-generation sequencing (Deeplex Myc-

TB) to identify resistance and explore the phylogenetics of *Mycobacterium tuberculosis* complex (MTBC) strains.

**Results:** Drug resistance profiles were obtained for 2,356 patients including 2,191 and 134 new and previously treated cases, respectively. The current estimated prevalence of RR-TB is 3.89% (2.78%-5.41%) and 5.38% (2.48%-11.30%) among new and previously treated cases, respectively. Preliminary WGS findings indicate high proportion of MTBC lineages 1 and 4 (both 43%), the latter with LAM as most common sub-lineage.

**Conclusions:** The prevalence of RR-TB among new cases has remained stable over time, pointing out that there is ongoing transmission and therefore need for better and more comprehensive screening for resistance.

### SOA23-973-18 An evaluation of the TB Prevention and Care Programme in Gweru District, Zimbabwe, 2022: the need for increased bacteriological coverage

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**Background:** The national TB program has onsite laboratories (with Gene Xpert and CXR services) and is supported by a partner with mobile screening trucks that are equipped with the same equipment. Despite the availability of the Xpert MTB-Rif, program data shows that Gweru district has low bacteriological coverage (36.5%) in 2021-2022 instead of the expected 90%.

The study evaluated the TB program in Gweru District to assess the inputs, processes, and outcomes of the program and determined the possible reasons for low bacteriological coverage.

**Design/Methods:** A descriptive cross-sectional study design using the CDC logic model for program evaluation was conducted in Gweru district. A sample of 110 patient records was selected. Structured key informant interviews and checklists were used to collect data from the key informants and TB facility records. Data were analyzed using Epi Info 7.2.4 statistical package to generate, frequencies, means, and proportions. Health worker knowledge of the TB program was assessed and categorized as acceptable and poor using the modified Bloom cut-off point. A thematic analysis of qualitative data was performed.

**Results:** Patient-related reasons for low bacteriological coverage included failure to produce sputum and health system related included intermittent Xpert cartridge stockouts. Approximately fifteen (14.6) percent of persons with presumed TB missed the opportunity to submit sputa for bacteriological assessment and not all

who submitted specimens received results. Bacteriological coverage was 68.1% which is below target. A high (10.0%) death rate was recorded, and 8/11 deaths were clinically diagnosed.

**Conclusions:** Low bacteriologic coverage poses multiple challenges including possible misdiagnosis which leads to unfavorable treatment outcomes and financial challenges to TB programs. Higher death rates were observed in clinically diagnosed individuals compared to bacteriologically confirmed individuals.

We recommended that all persons with presumed TB have specimens investigated for TB, and death audits be conducted, patient-level data analysis, and more detailed cohort analyses.

### SOA23-974-18 Analysis of whole-genome sequencing genotypic-phenotypic data for improved prediction of drug-resistant TB cases in Taiwan

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**Background:** Molecular testing using whole genome sequencing (WGS) offers the potential to revolutionize how TB drug resistance is identified. However there have been limited studies showing their practical application in resource constrained settings.

Here we describe the implementation of WGS in identifying DR-TB cases in Kaohsiung, Taiwan and compare it to standard drug susceptibility testing, leveraging existing infrastructure and resources.

**Design/Methods:** Between January 2019 to July 2021, all potential cases of TB in Kaohsiung, Taiwan were tested for drug resistance using phenotypic DST and whole genome sequencing. Cultures were collected and processed by partnering health centers and public health laboratories in the area. Specimens were deemed resistant on phenotypic DST if colonies grew on drug containing media at reference concentrations. Genotypic drug resistance was predicted if whole genome sequencing of the TB isolate was positive for one of the resistance conferring mutation catalogued in TB Profiler.

**Results:** A total of 1,936 TB isolates from 1,926 unique patients from Kaohsiung, Taiwan were prospectively processed for whole genome sequencing and phenotypic drug resistance testing. This comprised a coverage rate of ~85% for all new TB cases in the city during the study period.

Overall, we found that WGS performs very well compared to culture-based DST, reporting values as high as 90% for sensitivity and greater than 95% for specificity and accuracy across most of the drugs assessed. Additionally, when we use WGS data to predict prevalence of

drug resistance, the results agreed very well with what has been reported previously. Lastly, using our WGS results, we characterized the mutations most prevalent for each drug resistant strain and found that 3 or fewer mutations were responsible for over 50% of predicted resistance cases.

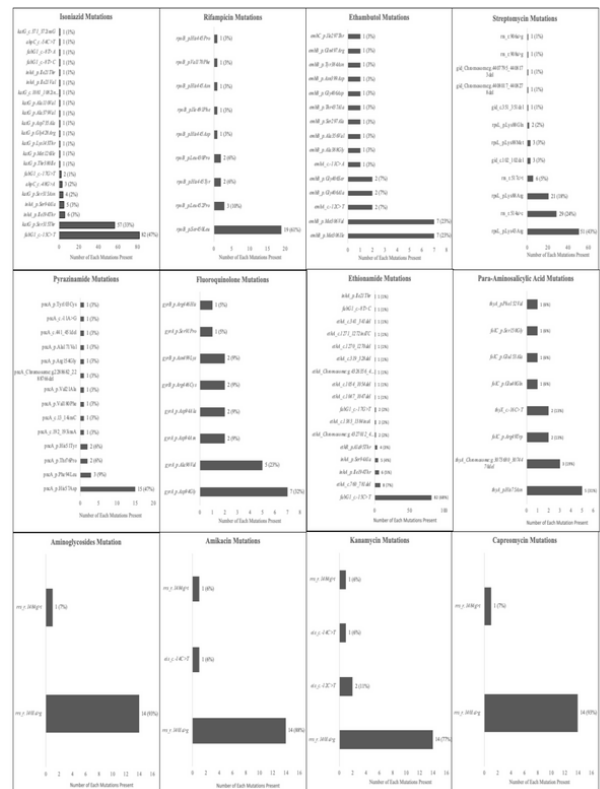


Figure. Distribution in resistance-conferring mutations across various anti-TB drugs.

**Conclusions:** Our study shows the many benefits WGS offers in identifying DR-TB cases and how this technology can be implemented in local public health settings.

### SOA23-975-18 Multicentric field validation of proof-of-concept of the utility of Trueprep-extracted DNA for line-probe assay testing

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**Background:** In National TB Elimination Program (NTEP) of India, for diagnosing TB and DR-TB, two sputum specimens are collected from presumptive TB patients. As *Mycobacterium tuberculosis* (MTB) is detected by Truenat at peripheral sites using Trueprep extracted DNA, the second specimen is transported to the linked reference laboratory for Line Probe Assay (LPA) testing for which the DNA is extracted again. To assess the feasibility of using DNA extracted by Trueprep for further FL and SL- LPA testing, NIRT with support from USAID's IDDS project established the proof of concept.

To evaluate the validity of the same in programmatic field conditions and assess the impact of transportation on DNA, the study is being carried out at 4 sites.

**Design/Methods:** A total of 518 MTB positive Trueprep extracted DNA along with second sputum specimen were transported to the linked reference laboratories (NIRT Chennai, NDTBC Delhi, RMRC Bhubaneswar, and IRL Ahmedabad) in cool chain from nine Truenat sites, selected to represent the country's geographies from South (2), North (2), East (2), and West (3) regions. DNA extracted by both the Trueprep and Genolyse methods was subjected to first line (FL) and second line (SL) LPA testing and results were compared.

**Results:** Among the Trueprep extracted DNA (N=518), interpretable results obtained for FL LPA were 462 (89%) and SL LPA were 456 (88%). Similarly, among the Genolyse extracted DNA, 432(83%) and 435 (83%) had interpretable results for FL and SL LPA respectively.

Out of the 518 samples tested, the Trueprep DNA with >10<sup>4</sup> cfu/ml value were 438 and there was 98.7% and 99.6% concordance between Trueprep and Genolyse DNA for FL LPA and SL LPA respectively.

**Conclusions:** Study has successfully validated that the Trueprep extracted DNA can be transported and utilized for obtaining valid FL and SL-LPA results at field settings.

### SOA23-976-18 Lateral-flow urine lipoarabinomannan test for TB diagnosis in people living with HIV in Nigeria: a case study from the states of Benue and Taraba

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**Background:** Tuberculosis (TB) is the most common cause of death in People Living with Human Immunodeficiency Virus (PLHIV). However, TB often goes undiagnosed as most PLHIVs with Advanced HIV Disease (AHD) are unable to provide quality sputum for bacteriological diagnosis. The lateral flow urine lipoarabinomannan (LF-LAM) assay is a point-of-care test, recommended by WHO for TB diagnosis in PLHIV. KNCV Nigeria with funding from USAID TB LON 1 & 2 grant procured and distributed LF LAM Ag test strips for TB diagnosis among clients at Antiretroviral Therapy (ART) Centers in Benue and Taraba state. The aim of this study is to showcase the TB Yield from LF-LAM diagnosis.

**Design/Methods:** Both states were provided with 200 strips of LF-LAM Ag test as this test is for a target population; All PLHIV (both old & newly identified clients) on treatment, whose CD4 Count were either <200, or were critically ill and presumed to have TB. Healthcare workers were sensitized, Lab staff received hands-on training, and demand creation was strengthened using TB Information, Education & communication materials and Job aids. This intervention was carried out for 3 months (April to June 2021).

**Results:** A sum of 194 clients were tested in both states. Of the 91 HIV clients tested in Benue, 13 (14.6%) were positive for TB, and of the 103 HIV patients tested in Taraba, 21 (20.4%) were positive for TB. The TB clients diagnosed from HIV clients receiving Antiretroviral Treatment were placed on TB treatment.

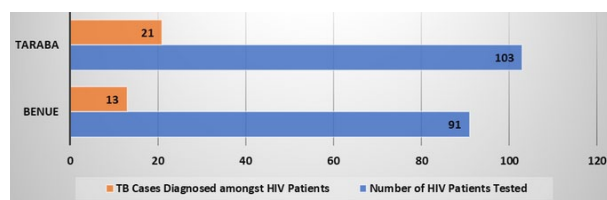


Fig 1: LF-LAM Test

**Background and challenges to implementation:** Tuberculosis (TB) is the most common cause of death in People Living with Human Immunodeficiency Virus (PLHIV). However, TB often goes undiagnosed as most PLHIVs with Advanced HIV Disease (AHD) are unable to provide quality sputum for bacteriological diagnosis. The lateral flow urine lipoarabinomannan (LF-LAM) assay

is a point-of-care test, recommended by WHO for TB diagnosis in PLHIV. KNCV Nigeria with funding from USAID TB LON 1 & 2 grant procured and distributed LF LAM Ag test strips for TB diagnosis among clients at Antiretroviral Therapy (ART) Centers in Benue and Taraba state. The aim of this study is to showcase the TB Yield from LF-LAM diagnosis.

**Intervention or response:** Both states were provided with 200 strips of LF-LAM Ag test as this test is for a target population; All PLHIV (both old & newly identified clients) on treatment, whose CD4 Count were either <200, or were critically ill and presumed to have TB. Healthcare workers were sensitized, Lab staff received hands-on training, and demand creation was strengthened using TB Information, Education & communication materials. This intervention was carried out for 3 months (April to June 2021).

**Results/Impact:** A sum of 194 clients were tested in both states. Of the 91 HIV clients tested in Benue, 13 (14.6%) were positive for TB, and of the 103 HIV patients tested in Taraba, 21 (20.4%) were positive for TB. The TB clients diagnosed from HIV clients receiving Antiretroviral Treatment were placed on TB treatment.

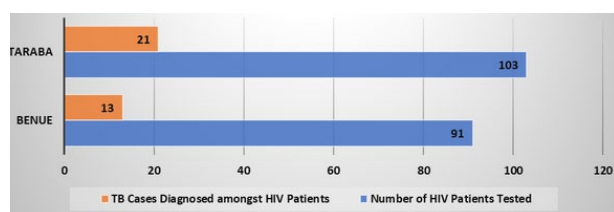


Fig 1: LF-LAM Test

**Conclusions:** Although the sample size was small due to the Target population (HIV clients), Lateral Flow Urine Lipoarabinomannan (LF-LAM) test gave an average TB yield of 17.5%. Following the inability of PLHIVs with ADH to provide quality sputum for bacteriological diagnosis, LF-LAM Ag test should be regularly available for TB Test in TB-HIV (PLHIV) coinfection settings.

## SOA23-977-18 Utility of lipoarabinomannan antigen detection in urine and cerebrospinal fluid for the diagnosis of tuberculous meningitis

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**Background:** Tuberculous meningitis (TBM), a devastating disease with more than 100,000 cases annually is associated with significant mortality. It is difficult to diagnose and has poor prognosis if treatment is delayed. WHO has recommended urine LAM detection for diagnosis of TB in HIV-infected individuals. Our study assessed the diagnostic accuracy of LAM in CSF and urine in immunocompetent adult TBM patients.

**Design/Methods:** In a Prospective study clinical specimens from patients with presumed TBM were processed using standard protocols. The CSF samples were processed for detection of *Mycobacterium tuberculosis* as per WHO recommendations (microscopy, culture(MGIT-960), GeneXpert(GX), followed by LAM antigen detection in both CSF and urine using lateral flow assay(Abbott(Alere)LFA).

Test	Reference Standard	Sensitivity n/N (%)	Specificity n/N (%)	PPV n/N (%)	NPV n/N (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
CSF LAM assay	Comprehensive Reference Standard	21/69 (30.4%)	11/11 (100%)	21/21 (100%)	11/59 (18.6%)	-	0.70
	Microbiological reference standard	10/23 (43.5%)	46/57 (80.7%)	10/21 (47.6%)	46/59 (77.9%)	2.25	0.70
	GX	9/19 (47.4%)	49/61 (80.3%)	9/21 (42.9%)	49/59 (83.0%)	2.41	0.66
	MGIT	5/12 (41.7%)	52/68 (76.5%)	5/21 (23.8%)	52/59 (88.1%)	1.7	0.7
Urine LAM assay	Comprehensive Reference Standard	24/69 (34.8%)	11/11 (100%)	24/24 (100%)	11/56 (19.6%)	-	0.65
	Microbiological reference standard	14/23 (60.9%)	47/57 (82.5%)	14/24 (58.3%)	47/56 (83.9%)	3.47	0.47
	GX	12/19 (63.2%)	49/61 (80.3%)	12/24 (50%)	49/56 (87.5%)	3.2	0.5
	MGIT	8/12 (66.7%)	52/68 (76.5%)	8/24 (33.3%)	52/56 (92.9%)	2.83	0.44

Table 1. Diagnostic performance of CSF and urine mycobacterial LAM assay for tuberculous meningitis.

**Results:** Overall, eighty hospitalized participants with presumed TBM were enrolled. We diagnosed definite TBM in 23 patients (28.7%) based on microbiologic

reference standards (MRS). (19 detected by GX; 12 detected by MGIT). Probable TBM was diagnosed in an additional 46 patients (57.5%) based on uniform case definitions. The remaining 11 non-TBM patients were diagnosed to have cryptococcal meningitis (CSF cryptococcal antigen /culture positive). CSF LAM LFA demonstrated sensitivity (43.5%) and specificity (80.7%) against MRS, and sensitivity (30.4%) and specificity (100%) in comparison to comprehensive reference standards (CRS). Urine LAM LFA demonstrated higher sensitivity (60.9%) and specificity (82.5%) against MRS and 34.8% sensitivity and 100% specificity against CRS. **Conclusions:** LAM LFA has proven to be useful diagnostic modality in patients with TBM. High specificity and positive predictive value in our study suggest that LAM LFA could be used as rule-in test for diagnosis of TBM. Also, better diagnostic performance of LAM LFA in urine compared to CSF suggest that non-invasive, easily collected urine sample can be used as bedside diagnostic modality for early diagnosis of TBM.

### SOA23-978-18 Urine metabolomics for the discovery of novel biomarkers for rifampicin-resistant TB

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**Background:** The very high burden of rifampicin resistance tuberculosis (RR-TB) and the very low detection of RR-TB cases are a major challenge that the world has been facing. Existing diagnostic tests are limited by poor sensitivity, high costs, delayed diagnosis and the need for adequate infrastructure and training.

**Design/Methods:** Drug susceptible tuberculosis (DS-TB) and RR-TB were recruited from Beijing Chest Hospital. This research was approved by the Ethics Committee of Beijing Chest Hospital, Capital medical university. All the methods and research protocol in this research were conducted by the Ethics Committee's existing guidelines. We used the UPLC-Q-Exactive-Orbitrap-MS/MS to provide a broader range of applications in RR-TB diagnosis.

**Results:** We included 80 patients, of whom 40(50%) had confirmed DS-TB, 40(50%) had confirmed RR-TB. During the entire experiment, variables with VIP value >1.0, P value <0.05, and |FC| >1.5 were considered to be poten-

tial differential metabolites. We investigated the possibility of differentiating RR-TB from DS-TB based on the molecular metabolite signatures. In this study, 1-Palmitoyl-2-Oleoyl-3-Linoleoyl-Rac-Glycerol, 2-Acetoxy-4-Pentadecylbenzoic Acid, 1-Cinnamoylpyrrolidine, C18-Sphingosine, Erucamide and Beta-Hydroxymyristic Acid were significantly upregulated in RR-TB. The downregulated metabolite abundance of Dihydroberberine, Dimethyl Sulfoxide, Choline, N,N-Dimethylarginine, Pyridoxine, D-Alanyl-D-alanine, Proline-Hydroxyproline, 4-(Cytisin-12-Amido)-Benzoic Acid, Phosphatidylethanolamine Lyso 20, (2-Oxo-2,3-Dihydro-1H-Indol-3-Yl) Acetic Acid, Cycloserine, 4-Pyridoxic Acid, Difluoro (Perfluoromethoxy) Acetic Acid and Beta-Alanine marked a high risk of RR-TB.

The accuracy, precision, sensitivity, specificity of the model were 93.75%, 95%, 92.68%, 94.87% for a specificity model for 20 potential diagnostic biomarkers. When these 20 metabolites were assessed in the test set, the area under the receiver operating characteristic curve (AUC) was 0.931 (95% CI 0.813-0.993).

**Conclusions:** UPLC-Q-Exactive-Orbitrap-MS/MS provides the most advanced technique for the selection of RR-TB metabolites with high stability and repeatability. After analysis, it was found that 20 metabolites with high diagnostic values were differentially expressed between RR-TB and DS-TB.

### SOA23-979-18 Evaluation of appropriate use of lateral-flow lipoarabinomannan and its sensitivity and specificity among presumptive TB patients in Lusaka Urban District, Zambia

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**Background:** In 2021, the Zambia Tuberculosis (TB) program adopted and rolled out the use of urine Lipoarabinomannan (LAM) as a diagnostic tool for TB in people with advanced HIV disease and additionally recommended the use of LAM in children <5 years with moderate or severe acute malnutrition and individuals with grade 4 or 5 chronic kidney disease irrespective of HIV status. We evaluated the use of urine LAM to establish adherence to the diagnostic algorithm and its sensitivity and specificity in the program setting.

**Design/Methods:** A retrospective analysis of 2021 program data collected from the TB laboratory, presumptive TB, and TB treatment registers in 15 facilities in Lusaka urban district.

**Results:** Of 2329 individuals tested with LAM, 2,315 (99%) had valid results, 1259 (54%) were male and 300 (13%) were aged < 5 years. Only 1514 (65%) had documented HIV results of which 677 (45%) were HIV positive. There was no documentation of the indication for LAM use in the HIV-negative group.

Overall, 790 (34%) were LAM positive of which 124 (16%) were children aged < 5 years and 383 (48%) were HIV positive. Among patients with valid LAM results, 682/2,315 (30%) had both GeneXpert sputum and LAM done and, the overall sensitivity and specificity of LAM was 17.9% (95% CI: 15.0 -20.8) and 89.8% (95% CI: 87.6 - 92.1), respectively.

The sensitivity of LAM in HIV-positive was 22.7% (95% CI:15.3-29.4) compared to 10.0% (95% CI: 5.2-14.8) in HIV-negative. The specificity of LAM in HIV positive was 88.1% (95% CI: 82.7-93.6) compared to 97.2% (95% CI: 94.6-99.8) in HIV negative.

**Conclusions:** The sensitivity of LAM was low in the program setting compared to available global evidence due to failure to adhere to recommended guidelines. The use of LAM in the wrong patient groups risks increasing the proportion of missed rifampicin-resistant TB.

## LATE BREAKER PRESENTATIONS WEDNESDAY 15 NOVEMBER 2023

### LB01 HIV-TB and other comorbidities late-breaker session

#### LB01-100-15 DOLPHIN TOO, weekly rifapentine and isoniazid for TB prevention in ART-naïve people with HIV initiating dolutegravir-based ART: a phase 1/2 study

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<sup>1</sup>Johns Hopkins University School of Medicine, Medicine, Baltimore, United States of America, <sup>2</sup>Aurum Institute, Clinical Research Division, Johannesburg, South Africa, <sup>3</sup>Vanderbilt, Medicine, Baltimore, United States of America, <sup>4</sup>Aurum Institute, Medicine, Johannesburg, South Africa.  
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**Background:** Short-course tuberculosis (TB) preventive therapy (TPT) with weekly isoniazid and rifapentine for 3 months (3HP) has high potential to improve outcomes in people with HIV living in high-endemicity areas for TB. A prior study of 3HP among virally suppressed individuals with HIV on dolutegravir (DTG)-based regimens found favorable safety and DTG pharmacokinetics; all remained virally suppressed. No data supports 3HP and DTG among ART-naïve people.

OUTCOMES and related parameters	Overall n=75	6H group n=25 # (%)	3HP group n=50 # (%)
Number (proportion) of participants with virologic suppression [HIV-1 RNA <50 copies/mL] at Week 12	67/75 (0.89) [0.80-0.95]	23/25 (0.92) [0.74-0.99]	44/50 (0.88) [0.76-0.95]
Unique participants w AE's	25 (33%)	11 (44%)	14 (28%)
AE's all grades	44 (100%)	25 (100%)	19 (100%)
AE Grade 1, n (%)	12 (27%) <sup>a</sup>	9 (36%)	3 (16%)
AE Grade 2, n (%)	31 (70%)	15 (60%)	16 (84%)
AE Grade 3, n (%)	1 (2%)	1 (4%)	0 (0%)
Treatment-related Grade 1 #Ppts	3 (4%)	1 (4%) <sup>a</sup>	2 (4%)
Treatment-related Grade 2 #Ppts	9 (12%)	2 (8%)	7 (14%)

<sup>a</sup> One participant had a treatment-related AE of vomiting which was attributed to BOTH DTG and TDF.

**Results:** There were 14/50 (28%) unique participants who experienced adverse events (AE's) in the 3HP arm and 11/25 (44%) in the 6H arm; all but 1 AE (an unrelated abscess requiring hospitalization) were Grade 1 or 2. Twelve treatment-related AE's occurred overall, 9/50 in the 3HP group (18%) and 3/25 in the 6H group (12%).

HIV viral load (VL) declined from study initiation by a median (IQR) of 4.3 (3.7-4.9) log<sub>10</sub> and 4.8 (4.1-5.3) log<sub>10</sub> respectively for 3HP and 6H in the first 3 months and 2.4 (2.1-2.7) log<sub>10</sub> and 2.1 (1.6-2.4) log<sub>10</sub> over the last 3 months. At week 12, viral suppression (VL < 50 copies/mL) was present in 44/50 (88%) and 23/25 (92%) participants in the 3HP and 6H groups, respectively.

**Conclusions:** Twelve doses of once-weekly isoniazid and rifapentine (3HP) TPT was well tolerated in a cohort of 50 ART-naïve individuals initiating dolutegravir-containing ART; high rates of viral suppression were achieved in both 3HP and 6H groups.

#### LB01-101-15 Results of integrated diagnosis of TB, COVID-19, hepatitis C virus and HIV among detainees and prisoners using GeneXpert in penal settings of Ukraine

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**Background:** Ukraine's HIV, tuberculosis (TB) and hepatitis C virus (HCV) rates are among the highest in Europe. During the last few years, there has been a high prevalence of TB, HCV, and HIV within Ukrainian prisons. COVID-19 pandemic and the Russian-Ukrainian war have limited access to TB, HCV and HIV services in Ukraine. Efforts to provide access to timely, comprehensive, integrated and person-centered health care services have been critical to combat TB, HCV, and HIV in Ukrainian prisons.

#### Results:

	2020	2021	2022
<b>Penitentiary population</b>	49730	46700	41800
<b>TB tested with Xpert MTB/RIF Ultra</b>	4157	5619	3948
Diagnosed with TB	486	554	330
<b>COVID-19 tested with Xpert</b>	-	6500	7517
Diagnosed with COVID-19	-	2572	98
<b>HCV tested with Xpert HCV VL</b>	314	-	1293
Confirmed HCV diagnosis	309	-	975
<b>HIV VL determined with Xpert HIV-1 VL</b>	1922	5679	4189
Undetectable HIV VL	1463	4646	3568

*Results of integrated diagnosis of TB, COVID-19, HCV and HIV among detainees and prisoners using GeneXpert in penal settings of Ukraine.*

During 2020-2022, 13,724 detainees and prisoners were TB tested using GeneXpert, 1,370 individuals (10%), were diagnosed with TB; 14,017 were tested for COVID-19, 2,670 (19%) were diagnosed with COVID-19; 1,607 were HCV tested and determined VL level, 1,284



(79,9 %) had confirmed HCV; HIV VL determination was conducted for 11,790 individuals, who are living with HIV and receive antiretroviral treatment for more than 6 months, 9,677 had an undetectable HIV VL. All individuals with a confirmed diagnosis were enrolled in treatment.

**Conclusions:** Implementation of an integrated person-centered approach using GeneXpert is highly effective in identifying TB, COVID-19, HCV and timely HIV VL determination, provide person-centered services and timely treatment start.

This approach allowed ensuring stable access to timely TB, COVID-19, HCV diagnosis, and HIV VL determination among detainees and prisoners, particularly, during COVID-19 pandemic limitations and the ongoing Russian-Ukrainian war.

### LB01-102-15 Optimising TB preventive treatment initiation among people with HIV in Cambodia: results of the OPTICAM Cluster randomised trial

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**Background:** Initiating people with HIV (PLHIV) on Tuberculosis Preventive Therapy (TPT) has been challenging for Cambodian HIV and TB programs. Shorter TPT regimens, capacity building, improved supply chain, patient information and programmatic supervision could contribute to increased TPT initiation.

**Results:** We consecutively enrolled 4047 PLHIV with 56.5% females and median age 45.0 [IQR 38.0, 52.0] years. Before the onset of the intervention, the average TPT coverage among PLHIV was of 47.1% (95% CI: [44.8; 49.3]) Vs 70.5% (95% CI: [59.1; 71.9]) pre/per intervention (OR: 0.62; 95% CI: [0.16; 2.38], p-value = 0.707).

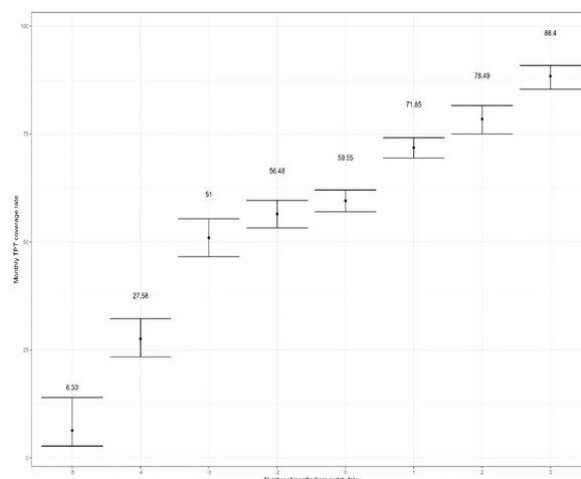


Figure. Mean and 95% CI of monthly TPT coverage rate by number of months from switching date, during the stepped-wedge period.

**Conclusions:** An approach including 3HP, comprehensive health care workers training and PLHIV information based on previously identified barriers was effective to reach a TPT coverage of 70.5% in adult PLHIV attending HIV clinic with previously low TPT initiation in adult PLHIV.

### LB01-103-15 Addressing TB-HIV intersectional stigma: co-developing a multi-level person-centred stigma reduction intervention in affected communities in South Africa

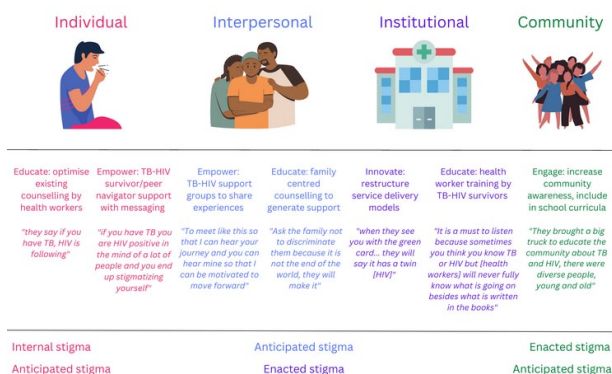
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**Background:** Addressing intersectional TB/HIV stigma is an urgent priority, yet targeted stigma reduction interventions are lacking. Our initial qualitative data from people affected by TB showed that anticipated and enacted stigma were major barriers to TB/HIV care engagement. We aimed to co-develop a multi-level person-centred stigma reduction intervention with HIV and TB affected communities in South Africa.

**Results:** At the individual level, participants recommended counselling to improve TB/HIV knowledge and provide ongoing support along the care journey. Partici-

pants recommended that TB survivors can guide messaging to foster stigma resilience, by highlighting that TB is curable and can affect anyone, and provide real-world examples of people (with and without HIV) who have experienced TB to decrease internal stigma. At the interpersonal level, support clubs and family-centred counselling were suggested to dispel myths related to TB/HIV and facilitate testing for TB/HIV in contacts. At the institutional level, health worker stigma training informed by insights from TB/TB-HIV survivors could improve existing counselling to reduce internal, anticipated, and enacted stigma.

Improved integration of TB/HIV care services and restructured service delivery models are needed to decrease anticipated and enacted stigma. At the community level, increasing knowledge and decreasing misconceptions through awareness-raising events, incorporating TB/HIV into school curricula, and outreach by community health workers, were seen as important.



**Conclusions:** Decreasing TB-HIV intersectional stigma requires a multi-level approach. Co-developing a person-centred intervention with affected communities is feasible and generates stigma intervention components that are directed and implementable, which should be prioritised as part of TB/HIV care integration.

### LB01-104-15 Bedaquiline use requires modifications to antiretroviral therapy, impacting the HIV viral load upon multidrug-resistant TB treatment completion

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**Background:** The antitubercular bedaquiline cannot be used with the antiretroviral efavirenz due to a drug-drug interaction. Many people living with human immunodeficiency virus (HIV) and multidrug-resistant tuberculosis (MDR-TB) will require a change to their antiretroviral regimen during MDR-TB treatment. The effect of this antiretroviral change on HIV viral load (HIVVL) among people with HIV who survive MDR-TB is unknown.

**Results:** Among 531 people with HIV and MDR-TB, average age was 37.4 years, 271 (51.0%) were male, and 259 (48.8%) took bedaquiline. Compared to those who did not take bedaquiline, those who did not experience an antiretroviral change due to taking bedaquiline (n=127) and those who were changed from efavirenz to a protease inhibitor due to bedaquiline use (n=22) were significantly less likely to have an undetectable HIVVL at the time of MDR-TB treatment outcome. Those who were changed from efavirenz to nevirapine due to bedaquiline use (n=110) did not have significantly different odds of an undetectable HIVVL than those who did not take bedaquiline. These significant associations remained when controlling for the nurse case management intervention, age, sex, baseline HIVVL, and length of MDR-TB treatment.

	n	Single Variable Model		Multivariable Model		
		OR	95% CI	aOR	95% CI	
ART Changes Related to BDQ Use	Did Not Take BDQ	272	Ref.	Ref.	Ref.	
	EFV to NVP	110	0.66	0.39-1.13	0.40	0.16-1.04
	EFV to PI	22	0.38*	0.15-0.94	0.19*	0.04-0.89
	No ART Substitutions	127	0.30***	0.19-0.48	0.27*	0.10-0.75

Legend: HIV, human immunodeficiency virus; HIVVL, HIV viral load; MDR-TB, multidrug-resistant tuberculosis; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; ART, antiretroviral therapy; ref., reference category; BDQ, bedaquiline; EFV, efavirenz; NVP, nevirapine; PI, protease inhibitor; \*, p<0.05; \*\*, p<0.01; \*\*\*, <0.001. Multivariable model adjusted for age, sex, presence of the nurse case management intervention, baseline HIVVL, and length of MDR-TB treatment.

**Conclusions:** Antiretroviral changes necessitated due to bedaquiline usage during MDR-TB treatment may negatively impact HIV viral suppression. Changes to antiretroviral regimens during MDR-TB treatment should be made cautiously, and clinicians may wish to choose nevirapine over protease inhibitors in the absence of newer antiretroviral options.

## LATE BREAKER PRESENTATIONS THURSDAY 16 NOVEMBER 2023

### LB02 The Union/CDC late-breaker session on TB (treatment and clinical trials)

#### LB02-105-16 A randomised, active-control, open-label phase 2A trial evaluating the bactericidal activity, safety and pharmacokinetics of TBA-7371 in drug- susceptible pulmonary TB

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**Background:** TBA-7371 is an investigational compound with demonstrated activity in murine TB models and an acceptable safety and pharmacokinetic profile in Phase 1 development.

**Results:** Among TBA-7371 doses, the greatest mean decline in CFU ( $\log_{10}$ CFU/ml/day) was observed in the 100mg thrice daily cohort (-0.130) followed by the 400mg daily cohort (-0.096), 100mg twice daily cohort (-0.086), 200mg daily cohort (-0.065), and 100mg daily cohort (-0.039) compared with HRZE (-0.203).

Similar findings were seen in liquid culture and sputum LAM, but narrower differences were seen between cohorts with sputum LAM, including HRZE.

$\geq 1$  adverse event (AE) occurred in 84% of TBA-7371 and 73% of HRZE participants. Most AEs were mild (Grade 1/2) in severity.  $\geq 1$  AE was reported in all TBA-7371 400mg daily participants; the incidence of Grade  $\geq 2$  AEs was higher in this cohort (80%) compared to all other cohorts (20-40%).

BA was positively associated with higher TBA-7371 minimum concentrations ( $C_{\min,ss}$ ) and exposures (AUC). Visual and cardiovascular AEs were associated with higher TBA-7371 maximum concentrations ( $C_{\max}$ ).

**Conclusions:** TBA-7371 exhibited a dose-dependent increase in BA measured by culture that was greatest with a fractionated daily dose of 300mg, which produced higher exposures and  $C_{\min,ss}$ . Overall, TBA-7371 demonstrated an acceptable safety profile. The increased frequency and severity of AEs and lower BA in the 400mg arm produced a less favorable risk-benefit profile for that dose.

Future TBA-7371 development should focus on optimizing exposure and  $C_{\min}$  while minimizing  $C_{\max}$ , potentially through a long-acting formulation, to best balance efficacy and safety.

	Statistic	TBA-7371 100mg Once Daily (N=15)	TBA-7371 100mg Twice Daily (N=15)	TBA-7371 200mg Once Daily (N=15)	TBA-7371 100mg Thrice Daily (N=17)	TBA-7371 400mg Once Daily (N=15)	All TBA-7371 (N=77)	HRZE (N=15)
Baseline $\log_{10}$ CFU/mL	Mean $\log_{10}$ CFU/mL (SD) [N]	6.05 (1.71) [15]	6.19 (1.21) [13]	6.49 (1.05) [14]	6.62 (0.67) [17]	6.46 (1.11) [15]	--	6.20 (0.69) [15]
Bactericidal Activity (BA) Solid Culture	$\Delta \log_{10}$ CFU /ml/day (90% CI) [n]	-0.039 (-0.074, -0.005) [15]	-0.086 (-0.12, -0.049) [13]	-0.065 (-0.10, -0.029) [14]	-0.13 (-0.16, -0.098) [17]	-0.096 (-0.13, -0.061) [15]	--	-0.20 (-0.24, -0.17) [15]
BA Liquid Culture (Mycobacterial Growth Indicator Tube [MGIT])	$\Delta$ Time to positivity (TTP) (hrs)/day (90% CI) [n]	2.33 (0.53, 4.14) [15]	4.14 (2.2, 6.09) [13]	3.25 (1.43, 5.07) [15]	5.55 (3.80, 7.29) [16]	3.77 (1.97, 5.57) [15]	--	13.88 (12.07, 15.68) [15]
BA Sputum LAM Concentration	$\Delta \log_{10}$ LAM concentration pg/ml/day (90% CI) [n]	-0.082 (-0.11, -0.056) [15]	-0.096 (-0.12, -0.067) [13]	-0.090 (-0.12, -0.063) [15]	-0.11 (-0.14, -0.089) [17]	-0.095 (-0.12, -0.068) [15]	--	-0.099 (-0.13, -0.073) [15]
Any AE	% (n/N)	73% (11/15)	93% (14/15)	87% (13/15)	71% (12/15)	100% (15/15)	84% (65/77)	73% (11/15)
Grade 1 and 2 AEs	% (n/N)	73% (11/15)	87% (13/15)	80% (12/15)	59% (10/17)	100% (15/15)	79% (61/77)	53% (8/15)
Day 14 $C_{\max}$	Mean ng/mL (%CV)	5,171 (27%)	5,342 (16%)	8,848 (15%)	6,683 (26%)	16,015 (16%)	--	--
Day 14 AUC <sub>0-24</sub>	Mean h*ng/mL (%CV)	37,869 (27%)	63,840 (28%)	71,415 (27%)	92,007 (26%)	141,533 (20%)	--	--
Day 14 $C_{\min,ss}$	Mean ng/mL (%CV)	187 (67%)	1,010 (53%)	356 (110%)	1,534 (44%)	694 (92%)	--	--

LB02-105-16 Table

## LB02-106-16 The effectiveness of levofloxacin for the treatment of latent TB infection among household contacts of patients with multidrug-resistant TB: The VQUIN MDR Trial

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**Background:** Prevention of drug-resistant TB is a leading global health priority. However, clinical trials evaluating the effectiveness of treating drug-resistant 'latent tuberculosis infection' (LTBI) to prevent disease progression are lacking.

**Results:** Between March 2016 and August 2019, 3,928 contacts were screened for LTBI. Prior to randomisation, 53 (1.3%) cases of co-prevalent confirmed TB were detected.

In total, 2,041 contacts met eligibility criteria, and were randomised to levofloxacin (n=1023) or placebo (n=1018). Their median age was 40 (IQR 28-52) years and HIV infection affected 8 (0.4%) people. The 30-month follow-up visit was attended by 1,998 (97.4%) participants.

Treatment was completed by 717 (70.1%) people given levofloxacin and 861 (84.6%) given placebo. The incidence of bacteriologically-confirmed TB was 6 (0.6%) in the levofloxacin group and 11 (1.1%) in the placebo group (incidence rate ratio 0.51; 95% CI 0.18 – 1.47, p=0.21).

Grade 3-5 adverse events occurred in 27 of 960 (2.8%) people taking at least one dose of levofloxacin and 18 of 962 (1.9%) people taking placebo. No acquired resistance to *M. tuberculosis* was observed among incident cases.

Intention to treat population	Levofloxacin	Placebo	Incidence rate (vs placebo)	p-value
Number of participants	1023	1018	--	--
Completed 30 months follow up	992 (96.9%)	996 (97.8%)	--	--
Total person-years of follow-up	2521	2518	--	--
Number of incident TB cases to 30 months				
Bacteriologically-confirmed TB	6 (0.6%)	11 (1.1%)	0.51 (0.18, 1.47)	0.21
Clinically diagnosed TB	1 (0.1%)	2 (0.2%)	not estimated	--
Bacteriologically or clinically-diagnosed	7 (0.7%)	13 (1.3%)	0.52 (0.20, 1.37)	0.19

**Conclusions:** The TB incidence rate was reduced among contacts in the levofloxacin group. However, the effect estimate was not statistically significant, with the confidence interval crossing the null. Levofloxacin was well-tolerated among adults and children.

## LB02-107-16 Efficacy and safety of levofloxacin preventive therapy in child and adolescent household contacts of multidrug-resistant TB: the TB-CHAMP double-blind placebo-controlled, cluster randomised trial

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**Background:** Multidrug-resistant (MDR) tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*) resistant to rifampicin and isoniazid, threatens global TB control. Approximately 2 million children are infected with MDR-*Mtb*, with about 30,000 progressing to disease annually.

There is currently no evidence from randomised-controlled trials on TB preventive treatment in people exposed to MDR-TB.

**Results:** 922 participants from 497 households were randomly assigned to receive levofloxacin (n=453) or placebo (n=469); 90% were <5 years, 27% with evidence of *Mtb* infection, 2% HIV-positive.

Five (1.1%) in the levofloxacin and 12 (2.6%) in the placebo arms developed TB (hazard ratio, respectively [HR] 0.44; 95% confidence interval[CI] 0.15-1.25; p=0.121); Figure.

In the pre-specified sensitivity analysis of incident TB based on site-adjudication, 4 (0.9%) children in the levofloxacin and 13 (2.8%) in the placebo arms developed TB. Four levofloxacin-arm participants vs. 8 placebo-arm participants developed grade  $\geq 3$  adverse events at least possibly related to study drug (HR 0.52; 95% CI 0.16-1.71;  $p=0.285$ ). Only one child developed tendonitis (grade 2, levofloxacin-arm), resolving after stopping drug.

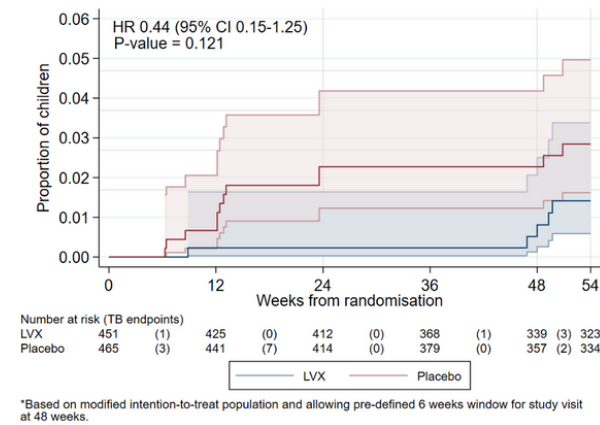


Figure.

**Conclusions:** There was a strong trend for levofloxacin efficacy in preventing TB in children/adolescents with household MDR-TB exposure. Levofloxacin was safe. This trial informs the evidence-base for MDR-TB preventive treatment.

**LB02-108-16 TB-PRACTECAL clinical trial: BPaLM, BPaLC and BPaL 24 week, all-oral regimens for rifampicin-resistant TB: Final outcomes at 24, 48, 72 and 108 weeks post-randomisation**

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**Background:** TB-PRACTECAL showed that a BPaLM regimen was superior to standard of care (SoC), and BPaL/BPaLC regimens were also effective at the 72-week primary endpoint.

Follow-up continued to 108-weeks. Optimal follow-up duration for 24-week regimens has not been established. We present final outcomes at 24-, 48-, 72- and 108-weeks post-randomisation.

**Results:** BPaLM had 8%, 9%, 12%, 14% unfavourable outcomes by week 24, 48, 72 and 108 respectively, BPaLC had 10%, 15%, 24%, 24%, BPaL had 10%, 13%, 14%, 22% and the SoC had 31%, 41%, 47%.

The risk differences to SoC were consistent at all time-points. Unfavourable outcome proportions increased over time, the largest change was in BPaL between week 72 and 108, mostly due to loss to follow-up (1-7%). At 108-weeks, 46.7% in SoC vs. 13.9% in BPaLM had unfavourable outcomes with an effect estimate of -32.8%, similar to 72-weeks.

For investigational arms, there was one additional recurrence over this period (9 versus 10). In contrast, by week-48, only 3/10 recurrences had been observed.

n (miTT population)	BPaLM (n=138)				BPaLC (n=115)				BPaL (n=111)			
	week 24	week 48*	week 72	week 108	week 24	week 48*	week 72	week 108	week 24	week 48*	week 72	week 108
unfavourable proportion	8.0%	8.80%	11.70%	13.90%	10.40%	14.80%	23.50%	24.40%	9.90%	12.60%	13.50%	21.60%
Risk difference (96.6% CI) †	-23.4% (-32.2% to -14.7%)	-29.9% (-39.4% to -20.5%)	-29.2% (-39.4% to -19.0%)	-32.8% (-42.6% to -22.9%)	-20.7% (-30.0% to -11.4%)	-23.9% (-34.3% to -13.5%)	-16.5% (-27.3% to -5.7%)	-21.4% (-32.5% to -10.4%)	-21.3% (-30.6% to -12.1%)	-26.1% (-36.3% to -15.8%)	-26.9% (-36.9% to -16.9%)	-23.8% (-34.9% to -12.6%)
Reasons for unfavourable outcome												
deaths	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.9%)	1 (0.9%)	0 (0%)	1 (0.9%)	1 (0.9%)	2 (1.8%)
early discontinuation	11 (8.0%)	11 (8.0%)	11 (8.0%)	12 (8.8%)	11 (9.6%)	11 (9.6%)	11 (9.6%)	11 (9.6%)	11 (9.9%)	11 (9.9%)	11 (9.9%)	11 (9.9%)
treatment failure	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.9%)	1 (0.9%)	1 (0.9%)	1 (0.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
loss to follow-up**	N/A	1 (0.7%)	4 (2.9%)	6 (4.4%)	N/A	4 (3.5%)	9 (7.8%)	10 (8.7%)	N/A	0 (0%)	0 (0%)	7 (6.3%)
recurrence**	N/A	0 (0%)	1 (0.7%)	1 (0.7%)	N/A	1 (0.9%)	5 (4.4%)	5 (4.4%)	N/A	2 (1.8%)	3 (2.7%)	4 (3.6%)

† CI=2-sided 96.6% CI for BPaLM, 95% for BPaLC/BPaL

\*\*Recurrence was the only planned outcome at week-48

\*\*Loss to follow-up and recurrence not possible at week-24

LB02-108-16 Table. Unfavourable outcomes in investigational regimens (death, treatment discontinuation, treatment failure, loss to follow-up, recurrence) at 24,48,72 and 108-weeks.

**Conclusions:** BPALM, BPALC and BPAL showed consistent effect estimates versus SoC at all measured time-points. Lost to follow-up between week-72 and week-108 changed with only infrequent additional recurrences. 72-weeks post-randomisation appears to be the optimal follow-up to detect recurrences in BPAL-based 24-week regimens.

### LB02-109-16 Pharmacokinetic predictors of hepatotoxicity in the HIRIF trial for drug-susceptible TB

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**Background:** Hepatotoxicity is frequent in the standard-of-care regimen for drug-susceptible tuberculosis, yet the association of each component drug with hepatotoxicity has not been fully characterized. The Phase 2B rifampin dose-ranging trial, HIRIF (NCT01408914), showed the potential of higher rifampin doses to shorten standard therapy without added toxicity. We leveraged the HIRIF trial to inform the association between the hepatotoxicity and the pharmacokinetics of rifampin and its companion drugs in standard therapy.

**Results:** Among 168 participants with available pharmacokinetic data, neither rifampin dose nor exposure was associated with the risk of grade 2+ ALT or AST elevation. Higher pyrazinamide exposure (hazard ratio [HR] 1.85 for every AUC<sub>0-6h</sub> 50 mg\*h/L increase), higher isoniazid exposure (HR 1.35 for every

AUC<sub>0-6h</sub> 5 mg\*h/L increase), and among a subset with known N-acetyl transferase 2 (NAT2) phenotypes, slow NAT2 acetylator status (HR 9.32 relative to fast NAT2 acetylator status, n=90) were associated with grade 2+ ALT or AST elevation in univariable analysis. In multivariable analysis, only pyrazinamide exposure was significantly associated with grade 2+ ALT or AST elevation.

Predictors	Patient, n	Event, n	Univariable HR (95% CI)	Multivariable HR (95% CI)
Rifampin AUC <sub>0-6h</sub> (for every 50 h*mg/L)	168	39	1.07 (0.58 - 1.96)	-
Pyrazinamide AUC <sub>0-6h</sub> (for every 50 h*mg/L)	168	39	1.85 (1.23 - 2.81)	1.85 (1.23 - 2.81)
Isoniazid AUC <sub>0-6h</sub> (for every 5 h*mg/L)	168	39	1.35 (1.04 - 1.76)	-
Rifampin 15 mg/kg/day (relative to 10 mg/kg/day)	60 (vs. 60)	16 (vs. 16)	0.99 (0.49 - 1.97)	-
Rifampin 20 mg/kg/day (relative to 10 mg/kg/day)	60 (vs. 60)	14 (vs. 16)	0.84 (0.41 - 1.71)	-
NAT2 intermediate acetylator (relative to NAT2 fast acetylator)	42 (vs. 16)	9 (vs. 1)	3.63 (0.46 - 28.62)	-
NAT2 slow acetylator (relative to NAT2 fast acetylator)	32 (vs. 16)	14 (vs. 1)	9.32 (1.22 - 70.92)	-

Abbreviation: ALT, alanine transaminase; AST, aspartate transaminase; HR, hazard ratio; CI, confidence interval; AUC<sub>0-6h</sub>, area under the concentration-time curve from 0 to 6 hours; NAT2, N-acetyl transferase 2.

*Table 1. Cox proportional hazards analysis of grade 2 or higher ALT or AST elevation among HIRIF trial participants treated for drug-susceptible tuberculosis.*

**Conclusions:** While higher exposures to pyrazinamide and isoniazid and slow NAT2 acetylator status were associated with increased hepatotoxicity, only pyrazinamide exposure was associated when considering these variables together. Rifampin exposure as achieved by doses of up to 20 mg/kg/day was not associated with hepatotoxicity in standard therapy, confirming previous findings of the HIRIF trial.

Our work provides valuable insights into the hepatotoxicity of the standard-of-care regimen for drug-susceptible tuberculosis.

## LB02-110-16 Clofazimine pharmacokinetics and safety in children with rifampicin-resistant TB

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**Background:** Clofazimine is a critical drug for the management of rifampicin-resistant tuberculosis (RR-TB). Current clofazimine dosing guidelines are largely based on expert opinion, with limited data on optimal paediatric dosing and safety.

**Results:** Twenty children were enrolled (median age 6 years; IQR 1.6-14.4; 6 male; 2 with HIV). A two-compartment model successfully described the data, with allometric scaling of clearances and volumes by weight. No other covariates were identified. The median AUC was >25% higher than the adult target in children across weight categories (Figure 1). There was one grade 3 adverse event (transaminitis) possibly related to clofazimine. There were 14 instances of QTcF  $\geq$  460ms and < 480ms in 6 participants; 5 were taking  $\geq$ 1 concomitant QTcF prolonging drugs; there was no QTcF >480ms. Pharmacokinetic-QTcF modeling showed a significant linear relationship with an increase of 0.02ms for every  $\mu$ g/mL of clofazimine with no effect of concomitant QT-prolonging drugs.

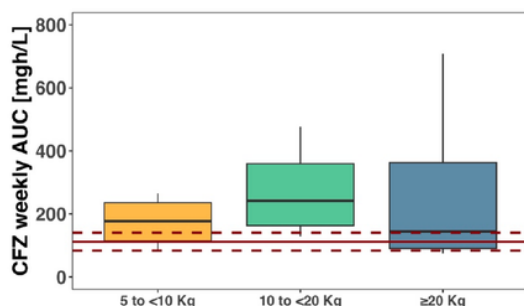


Figure 1. Area-under-the-concentration curve for clofazimine in children by weight group.

**Conclusions:** Current WHO-recommended clofazimine doses in children resulted in higher-than-expected exposures above target values, with a linear relationship between clofazimine exposure and QTcF at these doses. Lower clofazimine doses should urgently be evaluated in children.

## LB02-111-16 Memory T-cell composition contributes to lineage-specific host susceptibility to *M. tuberculosis*

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**Background:** Numerous studies show that host T cell-state composition affect susceptibility to TB and genome-to-genome studies suggest that the possibility of interaction between host and pathogen variation. We previously showed that interindividual differences in T-cell state abundance were associated with TB disease progression and that these differences likely represented intrinsic host immunity.

Here, we sought to determine whether human T-cell profiles underlie differential host susceptibility to specific *Mtb* lineages.

**Results:** Eleven (9.2%) former TB patients were infected with lineage 2, and 109 (90.8%) with lineage 4. Vd2 T cells were more abundant in the L2 than the L4 hosts (3.9% versus 1.4%, p-value < 0.0001). MASC analysis showed that Vd2 T cells were also expanded in the L2 patients (L2 versus L4; OR, 2.17; 95% CI, 1.41–3.34; Bonferroni adjusted p-value = 0.02).

**Conclusions:** Vd2 T-cell subpopulation abundance was higher in patients who had recovered from L2 infections compared to L4 infections. Previous studies have reported that Vd2 T-cells contribute to protective immunity and cytokine production against *Mtb* infection. The activation of Vd2 T-cells inhibits regulatory T-cells and mediates immune cell migration via IL-17 production during *Mtb* infection. The observation suggests that host T-cell composition is associated with specific *Mtb* lineages.

## **LB02-112-16 Differentially culturable tubercle bacilli quantified in sputum samples are associated with unfavourable treatment outcomes**

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**Background:** DCMtb do not form colonies on standard solid media but can be detected in extensively diluted liquid cultures, particularly those supplemented with *M. tuberculosis* culture filtrates (CFs) containing resuscitation promoting factors and other mediators.

We and others have shown that DCMtb frequently dominate bacillary populations in sputum and it has been suggested that their abundance provides a measure of bacillary persistence. If so, DCMtb quantification has potential to predict treatment outcomes and we address this question here.

**Results:** MPN and CFU determinations showed modest differentiation between favourable and unfavourable outcomes. However, the Resuscitation Index (RI,  $\text{Log}_{10}\text{MPN} - \text{Log}_{10}\text{CFU}$ ) clearly identified the unfavourable group in samples from 4 ( $p < 0.005$ ) and 8 ( $p < 0.05$ ) weeks.

Taking an RI threshold of 1.5 at 4 weeks gave an odds ratio of 12:1 for unfavourable outcome while an RI  $> 1.55$  at 8 weeks gave an odds ratio of 28:1.

**Conclusions:** In this retrospective study, detection of DCMtb in sputum collected at 4 and 8 weeks of treatment identified individuals who subsequently had unfavourable treatment outcomes.

Though technically demanding and time consuming, these results from 40 individuals provide evidence that outcomes can be predicted early in treatment and incentive to discover more amenable biomarkers that can inform both treatment and clinical trial management.



## LATE BREAKER PRESENTATIONS FRIDAY 17 NOVEMBER 2023

### LB03 The RIT/JATA student late-breaker session on lung health

#### LB03-113-17 Smoking induces cellular ageing and over production of reactive oxygen species in oral mucosal cells

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**Background:** The World Health Organization (WHO) estimates a 21% prevalence rate of smoking across the world that leads to about 6 million deaths per annum globally. Chemical components in cigarette smoke have been proven to cause over production of Reactive Oxygen Species (ROS). ROS in turn, alters the cell physiology which can lead to multiple oral and pulmonary pathologies.

We aimed to investigate the impact of smoking on the levels of ROS and its effects on cellular aging in oral mucosal cells.

**Results:** Smokers had higher percentage of ROS as compared to non-smokers (p value < 0.001). There was also over-expression of CYR61 gene as compared to non-smokers (p value= 0.001). While comparing ROS and cellular aging between young smokers and old smokers, surprisingly we found significantly higher % of ROS and up regulation of CYR61 gene expression in young smokers as compared to old smokers (p value 0.001 and <0.0001 respectively).

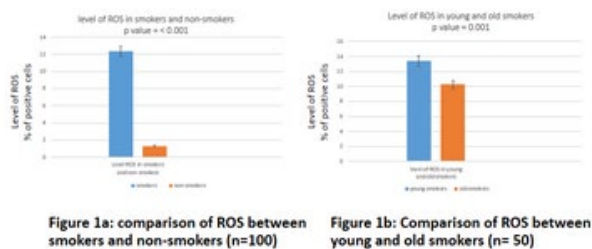


Figure 1. Comparison of ROS.

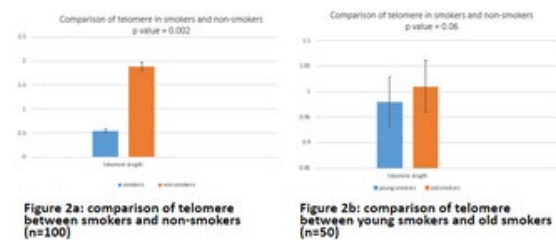


Figure 2. Comparison of telomere.

**Conclusions:** Smoking induces higher amount of ROS and cellular aging in oral mucosal cells. In young smokers, ROS and cellular aging were higher as compared to old smokers. This is alarming and might be leading cause of oral pathologies in the smoker.

#### LB03-114-17 Phylogenetic analysis of the first documented outbreak of SARS-CoV-2 variant XBB.1.16 in Botswana

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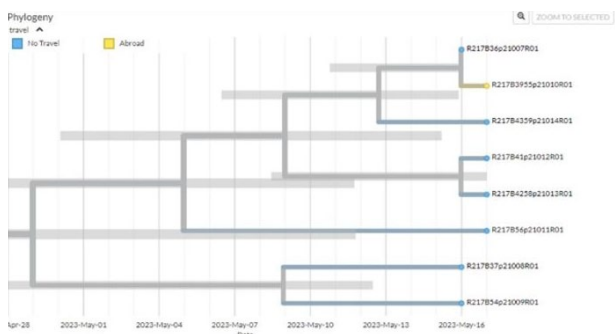
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**Background:** A recent outbreak of SARS-CoV-2 variant XBB.1.16 was identified in Botswana involving eight people with a common exposure, including one with recent travel to Germany and Tanzania. We used phylogenetic analysis to determine whether this outbreak occurred due to introduction by the person who traveled or existing community transmission.

**Results:** A total of 538 sequences were included in the time-scaled contextual tree, including eight outbreak sequences sampled on May 16 and 17. The most recent common ancestor (MRCA) of the outbreak samples was an internal node estimated at April 29 (confidence interval April 14 – May 12), and the nearest contextual sequences were from Canada, South Korea, the USA and India. Bayesian analysis of eight outbreak sequences identified the source as the individual with recent travel in 0.4% of sampled trees, and an unsampled individual in 90% of trees. BEAST2 analysis resulted in a similar estimate of time to MRCA as the contextual tree.



**Conclusions:** Our analysis suggests the outbreak was not likely due to introduction from the person with recent travel. Instead, that person may have acquired infection locally from an unsampled individual. It is unclear when this variant entered the country. Limitations of this analysis include high uncertainty in the timed phylogeny, and limited sequence data from the broader community in Botswana.

### LB03-115-17 Travel distance to rifampicin-resistant TB (RR-TB) treatment and its impact on loss to follow-up: the importance of continued RR-TB treatment decentralisation in South Africa

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**Background:** Incomplete rifampicin-resistant TB (RR-TB) treatment may lead to increased drug resistance and further transmission of RR-TB. Understanding why patients are lost from care is essential for TB control. This analysis examines the impact of travel distance to RR-TB treatment on loss to follow-up (LTFU), which has yet to be analyzed within South Africa (SA).

**Results:** Among 1444 participants, 75.7% successfully completed treatment and 24.3% were LTFU. The sample was 57.3% male, 54.9% unemployed, with 73.7% living with HIV. The median age was 35 (IQR:29-43) years and 71.9% had not completed secondary school. The overall median travel distance was 40.41km (IQR:16.78-62.57), with the median travel distances for individual treatment sites ranging from 12.50km (IQR:8.31-21.24) to 87.89km (IQR:62.57-103.81). A travel distance of greater than 40km increased odds of LTFU by 49% when adjusting for HIV status, age, gender, education level, rural residence, and treatment site, which were all significantly associated with LTFU in the final model (See Table 1).

	Final Multivariable Model <sup>1</sup>		
	OR	95% CI	p-value
≥40km from Treatment	1.49	(1.105, 2.016)	0.009
Rural Residence	0.67	(0.472, 0.971)	0.034
Age	0.97	(0.967, 0.990)	0.000
Male Sex	1.62	(1.251, 2.122)	0.000
Living with HIV	1.50	(1.116, 2.025)	0.007
Completed Secondary School	0.68	(0.509, 0.922)	0.013

<sup>1</sup>Analysis also controls for treatment site

Table 1. Odds of LTFU (N=1444).

**Conclusions:** Long travel distance to RR-TB treatment increases odds of LTFU. Factors behind this relationship may include transit cost or increased travel time. Despite past treatment decentralization efforts, interventions that bring RR-TB treatment closer to patients are still needed.

### LB03-116-17 Cost-effectiveness analysis of implementing medication monitors and differentiated care approach in South Africa

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**Background:** Digital Adherence Technologies (DATs), with a Differentiated Care Approach (DCA), may improve adherence to tuberculosis (TB) treatment. Within the TB Monitoring and Adherence Endpoints pragmatic cluster-randomised trial, we evaluated the cost-effectiveness of using the Wisepill evriMED 1000 device (medication monitor) to inform a DCA involving text messages, phone calls and home visits in three provinces of South Africa.

**Results:** With 1278 PWTB in the intervention arm and 1306 PWTB in the control arm, effectiveness was 81% and 50.8% in the intervention and control arms respectively. The total cost per patient treated for TB was \$114.28-\$206.32 (intervention) and \$100.21-\$155.73 (control), resulting in a societal incremental cost of \$21.73. Sensitivity analysis showed a decrease in provider costs when the device was re-used three times at intervention clinics with incremental costs to the provid-

	Gauteng		KwaZulu-Natal		Western Cape		Average cost	Average cost	Total	Total	Incremental difference
	Site 19	Site 09	Site 517	Site 518	Site 521	Site 525					
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control	
Study population									1 278	1 306	
Provider cost	81.93	39.28	66.39	8.97	64.95	26.96	71.09	25.07			
Patient cost	124.39	102.89	75.99	146.76	49.33	73.25	83.24	107.63			
Societal cost	206.32	142.17	142.38	155.73	114.28	100.21	154.33	132.70	197 229.54	173 306.97	23 922.57
Effectiveness (patients ≥80% adherence)									1 035.18	663.45	371.73
Incremental cost-effectiveness ratio (ICER) (Δ Costs/Δ Effects)											64.35

LB03-116-17 Table 1: Incremental cost-effectiveness ratio (ICER) of using an electronic monitor (Wisepill) and differentiated care approach.

er reducing from \$35.93-\$55.36 to \$21.73-41.17. Patient costs were \$49.33-\$124.39 per patient (intervention) and \$73.25-\$146.76 per patient (control) with indirect costs (foregone income) contributing to a large proportion of total costs at one intervention (66.2%) and two control (61.6% and 77.4%) clinics. The ICER was \$64.35.

**Conclusions:** The cost of achieving an additional adherent PWTB was estimated at \$64.35. Medication monitors and DCA can be considered a cost-effective option for scale-up if we negotiate a lower cost for monitors with manufacturers and ensure re-use of the devices, helping reduce provider costs.

### LB03-117-17 Finding the missing TB cases in Nigeria: Has community active case-finding helped in child TB diagnosis? Insights from Abia State, Nigeria

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**Background:** In Nigeria, Tuberculosis treatment coverage has increased from 30% to 40%. Despite these improvements, the proportion of TB Notification among children has remained at 7%. A significant proportion of children with TB miss out on care. This age group (0-14 yrs) has the lowest recorded number of incidences notified in Nigeria according to the 2022 TB report while Abia state child TB proportion has remained at less than 3% according to the National TB Program reports.

**Results:** 1583 (0-4 yrs) and 2667 (5-14 yrs) children were reached in the intervention. 230 (0-4 yrs) and 572 (5-14 yrs) children were TB presumptive, representing 15%

and 21% presumptive TB yield. 7 (0-4 yrs) and 29 (5-14 yrs) children were diagnosed with TB and started on TB treatment, representing 3% TB yield (0-4 yrs) and 5% (5-14 yrs) respectively. A total of 36 children (0-14 years) were started on TB treatment, representing a 4.45% yield in Child TB Notification.

		Abia State	
S/N	Data Elements	0-4 yrs	5-14 yrs
1	Total number of children reached	1583	2667
2	Total number of children screened	1583	2667
3	% of children screened	100%	100%
4	Total Number of Children with Presumptive TB	230	572
5	% of Presumptive TB yield	15%	21%
6	Total Number of Children Diagnosed with TB	7	29
7	Total Number of Children with TB placed on Treatment	7	29
8	% of TB yield	3%	5%
9	Number Needed to screen	226	92
10	Number Needed to Test	33	20

**Conclusions:** Community TB Prevention themed- interventions are efficient for Active Case finding especially for children age 0-14 yrs who are not able to present at the hospitals or health facilities without their caregivers.

### LB03-118-17 Case fatality among people with TB in a private sector treatment support programme in Bihar, India, during the first year of the COVID-19 pandemic

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**Background:** Due to COVID-19-related disruptions to TB programs, India has seen the largest drop in TB case notifications of any country globally. In the context of these disruptions, progress towards global and national TB elimination goals has been set back, making it urgent to assess case fatality among people diagnosed with TB during the pandemic.

**Results:** Of our random sample of 4,000 patients, n=2,962 (74.1%) answered the follow-up call. IPS-weighted in-treatment case fatality was 6.07% (95%CI: 5.22-6.93%). IPS-weighted post-treatment case fatality was 1.27% (95%CI: 0.79-1.79). These estimates were lower than pre-pandemic estimates (p=0.036 and p=<0.001 for in-treatment and post-treatment case fatality respectively).

Only age was a significant predictor of case fatality in both the weighted and unweighted models, with older individuals more likely to die (weighted model HR: 1.03, 95%CI: 1.02-1.05). Patients residing outside of their PPSA enrolment district had significantly higher case fatality in the unweighted model (HR: 1.50, 95%CI: 1.05-2.13), but not in the weighted model.

**Conclusions:** Although not higher than pre-pandemic estimates, the observed case fatality in this private sector cohort of people treated for TB during COVID-19 in Bihar, India is above the level needed to reach the 2025 and 2030 End TB Strategy targets for reductions in TB deaths, underlining the extent of pandemic-related setbacks to TB elimination.

### LB03-119-17 Brief tobacco cessation advice for persons with TB in Thailand

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**Background:** Pulmonary tuberculosis and smoking continue to be crucial health issues in Thailand. This study aimed to compare the outcome of a brief tobacco cessation intervention and conventional nursing care among persons with pulmonary tuberculosis.

**Results:** At a two-month follow-up, the proportion of the participants reporting the seven-day point prevalence abstinence was significantly higher in the experiment group than in the control group (40.0 percent vs 10.0 percent; *p*<0.05). The number of cigarettes per day decreased from 14.40 ± 6.57 and 13.93 ± 6.82 at the baseline to 3.50 ± 3.61 and 10.60 ± 5.93 at the end of the study in the experimental and control groups, respectively.

**Conclusions:** This brief tobacco cessation intervention had a promising outcome regarding smoking abstinence and smoking reduction. A long-term assessment of abstinence and continuing support are recommended.

### LB04 The Union/CDC late-breaker on TB (epidemiology and programmatic)

#### LB04-120-17 Increasing TB case detection through active case-finding and intensified case-finding in Rajshahi, Bangladesh

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**Background:** Despite multisectoral approaches to combat tuberculosis (TB), Bangladesh still misses 19% TB cases annually. Active Case Finding (ACF) and Intensified Case Finding (ICF) are recommended for early detection of TB in high TB-burden countries. USAID's Alliance for Combating TB in Bangladesh (ACTB) Activity initiated ACF and ICF activities to increase TB detection in Rajshahi, Bangladesh.

**Results:** Between October '22 - March '23, from activity sites, ACTB screened 16,06,039 individuals for TB. 39,209 (2%) TB presumptive were identified, and 33,209 (87%) were tested. Ultimately, 3,364 people were diagnosed with TB (Table-1) and 99.9% were enrolled for treatment. TB positivity rate was high (1,138/6597, 17%) at tertiary and secondary healthcare facilities.

Indicators	Tertiary and Secondary facilities (%)	Primary/Upazila facilities (%)	Community (%)	Total (%)
Persons screened for TB	2,85,687	9,66,189	3,54,163	16,06,039
TB presumptive identified	7,248 (3)	21,606 (2)	10,355 (3)	39,209 (2)
TB presumptive tested	6,597 (91)	18,913 (88)	8,501 (82)	34,011(87)
Total TB (all forms) identified	1,138 (17)	1,738 (9)	488 (6)	3,364 (10)
Pulmonary-Bacteriologically confirmed (B+)	817 (47)	259 (53)	1,453 (43)	1,454 (43)
Pulmonary-Clinically diagnosed (CD)	627 (36)	160 (33)	1,012 (30)	1,010 (30)
Extra-pulmonary (EP)	294 (17)	69 (14)	899 (27)	898 (27)
Persons with TB who started treatment	1,138 (100)	1,738 (100)	484 (99)	3,360 (100)

Table-1: ACF at Rajshahi Division (October 2022 to March 2023).

Over half (1,738, 51.7%) of early-stage TB were identified at primary healthcare facilities. Moreover, 488 (14.4%) TB identified from community may have been undiagnosed without ACF. Among all identified TB, 66% (2226/3364) were from primary healthcare facilities and communities. The combined approaches increased TB notification in the division. Post-ACTB intervention, national data (October '22 - March '23) of TB notifications (14,589) in Rajshahi increased, compared to the

same period in previous year (14,031). Detection increased by 9% in January - March '23 (7,614) compared to October - December '22 (6,973).

**Conclusions:** Simultaneous implementation of community-based ACF and facility-based ICF is effective for increasing early TB detection and reducing transmission. TB in community may remain undiagnosed with ACF. High TB-burden countries in similar settings can initiate this comprehensive approach to achieve End TB targets.

### LB04-121-17 Targeted active case-finding should be prioritised in settings with low notification rates: lesson learnt from TB case-finding among minorities in Cambodia

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**Background:** Cambodia's estimated TB burden is approximately 52,000 cases, while the NTP reported 30,017 notifications in 2019. It was demonstrated that there is still a large gap in case notifications (42%). Hard-to-reach minority communities mostly live without seeking health care when they face health problems. **Results:** Across three rural ODS, 28 communities were visited by the mobile ACF team on ACF days, resulting in a screening of 8,348 presumptive cases by CXR. 1,190 (14%) were tested by GeneXpert, resulting in the detection of 214 Bac+. A total of 440 new TB cases in all forms were put on treatment. New TB case notifications increased by +370% during a semester of ACF compared to the five-year trend of expected notifications. This translates into an estimated 321 TB patients being treated who would not have received care in the absence of the ACF intervention.

**Conclusions:** Hard-to-reach population groups are often unaware of the extent of the TB intervention in their communities and the potential for ACF. In settings with low notification rates, targeted ACF interventions such as this should be prioritized to reduce the pool of prevalent TB patients.

### LB04-122-17 Initial experience of delamanid-containing regimen implementation under the National TB Elimination Programme in India

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**Background:** The landscape of drug-resistant tuberculosis (TB) drug development has evolved over the past decade. Delamanid (DLM) is one of the recently endorsed drugs recommended by World Health Organization (WHO) for multi drug resistant TB (MDR-TB) treatment. In India, it was approved under the Conditional Access Programme of the National TB Elimination Program (NTEP) and was implemented in selected sites across the nation. We present the in-country early experience of the programmatic implementation of Delamanid for its efficacy and safety.

**Results:** A cohort of 462 DR-TB patients (Mean age 21.7±12.3 years) were initiated on Delamanid containing 24 – 30 months treatment regimen. Around 68.8% and 67.2% of patients showed culture conversion at the end of 3<sup>rd</sup> and 6<sup>th</sup> month respectively. Treatment success rate was observed as 62%. 11.7% adverse events including 92 deaths were reported. QTc prolongation was seen in 3.97% patients and only 2 patients required discontinuation of DLM. Further, those with prolonged QTc intervals were receiving clofazimine which could also potentially cause prolongation. Loss to follow-up was observed as 7.8%.

**Conclusions:** Delamanid containing regimen under conditional access programme in India has shown treatment success rate of 62% and death rate of 20%. Hence, India has mainstreamed Delamanid drug regimen under NTEP as group C drug as per WHO recommendation in longer oral regimen for MDR-TB.

### LB04-123-17 Results of operational research of a modified, shorter, all-oral treatment regimen for drug-resistant TB in Tajikistan

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**Background:** Main objective of the study was to determine the effectiveness of modified short-term all-oral regimen (mSTR) for rifampicin-resistant Tuberculosis (RRTB).

Sub-objectives were to determine:

- incidence of serious adverse events and adverse events of special interest (AEs) of severity grade  $\geq 3$ ;
- timing of sputum culture conversion;
- emergence of drug resistance to mSTR components;
- frequency of relapses after mSTR within 12 months after successful treatment.

**Results:** 102 patients were enrolled during 01 Oct 2020 – 30 Sept 2022: 82 patients cured, 11 completed treatment (91.1% success rate), 4 failed, 3 died, 2 - lost for follow-up.

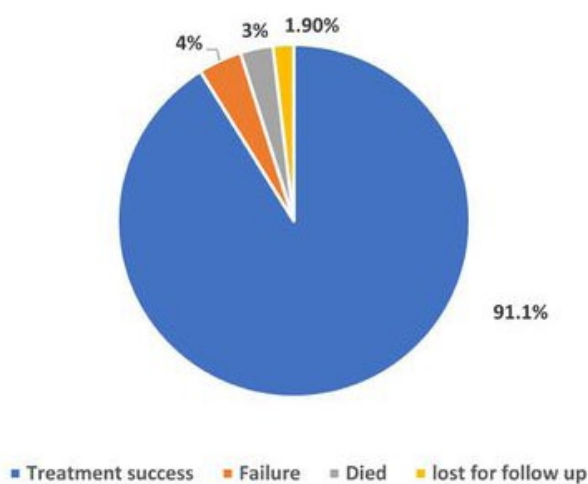


Figure. Treatment results of the patients on mSTR in Tajikistan, 1 Oct, 2020 - 30 Sept, 2022.

19 AEs were observed, 18 of them were managed with treatment continuation, 1 resulted in treatment termination.

Among 74 initially culture-positive patients in 12 cases conversion occurred after 1<sup>st</sup> month, in 20 cases after 2<sup>nd</sup> month, in 42 cases after 3<sup>rd</sup> month.

Among patients with successful treatment 1 relapse occurred during 12 months of observation.

In 3 cases additional resistance to fluoroquinolones was observed.

**Conclusions:** Based on positive results and safety profile, the National TB Program is expanding implementation of mSTR in Tajikistan.

## LB04-124-17 A prospective cohort study of long-term outcomes among people with multidrug-resistant TB in Vietnam

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**Background:** True rates of mortality and disease recurrence among people with multidrug-resistant (MDR-TB) are likely underestimated due to patient loss to follow-up. We estimated long-term rates of TB recurrence and mortality among a cohort of people treated for MDR-TB in Vietnam.

**Results:** We reached 1410/1535 (91.9%) patients enrolled in VQUIN between March 2016 and August 2019. Follow-up was complete in 88.4% (1357/1535), with 3.45% (53/1535) refusing. Median follow-up time since trial enrolment was 55.7 months (IQR: 45.1-68.1).

The rate of treatment success (composite of complete and cure) for the index MDR-TB episode was 83.7% (95% CI: 81.6-85.5). MDR-TB reportedly recurred among 3.82% (46/1410) of patients. The rate of MDR-TB recurrence was 7.44 (95% CI: 5.44-9.92) per 1000 person-years. Since enrolment, 243/1410 (26.3%) index patients died.

According to verbal autopsies, TB was the probable or confirmed cause of death in 39.5% (96/243) of index patients, with HIV leading to mycobacterial infection causing a further 7.00% (17/243) of deaths. Self-reported positive COVID-19 test result was not associated with increased mortality risk.

**Conclusions:** Despite high rates of reported treatment success, MDR-TB survivors in Vietnam have high risks of disease recurrence and mortality. Further work to address reversible factors associated with mortality and recurrence are critical to reducing the burden of MDR-TB in Vietnam.

## LB04-125-17 Diagnostic and treatment delay among rifampicin-resistant TB patients in China: a multicentre observational study

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**Background:** Rifampicin-resistant tuberculosis (RR-TB) patients experience complex diagnosis and treatment processes. This study aims to measure the diagnostic and treatment delay of RR-TB patients in China and investigate the relevant factors.

**Results:** A total of 98 RR-TB patients were surveyed. The median (IQR) diagnosis and treatment delay was 238 (80.8-430.5) days. Major delay occurred between TB diagnosis and identifying rifampicin resistance, with the median duration of 43 (3-161) days (Figure). Patients diagnosed with traditional drug susceptibility testing experienced a longer delay in identifying rifampicin resistance than those diagnosed with molecular testing (72 (45-153) vs 12 (1-166.2),  $p = 0.006$ ).

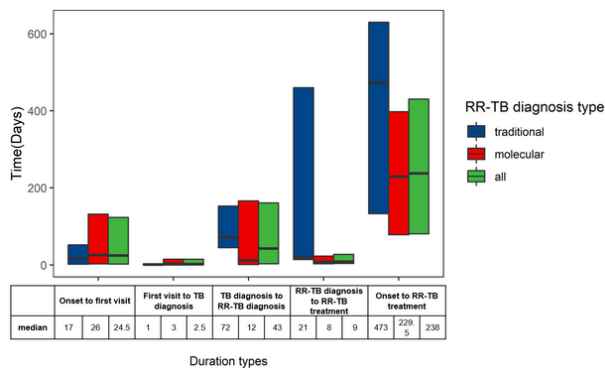


Figure.

Ignoring the effect of the duration for drug susceptibility testing, delay in identifying rifampicin resistance still exists. More precisely, 55.5% (10/18) and 47.5% (38/80) of participants received RR-TB diagnosis more than 60 or 14 days after their TB diagnosis in patients diagnosed with traditional drug susceptibility testing or molecular testing, respectively. Qualitatively, the most common reasons for this delay included the lack of awareness regarding drug susceptibility in presumptive TB, the absence of drug susceptibility testing capabilities, difficulties in obtaining pathogenic samples, and the high cost of the assay.

**Conclusions:** Although molecular drug susceptibility testing has helped decrease the diagnosis delay for RR-TB patients, delay in identifying rifampicin resistance in China remains longer than expected. Raising awareness and improving the availability and accessibility of drug susceptibility testing are needed.

## LB04-126-17 Reducing TB care cascade losses in the private sector: the results of a pilot intervention in eThekweni, South Africa

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**Background:** While TB is primarily addressed in South Africa's public sector, recent evidence suggests TB may be missed or delayed in the private sector. We introduced a pilot project in a high-TB burden Health District to connect private General Practitioners (GPs) to free TB testing in the public sector.

We aimed to

- Gauge GPs' willingness to participate and;
- Describe the patterns of TB diagnosed in the private sector.

**Results:** Half of approached GPs agreed to participate (158/313), 79.0% of whom underwent training ( $n=128$ ) and 47.7% submitted specimens ( $n=61$ ). Specimen yield and quality were high at 17.6% and 99.7%, respectively. About half of specimens submitted were from men (52.0%) and a third from clients living with HIV (33.9%). 107 clients were diagnosed with TB, more than half of whom were men (60.7%) and about half were known to be living with HIV (48.5%). Three clients were diagnosed with drug-resistant TB (2.9%). One hundred people with TB were linked to treatment, nearly all in the public sector (97.2%) in an average of 2 days (IQR 1-5). Two people with TB died before diagnosis by culture and six died during treatment.

**Conclusions:** The pilot was successful. One fifth (19.5%) of GPs submitted specimens without monetary incentives and helped link 100 clients to TB treatment expeditiously, suggesting a workable model for improving TB management in South Africa's private sector.

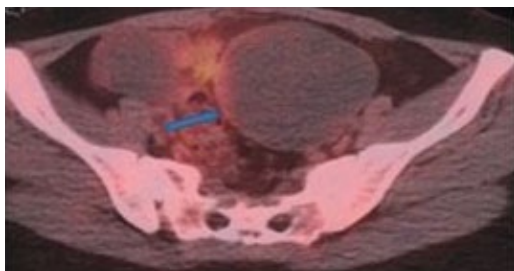
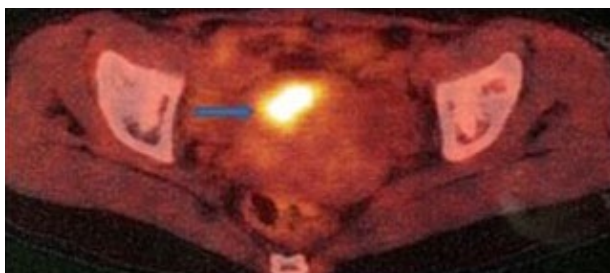
### LB04-127-17 Prevalence of genital involvement and tubo-ovarian masses in pulmonary TB in adolescent girls

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**Background:** Pulmonary TB (PTB) is common in adolescent girls and can cause involvement of genital organs, later on can causing infertility. The study aims to show the prevalence of genital involvement and tubo-ovarian masses in Pulmonary tuberculosis in an Adolescent girls.

**Results:** Out of 280 PTB adolescent girls, 42 (15%) had ultrasonic abnormalities in the form of tubo-ovarian masses in 34 (80.95%) (bilateral in 22 (52.38%), right sided 8(19%) and left sided in 4 (9.5%) cases. Other abnormalities were hydrosalpinx in 12 (28.57%), bilateral in 7(16.6%) and unilateral in 5 (11.9%), thin endometrium in 34 (80.95%), endometrial fluid in 18(42.8%), endometrial calcification in 2 (4.7%), endometrial synchiae in 4(9.5%), impaired endometrial vascularity in 12 (28.57%), ascites in 6(14.2%) and peritoneal omental thickening in 4 (9.5%) cases. Menstrual blood was positive for PCR in 18 (42.8%) cases but didn't show AFB on microscopy or culture in any case.

Figure 1 shows findings (A) F18 FDG-PET/CT study showing large cystic mass (arrow) with mildly increased FDG uptake (B) adnexal mass (arrow) with no FDG uptake. Subjects were treated with 6 months of ATT. USG and PET CT was normal in 38 patients (90.4%) but had persistent TO masses in 3 (7.14%) patients (without increase of FDG uptake) and uterine synchiae in 2 (4.7%) patients.



**Conclusions:** There is a high involvement of genital organs in pulmonary tuberculosis cases. Timely diagnosis and treatment can prevent permanent damage to genital organs thus can prevent future infertility.



## LATE BREAKER PRESENTATIONS SATURDAY 18 NOVEMBER 2023

### LB05 The Union late-breaker session on COVID-19

#### LB05-128-18 Durability of effectiveness of heterologous COVID-19 vaccine regimens: an analysis of national registration data from Thailand

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**Background:** Investigations into the durability of COVID-19 vaccine heterologous effectiveness have been primarily conducted in high-income countries. Limited evaluations of heterologous vaccine policies in lower- and middle-income countries (LMICs) are partly due to inadequate population databases.

This study aimed to assess the durability of vaccine effectiveness (VE) for heterologous vaccine sequences (HVS) against severe and fatal COVID-19 in Thailand.

**Results:** The study involved 52,580,841 individuals, with approximately 32% and 29% having received two-dose and three-dose common HVSs, respectively. Two-dose HVSs provided around 50% VE against severe and fatal COVID-19 for 2 months; however, the protection significantly declined over time. Three-dose HVSs sustained over 50% VE against both outcomes for at least seven months. The CoronaVac/CoronaVac/ChAdOx1 sequence demonstrated over 80% VE against both outcomes, without evidence of VE waning from model projection. Its final monthly measured VEs (95% CI) against severe and fatal COVID-19, seven months after the last dose, were 82% (80.3%, 84.0%) and 86.3% (83.6%, 88.7%), respectively.

**Conclusions:** The evidence that three-dose HVSs provide high and durable protection against severe and fatal COVID-19 should be taken into account as LMICs prepare for the next pandemic.

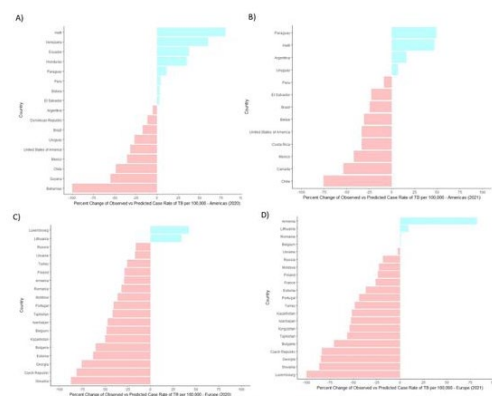
#### LB05-129-18 Impact of the COVID-19 pandemic on incarceration and TB notification rates among individuals who are incarcerated in Europe and the Americas

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**Background:** The COVID-19 pandemic has led to major disruptions in diagnosis, treatment, and care for tuberculosis programs globally. However, the impact of the pandemic on incarceration and tuberculosis notification rates among people who are incarcerated, a high-risk, vulnerable group, is unknown.

**Results:** Of the 101 countries in European and PAHO region, 79 and 41 countries were included for incarceration and notification rate outcomes, respectively. In Europe, most countries reported lower incarceration and tuberculosis cases per 100,000 persons in 2020 (28/40 and 17/19 countries) and 2021 (25/36 and 17/21 countries) than expected. The mean percent change between observed/predicted tuberculosis notification rates in 2020 and 2021 was -37%. Whereas, in the Americas, trends in incarceration and tuberculosis rates in prisons were highly heterogeneous; 9 (53%) countries had reduced notification rates in prisons in 2020 while 8 (47%) had higher notification rates (Figure).

The mean percent change between the observed/predicted tuberculosis notifications rates for the Americas was -6% in 2020 but decreased to -16% in 2021. Countries in the Americas with elevated notification rates during the pandemic were more likely to be countries with a high tuberculosis burden in prisons (e.g., Haiti, Venezuela, Peru, Paraguay).



**Figure 1** A) Percent change in the observed vs. predicted case rate of Tuberculosis per 100,000 persons who are incarcerated by country in the Americas for 2020 B) Percent change in the observed vs. predicted case rate of Tuberculosis per 100,000 persons who are incarcerated by country in the Americas for 2020 C) Percent change in the observed vs. predicted case rate of Tuberculosis per 100,000 persons who are incarcerated by country in Europe for 2020 D) Percent change in the observed vs. predicted case rate of Tuberculosis per 100,000 persons who are incarcerated by country in Europe for 2021. Red indicates that the observed was less than the predicted; Blue indicates that the observed was greater than the predicted.

**Conclusions:** Our findings suggest that the COVID-19 pandemic has substantially impacted tuberculosis notification rates in prisons, with especially substantial decreases throughout Europe.

### LB05-130-18 COVID-19 survivors-led intervention to increase vaccine uptake among female sex workers in Oyo State, Nigeria

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**Background:** Emerging evidence suggests that female sex workers (FSWs) face unique and profound risks from the COVID-19 pandemic. Most FSWs work without personal protective equipment during this outbreak; even wearing a mask is not welcomed by their clients. This paper, therefore, presents the outcome of COVID-19 survivors-led intervention to increase vaccine uptake among FSWs in Oyo State, Nigeria.

**Results:** Participants' with a good knowledge of COVID-19 increased from 12.6% before the training to 89.9% at the end of the training. At three months, 34.9% of the participants went for vaccination, which increased to 67.1% at six months.

**Conclusions:** Survivors-led intervention is effective in increasing sex workers' knowledge of COVID and uptake of vaccine. Involving survivors to share their experiences with their peers could be encouraged to ensure the success of similar programmes in the future.

### LB05-131-18 Can social activities be used to promote uptake of COVID-19 vaccination among younger men who have sex with men in Oyo State, Nigeria?

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**Background:** The COVID-19 pandemic reinforces health inequities among vulnerable populations, including men who have sex with men. Younger Men Who Have Sex with Men (YMSM) may be more impacted by the economic effects of COVID-19 and may be particularly vulnerable to reduced access to health services. This paper presents the outcome evaluation of social activities in promoting the uptake of COVID-19 vaccination among YMSM in Oyo State, Nigeria.

**Results:** Of 129 YMSM recruited for this intervention, 9 (6.98) were lost to follow-up. Respondents' mean age was 21.5 ± 2.2 years; 24.5% had completed secondary education, 43.6% were staying alone, and 12.9% had

parents who were not alive. Only 9.6% of the participants had a good knowledge of COVID-19 at baseline, which increased to 72.2% at the endline. None (0.0%) of the participants reported at baseline that they had taken the COVID-19 vaccine; at endline, 68.1% reported receiving it. Among these, only 58.5% showed evidence of this vaccination.

**Conclusions:** Social activities are effective in promoting the uptake of COVID-19 vaccination among *young men who have sex with men*.

### LB05-132-18 Remote aerosol SARS-CoV-2 transmission from clinical COVID patients to rodent sentinels

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**Background:** We performed studies investigating the feasibility of a human to animal (H2A) model system, to test whether patient generated respiratory bioaerosols hold infective capacity when traversing long distance airborne transport, within the built environment.

**Results:** In this study, seven (7) COVID-positive patients spent a cumulative 409.5 in-residence hours in the ward during a 17-day period. Two hundred and sixteen pair-housed golden Syrian hamsters (n=216) were exposed continuously to the ward ventilatory exhaust during this time. Analysis of available animal serum (n=146) collected at study termination indicated anti-SARS-CoV-2 IgG positivity (LOD 5.56 ng/ml) in over half (58.2%) of animals sampled.

**Conclusions:** Preliminary results support the concept of long-distance transport (>50 meters) of infectious viral bioaerosols generated from clinical patients remaining infective as evidenced by anti-SARS-CoV-2 antibodies in the rodent sentinels.

These findings also promote the posit that remotely generated SARS-CoV-2-containing bioaerosols may manifest as stochastically dictated disease induction rather than a deterministic threshold effect.

Further confirmatory studies are necessary to broaden our understanding of infection patterns in this idealized H2A transmission model system.

### LB05-133-18 Lessons learnt from COVID-19 modelling efforts for policy decision-making in lower- and middle-income countries

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**Background:** The COVID-19 pandemic has had devastating socio-economic effects. Mathematical modelling had a significant role in informing difficult trade-offs. There is little evidence on what approaches worked to guide policy decisions during the pandemic, especially in lower- and middle-income countries (LMICs). Guided by Graham’s knowledge-to-action framework, we sought to identify knowledge translation mechanisms, enabling factors, and the structures needed to ensure the successful translation of evidence to policy decisions for the pandemic and future emergencies

**Results:** We engaged with 147 researchers and 57 policymakers from 28 countries. We found the common knowledge translation mechanisms used during the pandemic included policy briefs, face-to-face debriefings, and dashboards. Some of the reported enabling factors included existing relationships and open communication between researchers and policymakers; trust and credibility of research institutions; stakeholder engagement throughout especially in the co-production of policy questions; and embeddedness of the researchers in the policymaking space. Factors required to strengthen knowledge translation included capacity building of modelling expertise and communication, improving on data infrastructure, sustained funding for modelling, and dedicated knowledge translation platforms.

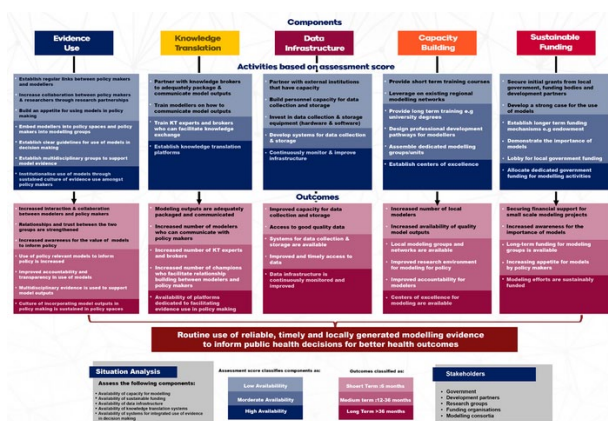


Figure 1.

**Conclusions:** Our study provided a better understanding of knowledge translation, especially in lower and middle-income countries in a global health crisis.

The findings were instrumental in co-creating a framework (Figure 1) that hopefully can be used in similar settings to guide evidence-based policy decision-making for future public health emergencies.

### LB05-134-18 Phone-based contacts and health outcomes in tele-case management for COVID-19 patients in Thailand: a retrospective cohort study

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**Background:** During the COVID-19 pandemic, case management became essential for emergency response. It includes assessment, planning, care coordination, evaluation, and advocacy for patients and their families, with effective communication between them and healthcare team being a key feature.

However, some studies lacked details on communication during self-isolation, and few evaluated patient outcomes when using phone calls or mobile applications.

Purposes (Code ICD-10-TM <sup>a</sup> )	total	Disease severity		
		Mild n (%)	Moderate n (%)	Severe n (%)
1. Screening, triage, and clinical assessment (999-01-90), n (%)	2,141	1,122 (52.4)	954 (44.6)	65 (3.0)
2. Interpreting preliminary results (999-00-00)				
2.1 Laboratory (011-04-00), n (%)	359	205 (57.1)	152 (42.3)	2 (0.6)
2.2 Assessment tools (012-05-00), n (%)	4	4 (100.0)	0	0
3. Drug administration (012-00-00), n (%)	942	482 (51.2)	448 (47.6)	12 (1.3)
4. Monitoring symptom changes (999-03-40)				
4.1 Vital signs, n (%)	3,782	2,258 (59.7)	1,489 (39.4)	35 (0.9)
4.2 Symptoms, n (%)	8,684	4,958 (57.1)	3,645 (42.0)	81 (0.9)
5. Nursing care (012-03-11)				
5.1 Health education, n (%)	397	244 (61.5)	153 (38.5)	0
5.2 Energy conservation/sleep enhancement, n (%)	83	42 (50.6)	41 (49.4)	0
5.3 Infection prevention control, n (%)	81	42 (51.9)	39 (48.1)	0
5.4 Nutrient intake, n (%)	1,019	558 (54.8)	460 (45.1)	1 (0.1)
5.5 Counseling, n (%)	51	28 (54.9)	23 (45.1)	0
5.6 Emotional support, n (%)	54	30 (55.6)	24 (44.4)	0
6. Discharge planning (999-95-40)				
6.1 Medical device delivery, n (%)	29	23 (79.3)	16 (55.2)	0
6.2 Referrals, n (%)	419	234 (55.8)	177 (42.2)	8 (1.9)
6.3 Phone calls, n (%)	8,980	5,080 (56.6)	3,808 (42.4)	92 (1.0)

<sup>a</sup>ICD-10-TM = International Classification of Diseases, Thai Modification

Table. Frequency of phone-based contacts and their purpose, using ICD-10-TM, nursing intervention codes, 2021 as a referential terminology for call categorization.

This study aimed to assess phone-based contacts in the tele-case management for COVID-19 patients in Thailand and examine the association between disease severity and the health outcomes.

**Results:** Between 28 July 2021 and 31 October 2021, a total of 8,980 phone calls were made to all patients, primarily for symptom monitoring, noting that a single call might serve multiple purposes. In contrast, counseling and emotional support calls were less frequent. This study showed positive health outcomes with no deaths or complications during discharge. It also found a statistically significant association between disease severity and health outcomes ( $C = .075$ ,  $p = .007$ ).

**Conclusions:** Daily phone calls are important for communication in tele-case management. However, counseling and emotional support should be given more emphasis and strengthened. Tele-case management proved to be a crucial strategy in ensuring patient safety across a diverse group with varying disease severity.

## TBSCIENCE 2023 ORAL ABSTRACTS

### TBS1B TB within the Global AMR fight: preventing drug resistance - Oral abstract presentations

#### TBS1B-10 The PanACEA SUDOCU trial shows sutezolid is a safe and effective oxazolidinone

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**Background:** Linezolid, an oxazolidinone, is a critical component of current multi-drug resistant tuberculosis (MDR-TB) treatment, but with toxicity limiting widespread use. Sutezolid is a novel oxazolidinone, with a hypothesized improved safety profile, only previously tested in humans in a 14-day monotherapy study.

**Methods:** The PanACEA Sutezolid Dose-Finding and Combination Evaluation (SUDOCU) study utilized a novel approach at defining the exposure-response relationship of a drug in a combination that would be usable in drug-sensitive (DS-) and MDR-TB, also allowing the assessment of late toxicities.

Participants with pulmonary DS-TB were randomised among five arms: no sutezolid, or sutezolid at doses of 600mg once-daily, 1200mg once-daily, 600mg twice-daily or 800mg twice-daily, added to bedaquiline, delamanid and moxifloxacin at standard doses for 12 weeks. After study treatment, participants received isoniazid and rifampicin for a further 14 weeks.

The primary efficacy endpoint was the slope of decline of bacterial load, measured by weekly MGIT TTP over 12 weeks. Evaluation of safety outcomes included oxazolidinone-class toxicities myelosuppression and neuropathy.

**Results:** 75 participants were enrolled in four sites in Tanzania and South Africa. No clinical neuropathy occurred during study treatment. One potential event of myelosuppression was noted: a person with HIV developed neutropenia <500/ $\mu$ l with a possible etiology of benign ethnic neutropenia. One participant experienced hepatotoxicity requiring treatment interruption. Pharmacokinetic-pharmacodynamic modelling, adjusting for baseline bacterial load and severity of lung damage, showed increased bacterial killing at higher sutezolid exposures ( $p=0.04$ ), without an apparent ceiling. The effect was estimated to 11.9% faster decline in bacterial load (95% confidence interval 0.5-26.8) at median sutezolid exposure, compared to no sutezolid.

**Conclusions:** In PanACEA SUDOCU, sutezolid given over 12 weeks at various doses showed no neuropathy nor myelosuppression, except one case of neutropenia with a possible alternative cause. Sutezolid improved bacterial killing when added to highly-potent backbone regimen.

#### TBS1B-15 Repurposing meropenem for TB and its role in the restoration of rifampicin activity for drug resistance

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Meropenem, in combination with amoxicillin/clavulanate, has demonstrated activity against drug-sensitive TB in early bactericidal activity (EBA) trials. In vitro, meropenem appears to restore rifampicin sensitivity in rifampicin-resistant (RR) TB strains. To see if this is true in patients with RR-TB, we evaluated this unconventional treatment strategy in an EBA trial in which we compared meropenem with vs. without rifampicin (NCT03174184, COMRADE).

Participants with RR-TB were randomized 3:2 to meropenem 2 g intravenously three times daily in combination with 500 mg/125 mg amoxicillin/clavulanate TID plus rifampicin 20 mg/kg once-daily (MeroAC+RIF) or MeroAC alone. Treatment was given for 14 days. Overnight sputum samples were collected serially and analysed to determine the change in colony-forming units ( $\log_{10}$ CFU) and time to positivity (TTP) over 14 days. CFU-EBA<sub>0-14</sub> and TTP-EBA<sub>0-14</sub> were determined using a model-based approach. Safety assessments were performed.

Of 52 participants enrolled at TASK in Cape Town, 14 (9 in MeroAC+RIF, 5 in MeroAC) stopped treatment early. 11% of participants on MeroAC+RIF and 7% on

MeroAC experienced grade 3 adverse events. The most common side effect was nausea and vomiting. In the MeroAC+RIF arm, the median CFU-EBA<sub>0-14</sub> (2.5th-97.5th percentiles) was -1.33 log<sub>10</sub>CFU (-3.64 to 0.15) and TTP-EBA<sub>0-14</sub> 136.91 hours (26.34 - 565.63). In the MeroAC arm, the CFU-EBA<sub>0-14</sub> count was -1.20 log<sub>10</sub>CFU (-2.66 to -0.05) and TTP-EBA<sub>0-14</sub> 114.85 hours (44.51 - 332.79). No exposure-response relationship was found and no significant difference in treatment response was detected across arms (Figure).

MeroAC is active against rifampicin-resistant TB, but dose-limiting toxicity and tolerability issues hamper its use. MeroAC failed to restore rifampicin activity against drug-resistant strains, contrary to findings in *in vitro* experiments.

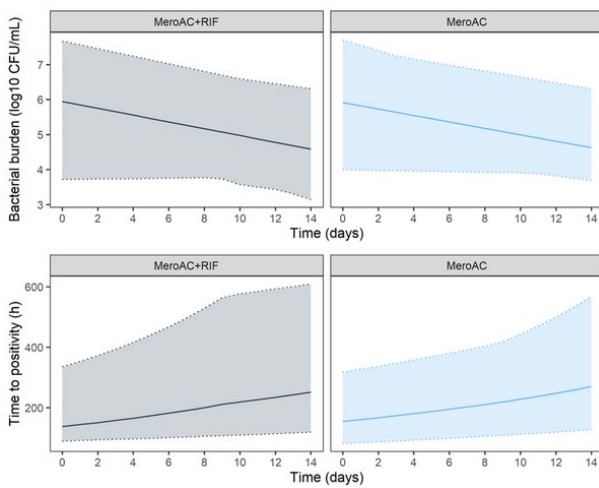


Figure.

Predicted individual CFU based on Bayes estimates of the final model. Lines show the median with a 95% confidence interval (shaded area).

### TBS1B-20 Sub-clinical drug-resistant TB missed by Xpert MTB/RIF in a rural South African community

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**Background:** Subclinical tuberculosis (TB) comprises up to half of prevalent pulmonary TB globally. The relevance of this to transmission of drug-resistant organisms is unknown.

**Methods:** Between 2018-2020, we conducted a community-based survey to characterize infectious and non-communicable diseases in a health and demographic surveillance area in rural KwaZulu-Natal, South Africa. For participants who reported any of the four WHO TB screening symptoms or had any chest x-ray abnormality, we collected sputum for Xpert MTB/RIF Ultra (Xpert), MGIT liquid culture (MGIT) and phenotypic drug sensitivity.

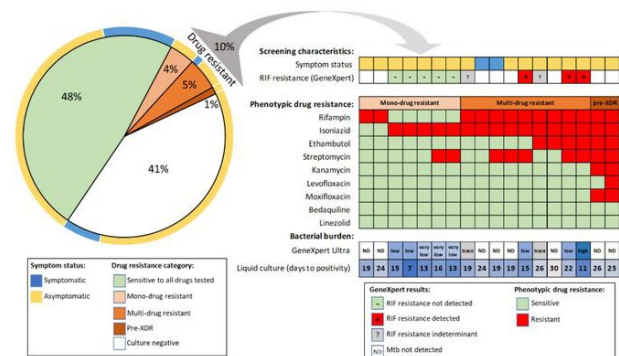


Figure 1.

**Findings:** Among 18,041 screened individuals, 174 (1.0%) had newly diagnosed microbiologically-confirmed TB, defined as either Xpert or MGIT positive sputum. Of these 82% (143/174) were asymptomatic according to the WHO 4 symptom screen and were defined as sub-clinical TB. Compared to people with symptomatic TB, those with subclinical TB had a similar Xpert cycle threshold (median 27.9 vs 28, p=0.8) and similar days to MGIT positivity (16.4 vs 15.3, p=0.8). Of those with microbiologically-confirmed TB, 10% (18/174, Figure 1, left) had phenotypic drug resistance with no difference

by symptom status (6.5% of symptomatic TB vs. 11% of subclinical TB,  $p=0.4$ ). Of the 18 drug-resistant isolates characterized (Figure 1, right), 88.9% (16/18) were from subclinical TB, 50% (9/18) were multi-drug resistant (MDR) and 11.1% (2/18) were pre-extensive resistant (pre-XDR). 13/18 (72.2%) had phenotypic evidence of rifampin resistance, but only 3/13 (23.1%) of these were identified by Xpert.

**Conclusions:** Individuals with subclinical, microbiologically-confirmed TB had similar bacterial burden and frequency of drug resistance as those with symptomatic TB. Eighty percent of rifampin-resistant strains were found in people with subclinical TB and three-quarters of these were “missed” by Xpert test. These findings highlight a substantial reservoir of drug-resistant TB that is unlikely to be detected by current, passive case-finding strategies.

### TBS1B-25 Moxifloxacin pharmacokinetic/pharmacodynamic studies indicate critical parameters in the hollow-fibre system for TB are currently overlooked

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The Hollow-Fiber system for Tuberculosis (HFS-TB) is a preclinical *in vitro* pharmacokinetic/pharmacodynamic (PKPD) tool qualified by the European Medicines Agency to underpin the anti-TB drug development. Bacteria growing in a bioreactor are subjected to different concentration-time exposures of drug(s) or drug combinations by mimicking their PK profiles. Preclinical data feed *in silico* mathematical modelling to efficiently inform Phase II/III clinical trial designs.

Despite advantages and potential benefits that HFS-TB could offer to public health stakeholders, this methodology is quite novel and no comprehensive recommendations, standard procedures or mandatory quality controls are established in the field. As such, reported studies provide insufficient data for intra-laboratory reproducibility, thereby omitting key parameters that may impact recommendations.

In this work, aiming to understand the impact of key HFS-TB parameters, we mimicked the PK profile of a moxifloxacin oral single dose of 400 mg QD and assessed: (i) bacterial growth dynamics of different strains in several medium composition, and (ii) drug compatibility with different types of cartridges.

Bacterial growth dynamics significantly varied in the different conditions tested (type of cartridge, growth media, etc...), with bacterial adaptation times impacting on antimicrobial activity. Monitoring of actual PK profiles in the extra-capillary space (ECS), where bacteria reside, was critical to depict PKPD relationships. Evidence showed a lag time between moxifloxacin was infused in the HFS and the desired concentration was reached in the central compartment and the cartridge's ECS; concentration at the ECS is related to the compatibility of the drug to the fibers of the cartridge and hardly reported.

Our data draw attention on multiple aspects of HFS-TB experiments that are currently overlooked and advise critical parameters that should be considered for future analysis of new drugs or combinations.

This work has received support from the Innovative Medicines Initiatives 2 Joint Undertaking (grant No 853989).

### TBS2D Correlates of protection as a guide to novel vaccine design and host-directed therapy - Oral abstract presentations

#### TBS2D-10 Functional heterogeneity of *M. tuberculosis*-specific-CD4 T-cells revealed by single-cell RNA-seq according to infection outcomes

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**Background:** There is a growing body of evidence indicating that control of *Mycobacterium tuberculosis* (Mtb) by CD4 T-cells involves mechanisms in addition to IFN- $\gamma$  production.

**Objectives:** We aimed to assess the full spectrum of Mtb-specific-CD4 T-cells in individuals controlling Mtb compared to those who developed symptomatic tuberculosis (TB).

**Methods:** Following PBMC stimulation with Mtb antigen pool, single-cell transcriptomic analysis on FACS-sorted Mtb-specific-CD4 T-cells (CD154+CD69+) was compared between three infection outcomes:

1. Symptomatic TB patients,
2. QuantiFERON (QFT)-positive Mtb-sensitized individuals,
3. TB “resisters” who were persistently QFT-negative TB household contacts with no parenchymal lesions on PET/CT scan .

**Results:** scRNA-seq analysis of 24,279 Mtb-specific-CD4 cells identified eight distinct T-cell subpopulations, with varying distribution across the three infection outcomes. Gene expression analysis showed that only a small proportion of cells exhibited high levels of Th1-related transcripts, traditionally associated with protective immunity (IFN- $\gamma$ , IL-2).

This IFN- $\gamma$  cluster was characterized by elevated expression of effector function and chemokine- transcripts including GM-CSF, CCL20, GZMB, CCL3, CCL4.

The remaining clusters encompassed the majority of Mtb-specific-T cells, with clusters enriched for Th2-associated transcripts (IL-4, IL-13, IL-5 – cluster 3, greater in QFT-positive), genes encoding for chemokines (CCL3, CXCL8 – cluster 7, only present in resisters) or metallothionines (MT1E, MT1X, MT1G – cluster 6, enriched in TB).

Finally, TNFSF8 expression (encoding CD153, a TNF superfamily molecule with proposed to control Mtb) was higher in the IFN- $\gamma$  cluster.

**Conclusions:** The Mtb-specific CD4 T-cell population is heterogenous and varies across different outcomes of infection, with the majority of subpopulations not exhibiting the characteristics of Th1 cells. The expression of genes encoding for chemokines and cytokines suggests a possible role for Mtb-specific-CD4 cells in immune cell differentiation and recruitment following TB exposure. Differential analysis of gene (and protein) expression amongst different groups will deconvolute T cell subsets contributing to TB protection.

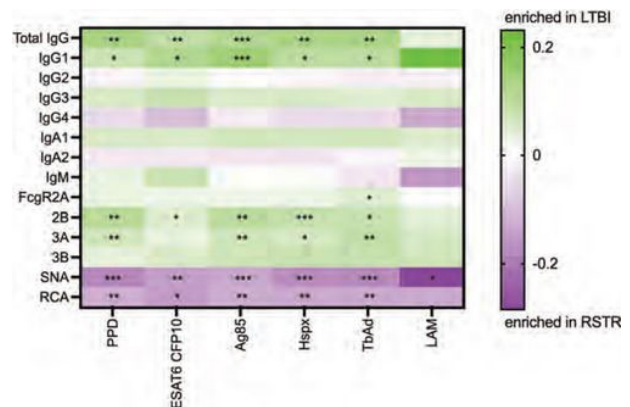
## TBS2D-15 Interferon- $\gamma$ -independent markers of *M. tuberculosis* exposure among male South African gold miners

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**Background:** The prevalence of tuberculosis among men who work in the gold mines of South Africa is among the highest in the world, but a fraction of miners demonstrate consistently negative results upon tuberculin skin testing (TST) and IFN- $\gamma$  release assay (IGRA). We hypothesized that these “resisters” (RSTRs) may display unconventional immune signatures of exposure to *M. tuberculosis* (Mtb).

**Methods:** In a cohort of RSTRs and matched controls with latent TB infection (LTBI), we profiled the functional breadth of Mtb antigen-specific T cell and antibody responses using multi-parameter flow cytometry and systems serology, respectively.

**Findings:** RSTRs and LTBI controls both exhibited IFN- $\gamma$  independent T-cell and IgG antibody responses to Mtb-specific antigens ESAT-6 and CFP-10. Antigen-specific antibody Fc galactosylation and sialylation were higher among RSTRs (RCA and SNA, respectively, in figure above). In a combined T-cell and antibody analysis, Mtb lysate-stimulated TNF secretion by T cells correlated positively with levels of purified protein derivative-specific IgG. A multivariate model of the combined data was able to differentiate RSTR and LTBI subjects.



**Interpretation:** IFN- $\gamma$  independent immune signatures of exposure to Mtb, which are not detected by approved clinical diagnostics, are readily detectable in an occupational cohort uniquely characterized by intense and long-term infection pressure. Further, TNF may mediate a coordinated response between Mtb-specific T-cells and B-cells.



**Funding:** NIH (R01-AI124348, R01-AI125189, R01-AI146072, 75N93019C00071), the Doris Duke Charitable Foundation, the Bill & Melinda Gates Foundation (OPP1151836, OPP1109001, OPP1151840), Mass Life Science Foundation, and Good Ventures Fund.

### TBS2D-20 Evaluation of tyrosine kinase inhibitor use for host-directed TB therapy accounting for human and mycobacterial variations

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Adjunctive host-directed therapy (HDT) is a new approach to reducing tuberculosis (TB) treatment length via stimulating host-mediated bacteria-killing mechanisms and/or reducing immunopathology. However, multiple challenges hampering successful strategies include response variations of the recipient human population and *Mycobacterium tuberculosis* (*Mtb*) complex (MTBC) lineage diversity causing TB.

Our project aims to understand how host and bacteria diversity influences response to tyrosine kinase inhibitors (TKI) to inform the selection and evaluation of HDT accounting for these diversities.

Monocytes were positively selected from venous blood from 114 TB patients three months post-standard anti-TB treatment in The Gambia. Overnight rested monocytes were infected with fluorescently-labelled clinical isolates of *Mtb*-lineage2, *Mtb*-lineage4, *M. bovis*, and West Africa dominant *Mycobacterium africanum* (*Maf*)-lineage5 and *Maf*-lineage6 at MOI 1 in the presence or absence of TKIs imatinib, gefitinib or erlotinib. Bacterial abundance was quantified by measuring fluorescence over seven days. Day 7 supernatant was col-

lected for Luminex quantification of 48 cytokines/chemokines/growth factors. We defined controllers as those with decreasing bacteria load and responders as those with lower bacterial fluorescence in TKI-treated compared to untreated over time. We regressed their association with demographic, clinical and microbiological parameters using a mixed-effect model in R.

There were 65% controllers, with *Mtb*-lineage2 (73%) being the most and *Maf*-lineage6 (60.4%) least controlled bacteria. Responders had a slight age-dependent increase in *Maf*-lineage6 control OR 1.04(1 – 1.08),  $p=0.04$ . TKI, with a relatively lower responders percentage among controllers, had the highest rate of responders in the non-controllers group. We identified a characteristic cytokines signature associated with TKI responders across MTBC lineages.

TKI-induced bacteria control varies according to recipient patients, and the response was lower for *Maf* lineages endemic in West Africa. HDT implementation should account for regional diversity. The cytokines and chemokines associated with TKI response could be developed as biomarkers of TB response to HDT treatment.

### TBS2D-25 In vitro selection, identification and in silico characterisation of *M. tuberculosis* epitopes binding to HLA-E peptide-binding groove for the design of a new multi-epitope TB vaccine

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*Mycobacterium tuberculosis* (*Mtb*) is the causative agent of tuberculosis (TB), which is the number one killer of people living with HIV-1. Despite the availability of BCG vaccine and being able to provide protection to children against pulmonary TB, its protective efficacy to people living with HIV-1 is still lacking. Interestingly, HLA-E is resistant to HIV-1 nef-mediated downregulation, therefore, antigen presentation dependent on HLA-E is less likely to be affected by HIV-TB co-infection. Also, HLA-E has an ability to present pathogen derived peptides to the adaptive immune system.

Thus, targeting *Mtb* specific HLA-E epitopes may be an advantage in TB vaccination. This study aimed at selecting, identifying and *in silico* characterize *Mtb* epitope peptides from *Mtb* secretome phage library for use in the design of a new multi-epitope TB vaccine.

In this study, we used affinity selection to screen the *Mtb* secretome phage library against immobilized recombinant HLA-E receptor. *Mtb* peptide epitopes binding to HLA-E receptor were identified by DNA sequencing. These peptide epitopes were docked into HLA-E receptor, to evaluate the potential interaction between the peptides epitopes and HLA-E. Eighteen (18) of the selected protein peptides were found to bind to HLA-E peptide groove with high binding affinity score.

These include immunogenic proteins and conserved hypothetical proteins, such as Rv1980c (Mpt64), Rv2875 (Mpt70) and Rv1566c.

Overall, since the identified *Mtb* peptide epitopes showed to have binding specificity to HLA-E peptide groove domain therefore, they have an ability to trigger both CD4+ and CD8+ T-cells, which warrants them to be potential TB vaccine candidates.

## TBS2E Mixed-theme Short Oral Abstract Presentations I

### TBS2E-10 BTZ-043 shows good safety and strong bactericidal activity in a seamless phase 1b/2a study in patients with pulmonary TB

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**Background:** New TB drugs are needed to shorten treatment and to counter rising resistance against new drugs, especially bedaquiline. BTZ-043 is the first-in-class benzothiazinone-DprE1-inhibitor with good activity and lesion penetration in mice, and prior evaluation in phase 1a.

**Design/Methods:** PanACEA-BTZ-043-02 was an adaptive seamless phase 1b/2a study in two South African sites. In phase 1b, doses were escalated in increments of 250mg with pre-specified decision-rules for seamless transition; in phase 2a, patients were randomised to receive BTZ-043 at 3 doses, or standard control. Sputum bacterial killing was assessed in liquid culture from overnight pooled samples.

Food effect on BTZ-043 exposure was assessed in phase 1b, drug-drug-interaction potential by probe drug cocktail or dolutegravir in phase 2a.

**Results:** 78 participants were enrolled and hospitalized for 14 days of treatment. Doses up to 1750mg were studied in phase 1a with doses of 250mg, 500mg and 1000mg advanced to phase 2b.

Safety was not dose-limiting with mild and moderate nausea being the most frequent AE and no toxicity signal; transaminases rose transiently and later declined

despite continued dosing. BTZ-043 pharmacokinetics was dose-proportional up to 1000mg. Food increased AUC by a factor of 2.99. Probe drug evaluations suggested a moderate inhibition of CYP2C9/OAT2 with a 1.7-2.5-fold increase in tolbutamide exposure.

Other mild interactions could not be excluded, but are not considered clinically significant. Bactericidal activity was in the range of rifampicin 10mg/kg, with  $-0.115$  (95% CI:  $-0.162$ ;  $-0.069$ )  $\log_{10}$  CFU/ml\*d at the highest dose with inferior killing in participants with low exposures.

**Conclusions:** To our knowledge, this was the first adaptive seamless phase 1/2 trial in TB patients accelerating bacterial activity and safety evaluation, determination of food effects and drug-drug-interactions. BTZ-043 was safe and effective over 14 days of dosing. BTZ-043 should be given with food, and can be safely co-administered with important TB drugs and dolutegravir.

### TBS2E-15 Understanding the risk factors for bedaquiline resistance

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Bedaquiline, a novel antimycobacterial drug that inhibits ATP synthesis, has shown great promise in the treatment of multi drug-resistant tuberculosis (MDR-TB). Reports of acquired resistance in patients receiving regimens containing bedaquiline, however, are becoming more and more common. Clinical resistance to bedaquiline most often occurs through the acquisition of mutations in the transcriptional regulator (*rv0678*) of an efflux pump which regulates iron in *Mycobacterium tuberculosis*.

In addition to being induced through exposure to bedaquiline, *rv0678* mutations have been found in treatment-naïve individuals. This implies the existence of a selection factor for bedaquiline resistance other than bedaquiline itself.

Identifying this selection factor could be key to preventing the development of further resistance to this critical weapon against MDR-TB.

To investigate this, isogenic *rv0678* mutants conferring resistance to bedaquiline were generated. These mutants were mixed with a wild-type strain, and exposed to either antibiotic or iron stress to determine if a fitness benefit to *rv0678* mutants exists in these conditions. An *rv0678* mutant conferring high levels of bedaquiline resistance was selected for both in the presence of rifampicin, a first-line antimycobacterial, and in the presence of an iron chelator.

This mutant did not confer significant resistance to rifampicin, as previously reported. This implies a benefit of *rv0678* mutants to rifampicin. Given that this mutant was also selected for in low-iron conditions, the benefit

in the presence of rifampicin may be related to the iron regulatory nature of the pump, rather than simple efflux. These data support literature suggesting *rv0678*, and its efflux pump, are upregulated upon rifampicin exposure. Thus, rifampicin may serve as a selection source for *rv0678* mutants *in vivo*.

Additional experimentation is needed to determine the mechanism for this selection. Understanding this mechanism has the potential to help inform treatment guidelines for this critical antibiotic, and subsequently improve patient outcomes.

### TBS2E-20 Verification of the revised critical concentration for rifampicin in the detection of disputed *rpoB* mutations

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**Background and objectives:** Disputed *rpoB* mutations in *Mycobacterium tuberculosis* are not easily detected by the BD MGIT drug susceptibility method. As a result, isolates harbouring disputed *rpoB* mutations may be classified as rifampicin susceptible despite harbouring rifampicin resistance conferring mutations.

These discordances negatively impact current tuberculosis (TB) control measures, leading to improper patient management and potential transmission of drug resistant strains. In response, the World Health Organization (WHO) has recently lowered the rifampicin critical concentration (cc).

While several studies have evaluated the phenotypic detection of disputed *rpoB* mutations, these have been conducted in countries with a low TB incidence. We sought to evaluate whether the revised critical concentration improves detection of disputed *rpoB* mutations on phenotype in a South African context.

**Method:** A total of 100 isolates were selected for the study, of which 37 isolates harboured the described disputed *rpoB* mutations Asp435Tyr, His445Asn, His445Cys, His445Leu, His445Ser, Ile491Phe, Leu430Pro, Leu452Pro and Ser441Gln, 29 high-confidence (non-disputed) rifampicin resistance conferring mutations Ser450Leu, His445Arg, His445Asp and His445Tyr, and 34 rifampicin susceptible isolates.

Rifampicin minimum inhibitory concentration (MIC) testing was performed for each isolate at 0.25, 0.5 and 1.0 µg/ml, with testing at the newly recommended cc of 0.5 µg/ml performed in triplicate to exclude the flip-flop effect for mutation exhibiting MICs bordering this concentration.

**Results:** Of the 37 disputed mutants, 19 (51.4%) were classified as rifampicin resistant at the revised cc. MIC distributions are shown for disputed, non-disputed and susceptible isolates in Table 1.

	RIF Susceptible		RIF Resistant		Total
	≤0.25	0.5	1	>1	
Disputed	15	3	5	14	37
Non-disputed	-	-	-	29	29
Susceptible	34	-	-	-	34

Table 1: MIC distribution of disputed *rpoB* mutations, non-disputed *rpoB* mutations and wild-type (susceptible) at the revised WHO critical concentration

**Conclusion:** The revised rifampicin critical concentration improves resistance detection of disputed *rpoB* mutations by only 50% in our setting. Further investigation on the critical concentration is warranted for programmes reliant on BD MGIT culture for drug susceptibility testing.

### TBS2E-25 Prediction of baseline linezolid neurotoxicity of multidrug-resistant TB treatment

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**Background:** Linezolid is a first-line component in the treatment of multidrug-resistant /rifampicin-resistant tuberculosis (MDR/RR-TB). It is highly efficient in the treatment against tuberculosis but neuropathic adverse events occur frequently, some of which remain irreversible even after drug discontinuation.

We aimed to identify genes and pathways that are associated with linezolid neurotoxicity before therapy initiation. Additionally, we aimed to identify and validate a host-RNA based biomarker that can predict linezolid neurotoxicity at baseline of treatment.

**Method:** Adult persons initiating MDR/RR-TB treatment including linezolid were prospectively enrolled in three independent cohorts in Germany. Clinical data and whole blood for RNA transcriptomic analysis were collected. The primary outcome was linezolid attributed peripheral and/or optic neuropathy.

A multistep model using a machine-learning algorithm was used for biomarker identification. The biomarker was validated in an additional fourth MDR/RR-TB patient cohort from Romania.

**Results:** A total of 52 patients from the three training cohorts received linezolid treatment. Of those, 23 (44%) developed neuropathies attributed to linezolid treatment. The majority were of grade 1 (39%) and grade 2 (58%) severity. Gene expression differed significantly before the initiation of treatment. Using feature selection, an algorithm containing nine genes out of 44,000 genes were found to predict neuropathic adverse events even before therapy was initiated.

In the validation cohort, 10 of 42 (24%) included persons developed grade  $\geq 3$  neuropathies. The prediction power for grade  $\geq 3$  neuropathies of the biomarker was moderate (area under the curve: 0.72, 95% CI: 0.54-0.90).

**Conclusion:** We identified a 9-gene RNA-signature that moderately predicts the occurrence of neuropathies due to linezolid before the initiation of MDR/RR-TB therapy.

### TBS2E-30 TB-HIV coinfection and TB's impact on the HIV reservoir in CD4 cells

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**Background:** The most deadly coinfection for people living with HIV (PLHIV) is tuberculosis (TB), which causes 1 in 3 deaths of PLHIV. Additionally, having had active TB confers increased all-cause mortality risk, even with effective treatment of HIV and TB. This suggests a persistent at-risk immunologic defect not reversed by effective treatment of both HIV and TB.

We hypothesize that this risk results from increased HIV reservoir, proviral DNA that is integrated into the DNA in cells of PLHIV, in those with TB coinfection.

**Methods:** We designed a case-control study to compare HIV provirus-containing CD4 in PLHIV with vs. without a history of active TB disease. Study participants were enrolled at GHEKIO in Port au Prince, Haiti. Intact and non-intact proviral DNA were quantified using droplet digital PCR of PBMC-derived CD4 cells. For a subset, Th1 and Th2 cytokines were assayed in plasma. Kruskal-Wallis tests were used to compare medians with tobit regression for censoring.

**Results:** We found that PLHIV with history of active pulmonary TB (n=20) had 7 times higher intact provirus than PLHIV without history of active TB (n=47) (794 vs 117 copies per million CD4, respectively;  $p < 0.0001$ ). In a confirmatory cohort, there was more intact provirus in PLHIV with (n=14) vs without (n=13) history of active

TB (66 vs. 0 per million CD4,  $p=0.15$ ), as well as more total detectable integrated proviral DNA (2247 vs. 343 per million CD4,  $p=0.029$ ). Additionally, we found the latter figure proportional to plasma IL-1beta, IL-2, and IL12p70 ( $p < 0.006$ ).

**Conclusions:** Our data show increased HIV provirus in PLHIV with history of active TB disease, which has implications for understanding why PLHIV with history of TB have higher all-cause mortality. It is our hope that consideration for coinfections, particularly TB, will be standardized as part of all HIV cure research.

### TBS2E-35 Targeting the acid sphingomyelinase pathway for *M. tuberculosis* clearance

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Tuberculosis remains a major global health problem. Although the available current drug regimen against tuberculosis provides protection, the advent of drug resistance advocates the development of potential host directed therapies.

We hypothesize that the acid sphingomyelinase (ASM) pathway is a potential therapeutic target for *Mycobacterium tuberculosis* (*Mtb*) clearance by repurposing FDA approved drug inhibitors of the ASM pathway.

To test our hypothesis, we extracted lipids from 30 *Mtb* granulomatous and 15 healthy human lung tissue specimens, and analysed them using an untargeted lipidomics-based approach with UHPLCQTOF-MS/MS. *In vitro* *Mtb*-infected host cells were treated with ASM inhibitors to assess their effect on *Mtb* burden in tuberculosis 2D or 3D models. Bactericidal efficacy was evaluated by measuring respective green fluorescent protein or luminescence expression and colony forming units. Bactericidal efficacy of the ASM inhibitors was also assessed in a TB mouse model.

The effect of treatment on phagosome acidification and phagosome-lysosome fusion in treated *Mtb*-infected THP-1 cells was assessed by staining with lysotracker and Hoechst dye.

Our results demonstrate that *Mtb* granulomatous tissue displayed a decrease in sphingomyelin levels, together with an increase in the levels of ceramides and glycosphingolipids vs healthy lung tissue. A dose dependent reduction in *Mtb* burden was found in THP1 cells and a significant reduction of *Mtb* growth was observed in an

*in vitro* granuloma model upon ASM inhibitor treatment. A substantial reduction in pulmonary *Mtb* burden was observed in the TB mouse model upon treatment. Lastly, inhibition of the ASM pathway promotes the acidification of the phagosome, facilitating *Mtb* clearance. Therefore, we conclude that treatment with ASM inhibitors reduces *Mtb* burden in all of the tested *Mtb*-infection models by promoting acidification of *Mtb* containing phagosomes. Our data suggest that targeting the ASM pathway as a potential therapeutic goal could treat tuberculosis and improve disease outcome.

### **TBS2E-40 Evaluating immune responses in an unblinded SMA-TB clinical trial: insights into the potential benefits of two host-directed therapies for TB treatment**

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Host-Directed Therapies (HDT) aim to shorten tuberculosis (TB) treatment duration and improve TB outcomes. Repurposed drugs with anti-inflammatory effects have been proposed as HDT for TB to minimise tissue damage, hyperinflammation, and long-term complications.

However, it is important to consider individual variability in patient response to HDT. The SMA-TB clinical trial is a multicenter randomized phase IIB study investigating the potential benefits of two common non-steroidal anti-inflammatory drugs, acetylsalicylic acid and ibuprofen, as adjunct therapies in people suffering pulmonary TB; being conducted in South Africa and Georgia (NCT04575519).

The present study focuses on assessing immune responses of 58 individuals enrolled in the SMA-TB CT, as well as clinical factors associated with prognosis and treatment response. In the study, 13 biomolecules linked to inflammation, TB severity, and treatment response were measured in plasma samples collected at different time points (baseline and weeks 2, 4, 8 and 24) using a Multiplex assay. Baseline results were examined for correlations with TB severity based on TB Score and a radiological score.

Preliminary findings indicate that only a few individuals had detectable levels of IFN-g, TNF-a, IL-6, IL-17A, CXCL-11 and MMP8. Levels of IP-10, CXCL-9, TREM-2, suPAR and VEGF-a decreased significantly during the treatment course. No correlation was found between the biomarkers and TB Score, but a weak but statistically significant positive correlation was observed between baseline levels of IP-10 and sUPAR and the radiological score.

Future steps include assessing whether these biomarkers can predict improvements in TB, stable sputum conversion, and overall TB outcomes. Additionally, a comprehensive analysis considering the treatment groups, will be conducted once the clinical trial is unblinded. This study has the potential to provide valuable insights into evaluating new HDT for TB treatment.

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### **TBS3A Mixed-theme Short Oral Abstract Presentations II**

#### **TBS3A-10 The development and accuracy of ultra-sensitive immunoassays to detect *M. tuberculosis* proteins in the urine of children with and without HIV**

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**Background:** Non-sputum tests for diagnosing childhood tuberculosis (TB) are urgently needed. We tested an electrochemiluminescence (ECL) immunoassay for *M. tuberculosis* (*Mtb*) lipoarabinomannan (LAM) and a new ultrasensitive, multiplex, ECL immunoassay for

three Mtb proteins (ESAT-6, CFP-10, and Ag85B) with urine collected from children enrolled in TB diagnostic studies in The Gambia, South Africa, Uganda and Peru.

**Methods:** The assays were conducted using the Meso Scale Diagnostics (MSD) U-PLEX® (LAM) or ultrasensitive S-PLEX® (protein panel) ECL assay formats. We calculated each assay's limit of detection (LOD) and measured the biomarkers in urine collected from children <15 years old being evaluated for pulmonary TB. Participants were classified as Confirmed, Unconfirmed or Unlikely TB based on NIH consensus definitions. We calculated the accuracy of each protein individually and combined.

**Results:** Amongst 519 children, the median (IQR) age was 4 years (2-7), 17% were living with HIV, and 17% were underweight. Assay LODs for LAM, ESAT-6, CFP-10 and Ag85B were 2,300, 78, 16, and 27 fg/mL, respectively. Specificity was high for all targets (97-100%), and sensitivity for Confirmed TB cases (n=130) was highest for LAM (35%) and Ag85B (39%) compared to ESAT-6 and CFP-10 (each at 13%). When Unconfirmed cases (n=129) were included, sensitivity for LAM and Ag85B reduced (Table).

Combining LAM and Ag85B improved sensitivity to 53% at 93% specificity while detecting an additional 17/129 (13%) Unconfirmed cases. Sensitivity was higher for LAM and Ag85B among children living with HIV (53%, 95% CI 35-71) and underweight (51%, 95% CI 34-68) at specificity  $\geq$  90%.

**Conclusions:** With ultra-sensitive assays, Mtb proteins can be detected in the urine of children with and without HIV at high specificity and similar sensitivity as LAM. Antigen combinations increased accuracy, and further improvement in the analytical sensitivity could inform a point-of-care, non-sputum TB test.

	Ag85B	CFP-10	ESAT-6	LAM
<b>Specificity</b>	97% (94%, 99%)	99% (96%, 100%)	100% (98%, 100%)	97% (93%, 98%)
<b>Sensitivity</b>				
<b>Confirmed TB</b>	39% (31%, 48%)	13% (8%, 20%)	13% (8%, 20%)	35% (27%, 44%)
• <b>HIV positive</b>	53% (35%, 71%)	27% (13%, 46%)	27% (13%, 46%)	53% (35%, 71%)
• <b>Underweight</b>	51% (34%, 68%)	26% (13%, 43%)	26% (13%, 43%)	51% (34%, 68%)
<b>Confirmed and Unconfirmed TB</b>	24% (19%, 30%)	7% (5%, 11%)	7% (4%, 11%)	21% (16%, 26%)

Specificity and sensitivity are provided as point estimates with 95% confidence intervals.

*Table. Sensitivity and specificity of four assays to detect Mtb proteins in the urine of children with presumed TB from The Gambia, Peru, South Africa and Uganda.*

### TBS3A-15 Diagnostic accuracy of plasma lipoarabinomannan (LAM) antibodies in combination with urine LAM in a high TB burden setting

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**Background:** Non-sputum triage tests are needed to improve tuberculosis (TB) case detection. Combining lipoarabinomannan (LAM) antibody testing with urine LAM detection has demonstrated improved sensitivity among people living with HIV (PLHIV). However, this has not been evaluated in populations including people without HIV.

**Methods:** We conducted a diagnostic accuracy study among adults with presumptive tuberculosis at two outpatient clinics in Kampala, Uganda. All participants had sputum tested for TB (Xpert Ultrax1 and MGITx2), urine tested using Alere Determine TB-LAM, and blood tested for HIV. Stored plasma samples were tested for LAM antibodies using ELISA. The sensitivity and specificity of LAM antibodies alone and in combination with Alere-LAM were calculated in reference to sputum TB test results.

**Results:** Among 227 participants, median age was 36 years (26-45), 143 (63%) were male, 98 (43%) were PLHIV (median CD4 count: 344 cells/ul), and 108 (48%) had confirmed TB. The sensitivity of Alere-LAM was 25% (95% CI: 17-34%) and specificity was 94% (95% CI: 88-98%). At the cut-point where Youden's index was maximized, LAM anti-IgG had higher sensitivity (59%, 95% CI: 49-69%, p<0.001) and lower specificity (83%, 95% CI: 75-89%, p<0.001). LAM anti-IgM had similar sensitivity (58%) but lower specificity (66%), compared to LAM anti-IgG. Combining LAM anti-IgG and anti-IgM with Alere-LAM further increased sensitivity (66%, 95% CI: 56-75%, p<0.001) but had lower specificity (85%, 95% CI: 77-91%, p=0.002) than Alere-LAM alone. At the cut-point that achieved 90% sensitivity as recommended for a TB triage test, specificity was low for LAM anti-IgG (28%) and LAM anti-IgM (13%) alone, or when combined with Alere-LAM (Anti-IgG+Anti-IgM:38%, Anti-IgG:35%, Anti-IgM:17%).

**Conclusion:** Combining LAM antibodies with Alere-LAM improved diagnostic accuracy for TB. However, neither Alere-LAM alone nor the combination of Alere-LAM and LAM antibodies achieved WHO target product profile accuracy thresholds for a TB triage test.

Diagnostic test or model	Cut-point that Maximizes Youden's Index		Cut-point that Achieves >90% Sensitivity		AUC
	Sensitivity	Specificity	Sensitivity	Specificity	
Alere LAM	0.25 (0.17 - 0.34)	0.94 (0.88 - 0.98)	--	--	--
Anti-IgG	0.59 (0.49 - 0.69)	0.83 (0.75 - 0.89)	0.91 (0.84 - 0.95)	0.28 (0.20 - 0.37)	0.74
Anti-IgM	0.58 (0.48 - 0.68)	0.66 (0.56 - 0.74)	0.91 (0.84 - 0.95)	0.13 (0.08 - 0.21)	0.61
Alere LAM + Anti-IgG	0.72 (0.63 - 0.80)	0.80 (0.71 - 0.87)	0.91 (0.84 - 0.95)	0.35 (0.27 - 0.45)	0.79
Alere LAM + Anti-IgM	0.69 (0.60 - 0.78)	0.65 (0.55 - 0.73)	0.91 (0.84 - 0.95)	0.17 (0.11 - 0.25)	0.68
Alere LAM + Anti-IgG + Anti-IgM	0.66 (0.56 - 0.75)	0.85 (0.77 - 0.91)	0.91 (0.84 - 0.95)	0.38 (0.29 - 0.47)	0.80

### TBS3A-20 A near-patient, non-sputum based, multiplex RT-PCR assay for TB diagnosis and disease monitoring

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Accurate diagnosis and estimation of risk in latent tuberculosis infection (LTBI) remains a major global health challenge. Rapid assays that can stratify different stages of TB infection and infer risk of TB progression are urgently needed. RISK6 is a 6-gene transcriptomic signature that can be utilised for diagnosis of tuberculosis, prediction of disease risk, and monitoring of treatment response, from whole blood samples.

The signature has been verified in multiple independent cohorts, including HIV infected and HIV uninfected individuals.

At >90% sensitivity, the RISK6 signature discriminates active tuberculosis (TB) from LTBI and healthy controls with a specificity >70%, meeting the WHO target product profile for a triage test.

Currently, the six individual transcripts are detected from cDNA using individual singleplex qPCR ThermoFisher TaqMan™ gene expression assays. We have developed a multiplex real-time PCR assay that simultaneously amplifies and detects all six RISK6 RNA transcripts directly from extracted RNA in a single reaction on a benchtop thermocycler.

Comparison of the 1-step multiplex assay (from RNA) and the six individual singleplex qPCR assays (from cDNA) was completed with 56 RNA samples extracted from venous blood, comprising 28 known LTBI samples and 28 known active TB samples. Excellent correlation was observed between the RISK6 scores generated by

the 1-step multiplex assay (from RNA) and the 6 individual singleplex qPCR assays (from cDNA) (Spearman correlation coefficient of 0.87) (Figure).

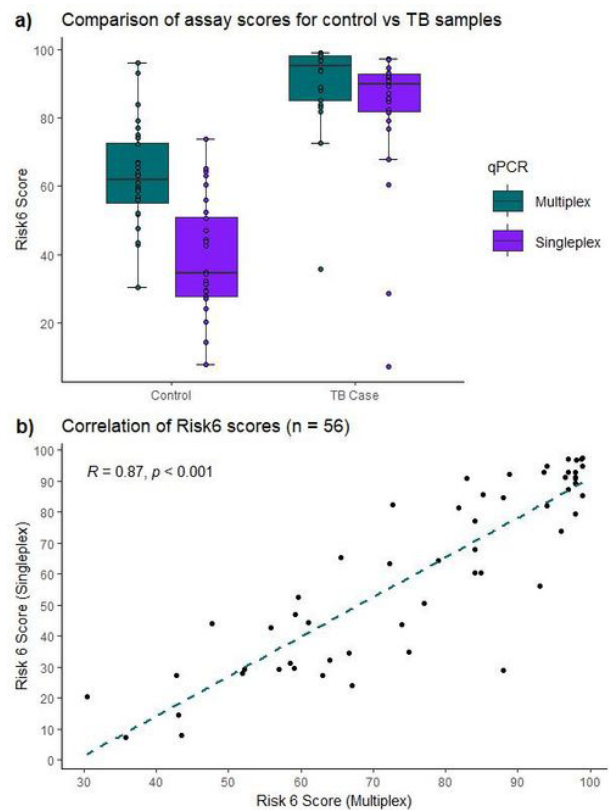


Figure.

Using the multiplex RT-PCR test, a RISK6 score could be generated using very small volumes of capillary blood (<100µl) from a fingerprick sample. We are developing the RISK6 multiplex RT-PCR assay into a test that can automatically generate a RISK6 score in approximately 30 minutes at the point of need, thus providing a much-needed testing solution and a move towards TB eradication.

### TBS3A-25 The plasma ratio of kynurenine to tryptophan is a biomarker of TB disease and treatment response in Ethiopian adults

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**Background:** *Mycobacterium tuberculosis* infection induces the enzyme indoleamine-2,3-dioxygenase-1 (IDO1), the rate-limiting step for metabolism of trypto-

phan to kynurenine, at a rate commensurate with bacterial burden. IDO1 activity is reflected in the plasma ratio of kynurenine to tryptophan (Kyn/Trp), which prior multicohort studies indicate is a biomarker of TB disease and treatment response.

We aimed to assess the performance of the plasma Kyn/Trp ratio for diagnosing TB disease in a population of Ethiopian adults with pulmonary TB and evaluate its utility as a marker of response to treatment.

**Methods:** We measured the plasma concentrations of tryptophan and kynurenine in HIV-negative persons with microbiologically confirmed drug-susceptible TB disease in Addis Ababa, Ethiopia (n=54). The plasma Kyn/Trp ratio at TB diagnosis was compared to household contacts of infectious TB cases with (n=92) and without (n=102) latent TB infection (LTBI), of whom 36 had a positive TB symptom screen and negative testing for TB disease. All persons with pulmonary TB were successfully treated with rifampin, isoniazid, pyrazinamide, and ethambutol, and plasma samples were analyzed in a subset after 2 months (n=25) and 6 months (n=14) of treatment.

**Results:** The plasma concentration of tryptophan was significantly decreased in persons with pulmonary TB at diagnosis versus all control groups ( $p < 0.001$  for all) while plasma concentrations of kynurenine and the Kyn/Trp ratio were significantly increased ( $p < 0.001$  for both; Figure 1).

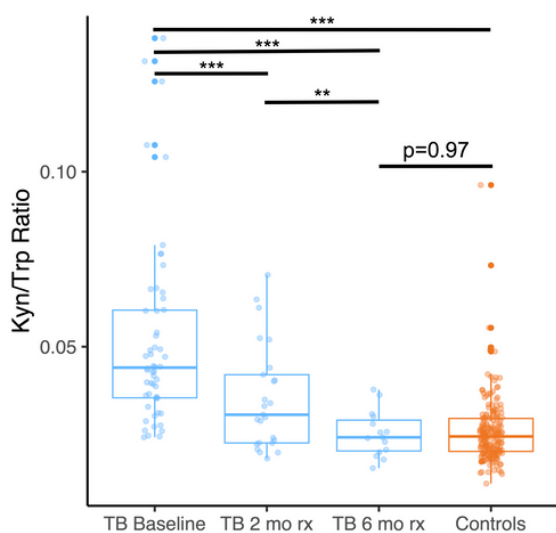


Figure 1.

The plasma Kyn/Trp ratio produced excellent classification accuracy for TB disease (AUC=0.9) and performed equally well when only controls with LTBI or TB symptoms were considered (AUC=0.92 and 0.9 respectively). We further found the plasma Kyn/Trp ratio decreased with TB treatment in a step-wise fashion after 2 and 6 months ( $p < 0.001$  and  $p = 0.002$  respectively).

**Conclusions:** These findings support use of the plasma Kyn/Trp ratio as a biomarker of TB disease and response to anti-TB treatment.

### TBS3A-35 Randomised community sampling reveals high-prevalence *M. tuberculosis* bioaerosol release in a TB-endemic setting

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Early-stage *Mycobacterium tuberculosis* (MTB) infection – encompassing latent, incipient, and subclinical tuberculosis (TB) – is increasingly recognized as a potentially significant contributor to TB transmission. However, despite their likely importance for TB control, these states remain poorly defined, and even less understood. This is largely due to technical challenges inherent in detecting small numbers of MTB-containing bioaerosols, and the long-held assumption that MTB transmission is predominantly driven by people with active TB disease.

Using the Respiratory Aerosol Sampling Chamber (RASC), we reported the capture of MTB-positive bioaerosols from ~90% of individuals on presentation with presumptive TB at the local community clinic, irrespective of final TB diagnosis. Moreover, through six-month follow-up of participants, we observed equivalent rates of decline in MTB bioaerosol release in TB patients undergoing standard chemotherapy and those with a negative TB diagnosis.

The spontaneous clearance of detectable MTB infection among untreated individuals was unexpected, and raised the possibility that periodic cycling between asymptomatic and subclinical disease states might occur frequently.

To investigate this possibility, we sought to determine the prevalence of MTB bioaerosol-positivity in our high-TB burden community in Masiphumelele. To date, utilizing randomized sampling based on allotment location, we have surveyed 177 individuals from our study site, 21% of whom are HIV positive. Within the community, 1% of sampled individuals were sputum-GenEXpert-positive (*i.e.*, asymptomatic TB) and 47% were QuantiFERON-TB Gold (QFT) positive. Most surprisingly, 66% of individuals produced a bioaerosol sample positive for MTB. Although a strong association was discernible between HIV status and QFT result, no association was evident between QFT status and MTB bioaerosol-positivity.



The unexpectedly high frequencies of MTB bioaerosol-positivity suggest that the disconnect between bacillary release and clinical symptoms (and, consequently, TB diagnosis) is common. In turn, this motivates for an urgent reframing of the prevailing paradigm of TB transmission and MTB infection.

### TBS3A-40 Spatiotemporal association between particulate matter air quality exposure and chest X-ray abnormality suggestive of TB on computer-aided diagnosis in Blantyre, Malawi

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**Background:** Air quality in many high TB prevalence countries falls far below WHO standards, with exposure to particulate matter a key risk factor for poor lung health. Chest X-ray screening for TB with computer-aided diagnosis software can accurately detect TB but may have suboptimal specificity where air quality is poor. We investigated the spatiotemporal variance in air quality and the relationship to scoring of TB on CAD-CXR in Blantyre, Malawi.

**Methods:** Fieldworkers undertaking surveys as part of a community cluster-randomised trial wore sensors (PurpleAir) to measure indoor air quality (PM<sub>2.5</sub>), with geolocation allowing spatial mapping. During the pre-trial prevalence survey, digital CXRs of randomly sampled adults were read by Qure.ai (version 2). We constructed a spatiotemporal integrated nested Laplace approximation model of air quality readings and CXR-CAD data were modelled using a linear mixed effects model.

**Results:** Between May 2019 and March 2021, 31,023 indoor PM<sub>2.5</sub> readings were taken from 3,363 households, and 11,562 adults underwent CXR-CAD, with a median CAD-CXR score of 0.158, IQR: 0.109-0.237. Spatiotemporal variation in air quality was found with predicted values for indoor PM<sub>2.5</sub> between 0 and 91.1 (Figure 1). Linear modelling showed increased PM<sub>2.5</sub> was associated with climate and varied with time of day. Higher scores for TB on CAD-CXR reading was associated with increased age (0.0018 95% CI 0.0015-0.002) and positive HIV status (0.028 95% CI 0.017-0.04).

**Discussion:** We found evidence of both exceedance of WHO guidelines for air quality and considerable spatiotemporal variation in Blantyre, Malawi. Ongoing work

to model air pollution with risk factors and CAD-CXR results will give an insight to whether this could be associated with lung damage as scored on CAD. Further research into air pollution on CXR findings in TB endemic settings will be needed to set appropriate thresholds for screening of TB disease.

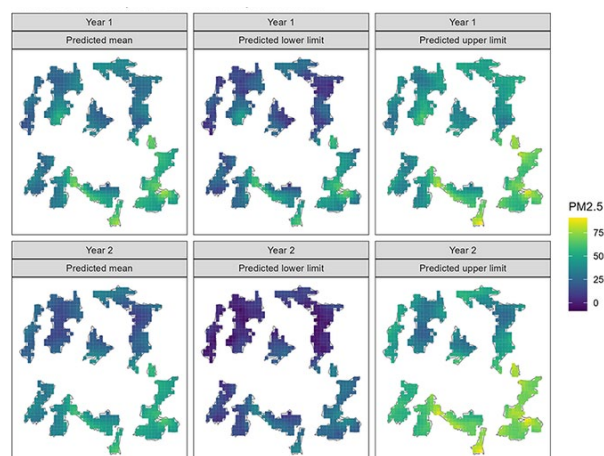


Figure 1. Predicted mean, upper and lower limits of indoor PM<sub>2.5</sub> for year 1 and 2, Blantyre, Malawi.

### TBS3C Earlier detection for easier treatment: thinking outside the sputum pot - Oral Abstract Session

#### TBS3C-10 Self-collection, dry storage and streamlined testing of tongue swab samples using commercial TB diagnostic platforms

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**Background:** Tongue swabs are emerging as viable alternatives to sputum for tuberculosis (TB) screening in settings where sputum collection is not practical. Material collected from the tongue dorsum is tested for *Mycobacterium tuberculosis* (MTB) DNA by qPCR.

Our recent study (Andama et al, 2022) showed that Cepheid Xpert MTB/RIF<sup>®</sup> Ultra can detect MTB in tongue swabs self-collected from Ugandan participants and stored in buffer, with 72% sensitivity and 100% specificity relative to a microbiological reference standard (MRS) incorporating sputum Xpert Ultra and culture.

In the current study, we evaluated a more convenient sampling protocol (self-swabbing with dry storage), combined with streamlined sample processing methods, for analysis of swabs in two commercial TB diagnostic tests: Xpert Ultra and Molbio TrueNat Ultima.

**Methods:** Up to 5 Copan FLOQSwabs were self-collected (under study worker observation) by South African participants (N = 199) with symptoms suggestive of TB. Swabs were placed into dry 2-mL tubes and frozen at -80 C. One swab per participant was tested on Xpert Ultra after a simplified 13-minute sample preparation protocol involving heating and vortexing. A second swab was tested on Truenat (without Trueprep processing) after a 36-minute preparation protocol that included heating and vortex bead-beating.

**Results:** Relative to a sputum MRS, Xpert Ultra was 75% sensitive and 100% specific when applied to dry swabs. TrueNat also exhibited high specificity at 97%, but lower sensitivity at 59%. Both platforms exhibited low error/failure rates (Xpert Ultra, 1%; Molbio, 2.5%).

	Relative to sputum Xpert Ultra		Relative to Sputum Xpert Ultra or Culture	
	Tongue swab Xpert Ultra	Tongue swab Truenat Ultima	Tongue swab Xpert Ultra	Tongue swab Truenat Ultima
Sensitivity; % (95% CI)	97/127; 76% (68%, 83%)	77/127; 61% (52%, 69%)	100/134; 75% (66%, 82%)	79/134; 59% (50%, 67%)
Specificity; % (95% CI)	69/72; 96% (88%, 99%)	68/72; 94% (86%, 98%)	65/65; 100% (94%, 100%)	63/65; 97% (89%, 100%)

Table. Sensitivity and specificity of relative to sputum microbiological references standards (N = 199).

**Conclusions:** Our streamlined protocol for Xpert Ultra enabled fast and easy testing of self-collected, dry-stored swabs with no loss of accuracy relative to previous methods. Further optimization is needed for Molbio testing of tongue swabs.

Overall, these results further support tongue swabs as non-invasive and exceptionally convenient samples for TB screening in settings where sputum collection is not practical.

### TBS3C-15 Urine high-resolution metabolomics identifies multiple putative biomarkers of TB disease in Ethiopian adults

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**Background:** High-resolution metabolomics (HRM) has the potential to identify novel biomarkers of tuberculosis (TB) disease to inform new point-of-care diagnostic tests. In a pilot study of Ethiopian adults, we sought to determine whether urine metabolites could differentiate persons with TB disease from persons without TB disease.

**Methods:** We performed HRM using liquid chromatography-mass spectrometry on urine samples from HIV-negative adults with microbiologically confirmed drug-susceptible pulmonary TB disease in Addis Ababa, Ethiopia (n=20). HRM analysis was also performed on samples from a group of household contacts with latent TB infection (LTBI) in whom TB disease had been excluded (n=20). Log<sub>2</sub> metabolite intensities were compared between groups using a linear regression model with p-values adjusted using a false discovery correction (FDR).

**Results:** Persons with TB disease had a median age of 27 years; 70% were male. We detected 7,427 metabolic features in negative ionization mode of which 5,909 were detected in ≥ 50% of samples. Several urine metabolites with high-confidence identities significantly differed between persons with TB disease and persons with LTBI. These included picolinic acid (intensity values 30.4 vs 25.1, p<0.0001), aminomuconic acid semialdehyde (26.4 vs 23.7, p<0.0001), methylnicotinamide (26.6 vs 21.6, p<0.0001), pyruvate (26.8 vs 25.4, p<0.0001), glycochenodeoxycholate sulfate (27.5 vs 26.4, p<0.0001), and N-acetylneuraminic acid (27.5 vs 26, p<0.0001).

Picolinic acid had perfect classification accuracy for TB disease (AUC=1.0) while the other five metabolites also accurately differentiated persons with TB disease from persons with LTBI (aminomuconic acid semialdehyde AUC=0.97, methylnicotinamide AUC=0.98, pyruvate AUC=0.93, glycochenodeoxycholate sulfate AUC=0.91, N-acetylneuraminic acid AUC =0.90).

**Conclusions:** In this pilot metabolomics study, we found multiple urine metabolites that differentiated persons with TB disease from their household contacts with LTBI. Larger prospective studies are warranted to determine whether these or other urine metabolites can be developed as biomarkers of TB disease to inform new point-of-care tests.

## TBS3C-20 Head-to-head comparison of the diagnostic accuracy of TB screening tests: chest-X-ray, Xpert TB host response and C-reactive protein

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**Background:** Accessible, accurate screening tests are necessary to advance tuberculosis (TB) case finding and early detection in high-burden countries.

**Methods:** We screened adults with  $\geq 2$  weeks cough presenting to primary health centers in the Philippines, Vietnam, South Africa, Uganda, and India. All participants received chest-Xray, venous or capillary Cepheid Xpert TB Host Response (HR) testing, and point-of-care C-reactive protein (CRP) testing (Boditech iChroma II). Chest-Xray images were processed using three computer-aided detection (CAD) algorithms (Delft Imaging CAD4TBv700, Qure.ai qXRv329, Lunit IN-SIGHTv314111).

We assessed diagnostic accuracy against a microbiologic reference standard (MRS) incorporating sputum Xpert Ultra x1 and liquid culture x2. Optimal cut points were chosen for each test that would achieve sensitivity  $\geq 90\%$  and maximize specificity against the MRS. Two-test screening algorithms were considered, defining a positive index test as a positive result on either test.

**Results:** Between July 2021-August 2022, 1,380 participants were enrolled. 625 (45%) were female, median age was 41 (interquartile range 29-55), 194 (14%) were living with HIV and 303 (22%) had confirmed TB.

At 90% sensitivity, all three CAD algorithms had comparable specificity (CAD4TB: 70.%, qXR: 71.5%, Lunit: 72.2%).

In head-to-head comparisons (with CAD represented by Lunit), CAD showed highest specificity when using a cut-point that achieves 90% sensitivity (72.2% vs. 65.2% for HR, difference 7.1%, 95% CI 3.3-10.7; 72.2% vs. 49.6% for CRP, difference 22.7%, 95% CI 18.9-26.4; Table).

For two-test screening algorithms, at 90% sensitivity, CAD-HR (specificity 79.4%) and CAD-CRP (specificity 74.0%) exceeded WHO target product profile (TPP) minimum accuracy thresholds and had higher accuracy than any test alone (Table).

	Quantitative value indicating positive test*	Specificity (95% CI)	Difference in specificity vs. CAD (95% CI)	Difference in specificity vs. HR (95% CI)	Difference in specificity vs. CRP (95% CI)
One-step screening					
CAD <sup>A</sup>	$\geq 5.48$	72.2% (69.5, 74.9)	-	7.1% (3.3, 10.7)	22.7% (18.9, 26.4)
HR	$\leq 1.3$	65.2% (62.3, 68.0)	-7.1% (-10.7, -3.3)	-	15.6% (12.1, 19.1)
CRP	$\geq 2.81$	49.6% (46.6, 52.6)	-22.7% (-26.4, -18.9)	-15.6% (-19.1, -12.1)	-
Two-step screening					
CAD-HR <sup>A</sup>	$\geq 43.02$ $\leq -1.92$	79.4% (76.8, 81.8)	7.1% (4.3, 10.0)	14.2% (11.3, 17.1)	29.8% (26.5, 33.1)
CRP-CAD <sup>A</sup>	$\geq 88.04$ $\geq 9.20$	74.0% (71.3, 76.6)	1.8% (0.4, 3.2)	8.8% (5.2, 12.4)	24.2% (20.8, 28.0)
CRP-HR	Did not achieve TPP targets	-	-	-	-

\*Cut points chosen to maximize specificity at a sensitivity  $\geq 90\%$

<sup>A</sup>Results for Lunit represent CAD

*Table. Accuracy comparison of TB screening tests using CAD, HR, and CRP*

**Conclusion:** In summary, CAD achieves TPP targets and outperforms HR and CRP. Combining screening tests further increased accuracy. Cost and feasibility of two-test screening algorithms should be explored.

## TBS3C-25 Open-source data to develop cough-based algorithms for TB: results from the CODA TB DREAM Challenge

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**Background:** Artificial intelligence (AI)-based cough sound analysis has the potential to provide a novel, low-cost and non-invasive approach to rapid TB screening. We report results of the Cough Diagnostic Algorithm for TB (CODA TB) DREAM challenge, an open-source data challenge to develop algorithms to classify TB status based on cough sounds and basic clinical data.

**Methods:** Symptomatic adults with presumptive TB were enrolled at outpatient clinics in India, Madagascar, the Philippines, South Africa, Tanzania, Uganda, and Vietnam. Clinical data (demographics, vital signs, basic physical examination features) were collected using standardized forms, two sputa were collected for

Xpert MTB/RIF Ultra and liquid culture, and at least 3 solicited coughs were recorded using the Hyfe Research app. Participants were divided randomly and evenly into training and test sets. Registered developers could access the training data and generate models to classify microbiological TB status based on 1) cough sound features only and 2) cough sound features and routinely available clinical data. Developers submitted their models for independent evaluation of diagnostic accuracy in the test set.

**Results:** A total of 19,402 cough sounds were collected from 2,143 participants (median age 40, 45.6% female, 14.8% living with HIV, 25.7% with microbiologically confirmed TB). Among 11 models submitted using cough sound features only, the area under the ROC curve (AUC) ranged from 0.65-0.74. The highest performing model had an AUC of 0.74 and achieved a sensitivity of 90% and specificity of 35% (Table 1). The addition of clinical data improved the AUC (range 0.78-0.83 for 6 models). The highest performing model had an AUC of 0.83, and specificity improved to 54% at 90% sensitivity.

Model	AUC	Sensitivity	Specificity
Cough Sound only	0.743	90.3%	35%
Cough Sound and Clinical Data	0.831	90.3%	53.9%

Table 1. Performance of the top cough sound models with and without clinical data to classify TB from the CODA TB DREAM Challenge

**Conclusions:** AI-based cough sound algorithms are promising as a TB triage test. Open-source data challenges should be further considered to accelerate the development and comparison of TB AI algorithms.

## TBS4B Observing the unobservable: tools, methods, and strategies for measuring transmission - Oral abstract presentations

### TBS4B-10 Does prevention of infection predict the prevention of disease following BCG vaccination? An individual patient data meta-analysis

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Prevention of disease (PoD) is the primary endpoint for tuberculosis (TB) vaccine trials, but there are no validated surrogate endpoints for late-stage trials. This study aims to assess the association between prevention of *M. tuberculosis* (Mtb) infection (PoI) following BCG vaccination and PoD using an individual patient data (IPD) meta-analysis of 15 studies.

Understanding this relationship has implications for vaccine development and trial design, as well as global TB control strategies.

We conducted an IPD meta-analysis from 15 randomized and non-randomized studies. Participants were followed up for incident Mtb infection (measured by TST or IGRA) and incident TB disease. Hazard ratios (HR) were calculated using longitudinal multilevel mixed effects modeling to assess the association between BCG vaccination and protection from infection, protection from disease without considering infection, and protection from disease given infection.

The meta-analysis included 23,094 individuals, with 67% being BCG vaccinated. BCG vaccination was associated with a lower percentage of TB disease, there was slight protection but close to no association for IGRA conversion, and a higher percentage of TST conversion. The hazard ratio (HR) for PoD ranged from 0.4 to 0.7, varying by study type. The HR for PoI ranged from 1 to 5.5, and for PoD among those infected from 0.4 to 0.8.

Preliminary findings indicate that BCG protects against TB disease, especially among individuals with likely Mtb infection. BCG did not demonstrate evidence of protection against Mtb infection using high TST and IGRA cut-offs.

Using low cut-offs, BCG increased the risk of Mtb infection, driven by TST cross-reactions. BCG showed limited protection against sustained IGRA conversion, and sustained IGRA conversion slightly predicted protection against TB disease.

These associations may be influenced by cross-reactivity of TST with BCG status, potential selection bias, and other confounding factors. Further research is needed to validate and refine these findings.

### TBS4B-15 Measuring changes in TB transmission using interferon- $\gamma$ release assay conversion surveys

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**Background:** A surrogate outcome for estimating reductions in *Mtb* transmission could be useful to evaluate the impact of interventions. Interferon-gamma release assay (IGRA) conversion measured via serial surveys among cohorts of initially-negative individuals — specifically adults, given their more generalizable contact patterns and higher exposure risks — has several advantages. Translating observed reductions in IGRA conversion to an estimate of transmission reduction, however, is not straightforward.

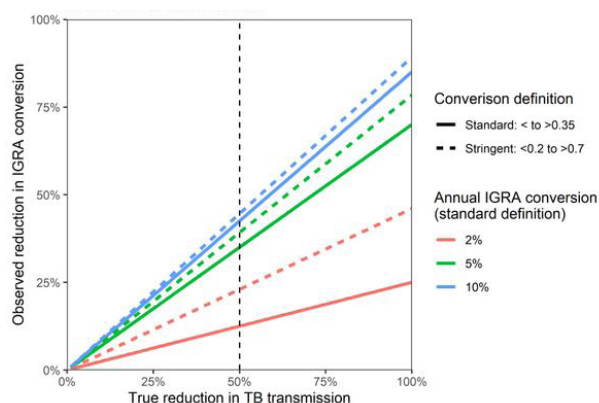
**Methods:** We developed a model of IGRA dynamics to simulate the impact of intervention-induced reductions in the true rate of *Mtb* transmission on IGRA conversion rates among initially IGRA-negative adults. Our model assumed the use of QuantiFERON-TB Gold In-Tube and included a persistent false-positive conversion rate that was fixed across transmission levels and true-positive conversion rates that varied with transmission.

Parameters came from a literature review of studies that conducted serial IGRA testing among cohorts of adults in high-burden countries.

We evaluated the sensitivity of estimated conversion reductions to different diagnostic cutoffs and conversion rates absent intervention.

**Results:** Assuming a pre-intervention IGRA conversion rate of 5% per year and a standard positivity cutoff (>0.35 IU/mL), a 50% reduction in the annual rate of *Mtb* transmission was projected to yield a 35% reduction in annual IGRA conversion (Figure).

Under these same assumptions, a more stringent definition of conversion (from <0.2 to >0.7 IU/mL) resulted in fewer conversions absent intervention (3.75% per year) but a higher observable reduction in conversion (42%). In settings with lower conversion rates absent intervention (and thus presumed lower transmission levels), the ratio of IGRA conversion reduction to true transmission reduction was lower.



Conversion levels under the more stringent definition are assumed to be 25% lower than conversion levels under the standard definition. Colors indicate conversion levels under the standard definition.

**Figure.** Observed reductions in annual IGRA conversion at two conversion cutoffs, varying levels of pre-intervention IGRA conversion, and reductions in annual *Mtb* transmission.

**Conclusions:** Changes in observed IGRA conversion levels will be smaller than true reductions in transmission, particularly in lower-transmission settings. Investigators should weigh traditional cutoffs with less specificity against more stringent cutoffs at which fewer conversions will be observed.

### TBS4B-20 Direct sputum sequencing reveals a high prevalence of mixed infections missed by conventional culture

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**Introduction:** Direct sputum whole genome sequencing (WGS) of *Mycobacterium tuberculosis* (*Mtb*) can identify within host genetic diversity that may signal impending resistance or treatment failure. High population genetic diversity within host can be the result of either a mixed infection or the microevolution of a single infecting strain, which may be missed in culture due to selective or enhanced growth of certain clones *in vitro*. Here we aimed to assess the within host *Mtb* diversity in a high burden setting utilising a well characterised patient cohort from Worcester, South Africa.

**Methods:** DNA was extracted from 87 baseline sputum sediment/culture pairs from 87 unique patients with rifampicin susceptible TB Xpert using a modified Zymo silica column-based DNA extraction method. *Mtb* DNA was enriched from the sputum sediment extract

using target capture. WGS was performed and output sequences were analysed using an in-house pipeline for the accurate detection of low frequency variants. All isolates were confirmed rifampicin susceptible by MIC testing.

**Results:** After quality control, sputum sediment/culture pairs from 74 unique patients were available for analysis. 12/74 pairs (16%) were concordant in the presence of a single lineage, while 43/74 sputum sediment samples (58%) showed evidence for mixed lineage infection not detected in culture. Mixed lineage infection (with strains from two different sub-lineages) were concordantly detected in sputum and culture for 1 patient. In one pair with mixtures, the lineages differed entirely from that found in the sputum pair. For 12/74 patients (16%) we identified a rifampicin resistance associated variant at an allele frequency of >10% in sputum but not in culture (Table 1). All variants except for 1, were found in samples designated as mixes.

Variant	Drug	Final confidence grading	Participants with variant present in sputum (AF > 10%) n = 74	Participants with variant present in culture (AF > 10%)
rpoB_S428T		Assoc with RI	4 (5.4%)	-
rpoB_Q432K	RIF	Assoc with R	1 (1.3%)	-
rpoB_S441A		Assoc with RI	7 (9.4%)	-

Table 1 Resistance associated mutations identified in direct sputum samples at AF > 10% according to the WHO Catalogue of mutations in *Mycobacterium tuberculosis* complex and their association with drug resistance.

**Conclusion:** Current results reveal mixed infection, and the presence of clinically relevant resistance markers go undetected by traditional culture based WGS.

### TBS4B-25 Identifying foci of TB transmission at the village-level in Moldova: a hierarchical multinomial logit approach to model genomic, spatial and epidemiologic data

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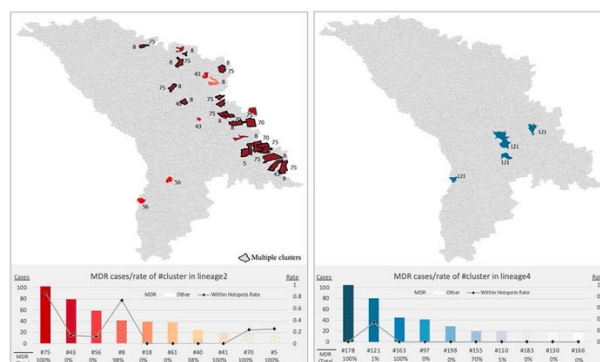
**Background:** The transmission of MDR-TB in Moldova remains a serious challenge, with an estimated 23% of new and 48% of previously treated TB cases with MDR in 2022. A prospective genomic epidemiology study of incident cases occurring in 2018 and 2019 found that 92% of MDR-TB was the result of transmitted MDR. The MDR phenotype was concentrated among two *M. tuberculosis* lineages: L2.2.1 (Beijing) and L4.2.1 (Ural).

**Objective:** We sought to identify villages in Moldova where local transmission of TB and MDR-TB was focused.

**Methods:** 35 large transmission clusters (i.e., at least 10 cases) were identified using TreeCluster. We developed a hierarchical Bayesian multinomial logit model for transmission clusters of each lineage, with both individual-level (i.e., age, gender) and village-level variables (i.e., population density, poverty).

**Results:** Transmission foci of Beijing and Ural strains had distinct spatial distributions (Figure). 28 villages were identified as foci of local transmission Beijing clusters; these villages were predominantly located in Transnistria (eastern border of the country).

In contrast, only 5 villages were identified as foci of local transmission of one Ural cluster, none of which were in Transnistria. Notably, nearly 80% of cases within the largest transmission cluster of Beijing strains (cluster #75, n=102), comprised entirely of MDR-TB, were concentrated in specific villages, while the largest transmission cluster of Ural strains (cluster #178, n=105), comprised almost entirely of MDR-TB, had no area of geographic focus.



**Conclusions:** Our results revealed the significant differences in the spatial distribution and local concentration of Beijing and Ural transmission clusters. A better understanding of the extent to which host factors, pathogen characteristics, and environmental conditions contribute to these differences in local transmission is needed. Our modeling framework allows for such additional investigation, as new variables can easily be incorporated to explore the factors that influence local transmission.

## TBSCIENCE 2023 E-POSTERS

### TBS-EP01 TBScience 2023 - Moderated E-Poster Session I

#### TBS-EP01-01 First-time-in-human study and prediction of therapeutic Phase IIa dose for alpipectir, a potent first-in-class anti-tuberculosis drug

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The clinical candidate alpipectir (BVL-GSK098) overcomes resistance to and potentiates the activity of ethionamide against *M. tuberculosis* and is currently under development for the treatment of TB.

Here we report the results from the Phase 1 study (NCT04654143) to investigate the safety, tolerability, pharmacokinetics (PK) and food effect of alpipectir administered as single and multiple oral doses in healthy volunteers. In part A, single doses of alpipectir (0.5, 1.5, 4, 10 (fasted and fed), 25 and 40 mg) were administered in 7 cohorts. In part B, repeat doses of 5, 14 and 30 mg were administered QD for 7 days in 3 cohorts.

Alpipectir was well tolerated and demonstrated an acceptable safety profile at the doses tested. No clinically relevant safety findings were identified in the participants treated during Part A or Part B.

Alpipectir showed rapid absorption after a single dose ( $T_{max}$  range of 0.75-1.5h) with dose-proportional increases in exposure ( $C_{max}$  and AUC). Following repeat dosing, accumulation of alpipectir was observed with a more profound effect on AUC compared to  $C_{max}$  and with steady state being achieved by the last day of treatment. Food affected the PK of alpipectir characterised by a slower absorption and lower  $C_{max}$ . Administration with food increased the AUC by approximately 20% compared to the fasted conditions.

A population PK model was used during dose escalations as well as to predict the therapeutic dose range of alpipectir for the ongoing phase IIa trial (NCT05473195).

Alpipectir is the first example of a small molecule targeting bacterial transcription regulators in clinical development, a ground-breaking approach with the potential to create a paradigm shift in the treatment options for TB.

#### TBS-EP01-02 Grading of associations between *M. tuberculosis* genotype and antibiotic resistance

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**Background:** Genotype-based resistance prediction has revolutionized tuberculosis care due to its speed and low cost. Yet our knowledge of genetic markers of resistance requires continuing review as larger sequencing datasets become available. It is also critical to characterize emerging resistance to novel drugs, but the relative rarity of resistance limits the statistical power of direct association methods.

Regression models can increase power and estimate the effects of co-occurring or correlated genetic features on resistance.

**Methods:** A dataset of 52,567 *Mycobacterium tuberculosis* (Mtb) isolates was curated by the WHO with support from FIND. To identify mutations associated with resistance, we built single-drug L2-penalized logistic regression models associating binary phenotypes (R/S) with mutations in Mtb genes known (Tier 1) and hypothesized (Tier 2) to affect resistance.

We corrected for population structure using genome-wide principal components. Final prediction models were built using all mutations significant by permutation test.

**Results:** Binary resistance prediction models for five novel drugs and two fluoroquinolones achieved state-of-the-art accuracy (Figure 1A).

For all drugs, Tier 2 mutations improved model goodness-of-fit (likelihood ratio test,  $p \ll 0.01$ ). We assigned mutations to 5 grades depending on the strength of evidence, grading more mutations than the published catalogue (Figure 1B).

Frameshift mutations in *Rv2752c* and *glpK* are associated with higher odds of fluoroquinolone resistance. For clofazimine, linezolid, delamanid, and pretomanid, the proportion of resistant isolates in the data is very low (2-4.5%); therefore, fewer than five associations with low individual predictive sensitivities (0.6-26%) were made per drug.

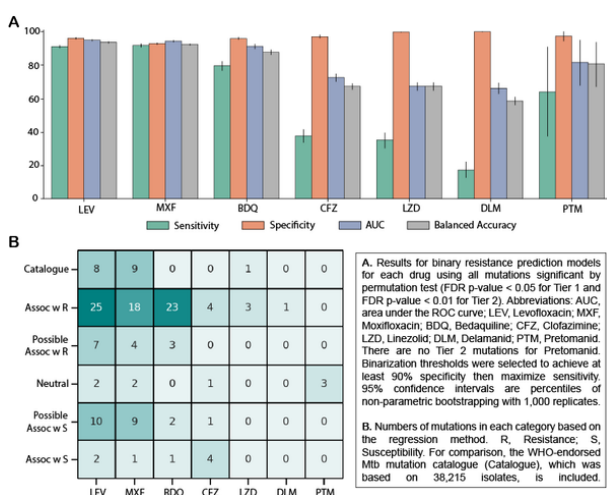


Figure 1.

**Conclusion:** L2-penalized logistic regression can:

1. Associate mutations with resistance with high power and;
2. Build accurate predictive models of resistance.

However, logistic regression models are still limited by the low prevalence of resistance to new drugs. More data or complex models may be needed to estimate the effects of rare mutations on drug resistance.

### TBS-EP01-03 Developing a platform to evaluate mycobacterial drug resistance through CRISPR-mediated knockdown of essential and non-essential genes

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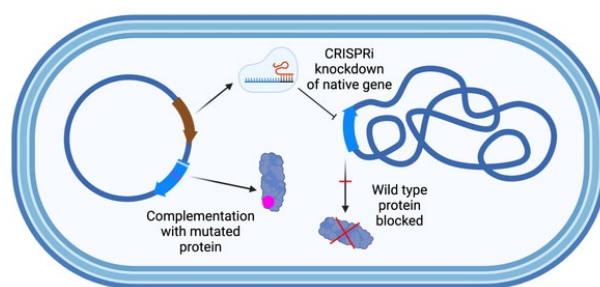
**Introduction:** Genetic techniques have >80% sensitivity for predicting *Mycobacterium tuberculosis* (*Mtb*) resistant to rifampicin, isoniazid, and fluoroquinolones. However their sensitivity is much lower for the constituents of the new BPAL regimen (40% for linezolid, 0% for bedaquiline/pretomanid) and new drugs in the clinical pipeline as few resistance associated variants (RAVs) for these drugs have been identified.

We developed a technique to evaluate specific variants in mycobacteria *in vitro* to evaluate association with resistance by CRISPR interference (CRISPRi) knockdown of genes of interest and complementation with an edited mutation-containing version.

**Methods:** We used a CRISPRi system containing *Streptococcus thermophilus* dCas9 (dCas9<sup>Sth1</sup>) to induce knockdown of genes in *Mycobacterium smegmatis* (*Msm*) and *Mycobacterium marinum* (*Mmar*). Single guide RNAs (sgRNAs) were designed and cloned into a plasmid with expression induced by anhydrotetracycline (ATC). Complemented genes containing mutations of interest were synthesised and cloned into the same plasmid under constitutive expression (figure).

The plasmid was transformed into *Msm/Mmar*, with subsequent culture in 7H10 and minimum inhibitory concentrations (MICs) calculated at day 2 (*Msm*) or 7 (*Mmar*).

**Results:** sgRNAs were designed for *Msm* against *gyrA* (essential gene, RAVs cause target-based fluoroquinolone resistance), and for *Mmar* against *gyrA*, *mmpR5* (non-essential, RAVs cause off-target bedaquiline resistance) and *fbiC* (non-essential, RAVs cause off-target pretomanid resistance). CRISPRi knockdown of *gyrA* in both *Msm* and *Mmar* led to elimination of bacterial growth at all concentrations of moxifloxacin, while complementation with a mutated version restored growth. Knockdown of *mmpR5* and *fbiC* led to an increase in MIC against bedaquiline and pretomanid respectively.



**Conclusion:** CRISPRi inducible knockdown combined with plasmid complementation is a strategy that can be used to evaluate putative RAVs in both essential and non-essential genes. It has the potential to be used to rapidly evaluate multiple potential RAVs against new drugs in *Mtb*.

### TBS-EP01-04 A clinical decision support system to empower doctors and nurses treating drug-resistant TB in the BPALM era

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Rifampicin-resistant tuberculosis (RR-TB) remains a global threat with almost 500,000 new cases annually. In 2020, we developed a treatment recommender clinical decision support system for (CDSS) to automate RR-TB treatment individualization using whole genome sequencing (WGS) results. To support the implementation of BPAL(M) regimens, we revised the CDSS.

First, we developed a system to predict the *Mycobacterium tuberculosis* (*Mtb*) strain phenotype for each of the 23 TB drugs as sensitive, very low, low (<25%),



moderate (25 to 60%), or high (>60%) probability of resistance, or resistant. This classification is based on a combination of phenotypic information on genomic variants in the WHO catalogue and expert rules derived from literature review.

Next, machine learning methods were applied to expert feedback on CDSS treatment recommendations to develop the optimal regimen for each patient. The CDSS recommends BPALM when the *Mtb* strain is fully susceptible to BPALM (wild type for all Bedaquiline, Pretomanid, Linezolid and Moxifloxacin resistance conferring genes) or when WGS predicts a very low or low probability of resistance to these drugs.

The CDSS recommends strengthening BPALM to a 5-drug BPALM*plus* regimen by adding one drug when the strain is susceptible to fluoroquinolones and has a moderate probability of resistance to B, Pa or L.

Similarly, the tool recommends a 5-drug BPAL*plus* regimen by adding two drugs to BPAL when the strain is fluoroquinolone resistant and there is a moderate probability of resistance to B, Pa or L. A fully individualized regimen is recommended when the strain is resistant to B, Pa or L or when the probability of such resistance is high.

Complementing the implementation of BPAL(M) with WGS and the CDSS could improve RR-TB treatment outcomes and protect the longevity of the BPAL(M) regimens by mitigating the risk of resistance amplification in routine care settings.

### TBS-EP01-05 Hollow-fibre system and Kramnick mouse model data show the efficacy and safety of delpazolid superior to linezolid

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**Background:** Delpazolid, a novel oxazolidinone, was studied for safety and efficacy in a Kramnick (C3HeB/FeJ) mouse model and in the Hollow Fiber System (HFS). These studies were conducted in parallel with the DECODE clinical trial to provide a deeper understanding of delpazolid prior to later trials.

**Design/Method:** C3HeB/FeJ mouse experiments were conducted at the research facilities of the Veteran's Health Research Institute. C3HeB/FeJ mice received bedaquiline and delamanid (BD), BD+linezolid(LZD), BD+delpazolid(DZD), INH/RIF/PZA or were untreated controls. Groups of six mice each were sacrificed after eight weeks or twelve weeks to assess bacterial load and surviving mice were followed for 12 weeks for reactivation.

HFS modeling was conducted at Praedicare Inc., Dallas, Texas. Studies included the semi-dormant model and the intracellular model. PK/PD relationships were generated with Monte Carlo simulations of 10,000 patients receiving QD doses of 400 mg, 800 mg, 1,200 mg or BID 800 mg. Additionally, delpazolid and linezolid were assessed for mitochondrial toxicity.

**Results:** In C3HeB/FeJ mice, delpazolid was superior to linezolid in the number of mice with zero CFU recovered after 8- or 12 weeks treatment or 12 weeks observation after 8- or 12-weeks treatment. Consistent with some other reports, the results in the BD only group were better than BD+linezolid at all time points.

In the HFS system delpazolid demonstrated good sterilizing activity and was active against intracellular bacteria. A dose of 1200 mg QD or 800 mg BID would achieve an optimal microbial effect. Delpazolid demonstrated no mitochondrial toxicity while linezolid showed the expected level of toxicity.

**Conclusions:** Delpazolid shows an excellent safety and efficacy profile in a Kramnick model and the HFS. If these results are confirmed in the DECODE trial, delpazolid will be well characterized for design of a Phase 2B or 3 clinical trial.

### TBS-EP01-06 Monitoring TB treatment response: the role of drug resistance and pre-treatment bacillary load

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**Background:** Drug resistant tuberculosis (DR-TB) is on the rise especially among the previously treated people. We evaluated the utility of tuberculosis Molecular Bacterial Load Assay (TB-MBLA) for monitoring treatment response of DR-TB under the Triage Test for All Oral-TB DR-TB regimen (TRiAD) study in Ethiopia, Nigeria, and South Africa.

**Methods:** Presumptive cases were tested for TB and rifampicin resistance using Xpert MTB/RIF Ultra. Positive cases were tested for multidrug resistant TB (MDR-TB) using the Xpert XDR cartridge and triaged to receive the most appropriate treatment according to resistance profile.

Treatment response was measured by smear microscopy, Mycobacterial-Growth-Indicator-Tube (MGIT) culture and TB-MBLA (estimated colony forming units per millilitre – eCFU/ml). Linear regression and Kaplan Meier curve analysis were applied to assess difference in

the rate of bacillary load clearance and impact of pre-treatment bacillary load/drug resistance on treatment outcomes.

**Results:** Overall, pre-treatment bacillary load (PBL) was  $3.4 \pm 2.1 \log_{10} \text{CFU/ml}$ , corresponding to MGIT time-to-culture-positivity of  $17.5 \pm 12.7$  days and smear grade  $1.3 \pm 0.7$ . Median age was 34 years with 75% (41/54) being male. 61% of the participants had TB-MBLA follow-up data and were considered for treatment response analysis. Rifampicin monoresistant (RR-TB) participants cleared bacterial load faster,  $0.87 \log_{10} \text{eCFU/ml/month}$  than MDR-TB,  $0.70 \log_{10} \text{eCFU/ml/month}$ ,  $p < 0.0001$ .

Comparison with a Ugandan drug susceptible (DS-TB) cohort treated with standard first-line HRZE, revealed that PBL was higher in DS-TB patients but cleared faster,  $1.15 \log_{10} \text{eCFU/ml/month}$  overtaking DR-TB,  $0.82 \log_{10} \text{eCFU/ml/month}$  by month-2 of treatment,  $p < 0.0001$  (Figure 1).

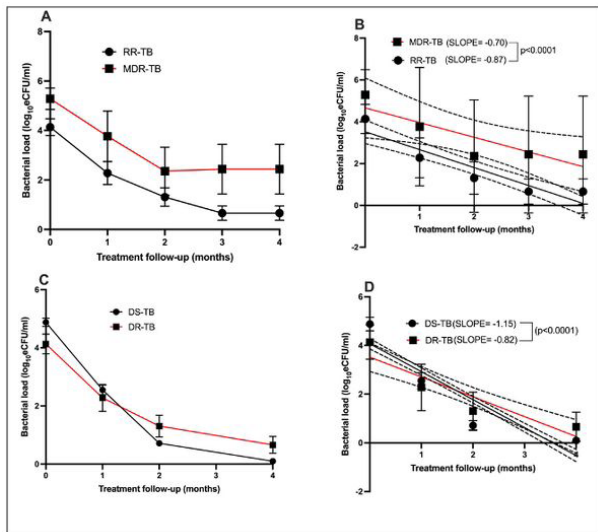


Figure 1: Treatment response among DR-TB and DS-TB participants from baseline to month 4 of treatment. A) Treatment response curves of RR-TB (black curve) and MDR-TB (red curve) and B) is the linear regression analysis of the rate of clearance (SLOPE) between the two forms of TB. C) Treatment response curve of DRTB (red curve) compared to a Ugandan DS-TB cohort (black curve), and D) regression analysis of the SLOPE of DRTB versus DS-TB. Dotted lines in B and D are 95% CI bands of the regression line.

The risk (hazard ratio) of not converting to negative by month-2 of treatment in patients with high PBL and DS-TB was 2.7,  $p = 0.01$  compared to 4.9,  $p = 0.02$  in patients with high PBL and DR-TB.

**Conclusion:** The results show that a combination of high PBL and DR-TB increases the risk of failing treatment. Xpert XDR cartridge/TB-MBLA can detect these patients very early and ensure appropriate clinical management is provided.

## TBS-EP01-07 A handheld 6-lead device for monitoring QTc interval during drug-resistant TB treatment in limited-resource settings

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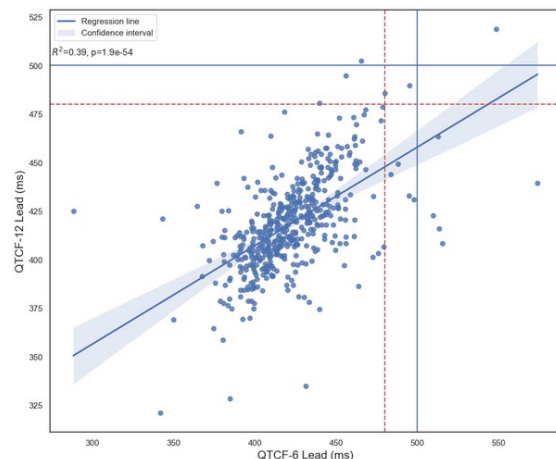
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**Background:** Modern treatment regimens for rifampin-resistant tuberculosis (RR-TB) have QT-prolonging potential requiring electrocardiographic monitoring. Handheld 6-lead ECG devices may facilitate RR-TB regimen scale-up but have not been validated for research or clinical use in high TB burden settings.

**Methods:** We prospectively determined the longitudinal diagnostic accuracy of a handheld 6-lead ECG monitor (KardiaMobile® 6L) versus reference standard 12-lead ECGs across consecutive patients recruited into the phase III BEAT Tuberculosis trial utilizing up to four concurrent QT-prolonging drugs. We further assessed agreement and repeatability of each modality, and conducted a qualitative survey assessing feasibility of the 6-lead ECG.

**Results:** During the study period, 2,070 and 2,015 total 12-lead and 6-lead ECG QTc measurements were obtained, 5% and 11.7% of which were indeterminate. Among 170 participants across 489 clinic visits, the mean 12-lead and 6-lead ECG QTc was 418 milliseconds (ms) (range, 321-519 ms; SD 23.8 ms) and 422 ms (range, 288-574 ms; SD 27.3 ms; [ $r^2 = 0.4$ ]); the inherent QTc variability was  $\pm 22.0$  ms and  $\pm 50.2$  ms, respectively. At a 500 ms QTcF cutpoint, the 6-lead ECG correctly classified 483 (98.8%) cases, with one (0.2%) false-negative and five (1%) false-positives, for a positive and negative predictive value of 16.7% and 99.8%, respectively. The mean increase in 12-lead QTcF from baseline to week 24 was 8.5 ms, with four (2.1%) patient visits exceeding QTcF 500 ms. The handheld device was feasible and easier to use than formal 12-lead ECG.



**Conclusion:** The handheld 6-lead ECG device has high negative predictive value and therefore performs well as a triage test to determine which patients should undergo reference standard 12-lead ECG. Trial participants received up to four QTc-prolonging anti-TB medications, though QTc rarely exceeded 500 ms. International guidelines should reconsider whether monitoring be risk stratified rather than be required for all patients.

### TBS-EP01-08 Contezolid can replace linezolid in a novel combination with bedaquiline and pretomanid in a murine TB model

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Linezolid (L) exhibited additive bactericidal and sterilizing activity when combined with bedaquiline (B) and pretomanid (Pa) in mouse models of TB. The resulting 3-drug “BPaL” regimen later proved to be an effective 6-month, oral regimen for extensively drug-resistant and refractory multidrug-resistant tuberculosis.

Despite the efficacy of the BPaL regimen, the dose- and duration-dependent toxicity of linezolid compromises its utility. Contezolid is a new oxazolidinone with *in vitro* and *in vivo* activity against *Mycobacterium tuberculosis* comparable to that of linezolid.

It was recently approved by the National Medical Products Administration in China for the treatment of complicated skin and soft tissue infections; and it has already been used off-label in tuberculosis treatment.

Pre-clinical and phase 1,2 and 3 studies suggest it may be less toxic than linezolid, making contezolid a potential candidate to replace linezolid in treatment of drug-resistant tuberculosis.

We evaluated the dose-ranging activity of contezolid, alone and in combination with BPa, and compared it with linezolid at similar doses, in an established BALB/c mouse model of tuberculosis. Contezolid had an MIC of 1 µg/ml, similar to linezolid, and exhibited similar bactericidal activity in mice.

Addition of each oxazolidinone increased the bactericidal activity of BPa, although only linezolid 100 mg/kg and contezolid at 100 or 200 mg/kg increased the activity of the BPa combination in a statistically significant fashion. BPa plus contezolid at 200 mg/kg produced the lowest mean CFU count, but was not statistically superior to BPa with linezolid at 100 mg/kg.

Contezolid-resistant mutants selected *in vitro* had 10-fold increases in contezolid MIC and harbored mutations in the *mce3R* gene. These mutants did not display cross-resistance to linezolid. Our results indicate that

contezolid has potential to replace linezolid in regimens containing bedaquiline and pretomanid and likely other regimens.

### TBS-EP01-09 In vitro efficacy of the diarylquinoline TBAJ-587 and its metabolites against *M. tuberculosis*

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The first-in-class diarylquinoline (DARQ) bedaquiline (BDQ) was recently added to the WHO essential medicines list for drug-resistant tuberculosis. Improved efficacy may be possible beyond current doses, but adverse effects limit evaluation of higher exposures.

TBAJ-587 is a next-generation DARQ with improved anti-*Mycobacterium tuberculosis* (Mtb) activity and safer properties than BDQ. Its dose optimization is under evaluation within the ERA4TB consortium.

This study evaluated the *in vitro* efficacy of TBAJ-587 and its main metabolites (M2, M3 and M12) under standard conditions (ST) and different carbon sources (more relevant to the site of infection) by minimal inhibitory concentration (MIC) and time-kill (TKA) assays coupled to actual drug measurements over time.

TBAJ-587 scored lower MIC values than BDQ in the 8 conditions tested. In TKA, TBAJ and its metabolites exhibited bactericidal effect at  $\geq 5 \times \text{MIC}$  values, while  $1 \times \text{MIC}$  and  $2 \times \text{MIC}$  resulted in a bacteriostatic effect that led to bacterial regrowth, not associated to compounds' instability, and isolation of mutants with a 4-fold increase in their MIC.

Drug measurements over time demonstrated extensive non-specific binding of the compounds to the polystyrene plastic-ware resulting in lower-than-expected effective concentrations in ST and fatty acids (FA) cultures, but not in cholesterol. The detergent tyloxapol (added to the cholesterol broth) limited binding to the plastic-ware, thus maintaining TBAJ-587 concentrations closer to expected values.

The PKPD analysis demonstrated that the unbound fraction in solution was effective overtime. Thus, Mtb was killed with lower exposures of TBAJ-587 and M3 than expected in ST and FA broths, indicating a likely underestimation of the activity in *in vitro* assays using polystyrene plastic-ware, the most commonly used in antimicrobial research.

This work has received support from the Innovative Medicines Initiatives 2 Joint Undertaking (grant No 853989).

### TBS-EP01-10 In vitro susceptibility testing of GSK656 against *M. tuberculosis* complex isolates to establish the epidemiological cut-off values and the distribution of minimum inhibitory concentrations

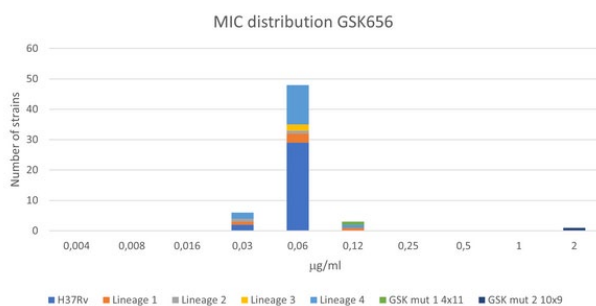
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**Introduction:** GSK3036656 (GSK656) is a novel Benzoxaborole targeting *Mycobacterium tuberculosis* complex (MTBC) leucyl-tRNA synthetase. The proposed use of GSK656 in Phase 2 combination regimen studies calls for the establishment of a robust phenotypic drug susceptibility testing (DST) method and a properly set breakpoint.

A first step in this direction is the establishment of an *in vitro* standardized test based on the EUCAST protocol and the identification of the MIC distribution for the reference strain H37Rv ATCC 27294 and phylogenetically diverse clinical isolates.

**Methods:** To reach this objective, we tested H37Rv ATCC 27294 (31 independent replicates) and a panel of 25 phylogenetically diverse clinical isolates, showing different phenotypic resistant pattern to 1<sup>st</sup> and 2<sup>nd</sup> line drugs, using serial 2-fold dilutions from 0,004 to 0,5 µg/mL. Isoniazid was used as control drug against the H37Rv strain (serial 2-fold drug dilutions 0,008 to 1 µg/mL).

**Results:** We observed a similar distribution of GSK656 MICs for H37Rv and the phylogenetically diverse clinical isolates, without no verifiable associated lineage effect. The MIC mode and the provisory ECOFF were identified respectively at 0.06 and 0.125 µg/mL (Fig 1). Moreover, the two-laboratory derived low/high level resistant isolates showed an MIC of 0,12 and 2 µg/ml as expected.



**Conclusion:** In conclusion, based on the identified MIC distribution we propose a provisory critical concentration of 0.125 µg/mL for GSK656.

### TBS-EP01-11 NAT2 acetylator status associated with drug-resistant TB in Thailand

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The N-acetyltransferase 2 (NAT2) acetylator status significantly influences drug metabolism and tuberculosis (TB) treatment outcomes. NAT2 slow acetylation leads to elevated isoniazid (INH) blood concentrations, thereby increasing the risk of drug-induced liver injuries.

On the other hand, NAT2 rapid acetylation results in low blood INH concentrations, raising the likelihood of treatment failure, relapse, and death.

We hypothesize a possible association between NAT2 rapid acetylator status and drug-resistant *M. tuberculosis* as a consequence of inadequate treatment.

The research was conducted in Chiang Rai Province, Thailand, as part of an integrative study on human and pathogen genomics of TB. We enrolled TB patients confirmed via culture and over 15 years old.

The study determined NAT2 rapid, intermediate and slow acetylators using SNPs from six loci of the SNPs including rs1041983, rs1801280, rs1799929, rs1799930, rs1208 and rs179993.

We identified six NAT2 haplotypes (NAT2\*4, \*5B, \*6A, \*7B, \*12A and \*13A), and individuals were classified into rapid, intermediate or slow acetylators.

We stratified participants by their TB treatment history and analyzed the association between NAT2 acetylator status and drug resistance against INH, rifampicin and both.

Of those with NAT2 genotype and drug resistance results (n=1032), 399 (38.7%) had previous TB treatment history. 133 patients with prior TB treatment history exhibited at least one drug resistance. Among them, patients with rapid and intermediate NAT2 acetylators showed higher INH resistance rates (18.2% and 25.1%) compared to slow acetylator (13.5%).

After adjusting for age, sex and ethnicity, rapid and intermediate acetylator status showed 1.89 (95% CI: 1.03-3.45) higher odds of drug resistance compared to slow acetylators.

In conclusion, our findings suggest that NAT2 rapid and intermediate acetylator status might increase the risk of TB drug resistance.

### TBS-EP01-13 Investigation of bedaquiline-resistance in *Mycobacterium tuberculosis* isolates from patients with drug-resistant tuberculosis at the Dr George Mukhari Tertiary Laboratory

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Tuberculosis (TB) is a major global health concern worsened by the spread of drug resistant *Mycobacterium tuberculosis* (*Mtb*) strains. Bedaquiline (BDQ) was licensed in 2012, and rolled out nationally in South Africa in 2015, to strengthen the current regimens in the treatment of drug-resistant strains and improve patients' outcome.

The purpose of this study was to investigate BDQ-resistance in *Mtb* isolates from patients with drug-resistant-TB at Dr George Mukhari Tertiary Laboratory.

One hundred and fifty consecutive residual drug resistant isolates were collected from routine clinical specimens from June 2020 to February 2021 and included in the study, for target and non-target sequencing.

Of the 150 isolates, 78 (52%) were from Gauteng, 59 (39.3%) Northwest and 13 (8.6%) from Mpumalanga. Of all the drug resistant-TB cases, 128 (85.3%) were new cases.

Target sequencing was done in all the isolates targeting three genes associated with BDQ resistance (*pepQ*, *Rv0678* and *atpE*). Of the 150 isolates, 12 (30%) had substitution mutation in the *pepQ* gene while 3 (3.8%) had deletion and substitution mutation in the *Rv0678*. For the *atpE* gene, 1 (2.1%) isolate had both substitution and deletion mutations. Non target sequencing was done in 19/150 (12.6%) pre-XDR isolates, of which 14 (73.6%) were resistant to both BDQ.

These mutations were found in the *mmpR* (*Rv0678*) gene encoding the MmpS5–MmpL5 efflux pump repressor associated with BDQ resistance. The predominant lineages were found to be the India-Oceanic and Euro-American lineages.

To improve treatment outcomes in patients with DR-TB strains, the availability of comprehensive and rapid genotypic and phenotypic drug susceptibility testing is a key to effective and timeous treatment that will help to prevent the emergence of drug resistant *Mtb* strains and further reduce transmission of resistant strains within communities.

### TBS-EP01-14 Interaction Between Host Defence Peptides and Mycobacteria

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*Mycobacterium tuberculosis* is resistant against the antimicrobial activity of a large number of host defence peptides (HDPs), which are active against other Gram-negative or –positive bacteria. One reason for this resistance is the unique structure of the mycobacterial cell wall. Mycobacteria produce a thick mycolate-rich outer glycolipid layer which functions as an exceptionally efficient barrier.

We demonstrated that the membrane forming properties of trehalose dimycolate (TDM), as one of the important components of the mycobacterial outer barrier, are unique. TDM, which is organized in domains, leads to an increase of the overall membrane stability by a factor of three.

We used reconstituted planar lipid bilayers composed of TDM and phospholipids to perform electro-physiological experiments for determining the membrane permeabilizing activity of different HDPs. Atomic force and Scanning Electron microscopy was used to characterize the surface topography of reconstituted membranes and mycobacteria.

X-ray synchrotron experiments were performed to analyse the molecular organization of the membranes. The biophysical results were compared with results from anti-mycobacterial killing assays.

Interestingly LL32, which is the highly active fragment of human cathelicidin, induced dramatic changes in the membrane morphology without inducing a significant permeabilization. We developed new HDPs with significantly increase activities against *Mtb* and no haemolytic activity.

### TBS-EP01-15 Antimicrobial resistance stewardship: lessons learned from drug-resistant tuberculosis programs – a scoping review

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**Background:** Antimicrobial resistance (AMR) is a growing public health threat due to the slow development of new antimicrobials and the increasing use of these drugs. Globally, drug-resistant microorganisms contribute to around 700,000 deaths, with 200,000 attributed to drug-resistant tuberculosis (DR-TB).

**Objective:** This scoping review aims to identify interventions in DR-TB control that have demonstrated higher treatment success rates than the global average in low- and middle-income countries (LMICs), with the goal of informing global AMR stewardship efforts.

**Design:** In June 2021, a literature search was conducted in the MEDLINE and Embase databases. We selected original articles published in English that focused on observational cohort studies, clinical trials, systematic reviews, and mixed methods studies of adult pulmonary DR-TB patients from 2008 - 2018 in LMICs, with documented end-of-treatment outcomes. Data were extracted, collated, charted, and mapped against the 2019 WHO Practical Toolkit on Antimicrobial Stewardship Programs in Healthcare Facilities in LMICs.

**Results:** We identified 3348 articles. After the removal of duplicates, 2693 articles were screened for eligibility based on title and abstract, resulting in a remainder of 370 articles that were reviewed based on full text. In total, 53 articles met the eligibility criteria.

We found that interventions in the context of DR-TB closely align with the principles outlined in the WHO's practical toolkit on Antimicrobial Stewardship Programs.

However, inconsistencies were identified in antibiotic prescription practices and patient treatment adherence. Out of the 42 documented intervention types, key interventions included directly observed treatment (27 articles), adverse event monitoring (26 articles), and prioritizing DR-TB in National Action Plans (22 articles).

**Conclusion:** Our review highlights the strong alignment between DR-TB interventions and the WHO's practical toolkit on Antimicrobial Stewardship Programs, except for antibiotic prescription practices and patient treatment adherence. Addressing these areas of inconsistency could enhance global AMR stewardship.

### TBS-EP01-16 Investigating West African *M. tuberculosis* complex lineages response to new anti-tuberculosis treatment approaches

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Tuberculosis is caused by *Mycobacterium tuberculosis* (*Mtb*) complex (MTBC) lineages. There are nine MTBC lineages worldwide, all found in Africa. Some lineages are distributed globally (lineage 2 and 4), while others are restricted to specific geographical locations, such as *M.africanum* (lineages 5 and 6), where are mainly found in West Africa.

Despite this diversity, drug-susceptible TB is treated with the same antibiotic combination for six months. MTBC lineages' genetic diversity has been shown to affect treatment response. Therefore, new drugs accounting for this diversity are needed to control TB.

Here, a total of 285 MTBC isolates from The Gambia with whole genome sequence data were used to identify important genetic mutations for structural bioinformatics analysis. Representative isolates of MTBC lineages were transformed using a reporter gene-tagged plasmid to confer luminescence and green fluorescence protein expression to bacilli. The direct effect of antibiotics was tested in the presence of the bacteria to determine the half-maximal inhibitory concentration 50 (IC50) of each drug against the transformed MTBC lineage. The IC50 values were then aligned with the genetic variation in each lineage to derive an association.

The results revealed that some mutations within established drug resistant genes differed in MTBC lineages. The IC50 for rifampicin was 0.001-0.002, 0.003-0.004, 0.004, 0.007 and 0.008 for *M.africanum* lineage 6, *Mtb* lineage 2, *M. bovis*, *Mtb* lineage 4 and *M.africanum* lineage 5, respectively. *M.africanum* lineage 6 had a lineage-specific mutation in the *rpoB*, but also *fabG1* and *gyrA/B* genes. *Mtb* lineage 4 had only a mutation in the *katG* gene, related to isoniazid resistance.

Overall, we have built a pipeline to integrate the genetic variation of MTBC isolates circulating in West Africa with phenotypic antibiotics' susceptibility. This will be used to understand the molecular determinants of West African MTBC lineage responses to existing and new anti-TB drugs.

### TBS-EP01-18 Development of low-cost oligonucleotide ligation assay and lateral flow test to detect multidrug-resistant TB

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Treatment regimens for tuberculosis (TB) rely on antimicrobial drugs such as rifampin and isoniazid. However, high levels of antimicrobial resistance can lead to poor treatment outcomes and further transmission of TB and multi-drug resistant TB (MDR-TB). Screening for MDR-TB can be complicated by the long turnaround time involved in existing methods such as line probe assay. Point-of-care MDR-TB tests such as Xpert are available but require access to >\$US10k custom equipment. To this end, we have developed a near-point-of-care, low-cost oligonucleotide ligation assay “OLA-Simple” platform to detect single nucleotide polymorphisms (SNPs). OLA-Simple contains four main steps: sample preparation, amplification of regions containing mutations, allele-specific probe ligation, and visual detection of the ligated products by lateral flow test (LFT). Here we develop PCR primers and ligation probes and optimize assay conditions to detect rifampin-resistant TB mutations within the *rpoB* gene (i.e., D435V, D435Y, H445Y/D, H445L, S450L/W, S450L/W, and L452P). Primers and probes were designed based on the consensus sequence of ~4,000 MTB complexes (European Nucleotide Archive). Ligation reaction is carried out in the presence of wild-type (WT) or mutant (MUT) MTB amplicon mixed with ligase and three different probes: a 5'-phosphorylated, 3'-biotinylated common probe, a 5'-digoxigenin-tagged WT probe, and a 5'-fluorescein-tagged MUT probe. The resultant ligation product is detected using anti-biotin-conjugated gold nanoparticles on custom 3D-printed LFT consisting of a biotin control line, anti-digoxigenin WT line, and anti-fluorescein MUT line. Across all the seven rifampin-resistant mutations, we observed expected results with visible MUT bands in samples with MUT alleles and visible WT bands in samples with WT alleles. Similarly, software analysis revealed a significant difference between the MUT signal intensities of samples with MUT vs. WT alleles. In summary, the work present is a significant step toward increasing access to low-cost MDR TB testing.

### TBS-EP01-19 Unconjugated peptides comprising *M. tuberculosis* heat shock protein and *S. aureus* peptidoglycan generate broadly reactive antibodies to Gram-positive bacteria

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**Background:** Antimicrobial Resistance (AMR) is a global threat to public health. *Mycobacterium tuberculosis* (MTB) is one of the high priority pathogens among drug-resistant bacterial strains that contribute to AMR. Peptide vaccines comprising multiple epitopes specific to MTB and common to gram-positive bacteria could provide a novel approach towards designing a vaccine that combats AMR, while also targeting tuberculosis. Previous studies have shown that antibodies to Peptidoglycan (PGN) were opsonic against gram-positive bacteria and MTB.

In this study, we demonstrate that unconjugated peptides comprising MTB heat shock protein (HSP16.3), TB Pep01, and PGN from *Staphylococcus aureus* (SA), generated cross-reactive antibodies against mycobacteria and other gram-positive bacteria.

**Methods:** ICR mice were immunized with 1, 10, and 20 µg of TB Pep01 and ultrapure PGN, formulated with AddaVax™ adjuvant. Serum IgG1 titers to TB Pep01, PGN, and various gram-positive bacteria including MTB were analyzed by indirect fixed ELISA. Titers to *Mycobacterium smegmatis* (SMEG), *Staphylococcus epidermidis* (SE), *Staphylococcus aureus* (SA), *Bacillus subtilis* (BS) and Group B Streptococcus (GBS) were also assessed using live bacteria ELISA.

**Results:** Robust and broad IgG1 antibodies were induced to both PGN and TB Pep01 and demonstrated higher titers with 10 and 20 µg doses, compared to 1 µg. A dose response was also observed in the binding of antibodies to fixed and live mycobacteria, staphylococci, streptococci, and bacilli.

**Conclusion:** Unconjugated peptides comprising MTB HSP16.3 and PGN from SA generated broadly reactive antibodies to MTB, SMEG, SE, SA, BS and GBS. Antisera are currently being tested for opsonophagocytic killing activity against mycobacteria and staphylococci. Combining MTB-specific epitopes with common epitopes among gram-positive bacteria could be a useful strategy for mitigating the global threat of AMR and provide novel treatment options for tuberculosis. Moreover, unconjugated peptides targeting epitopes of multiple pathogens provide a cost-effective, easily scalable approach for vaccine design.

## TBS-EP02 TBScience 2023 - Moderated E-poster Session II

### TBS-EP02-02 MIC distribution and the prevalence of drug resistance in multidrug-resistant TB in the Philippines

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The Philippines is one of the countries with a high burden of TB and DR-TB, and quality-assured drug susceptibility testing is needed to confirm drug resistance. Furthermore, the critical minimum inhibitory concentration (MIC) of these drugs and the prevalence of resistance in the local environment remain unknown.

We tested a total of 188 MDR-TB isolates registered with PMDT were randomly selected in this preliminary analysis. The reference values used for the MIC ranges of MFX, BDQ, DLM and LZD and the critical concentration of MGIT were based on the latest CLSI and WHO standards respectively. MIC resistance categories were determined by comparing the obtained MIC distribution with MGIT-AST results, and the frequency of resistance for each drug was determined. For MFX, resistance-related genes were confirmed by WGS.

The tentative MIC resistance rates were as high for MFX (18.4%), followed by LZD (8.0%), BDQ (0.5%) and DLM (0.5%); The area of technical uncertainty or intermediate category was set at 1mg/L for MFX. MGIT-AST results showed that MFX resistance was highest (17.8%), followed by BDQ (1.1%) and LZD (0.5%), but no isolates were resistant to DLM. For comparison of phenotypic MFX resistance by MGIT-AST and results with WGS, 2 isolates with the *gyrA* A90V mutation (2/26:12.5%) were found to be phenotypically susceptible, while all 12 strains with the D94G mutation were resistant with MGIT-AST (100%). Hetero-resistant (n=6) and isolates with no mutations (n=8) were also found.

In conclusions, the MIC distribution proposed in this study also indicates that the clinical breakpoint (CB) and quality control strain tolerance for X/MDR-TB treatment may be influenced by the MIC distribution.

The results of this preliminary analysis may warrant a comprehensive review of existing MICs and possible changes to the current MIC plate design. Further detailed analysis by WGS is required (currently ongoing).

### TBS-EP02-03 Risk factors for fluoroquinolone resistance among patients with second-line drug-resistant TB evaluated in Uganda

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Despite the emerging burden of second-line resistance, the emergence of fluoroquinolone resistance and the risk factors among patients living with mono and multi drug resistant TB has not been extensively studied in Uganda.

This study aimed at determining the risk factors for fluoroquinolone resistance among patients with second line-drug resistant tuberculosis from mono and multi-drug resistant tuberculosis isolates previously evaluated samples in Uganda.

This was a case-control study conducted on 240 mono and multi-drug resistant tuberculosis patient samples referred to the national tuberculosis reference laboratory and evaluated for second-line drug resistance between the months of June 2017 and December 2019. Data for the study were collected using the laboratory information system, which extracted information on drug-resistant TB patients and relevant metadata. Data on mutations and clinical/demographic information were entered, sorted, cleaned, and organized in Microsoft Excel.

The data were then imported into STATAv15 for cross-tabulation and descriptive statistics. The study employed a nested case-control sampling approach, where cases were identified from a larger cohort study population, and controls were selected from the same cohort.

Linear logistic regression and correlation analyses were conducted to explore the relationships between the dependent and independent variables. In total 72/574 (12.54%) were characterized as second line drug resistant strains using rapid molecular line probe assay analysis.

Predominant mutations (26) conferring high-level resistance to Moxifloxacin were found to frequently occur in the *gyrA* D94G locus, followed by the *gyrA* A90V locus (25) and least (01) in the *gyrB* locus. Clinical factors, specifically RIF/INH Resistance and Treatment outcome, showed significant associations with fluoroquinolone drug resistance at coefficients of 0.3077 ( $p < 0.001$ ) and -0.0972 ( $p = 0.003$ ), respectively.

The study findings suggest that public health initiatives should prioritize tackling RIF/INH resistance and treatment outcomes as key areas for intervention to combat fluoroquinolone drug-resistance among drug-resistant TB patients.



## TBS-EP02-05 Metabolic inhibitors mitigating sepsis and TB-induced DNA hypermethylation

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**Background:** Severe and chronic infections, such as sepsis and Tuberculosis (TB), lead to epigenetic-mediated immune suppression. Cancer studies have demonstrated that perturbations in intracellular metabolites trigger global changes in the epigenetic landscape.

**Methods:** We applied complementary approaches, including data mining public tuberculosis (*GSE42834*) and sepsis (*GSE154918*) datasets, an in vitro LPS-stimulated macrophage tolerance model, DNA methylation (Methyl EPIC), confocal microscopy, and reverse phase protein array (RPPA) to investigate mechanisms of reversing post-infection immune suppression. Metabolic inhibitors rapamycin, everolimus, metformin, BAY1436032, DON and GLYNAC were used.

The results from vitro studies were validated in vivo among TB participants who received standard of care antibiotics (SOC) with and without the metabolic inhibitor everolimus.

**Results:** Patients with TB and sepsis both demonstrate increased expression of genes involved in glycolysis and the tricarboxylic acid (TCA) cycle, which correlated with an increase in DNA methylation. LPS-tolerized human monocytes developed DNA hypermethylation that overlaps with epigenetic profile changes in humans with sepsis and TB. LPS induced the TCA enzymes isocitrate dehydrogenase, citrate synthetase, as well as DNMT3B to translocate into the nucleus. Inhibition of metabolic overactivation blocked LPS-induced immune suppression and DNA hyper-methylation.

Phase 2 TCA metabolites succinate and itaconate mimicked LPS-induced immune suppression and DNA hyper-methylation. In vivo, humans with TB who received SOC plus the everolimus are rescued from DNA hyper-methylation marks.

**Conclusion:** Metabolic activation via the TCA cycle regulates DNA methylation and immune tolerance and metabolic inhibitors restore immune responsiveness and lower DNA hypermethylation. In vivo, metabolic inhibitor everolimus inhibits DNA hypermethylation and associates with improved lung function.

## TBS-EP02-06 Post-TB DNA hypermethylation correlates with improved lung function

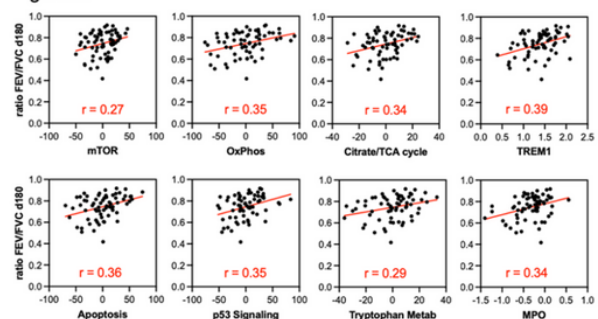
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During successful TB therapy, 10-20% of patients have worsening lung function despite microbial clearance. DNA methylation are heritable epigenetic marks that regulate immunity. We previously demonstrated that TB patients have long-lasting DNA hypermethylation scars that limits Mtb-specific peptides (ESAT-6 and CFP-10) and non-specific (BCG and mitogen) immunity. It is unclear how DNA methylation status effects lung function recovery during TB therapy.

Leveraging PBMCs available from a previously described HDT clinical trial, DNA was isolated from 73 micro-confirmed TB participants with spirometry data at baseline and end of therapy (EOT). Despite successful therapy, 26%, 28%, and 44% had worsening FEV1, FVC, or FEV1/FVC, respectively. CRP levels, used as a marker of inflammation, decreased in almost all TB participants, but did not correlate with improved lung function ( $r = -0.08$ ;  $p = 0.49$ ).

Improved lung function correlated with DNA hypermethylation. Specifically, improved lung function (with improved FEV1 and FEV1/FVC) associated with DNA hypermethylation in mTOR signaling, OxPhos, apoptosis, TCA cycle, and p53 signaling (Fig 1).

**Figure 1:** End of therapy (day 180) FEV1/FVC ratio correlates with increased promoter DNA methylation of the mTOR, Oxidative phosphorylation, TCA cycle, apoptosis, p53, and tryptophan metabolism pathways and of the TREM1 and MPO genes.



Improved FVC correlates with DNA hypermethylation in mTOR signaling and one-carbon metabolism. Worsening lung function during successful therapy overlapped with previously identified methylation changes associated with systemic inflammation, including DNA methylation changes in TNF-NFKB pathway, p53, PI3K-mTOR signaling, and VEGF signaling.

WGCNA analysis identified a module of hypermethylated promoters that correlated with EOT FEV1/FVC ( $r=0.34$ ;  $p = 0.005$ ). This module of promoters identi-

fied that hypermethylation of TREM1 and MPO correlating with EOT FEV1/FVC ( $r = 0.39$  and  $0.34$ , respectively;  $p < 0.01$ )

In summary, while DNA hypermethylation induces immune suppression, this data demonstrates that it is associated with improved lung function during TB therapy. This suggests that HDT will need to balance healing some DNA methylation scars without inducing additional lung pathology.

### TBS-EP02-07 Interferon- $\gamma$ -independent immune markers of *M. tuberculosis* exposure among HIV-exposed and unexposed infants

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**Background:** HIV-exposed uninfected (HEU) children may be at increased risk for *M. tuberculosis* (Mtb) infection compared to HIV-unexposed children (HUU). Clinical tests to identify Mtb infection (tuberculin skin test [TST] and interferon- $\gamma$  [IFN- $\gamma$ ] release assay [IGRA]) may have decreased performance due to BCG cross-reactivity or reduced IFN- $\gamma$  production in early life. We hypothesized non-IFN- $\gamma$  responses would identify additional children, and HEU infants would be more likely to exhibit Mtb sensitization.

**Methods:** We performed TST (12 and 24 months) and collected PBMCs (6 weeks, 12 and 24 months) from HEU and HUU infants in Kenya. PBMCs were incubated overnight with CFP-10/ESAT-6 peptide pool. CD4 T cell expression of IFN- $\gamma$ , IL-2, and TNF was measured by flow cytometry.

Probability of TB-specific CD4 T cell responses was estimated using Bayesian hierarchical mixture model approach (MIMOSA); cytokine responses with posterior probability of response  $\geq 95\%$  and false discovery rate  $< 0.05$  were considered positive. TST  $\geq 10$  mm was considered positive.

**Results:** Among 87 infants with PBMCs evaluated (HEU: 39 [45%], HUU 48 [55%]), 17 (19.5%) exhibited CFP-10/ESAT-6 specific responses at any time point (IFN- $\gamma$ +: 4 [4.6%], IL-2+: 11 [12.6%], TNF+: 6 [6.9%]), including 2 with IL-2+TNF+ and 1 with IFN- $\gamma$ +IL-2+TNF+ responses; 1/87 (1.1%) had a positive TST. IL-2 and/or TNF identified 3.5-fold (16.1 vs. 4.6% RR 3.5 [95% CI 1.23-9.98]) more infants vs. IFN- $\gamma$  alone, while any TB-specific cytokine identified 16 times (19.5 vs. 1.2% RR 16.0 [95% CI 2.12-120.6]) more infants than TST alone. The proportion of HEU and HUU infants with any TB-specific cytokine response was similar (23.1 vs. 16.7%, RR 1.2 [95% CI 0.73-2.09]), though HEU infants were more likely to have TNF+ responses (12.8 vs 2.1%, RR 2.0 [95% CI 1.28-3.09]).

**Conclusion:** TB-specific IFN- $\gamma$ -independent cytokine responses identified additional infants with Mtb sensitization, potentially missed by TST and IGRA, with TNF responses more common among HEU infants.

	Overall				6 weeks				12 months				24 months			
	Overall† N=87 n (%)	HEU N=39 n (%)	HUU N=48 n (%)	p*	Overall N=51 n (%)	HEU N=19 n (%)	HUU N=32 n (%)	p*	Overall N=77 n (%)	HEU N=35 n (%)	HUU N=42 n (%)	p*	Overall N=22 n (%)	HEU N=4 n (%)	HUU N=18 n (%)	p*
CFP-10/ESAT-6 (any+) #	17 (19.5)	9 (23.1)	8 (16.7)	0.453	1 (2.0)	1 (5.3)	0	0.190	12 (15.6)	8 (22.9)	4 (9.5)	0.108	4 (18.2)	0	4 (22.2)	0.297
IFN- $\gamma$ +	4 (4.6)	2 (5.1)	2 (4.2)	0.831	--	--	--	--	4 (5.2)	2 (5.7)	2 (4.8)	0.851	--	--	--	--
IL-2+	11 (12.6)	4 (10.3)	7 (14.6)	0.546	--	--	--	--	7 (9.1)	4 (11.4)	3 (7.1)	0.515	4 (18.2)	0	4 (22.2)	0.297
TNF+	6 (6.9)	5 (12.8)	1 (2.1)	<b>0.049</b>	1 (2.0)	1 (5.3)	0	0.190	5 (6.5)	4 (11.4)	1 (2.4)	0.231	--	--	--	--
TST+‡	1 (1.2)	1 (2.6)	0	0.274	n/a	n/a	n/a	n/a	1 (3.5)	1 (2.9)	0	0.275	--	--	--	--

† Includes participants who were positive by any CFP-10/ESAT-6+ specific cytokine or TST at any timepoint

\* Test of proportions between HEU and HUU

# Bayesian hierarchical mixture model approach (MIMOSA); cytokine responses with posterior probability of response  $\geq 95\%$  and false discovery rate  $< 0.05$  were considered positive

‡ TST positive  $\geq 10$ mm

TBS-EP02-07 Table. Prevalence of CFP-10/ESAT-6-specific responses and TST positivity among HIV-exposed uninfected (HEU) and HIV-unexposed uninfected (HUU) infants in Kenya at 6 weeks, 12 months, and 24 months of age, N=87.

### TBS-EP02-08 Searching for suppression: myeloid-derived suppressor cells in TB granulomas

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Multidrug resistant TB remains a major clinical challenge world-wide and host-directed therapies have been proposed as adjunctive therapy in cases of Mtb drug resistance. Recently, it has been suggested that pharmacologic modulation of myeloid-derived suppressor cells (MDSC) may be an alternative to antimicrobial therapy for TB. MDSC are a transient immature myeloid cells that have been shown to block T cell-activation by recruiting T-regulatory lymphocytes.

In cancer, MDSC have been associated with immune-suppression and dampening of the host's immune response locally in tissue microenvironments, but the role of MDSC in *Mycobacterium tuberculosis* (Mtb) disease progression is unclear.

In order to determine if MDSC could be a useful target for adjunctive therapy for TB disease in immune suppressed populations, we wanted to investigate their role in TB disease.

Using spatial transcriptional profiling and highly multiplexed tissue cyclic immunofluorescence, we profiled a series of histologically distinct granulomas identified on H&E- stained sections of surgical lung resection specimens from four individuals with culture confirmed Mtb infection. Distinct transcriptional profiles were associated with different granuloma maturation states and degree of T lymphocyte infiltration.

In transitional granulomas, that were non-necrotizing and characterized by variable degrees of fibrosis, we identified increased co-expression of suppressor genes such as S100A8/S100A9 and IDO with myeloid markers (CD14, CD68, CD163) consistent with the presence of monocyte-like myeloid-derived suppressor cells (Mo-MDSC).

Analysis of multi-plexed IF (mIF) from serial sections confirmed the co-expression of suppressive proteins with myeloid cells consistent with the presence of MDSC in human tuberculosis.

Notably, the highest expression of suppressive genes was detected in granulomas that lacked significant T cell infiltrates or necrosis suggesting that MDSC may have a distinct role in tuberculosis pathology that differs from what has been described in tumor microenvironments.

### TBS-EP02-09 Diminished TB-specific T-cell responses during pregnancy in women with HIV and the effect of isoniazid preventive therapy

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**Background:** Risk of tuberculosis (TB) progression appears increased in pregnancy and early postpartum and is associated with adverse maternal-infant outcomes. We previously described suppression of *Mycobacterium tuberculosis* (Mtb)-specific CD4+ T-cell responses (associated with TB progression) during the third trimester irrespective of HIV coinfection.

In this study, we evaluated the impact of pregnancy on Mtb-specific CD4+ T-cell responses in women with HIV (WHIV) with prior TB sensitization determined by a positive QuantiFERON-TB Gold Plus (QFT-Plus), and the interaction of isoniazid preventive therapy (IPT) on immune responses to Mtb.

**Methods:** We measured adaptive immune responses among participants (n=33) with persistently positive QFT-Plus tests during pregnancy (20-34 weeks), 6-weeks postpartum, and 12-months postpartum enrolled in the Maternal Infant TB infection Incidence and Prevalence Study (MITIPS) in Western Kenya. Using cryopreserved peripheral blood mononuclear cells (PBMC), we quantified frequency of Mtb (ESAT6/CFP10) specific CD4+ T-cell cytokines IFN $\gamma$ , IL-2, and TNF $\alpha$  with intracellular cytokine staining, performed dimensional reduction techniques applying COMPASS to create a total functional score (FS), and compared groups using nonparametric ANOVA.

**Results:** Among 21 WHIV (median CD4 = 570, IQR 493-802 and 90% with undetectable viral load), we observed Mtb-specific cytokine responses in WHIV were significantly lower during pregnancy than at 12 months postpartum (median FS 0.009 vs 0.12, p=0.03) (Figure-1). WHIV who received IPT during current pregnancy (n=6) had significantly diminished Mtb-specific T-cell responses during pregnancy compared to 12 months postpartum (median FS  $1.6 \times 10^{-6}$  vs 0.13, p=0.02). The magnitude of reduction was greater in this group compared to WHIV who either received IPT before current pregnancy or never (n=15, median FS 0.02 vs. 0.12, p=0.3).

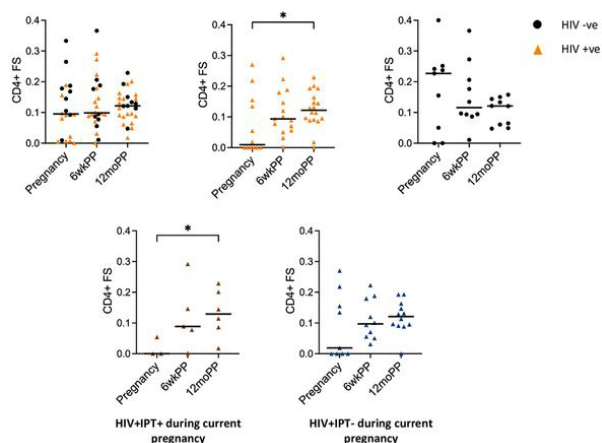


Figure 1. CD4+ T-cell functional score (FS) generated from COMPASS analysis, is diminished during pregnancy in women with HIV.

**Conclusion:** Pregnancy decreased TB-specific immune responses in WHIV, which was further decreased by IPT. Studying the interplay of pregnancy, HIV, and IPT in Mtb-specific immune responses may shed light on TB prevention during pregnancy.

### TBS-EP02-10 A comparison of immune profiles in the lung and the blood from post-TB patients in The Gambia

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**Introduction:** Tuberculosis (TB) is the leading cause of death from a single infectious disease. Despite successful treatment in most TB patients with drug-susceptible TB, at least 50% continue to present with signs of chronic inflammation, fibrosis, bronchiectasis, and airflow limitation years after treatment, leading to significant morbidity and mortality.

While Post-TB lung disease is common, the inflammatory profile and lung micro-environment post-cure have not been well described. The aim of this study was to compare immune profiles in the lung and blood of Post TB patients.

**Methods:** Twelve adult participants who had successfully completed TB treatment at least 2 years prior to the study were recruited. Paired peripheral blood mononuclear cell (PBMC) and bronchoalveolar lavage (BAL) samples were collected from each participant, and the proportion of antigen-specific CD4+ T cells expressing different cytokines (IL17a, IL22, IL2, TNF $\alpha$ , and IFN $\gamma$ ) was analyzed using flow cytometry.

**Results:** CD3+CD4+ lymphocyte levels were significantly higher in PBMCs compared to BAL cells. However, TNF- $\alpha$  and IFN- $\gamma$  expression on CD4 T cells was higher in BAL compared to PBMCs. No significant difference was found between BAL cells and PBMC for IL22 and IL17a. Also, the expression of IL2 in PBMC strongly correlates with lung function by spirometry ( $r=0.78$ ).

**Conclusion:** Post-TB patients show a higher level of Th1 response in the lungs compared to the blood, suggesting ongoing or unresolved inflammation in the lung's years following TB treatment. Further analysis of activation and memory markers on CD4 T cells will provide a better understanding of the lung's pathophysiology post-TB treatment.

### TBS-EP02-11 An autologous human dendritic cell vaccine from extensively drug-resistant TB patients polarises antigen-specific polyfunctional and cytotoxic T-cell responses that are bactericidal to *M. tuberculosis*

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**Background:** Extensively drug-resistant tuberculosis (XDR-TB) is an increasing public health concern as drug resistance is outpacing the drug development pipeline. Alternative immunotherapeutic approaches are needed. **Methods:** DCs were cultured from XDR-TB patient-derived peripheral blood monocytes (n=30) by maturation with *M.tb*-specific antigens, with/without a maturation cocktail (interferon- $\gamma$ , interferon- $\alpha$ , CD40L, IL-1 $\beta$ , and TLR3, TLR7 and TLR8 agonists). Two peptide pools were evaluated:

i. An ECAT peptide pool (ESAT6, CFP10, Ag85B and TB10.4 peptides)

ii. A PE/PPE peptide pool (PE and PPE peptides).

A sonicated lysate of HN878 served as an antigen control. DCs were assessed for the expression of key maturation markers and the secretion of Th1-polarising cytokines. The ability of the DC-primed PBMCs to restrict the growth of *M.tb*-infected monocyte-derived macrophages was evaluated using an *in vitro* mycobacterial containment assay.

**Results:** In patients with XDR-TB, DCs matured with *M.tb*-antigen+cocktail, compared to DCs matured with *M.tb*-antigen only, showed significantly higher upregulation of key co-stimulatory molecules, CD80, CD83, CD86, and CCR7 ( $p<0.001$  for all comparisons), and higher secreted levels of the IL-12p70 (0.67 versus 0.01ng/mL/ $10^6$  cells;  $p<0.001$ ). The matured DCs enhanced antigen-specific CD8+ T-cell responses to ESAT-6 ( $p=0.05$ ) and Ag85B ( $p=0.03$ ).

Furthermore, containment was significantly higher with *M.tb*-antigen+cocktail versus antigen alone ( $p=0.0002$  for PE/PPE). PE/PPE+cocktail-matured DCs achieved a higher magnitude of containment compared to ECAT+cocktail-matured DCs (50%, IQR:39-75, versus 46%, IQR:15-62,  $p=0.02$ ).

**Conclusions:** In patients with XDR-TB, an effector response primed by the PE/PPE peptide pool and cocktail-matured DCs was capable of restricting the growth of *M.tb in vitro*. These data support the generation of a DC-based immunotherapeutic intervention for therapeutically destitute patients with DR-TB. Further mechanistic studies and future phase 1 human clinical studies are warranted.

### TBS-EP02-12 Persistent inflammation and impaired redox homeostasis in TB survivors: implications for host-directed therapies

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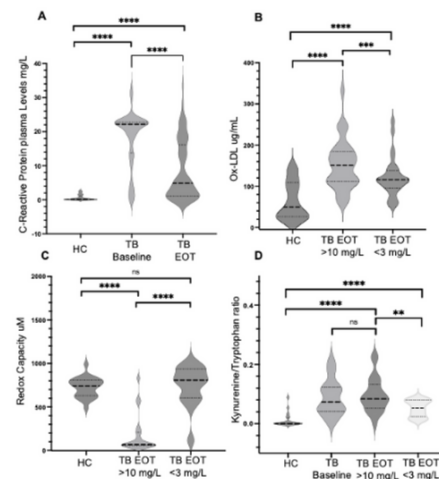
Despite antimicrobials killing the *M.tb* bacilli, after successful TB treatment, survivors have a 3.7-fold increased risk of mortality due to increased rates of cardiovascular disease, cancer, respiratory disease, and recurrent infections. The majority of TB survivors have persistent inflammation despite becoming culture negative completing antibiotics. Upon immune activation, electrons leak out of the mitochondria, forming lipid peroxide radicals that can propagate a chain reaction of persistent inflammation known as lipid peroxidation.

We hypothesized that post-TB persistent inflammation is driven by lipid peroxidation and is inversely associated with redox capacity.

From 2014 to 2020, 325 participants with pulmonary TB and 400 asymptomatic healthy household contacts were monitored for 12 months, with blood collected at baseline and after completion of successful TB treatment (EOT). Inflammation, lipid peroxidation, redox capacity, and immune activation were evaluated by measuring plasma C-reactive protein (CRP) levels, 4-hydroxynonenal (HNE)-LDL, Trolox antioxidant reducing capacity, and Indoleamine 2,3 dioxygenases (IDO) activity, respectively.

Among TB participants with successful therapy, 60% still had abnormal inflammation (CRP > 3 mg/dL). HIV coinfection, gender, and age were not found to be associated with elevated post-TB inflammation. Failure to

normalize CRP at EOT was associated with increased lipid peroxidation (oxLDL;  $p<0.001$ ). Similarly, elevated EOT CRP was associated with decreased redox capacity (Trolox) ( $p<0.001$ ). Both the TB participants with persistent and normalized inflammation demonstrated persistent immune activation (elevated IDO activity as measured by Kynurenine: Tryptophan ratios) at EOT (Fig 1).



**Fig.1 (A):** In this study, C-reactive protein (CRP) levels were measured in tuberculosis (TB) participants and healthy household contacts. The healthy contacts had a median CRP level of less than 2 mg/L, indicating low inflammation. In contrast, TB participants had significantly higher CRP levels, with a median of 21 mg/L at the beginning of the study. However, after successful therapy (EOT), their CRP levels decreased to 8 mg/L. Previous research has linked CRP levels exceeding 3 mg/L to an increased risk of cardiovascular disease (CVI). Alarmingly, at the end of TB therapy, 60% (114 out of 190) of TB participants still had CRP levels exceeding mg/L, suggesting persistent inflammation and a potential elevated risk of CVD. (B) Oxidized-LDL was measured in TB individuals with High Levels of CRP < 10 mg/L (n=30) vs Low CRP levels < 3 mg/L (n=28). (C) Trolox antioxidant capacity of Trolox was assessed in three groups: tuberculosis (TB) participants with high CRP levels (>3 mg/L) (n=39), TB participants with low CRP levels (<3 mg/L) (n=31), and healthy controls (n=25). (D) Plasma Kynurenine to Tryptophan ratio was evaluated in TB individuals with persistent augmented level of CRP (n:19) at baseline and Healthy Controls. At the end of Therapy, the KYN: TRYP was evaluated in 1 individuals with high (n:22) and Low CRP levels (n:17).

The data demonstrate that most TB participants continue to experience inflammation, immune activation, lipid peroxidation, and decreased redox capacity despite successful TB treatment. The inability to quench lipid peroxidation likely perpetuates persistent inflammation. Future studies need to evaluate if persistent inflammation, lipid peroxidation, and/or redox capacity can help predict post-TB morbidity and mortality and if lifestyle and host-directed therapies targeted this pathology could improve post-TB outcomes.

### TBS-EP02-13 Innate tolerization of myeloid cells to Mycobacterium tuberculosis glycolipids

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Mycobacterial glycolipids make up a large part of the bacterial cell wall and closely interact with innate immune cells, influencing their response upon infection. Therefore, to better understand resistance and control mechanisms in TB, it is important to investigate the innate immune response to mycobacterial glycolipids.

Lipoarabinomannan (LAM) and phosphatidyl-myoinositol mannoside (PIM) are major glycolipid components of the Mtb cell wall and have exhibited immunomodulatory properties of the host's innate immune cells. Among observed effects was a dampened cytokine production among myeloid cells in patients with latent TB compared to healthy controls. This suggests that monocytes could be tolerized in TB infection, perhaps contributing to evasion of active TB disease.

We investigated innate tolerization mechanisms by stimulating monocytes and monocyte-derived macrophages (MDMs) with Mtb glycolipids. We consequentially demonstrated induced tolerization of monocytes and MDMs to PIM whereas stimulations with LAM gave varied results. Blockade of TLR2 prior to glycolipid stimulation indicated a significant but not complete reliance on TLR2 as a receptor for tolerization by PIM.

### TBS-EP02-14 Altered interleukin-6 signalling and risk of TB disease: a meta-analysis and trans-ancestry Mendelian randomisation study

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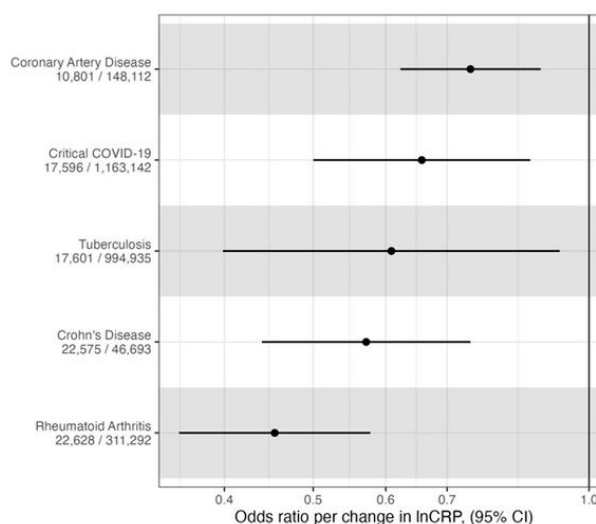
**Introduction:** The role of ubiquitous IL-6 responses in determining human tuberculosis (TB) disease risk is unknown. IL-6 inhibitors, such as tocilizumab, are thought to increase the risk of progression to TB disease, and screening for latent TB prior to using these drugs is widely recommended.

To assess the effect of altered IL-6 activity on TB disease risk, we used single nucleotide polymorphisms (SNPs) in and near the IL-6 receptor (*IL6R*) gene, focusing on the non-synonymous variant, rs2228145, for which the C allele contributes to reduced classical (*cis*) IL-6 signalling activity.

**Methods:** We identified 16 genome wide association studies (GWAS) of TB disease, including 12 from the International Host TB Genetics Consortium. Effect estimates were extracted for each additional copy of the rs2228145 C allele. Mendelian randomisation (MR) analyses were performed using rs2228145-C alone

weighted on CRP reduction, or using a trans-ancestry, multiple SNP approach with IL6R plasma protein as exposure.

**Results:** Sixteen GWAS were included, collating 17,601 cases of TB disease and 977,334 controls across four continents. For each additional rs2228145-C allele, the odds of TB disease reduced (OR 0.94, 95% CI 0.91–0.97,  $p=2.9 \times 10^{-5}$ ). MR analyses supported these findings, with decreased odds of TB disease with readouts of reduced IL-6 signalling: for each natural log CRP decrease, OR 0.50 (0.39 - 0.71),  $p = 2.9 \times 10^{-5}$ , and for increase in IL6R plasma protein, OR 0.94 (0.92-0.96),  $p = 6 \times 10^{-9}$ . These effects were comparable in size and direction to those observed in severe COVID-19, Crohn's disease and rheumatoid arthritis in which IL-6 antagonism has beneficial therapeutic effects.



**Conclusions:** Our findings establish a causal relationship between IL-6 signalling and the outcome of TB infections, suggesting IL-6 antagonists do not increase the risk of TB disease but rather should be investigated as adjuncts in its treatment.

## TBS-EP02-15 T-helper cell subsets and integrin $\alpha 4\beta 7$ and $\alpha 4\beta 1$ expression in TB-HIV co-infection

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**Background:** CD4<sup>+</sup> T cell responses are crucial for *Mycobacterium tuberculosis* (Mtb) control. HIV mediated depletion of Mtb-specific CD4<sup>+</sup> T cells leads to increased susceptibility to tuberculosis (TB), faster disease progression and increased risk of TB reactivation.

**Methods:** Using the samples from the CAPRISA 011 Improving Retreatment Success (IMPRESS) trial (n=70) we characterised memory CD4<sup>+</sup> T cell phenotypes in TB-infected and TB/HIV co-infected participants. Additionally, we assessed the impact of TB treatment completion on the changes in memory CD4<sup>+</sup> T cell phenotype as well as characterised the effect of systemic CD4<sup>+</sup> T cell subsets during active TB on the presence of cavitory disease and time to Mtb clearance.

**Results:** A higher percentage of Th2 (p=0.0267) and lower percentage of Th9 cells (p=0.0001) were observed in TB/HIV co-infected participants compared to healthy controls. TB/HIV co-infected participants had a significantly lower percentage of Th17.1 (p=0.0263) and higher percentage of CCR6<sup>+</sup>DN (p=0.0299) and CCR6<sup>+</sup>DP (p=0.0144) cells compared to TB-infected participants. TB/HIV co-infected participants had a higher percentage of  $\alpha 4\beta 1$  and  $\alpha 4\beta 7$  expressing memory CD4<sup>+</sup> T cells in comparison to healthy controls.

Additionally, TB/HIV co-infected participants had higher percentage of  $\alpha 4\beta 7$  (p=0.0011) and  $\alpha 4\beta 7^{\text{hi}}$  (p=0.0425) expressing memory CD4<sup>+</sup> T cells compared to TB participants. Following TB treatment completion, we observed a significant increase in percentage of CCR6<sup>+</sup>DP cells (p=0.0481) in the total cohort. We observed no significant association between memory CD4<sup>+</sup> T subtypes with time to culture conversion and cavitory disease in the total cohort and among TB/HIV co-infected individuals, likely due to limited sample size.

**Conclusion:** During active TB, HIV induces changes in CD4<sup>+</sup> T cell subset distribution and lymphocyte trafficking marker expression that may have detrimental effects on Mtb control.

## TBS-EP02-16 Interleukin-2 and interleukin 17/17a in outpatient adults with diabetes and tuberculous infection in Uganda

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**Introduction:** The bi-directional relationship between diabetes mellitus (DM) and tuberculosis (TB) is a subject of scientific inquiry, especially in Sub-Saharan Africa where the two disease burdens are converging. Improved understanding of the immunological intersections of TB infection (TBI) and diabetes mellitus can contribute to effective host-directed therapies (HDT) to improve treatment outcomes. IL-2 inhibits T-helper cell 17 (Th17) and stimulates regulatory T-cells and may result in inhibition of antimycobacterial activity in high concentration leading to persistence of TBI; while IL-17/IL-17a is a pro-inflammatory cytokine that promotes neutrophil activation. HDT targeting IL-2 may improve antimycobacterial activity and promote clearance of TBI while inhibition of IL-17/IL-17a may hinder effective pathogen clearance. Elevated IL-2 and IL-17 are associated with chronic kidney disease that may further increase risk of TBI.

**Methods:** we conducted a cross-sectional study among adults living with DM attending an outpatient clinic at a national referral hospital in Uganda. We determined the TBI status using venous blood tested using QuantiFERON®-TB Gold Plus® (QFT-Plus) test protocols. Supernatants were tested using Luminex assays to determine interleukin (IL)-17/IL-17a and IL-2 cytokine concentrations. Data was exported to STATA v.16 and analysed for descriptive statistics; and differences in cytokine concentrations determined using Mann Whitney U test while Pearson's correlation coefficient and scatter plots were used to explore relationships between glycaemic control and cytokine concentrations.

**Results:** Of 159 participants, 76.7% (122) were female, 77.4% (123) had HbA1c  $\geq 7\%$  and 66.7 (106) had TBI. DM individuals with TBI had higher levels of IL-17/IL-17a (medians 146.8 vs 141.0 pg/ml, p = 0.04), IL-2 (1038.4 vs 329.0 pg/ml, p<0.01). Weak positive correlations were observed between HbA1c and cytokine concentrations.

**Conclusion:** The cytokine profile in DM individuals with and without TBI differed. Further research is recommended to determine the temporal attributes of these differences.

## TBS-EP02-17 Protein kinase C $\delta$ , a critical hub for immunomodulatory functions in macrophages during *M. tuberculosis* infection

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Tuberculosis (TB) has reached epidemic levels and emerged as the second deadliest infectious disease globally after CoVID-19. By evolving the ability to evade host defense via intrinsic mechanisms, *Mycobacterium tuberculosis* (Mtb), the etiological agent of TB has been deleterious to human health and has necessitated novel therapeutic interventions, the primary notion to combat Mtb infection.

Hence, the identification of host-modulating candidate genes involved in macrophage immune evasion and putative pathogen-killing pathways during Mtb infection is crucial.

One such candidate gene with potential novel therapeutic intervention, Protein Kinase C –  $\delta$  (PKC $\delta$ ), in an experimental mouse model of global PKC $\delta$  knockout (PKC $\delta$ -/-) revealed mechanistic alterations enhancing the susceptibility to various infectious diseases including Mtb infection.

However, the macrophage-specific role of PKC $\delta$  during Mtb infection remains unknown. Because the pulmonary microenvironment during Mtb infection is majorly governed by macrophages, initiating an innate and skewing adaptive immune response, we have exploited the role of PKC $\delta$  in macrophages using the macrophage-specific PKC $\delta$  knockout mice (*LysMcrePKC $\delta$ flx/flx*). An early lymphocytic immune response, increased neutrophil turnover, and reduced inflammatory macrophages are all accompanied by PKC $\delta$  deficiency in macrophages, which was abolished in the chronic stage of infection.

Bone-marrow-derived macrophages from *LysMcrePKC $\delta$ flx/flx* murine model further showed that the disease susceptibility is a consequence of an array of cellular intrinsic mechanisms and dysregulated metabolism which are modulated by PKC $\delta$ .

Furthermore, increased expression in bronchoalveolar lavage (BAL) samples from active TB patients and increased bacterial burden in PKC $\delta$  silenced human monocyte-derived macrophages with decreased pro-inflammatory cytokine response strongly signify PKC $\delta$  as a key hub for immunomodulatory functions during Mtb infection.

## TBS-EP03 TBScience 2023 - Moderated E-poster Session III

### TBS-EP03-01 Accuracy of a PCR-based gene signature for the triage of childhood pulmonary TB

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**Background:** Novel approaches are needed for triage among children with presumptive TB. We evaluated the diagnostic accuracy of a PCR-based three-gene RNA signature (Xpert Host Response, Xpert-HR, Cepheid, USA) among children from Uganda and the Gambia.

**Methodology:** We prospectively enrolled children 0-9 years old with presumptive TB. All participants completed standard TB evaluation including Xpert MTB/RIF Ultra and mycobacterial culture on respiratory specimens. Venous or capillary blood was collected for Xpert-HR testing using the GeneXpert platform per manufacturer recommendations. A TB score was calculated based on the cycle threshold value of three genes: (GBP5-DUSP3)/2 - TBP.

We calculated the area under the receiver operating characteristic curve (AUC) based on a microbiological or composite reference standard (MRS or CRS, respectively), and determined the specificity at a cut-off



closest to 90% sensitivity. We compared the accuracy of Xpert-HR to the clinical prediction score from the World Health Organization (WHO) treatment decision algorithm.

**Results:** We included 128 children (median age 3 years, IQR 1-6), of whom 15 had Confirmed TB, 73 had Unconfirmed TB, and 40 had Unlikely TB. The AUC of Xpert-HR was 0.71 (95% CI 0.55-0.86) using the MRS, and 0.59 (95% CI 0.49-0.70) using the CRS. At a sensitivity of 87%, the specificity of Xpert-HR was 30.1% (95% CI 21.8- 39.4) using the MRS, but 5.0% for the CRS (95% CI 0.61-16.9, Table). Xpert-HR was more specific than the WHO treatment decision algorithm clinical score using the MRS (30.1% vs. 4.4%,  $p < 0.001$ ), but had similarly low specificity using the CRS (5% vs. 10%,  $p = 0.41$ ).

	MRS (N=128)		CRS (N=128)	
	Sensitivity % (95% CI)	Specificity % (95% CI) / p value	Sensitivity % (95% CI)	Specificity % (95% CI) / p value
Xpert-HR	86.7 (59.5-98.3)	30.1 (21.8-39.4)	87.5 (78.7-93.6)	5.0 (0.61-16.9)
WHO Treatment Decision Algorithm A	100.0 (78.2-100.0)	4.4 (1.5-10.0)	98.9 (93.8-100.0)	10.0 (2.8-23.7)
Difference in specificity		25.7% $p < 0.001$		5% $p = 0.41$

Table 1. Comparison of Cepheid Host Response Cartridge to the World Health Organization Integrated Treatment Decision Algorithm Among Children Younger than 10 Years Old (N=128).

**Conclusions:** Xpert-HR had only moderate accuracy but greater specificity for microbiologically-confirmed childhood TB than the WHO treatment decision algorithm. Additional genes or complementary tests may be needed to improve specificity, especially for detection of Xpert MTB/RIF Ultra- and culture-negative TB.

## TBS-EP03-02 Multi-country metabolomic assessment of urine for the diagnosis of paediatric TB

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**Background:** Current tests for TB disease in children have suboptimal accuracy and rely on respiratory samples which are difficult to obtain. There is great need for new TB diagnostics that utilize non-sputum biospecimens such as urine.

We aimed to determine whether high-resolution metabolomic (HRM) profiling of urine could identify novel biomarkers of TB disease.

**Methods:** We collected urine samples from prospectively enrolled children 0-14 years being evaluated for TB disease in Uganda, The Gambia, and South Africa. All children underwent a standard clinical evaluation and were followed up after 3 months.

Children were classified as Confirmed, Unconfirmed, or Unlikely TB per the NIH consensus definitions. We used liquid chromatography/mass spectrometry for HRM analysis of urine samples. All analyses were adjusted for age, sex, and HIV status.

**Results:** Of the 382 children enrolled, 94 (25%) were classified as Confirmed TB, 96 (25%) as Unconfirmed TB, and 192 (50%) as Unlikely TB (Table 1).

	Confirmed TB n=94	Unconfirmed TB n=96	Unlikely TB n=192
<b>Age:</b>			
<5 years	57 (60%)	64 (67%)	127 (66%)
5-9 years	24 (26%)	19 (20%)	43 (22%)
10-14 years	13 (14%)	13 (13%)	22 (11%)
<b>Female Sex</b>	46 (49%)	34 (35%)	89 (46%)
<b>HIV Positive</b>	28 (30%)	20 (21%)	40 (21%)
<b>Country:</b>			
South Africa	43 (46%)	19 (20%)	50 (26%)
The Gambia	28 (30%)	28 (29%)	61 (32%)
Uganda	23 (24%)	49 (51%)	81 (42%)

Table 1.

Urinary metabolites with high-confidence identification that differentiated children with Confirmed TB from children with Unlikely TB were picolinate (adjusted  $p = 0.005$ ), neopterin ( $p = 0.01$ ), and dihydroneopterin ( $p = 0.01$ ). The area under the curve (AUC) and 95%

confidence interval of the receiver operating characteristic (ROC) curve was 0.66 (0.59-0.73) for picolinate, 0.65 (0.59-0.72) for neopterin, and 0.66 (0.59-0.73) for dihydroneopterin. The AUC for the metabolic signature of picolinate, neopterin, and dihydroneopterin combined was 0.72 (0.65-0.78).

For children and adolescents living with HIV, the AUC for this signature was 0.77 (0.64-0.89), and for HIV-negative children it was 0.70 (0.62-0.78). When this metabolic signature was used to compare children with Unconfirmed TB to those with Unlikely TB, the AUC was 0.61 (0.54-0.68).

**Conclusion:** Metabolomic analysis of urine in children from three African countries revealed that urine picolinate, dihydroneopterin, and neopterin are potential biomarkers for the diagnosis of TB disease in children independent of HIV-status.

### TBS-EP03-03 Performance evaluation of the Cepheid 3-gene test for active pulmonary and extrapulmonary TB

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**Introduction:** With 4 million TB cases undetected yearly (WHO), new diagnostic tools are needed. Cepheid's *MTB Host Response RUO (MTB-HR)* prototype for GeneXpert®, is a PCR method based on a modified 3-gene signature associated to active TB (Sweeney, *Lancet Respir Med.* 2016) generating a score from mRNA expression in blood. MTB-HR is currently being evaluated for diagnosis of pulmonary TB in high-endemic countries, reaching the WHO triage test target for active TB (Interim results, Sutherland, *Clin Inf Dis.* 2022). This is the first evaluation of MTB-HR in all forms of TB disease.

**Aims:** Evaluation of MTB-HR as a point-of-care test for pulmonary (PTB) and extrapulmonary TB (EPTB) in venous and capillary blood compared to a combined diagnostic work-up.

**Methods:** Individuals  $\geq 18$  years with presumed or recently diagnosed active TB ( $\leq 3$  days treatment), were enrolled at Karolinska University Hospital, Sweden. Venous and capillary blood samples were analysed in parallel on-site with MTB-HR in addition to microbiological testing for TB (microscopy, PCR and culture) and clinical investigation. Patients were categorised as active TB or non-TB based on final diagnosis. MTB-HR test results were given as a score based on Ct-values of GBP5, DUSP3 and TBP.

**Results:** 311 patients were included in the analysis, of which 107 with active TB disease; PTB 66/EPTB 41. The TB-diagnosis was bacteriologically confirmed in 102 (95%) patients, of which 97 culture-positive.

The AUC (area under the curve) for the MTB-HR test was 0.828 (0.758-0.898) for PTB and 0.835 (0.772-0.898) for EPTB, translating to an overall (Youden index) sensitivity of 70.1% (61.7-78.5) and specificity of 84.2% (78.9-89.2). No significant difference (DeLong,  $p=0.9153$ ) was detected between venous and capillary samples at diagnosis.

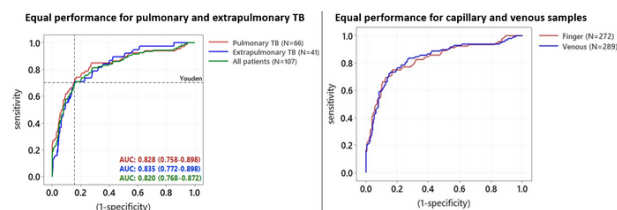


Figure 1. ROC-curve of MTB-HR performance in pulmonary TB (red), extrapulmonary TB (blue) and all TB cases (green)

**Conclusion:** MTB-HR shows great potential to improve diagnosis of both EPTB and PTB and with equal performance in venous and capillary samples.

### TBS-EP03-04 Diagnostic performance of Deeplex Myc-TB and Oxford Nanopore Technologies kits on *M. tuberculosis*-confirmed stool samples

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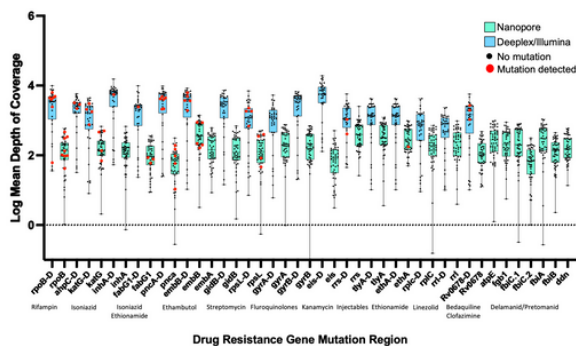
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**Background:** Stool is now recommended as a first line diagnostic specimen for Pulmonary tuberculosis in children and people living with HIV who have difficulty producing sputum; however, stool-based *M. tuberculosis* culture and drug susceptibility testing has poor yield.

Leveraging specialized DNA extraction protocols, stool-based targeted next-generation sequencing (tNGS) can provide rapid and comprehensive drug susceptibility information.

**Methods:** DNA was isolated from stool samples (n=48) provided by a cohort of participants with microbiologically confirmed TB in Eswatini. The presence of *M. tuberculosis* DNA was confirmed with an in house quantitative real-time PCR. Deeplex® Myc-TB [Deeplex] and Oxford Nanopore Technologies TB resistance [ONT] kits and recommended sequencing platforms (Illumina and ONT MinION, respectively) and pipelines were used for analysis.

**Results:** ONT and Deeplex detected *M. tuberculosis* in 94% (45/48) and 73% (35/48) of specimens. Overall, mDST was successful in 33 matched stool samples using both the ONT and Deeplex kits. Compared to the reference standard of phenotypic DST (PdST), sensitivity for detection of *M. tuberculosis* by 0.938 (95% CI 0.828, 0.987) by ONT and 0.729 (95% CI 0.582, 0.847) by Deeplex. Results were concordant in 29/33 (87.9%) stool samples, 3/33 (9.1%) and 1/33 (3%) mutations were detected *aphC* and *pncA* genes occurring at 1,8-4.33% frequencies were only detected by Deeplex kit; were also INH resistant by pDST. Overall Rifampicin resistance prediction was as follows; MDR (12.1%; 4/33) and pre-XDR (9.1%; 3/33) with *rpoB* I491F (RIF) and M146T mutations (BDQ and CFX).



**Conclusion:** Both the ONT and Deeplex tNGS assays can provide comprehensive mDST results from stool and identify the RIF conferring *rpoB* I491F mutation which is of epidemiological importance in Eswatini. Stool-based mDST could dramatically improve TB control in TB/HIV and MDR high burden settings where the majority of TB patients are living with HIV.

**TBS-EP03-05 Blood RNA biomarkers vs. C-reactive protein for TB screening in people living with HIV prior to antiretroviral therapy initiation**

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**Background:** Undiagnosed tuberculosis (TB) remains a major threat for people living with HIV (PLHIV). We sought to evaluate the diagnostic accuracy and clinical utility of blood transcriptomic biomarkers and CRP for pre-antiretroviral therapy (ART) TB screening. **Methods:** We enrolled consecutive adults referred to start ART at a community health centre in Cape Town, South Africa, irrespective of symptoms. Sputa were ob-

tained (using induction if required) for two liquid cultures. Whole-blood RNA samples underwent transcriptional profiling using a custom Nanostring gene-panel. We measured the diagnostic accuracy of seven RNA biomarkers for *Mycobacterium tuberculosis* culture status, using area under the receiver-operating characteristic curve (AUROC) analysis, and sensitivity/specificity at pre-specified thresholds (two standard scores above the mean of healthy controls; Z2).

Clinical utility was assessed using decision curve analysis. We compared performance to CRP (threshold  $\geq 5\text{mg/L}$ ), and the World Health Organisation (WHO) four-symptom screen (W4SS).

**Results:** A total of 707 PLHIV were included, with median CD4 count 306 cells/mm<sup>3</sup>. Of 676 with available sputum culture results, 89 (13%) had culture-confirmed TB. The seven RNA biomarkers were moderately to highly correlated (Spearman rank coefficients 0.42-0.93) and discriminated TB culture-positivity with similar AUROCs, but none statistically better than CRP (Table). Diagnostic accuracy was similar across CD4 count strata, but lower among W4SS-negative (AUROCs 0.56-0.65) compared to W4SS-positive participants (AUROCs 0.75-0.84). The RNA biomarker with highest AUROC point estimate was a 4-gene signature (Suliman4; Table). In decision curve analysis, Suliman4 and CRP had similar clinical utility to guide confirmatory TB testing, but both had higher net benefit than W4SS.

Biomarker	AUROC	Sensitivity	Specificity	Positive predictive value	Negative predictive value	p
Suliman4	0.8 (0.75 - 0.86)	0.83 (0.74 - 0.9)	0.59 (0.55 - 0.63)	0.23 (0.19 - 0.28)	0.96 (0.93 - 0.97)	0.320
RISK6	0.79 (0.74 - 0.85)	0.91 (0.83 - 0.95)	0.39 (0.35 - 0.43)	0.18 (0.15 - 0.22)	0.97 (0.94 - 0.98)	0.575
Sweeney3	0.79 (0.73 - 0.85)	0.92 (0.85 - 0.96)	0.28 (0.25 - 0.32)	0.16 (0.13 - 0.2)	0.96 (0.92 - 0.98)	0.608
Gliddon3	0.79 (0.73 - 0.84)	0.89 (0.81 - 0.94)	0.31 (0.28 - 0.35)	0.16 (0.13 - 0.2)	0.95 (0.91 - 0.97)	0.608
CRP	0.78 (0.72 - 0.83)	0.85 (0.77 - 0.91)	0.48 (0.44 - 0.52)	0.2 (0.16 - 0.24)	0.96 (0.93 - 0.97)	Reference
BATF2	0.75 (0.69 - 0.8)	0.82 (0.73 - 0.89)	0.53 (0.49 - 0.57)	0.21 (0.17 - 0.25)	0.95 (0.92 - 0.97)	0.405
Roe3	0.74 (0.68 - 0.8)	0.73 (0.63 - 0.81)	0.61 (0.57 - 0.65)	0.22 (0.18 - 0.27)	0.94 (0.91 - 0.96)	0.320
Zak11	0.73 (0.68 - 0.79)	0.56 (0.46 - 0.66)	0.77 (0.73 - 0.8)	0.27 (0.21 - 0.34)	0.92 (0.89 - 0.94)	0.320
WHO 4 symptom screen	0.63 (0.58 - 0.68)	0.79 (0.69 - 0.86)	0.47 (0.43 - 0.51)	0.18 (0.15 - 0.23)	0.94 (0.9 - 0.96)	<0.001

**Interpretation:** RNA biomarkers showed better clinical utility than symptom-based screening to guide confirmatory TB testing pre-ART initiation, but their performance did not exceed that of CRP, and fell short of WHO targets. Interferon-independent approaches are required to improve accuracy of host-response biomarkers to support pre-ART TB screening.

### TBS-EP03-06 Host blood protein biomarkers to triage active TB disease: a systematic review and meta-analysis

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**Introduction:** Newer diagnostics that do not rely on sputum are needed to find undiagnosed tuberculosis (TB) cases. The World Health Organization target product profile (TPP) for a non-sputum-based point of care (POC) test to triage active TB requires a minimum sensitivity >90% and specificity >70%. Our objective was to identify host blood protein biomarkers meeting TPP criteria.

**Methods:** A systematic literature review following PRISMA guidelines was conducted. Data extraction and quality assessment with QUADAS-2 were completed for included studies. Biomarkers with at least four results were meta-analysed.

**Results:** From 3,835 results screened, 48 studies were included (33 pulmonary TB (PTB), 9 extrapulmonary TB (EPTB), 2 combined PTB and EPTB, and 4 paediatric). Only adult PTB results are reported here. The studies had a low risk of bias regarding the reference standard but an intermediate/high risk of bias in the other three design domains. Important biasing factors were the use of case-control studies and control groups without symptoms of presumed TB. Most assays were not POC tests and used cut-off-values not validated for TB. Twelve individual biomarkers and two signatures met TPP criteria in single studies. In a HIV-negative population the sensitivities and specificities of the best performing biomarkers were: CRP (95.2%, 93.3%), HO-1 (91.8%, 94.9%), IP-10 (94.6%, 93.3%), OPN (94.6%, 93.3%), MMP-1 (98.5%, 100%), TIMP-2 (100%, 95.5%) and TIMP-4 (98.5, 95.5%). CD14 performed well in a HIV-positive population (sensitivity 95%, specificity 96%). The best performing signature was HO-1 and MMP-1 (sensitivity 97.9%, specificity 100%). Four biomarkers were meta-analysed but none of the pooled sensitivities and specificities met TPP criteria: CRP (86%, 61%), HO-1 (84%, 87%), IP-10 (85%, 80%), and MIG (76%, 67%) (Table).

Biomarker	Number of studies	Total sample size	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)
CRP	16	5568	86% (82%-90%)	61% (50%-72%)
HO-1	4	490	84% (68%-100%)	87% (73%-100%)
IP-10	4	713	85% (74%-96%)	80% (65%-95%)
MIG	4	908	76% (61%-90%)	67% (32%-100%)

**Conclusion:** Our review found few individual biomark-

ers that met TPP criteria. Additional studies of biomarker signatures designed for TB triage at POC are now needed.

### TBS-EP03-07 The MARTI-TB assay for the detection of anti-mycolate antibodies as biomarkers for TB and monitoring response to chemotherapy

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Antibodies to mycobacterial lipid antigens appear to have potential use as biomarkers of tuberculosis infection, in particular those directed to mycolate antigens occurring in the mycobacterial cell wall. In contrast to antibodies to mycobacterial protein antigens, antibodies to mycolate antigens appear to be independent of HIV co-infection, appear to have no long-term immune memory in humans (allowing for serial testing to follow treatment response or progression of infection to disease) and can accurately distinguish between TB-positive and TB-negative human patients.

Our team has developed a handheld electro-impedimetric biosensor method (MARTI-TB assay) as a test whereby anti-mycolate antibodies can be detected in serum samples. Packaging the procedure as a smartphone-linked POC kit incorporating microfluidic separation, that can detect TB infection from a single drop of blood based on the proven lab-based assay technique, is in progress.



In a preliminary assay series of 60 blinded serum samples from a random mix of 14 culture-positive TB patients and 46 IGRA-negative controls, the MARTI-TB test showed 95% accuracy to distinguish between TB-positive and TB-negative serum samples. These early

results suggest that the MARTI-TB assay can detect anti-mycolate antibodies in serum samples from presumptive TB patients by the electro-impedimetric biosensing of antibody binding to mycolate-coated screen-printed carbon electrodes.

Currently, the utility of MARTI-TB for monitoring treatment response in TB patients is being assessed in a bacteriologically and immunologically well-characterised plasma-sample series from treatment-compliant TB patients vs healthy controls, collected pre-treatment and at 1, 2 and 6 months following initiation of treatment.

### TBS-EP03-08 Using the Cepheid 3-gene test to measure mRNA expression in blood, a potential biomarker for monitoring treatment response in active TB

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**Introduction:** There is no biomarker to accurately monitor treatment response in active TB. As shorter treatment regimens are introduced, the need to identify patients that qualify will likely increase.

Cepheid's *MTB Host Response RUO (MTB-HR)* prototype for GeneXpert™ is based on a modified 3-gene signature (Sweeney, *Lancet Respir Med.* 2016) generating a score from mRNA expression in blood associated to active TB. A previous study on biobanked blood indicates normalisation of the score during treatment of pulmonary TB.

**Aims:** Point of care evaluation of MTB-HR for treatment monitoring in pulmonary (PTB) and extrapulmonary TB (EPTB).

**Methods:** Adults  $\geq 18$  years with active TB were enrolled at Karolinska University Hospital, Sweden. Venous and capillary blood samples were analysed on-site with MTB-HR at diagnose ( $\leq 3$  days treatment), week 1, 2, monthly until 6 months and then every 3 months until end of treatment (EOT), with a last follow-up 3-6 months after EOT. Clinical data and clinician's assessment of treatment response were collected.

**Results:** 107 patients were included (PTB 66/EPTB 41), the TB-diagnosis was bacteriologically confirmed in 102 (95%). Scores per time point of 98 individuals with  $\geq 4$  MTB-HR results are presented.

Overall, the MTB-HR score normalises during treatment in individuals with an initial score below cut-off. Based on the timepoint when a cut-off (Youden index) for the test is passed, 36 study subjects (37%) passed at 2 months or less with the majority of those (28/29%) within the first month, while 15 (15%) passed it at 4

months. Certain individuals pass at  $\geq 6$  months (9/9%) or do not reach the cut-off during follow-up (8/8%). In the latter group, 4 had extensive TB-disease.

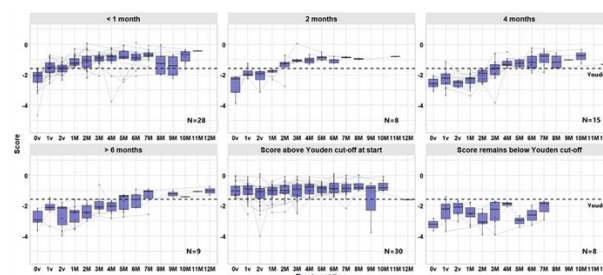


Figure. MTB-HR scores in 98 individuals during treatment for active TB, separated into six groups by timepoint MTB-HR score passes the Youden index cut-off. In 30 individuals the score is above cut off at start.

**Conclusion:** MTB-HR could potentially identify individuals responding quickly to treatment, and may serve as an aid in treatment decisions and guide evaluation of new treatment regimens.

### TBS-EP03-09 Blood RNA signatures outperform C-reactive protein in triaging extrapulmonary TB lymphadenitis and pericarditis

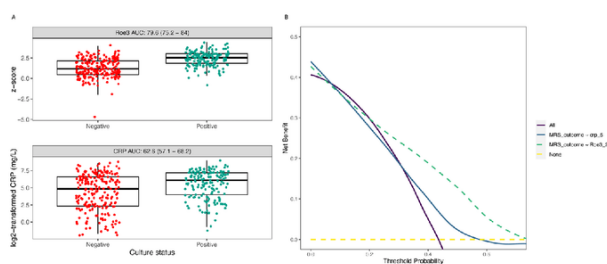
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**Background:** Limited data are available on the performance of blood RNA biomarkers of tuberculosis (TB) in patients with extrapulmonary TB (EPTB). We addressed this limitation focusing on TB lymphadenitis and in TB pericarditis in the hyperendemic setting of Cape Town, South Africa.

**Methods:** We enrolled 384 consecutive adults being investigated for TB lymphadenitis (N=289) or TB pericarditis. *Mycobacterium tuberculosis* (Mtb) culture was performed in tissue from disease sites.

Discrimination of culture positive and negative cases was evaluated using each of seven blood RNA signatures, benchmarked against blood C-reactive protein (CRP) by area under the receiver-operating characteristic curve (AUROC), and sensitivity/specificity at predefined thresholds two standard scores above the mean of healthy controls for RNA signatures and CRP > 5 mg/L. Decision curve analysis evaluated the clinical utility of the best performing blood RNA signature and CRP.

**Results:** In TB lymphadenitis all seven blood RNA signatures achieved statistically comparable discrimination with AUROC point estimates ranging 0.73-0.79, statistically superior to CRP. Similar findings were mirrored in TB pericarditis. In pooled analysis of both EPTB syndromes the best performing blood RNA signature, 'Roe3' achieved an AUROC of 0.80 (0.75-0.84) compared to CRP AUROC of 0.64 (0.57-0.66). At predefined thresholds for each test, the Roe3 signature provided 70% sensitivity and specificity, and CRP provided 88.3% sensitivity and 32.5% specificity, both falling short of 90% sensitivity and 70% specificity proposed by the WHO target product profile (TPP). In decision curve analysis, Roe3 achieved greater net benefit than other approaches if services are aiming to reduce the number needed to investigate for TB to less than 5 in order to identify each case.



**Diagnostic accuracy of blood RNA biomarkers for tuberculosis screening in presumptive extrapulmonary tuberculosis (EPTB).**  
**A)** Blood RNA biomarker, Roe3, and CRP discrimination of Mycobacterium tuberculosis spectrum culture positivity (vs. NBT). Scores are shown as boxplots for Roe3 and log2-transformed CRP (mg/L). The performance was analyzed using the area under the receiver operating characteristic curve (AUROC) with 95% confidence intervals.  
**B)** Decision curve analysis assessing the clinical utility of the highest performing biomarker, Roe3, and CRP (vs. WHO TPP) (70% positive vs. false positive rate weighted by case:well ratio) for investigators all and investigate more aggressively across the range of threshold probabilities that could be used to trigger confirmatory investigations for EPTB is compared to that of decisions to investigate patients with a CRP >10mg/L and a Roe3 score of ≥2.

**Interpretation:** RNA biomarkers show better accuracy and clinical utility to trigger confirmatory TB testing in patients with TB lymphadenitis and TB pericarditis but still fall short of the WHO TPP for TB triage tests.

### TBS-EP03-10 Diagnostic performance of transcriptomic signatures for pulmonary TB in symptomatic individuals across the African continent

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**Background:** Twenty transcriptomic signatures with promise for development of non-sputum-based triage tests for tuberculosis (TB) have been developed. This study aimed to determine which blood transcriptomic signature(s) have the best diagnostic performance for distinguishing between TB cases and individuals with other respiratory diseases (ORDs).

**Methods:** Study participants presenting with symptoms that required investigation for TB, were recruited from primary health care clinics in Ethiopia, South Africa, Malawi, Namibia, Uganda, and The Gambia. TB was

diagnosed based on clinical, microbiological, and radiological findings. Twenty transcriptomic signatures were measured in whole blood samples using multiplex qRT-PCR with signature scores generated from Ct values. Diagnostic performance was benchmarked against the WHO target product profile (TPP) for a non-sputum TB triage test.

**Results:** Among 541 individuals, 158 had definite and 32 probable TB, while 389 had ORDs. Ten signatures achieved equivalent performance (Satproedprai7: AUC 0.83 [95% CI 0.79-0.87], Jacobsen3: 0.83 [0.79-0.86]; Suliman2: 0.82 [0.78-0.86]; Roe1: 0.82 [0.78-0.86]; Kaforou22: 0.82 [0.78-0.86]; Sambarey10: 0.81 [0.77-0.85]; Penn-Nicholson6: 0.81 [0.77-0.84]; Duffy9: 0.81 [0.76-0.86]; Gliddon3: 0.8 [0.75-0.85]; and da Costa3: 0.79 [0.75-0.83]) for differentiating patients with ORDs from all TB patients.

With specificity benchmarked against the WHO TPP (70%), these ten signatures achieved sensitivities between 75% (95% CI 68-81) and 81% (74-86). Factors associated with signature scores included HIV infection and country. Country-specific analyses showed that signatures such as Satproedprai7 and Penn-Nicholson6, met the minimal TPP criteria for a triage test in Ethiopia, Malawi, and South Africa.

**Conclusions:** None of the signatures met the TPP criteria when all countries were combined, but several signatures met the minimum criteria in some countries.

**Funder:** South African Medical Research Council

### TBS-EP03-11 Gene signatures for monitoring treatment response among TB patients in Brazil

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**Background:** The WHO recommends sputum smear microscopy or culture at the end of the intensive phase of TB treatment in adults, however these are poor predictors of treatment failure and other adverse outcomes. There are currently no rapid, non-sputum biomarkers in clinical practice for monitoring response to TB treatment, and predicting cure, risk of treatment failure, or recurrent TB disease.

**Objectives:** To evaluate parsimonious host-response blood transcriptomic signatures for monitoring treatment response and predicting cure in adults with pulmonary TB.

**Methods:** We measured six published parsimonious transcriptomic signatures (Table) by microfluidic real-time qPCR on whole blood RNA samples collected from 48 drug-sensitive pulmonary TB patients in Brazil at the start, month 2, and after completion of 6 months of standard TB treatment, and 99 healthy close contacts (77 IGRA– and 22 IGRA+). All TB patients had clinical cure by six months, and did not have recurrence through 2 years of follow-up. Score distributions were compared between timepoints and groups using Wilcoxon signed-rank and rank-sum tests, respectively, and receiver operating characteristic area under the curve (AUC).

**Results:** Signature scores were lower through month 2 ( $p < 0.05$ ) and completion ( $p < 0.0001$ ) of treatment compared to baseline. Accordingly, all signatures were able to differentiate TB patients prior to treatment from those who had received 2 months (AUC 0.63–0.76) or 6 months (AUC 0.77–0.92) of treatment (Table). Signature scores in cured TB patients were not different from those of healthy (IGRA– and IGRA+) close contacts (AUC 0.48–0.59;  $p > 0.1$ ).

	AUC (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Maertzdorf4	0.89 (0.83–0.96)	91.7 (83.3–97.9)	75.0 (62.5–87.5)
Penn-Nicholson6	0.89 (0.82–0.96)	91.8 (83.7–98.0)	73.5 (61.2–85.7)
Suliman4	0.92 (0.86–0.97)	91.5 (83.0–97.9)	78.7 (66.0–89.4)
Sweeney3	0.77 (0.68–0.87)	91.7 (83.3–97.9)	43.8 (29.2–58.3)
Thompson5	0.85 (0.77–0.92)	91.8 (83.7–98.0)	63.3 (49.0–77.6)
Francisco2	0.80 (0.71–0.89)	91.7 (83.3–97.9)	54.2 (39.6–68.8)

Table: Prognostic performance for differentiating baseline from end of treatment signature scores.

**Conclusion:** Signatures were able to track response to TB treatment and differentiate start of treatment from cure timepoints. Scores among individuals who had successfully completed treatment were similar to those of healthy IGRA+ and IGRA– controls. Host-blood parsimonious transcriptomic signatures have potential to monitor TB treatment response and determine successful clearance of *Mycobacterium tuberculosis*.

**TBS-EP03-12 *M. tuberculosis*-derived cell-free DNA detection in peripheral blood for TB diagnosis: the CRISPR-TB assay**

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**Background:** *M. tuberculosis* (Mtb)-derived cell-free DNA has potential for non-sputum-based TB diagnosis, but improved performance is needed. We developed a CRISPR/Cas12a-based TB assay (CRISPR-TB) that detects Mtb-specific multicopy insertion element (IS6110) in cell-free DNA (cfDNA) isolated from 200µl plasma samples.

**Methods:** We evaluated CRISPR-TB using cryopreserved plasma from 46 adults with pulmonary TB not yet on TB treatment (TB+, Xpert Mtb/RIF or Xpert Ultra+ on sputum) including people with HIV (PWHIV), and 50 adults without TB (TB-) (primarily household contacts without TB) enrolled in the TB Aerobiology, Infectiousness, and Transmission (TBAIT) study in Kenya. In pilot evaluation we used all available samples to define a cfDNA-positive threshold optimizing sensitivity and specificity based on Youden’s J statistic, and used logistic regression (or Fisher’s exact, as appropriate) to investigate correlates of CRISPR-TB positivity.

	TB* N=46 n (%) or median (IQR)	No TB N=50 n (%) or median (IQR)
Age, years	35.5 (27.0-41.5)	33.7 (24.4-38.5)
Female sex	9 (20%)	38 (76%)
PWHIV	14 (30%)	2 (4%)
Sensitivity	38/46 83% (95% CI 69-92)	-
Specificity	-	45/50 90% (95% CI 78-97)

\*Xpert MTB RIF or Xpert Ultra positive on sputum

*Evaluation of CRISPR-TB detected Mtb cell-free DNA in peripheral blood for TB diagnosis*

**Results:** Among 46 adults with TB, 9 (20%) were female, median age was 36 years (IQR 27-41), 14 (30%) were PWHIV. CRISPR-TB sensitivity was 83% (95% CI 66-92) among all TB+ participants; specificity was 90% (95% CI 78-97) for those without TB based on a positive cfDNA threshold of 6648 arbitrary units (a.u.) (Youden’s J statistic = 0.726).

Among 14 participants with TB-HIV, sensitivity was 100% (95% CI 77-100). Median Mtb cfDNA concentration was higher among participants with TB only (13664 a.u. [IQR 7315-30017]) and TB-HIV (33099 a.u. [IQR 13536-39614]), compared to participants without

TB (1894 a.u. [IQR 1727-4445] (both  $p < 0.0001$ ). CRISPR-TB positivity was associated with male sex (male 61% [30/49] vs. female 28% [13/47], OR 6.62 [95% CI 2.23-19.62]  $p = 0.001$ ), HIV-positive status (HIV+ 100% [16/16] vs. HIV- 34% [27/80]  $p < 0.001$ ).

**Conclusion:** In pilot evaluation, CRISPR-TB identified adults with TB including PWHIV, approaching diagnostic performance of the WHO-recommend target profile for non-sputum diagnostics, using minimal blood volumes.

### TBS-EP03-14 Evaluation of a molecular test based on single tube-nested PCR for colourimetric detection and confirmation of *M. tuberculosis*

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The aim of the study was to establish a novel format of molecular test based in STNPCR with detection by ELISA assay using microtiter plates of amplified fragments of the target, IS6110, a specific gene of *Mtb* complex. The study first defined the technical parameters of the STNPCR-ELISA assay. The sensitivity and specificity of the STNPCR-ELISA were evaluated and defined. A total of 315 biological samples from patients with and without pulmonary and extrapulmonary TB were used on this study.

The STNPCR-ELISA System was developed and optimized for TB by the team based on validated similar systems for various infected diseases. The probe used on microplates on ELISA assay presented 100% specificity with the IS6110 target. Two different plates, both from Thermofisher, were tested and ImmunoplateMaxisorp™ microtiter plate demonstrated better reproducibility when compared to Nunc Immobilizer™.

The detection limit of *Mtb* genomic DNA (H37Rv) was 1pg/μl, diluted in Milli-Q® water; 1fg/μl diluted in urine; 10pg/μl diluted in blood; 1fg/μl diluted in pleural fluid and 1fg/μl diluted in sputum samples. The sensitivities on STNPCR-ELISA System ranged from 55% (plasma) to 75% (pleural fluid) and specificities varied from 51% (urine) to 100% (pleural fluid).

All sensitivities, in different clinical samples compared to sputum, was statistically the same, as detailed on table 1.

The STNPCR-ELISA System presented a simple and operational method, which uses equipment's already existing in laboratories of diagnostic routine. This system could be an interesting alternative way to be used as complementary diagnostic method. Other valuable point is the high measured accuracy in all tested samples,

with values equals of sputum (gold standard sample), independently of clinical form of TB. It is important to emphasize that the study still needs validation.

Sample compared to sputum	Cut-off on ELISA	Sensitivity	Specificity	X <sup>2</sup> Test	CI=95% (X <sup>2</sup> )	p-values	n
Plasma vs. Sputum	0.110	55.5% - Plasma	80% - Plasma	0.57	-14.5% - 28.8%	0.45	98
PBMC vs. Sputum	0.090	72.3% - PBMC	54.3% - PBMC	0.46	-11.8% - 30.7%	0.50	100
Urine vs. Sputum	0.092	61.3% - Urine	51.5% - Urine	0.08	-20.2% - 23.1%	0.78	95
Pleural Fluid vs. Sputum	0.081	75% - Pleural fluid	100% - Pleural Fluid	0.18	-34.4% - 39.6%	0.67	5
Sputum	0.164	64.7% - Sputum	66.7% - Sputum	--	--	--	20

Table 1: Comparison of sensitivities on STNPCR-ELISA System on biological samples with sputum.

### TBS-EP03-15 Optimising sample treatment methods to reduce the confounding effect of cell-free DNA on live *M. tuberculosis* quantitation and the sputum microbiome

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**Background:** Measuring microbial DNA is important for assessing the impact of antibiotics on the microbiome, which can increase extracellular DNA. This can distort the results of PCR and cause false positives. We investigated whether nucleic acid dyes, i.e., propidium monoazide (PMA) and PEMAX, as well as DNase I, could reduce this phenomenon in the context of tuberculosis (TB).

**Methods:** PCR [16S *Mycobacterium tuberculosis* complex (*Mtb*) qPCR and Xpert MTB/RIF] was done on a dilution series of *Mtb* treated with PMA, PEMAX, or DNase I in 7H9 liquid media. Using 16S qPCR and sequencing, we compared untreated and (PMA-, PEMAX-, or DNase I-) treated patient sputa before TB antibiotic treatment (Cohort A: n=20) and, separately, at the beginning and end of a 24-week treatment period (Cohort B: 19 TB cases, PEMAX only).

**Results:** PMA and PEMAX treatment lowered PCR-detected mycobacterial load compared to untreated controls in both the dilution series and Cohort A sputa. In sputum, treatment with PMA or PEMAX reduced alpha diversity and increased compositional distance (beta



diversity). PEMAX treatment enabled the detection of mycobacterial reads in 8 out of 9 (89%) TB cases where none were detected in untreated samples.

Untreated and PEMAX-treated Cohort B sputa had similar alpha diversity before antibiotics (week 0) but differed at week 24. When beta diversity was compared between timepoints, only PEMAX treatment revealed differences. PEMAX also identified differentially enriched taxa at the beginning and end of TB treatment, which were not identified in untreated samples. DNase I had negligible effects.

**Conclusions:** PMA and PEMAX (but not DNase I) reduced the sequencing of extracellular DNA from non-intact taxa, which likely increased the proportion of *Mycobacterium* detected. Furthermore, PEMAX may be useful for characterizing microbiome shifts in the presence of antibiotics, particularly in the case of TB, where treatment regimens are lengthy.

### TBS-EP03-16 Assessment of TB case notification in the Eastern Region, Ghana: record linkage of three TB registries

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**Background:** Under-reporting of tuberculosis (TB) is a major global health concern. In most low and middle-income countries, due to the limited resources, the surveillance systems are not robust and, hence, estimates of TB case detection and notification are often not reliable. In Ghana, although the district TB registry data serves as the main TB notification data on which national TB programmes planning decisions are based, the data contained in the registers are deemed to be incomplete. This study assessed the completeness of TB case reporting in the Eastern Region of Ghana.

**Methods:** We analyzed data of TB cases diagnosed from five randomly chosen districts of the Eastern Region between 2016 and 2017. We performed linked analysis of

three TB registers using record linkage to prepare for the capture-recapture approach and compared the records across the registries to identify unreported cases. Record linkage was conducted using name, age and sex as matching variables.

**Results:** Of the 773 bacteriologically confirmed unique pulmonary tuberculosis (PTB) cases in the three registers linked, 369 were in the district TB registry with an additional 404 (134 in treatment registers, 238 in laboratory plus 32 cases recorded in both registries) cases only known to the laboratory and treatment register data sources. Hence, the proportion of bacteriologically confirmed PTB cases not documented in the district TB registry was 52.3% (404/773). The district TB register and health facility treatment registers recorded the highest overlap of 156 cases (20.2%).

**Conclusion:** We found low levels of matching PTB case in all three registries. Hence, the observed reporting of the most infectious TB cases in the study area is too low, emphasizing the need for improved surveillance systems and reporting pathways, and enhanced efforts to accurately describe the current burden of TB in Ghana.

Key words: Under-reporting, notification, tuberculosis, record linkage, Ghana

### TBS-EP03-17 Detection of *M. tuberculosis* using fluorescence spectroscopy and machine learning algorithm

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In this study, fluorescence spectroscopy together with chemometric technique has effectively been used for analyzing respiratory infectious disease *mycobacterium tuberculosis*. This research work is based on fluorescence emission of *mycobacterium bacillus*. Samples used in this study were collected from tuberculosis (TB) suspected patients of various areas of Khyber Pakhtunkhwa, Pakistan.

Further, all these samples were cultured in the Provisional Reference Lab, Hayatabad Medical Complex (HMC) Peshawar. The fluorescence spectra from all these samples have been acquired using 405nm wavelength for excitation.

The differences in the fluorescence emission spectra between TB positive, TB negative and cultured media samples has been found at peak emission wavelengths arises at 465 nm and 490 nm. The differences between TB positive and negative samples were seen both in the intensities as well as shift in their fluorescence emission peaks.

For highlighting the spectral differences, Principal Component Analysis (PCA) is applied on the fluorescence emission data collected from the three sets of samples. PCA clearly cluster the data into three different groups

based on features extracted from their fluorescence emission data. These results suggest that fluorescence spectroscopy could be used for identification of mycobacterium bacillus in the sputum samples of the suspected individual at mass scale.

Furthermore, this technique is fast, cost effective and user friendly that could be used effectively for the early detection of mycobacterium bacillus in the suspected individual.

### TBS-EP03-18 TB screening and incidence of TB in children in 2016-2022 in Belarus

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**The aim** of the study was to research TB screening and TB incidence in children during 2016-2022 in Belarus.

**Methods:** Data from the state statistical reporting on medical care for children in Belarus for 2016-2022 were used. The number of children screened for TB and the average annual growth rate (AAGR) of the number of children screened for TB were calculated. The incidence of TB in children and AAGR of TB incidence were calculated.

**Results:** In 2016-2022, on average per year, 96522,7 children aged 0-17 years old were examined for TB using fluorography. AAGR of the number of children examined for TB using fluorography was +1,4%.

In 2016-2022, TB screening of children using skin tests (Mantoux test or Diaskintest) was significantly reduced. On average per year, 139038,6 children aged 0-14 years old were examined for TB using skin tests. AAGR was -20,5%. On average per year, 62009,1 children aged 15-17 years old were examined for TB using skin tests. AAGR was -13,2%.

Reduced TB screening was accompanied by a decrease in TB incidence.

In 2016-2022, TB incidence in children aged 0-14 years old decreased from 0.8 per 100,000 children (2016) to 0.5 (2022). AAGR of TB incidence in children was -15%. TB incidence in children aged 15-17 years old decreased from 8.2 per 100,000 children (2016) to 2.9 (2022). AAGR of TB incidence in children was -21,4%.

**Conclusions:** In 2016-2022, TB incidence in children aged 0-14 and 15-17 years old decreased significantly. AAGR was -15% and -21,4%. However, the decrease in TB incidence was associated with a decrease in TB screening using skin tests. This is an unfavorable trend. AAGR of the number of children examined for TB using skin tests decreased by -20,5% in children aged 0-14 years old and by -13,2% in children aged 15-17 years old.

### TBS-EP04 TBScience 2023 - Moderated E-poster Session IV

#### TBS-EP04-01 Clinical and imaging findings of patients with culture-negative pulmonary TB in a TB-endemic setting

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**Introduction:** Lowenstein-Jensen (LJ) culture has been the most sensitive TB detection method among the currently available TB laboratory diagnostics however, it misses more than 40% of tuberculosis (TB) including cases missed by geneXpert and smear microscopy. Culture negative pulmonary TB (CNPTB) patients have been diagnosed clinically supported with imaging findings, potentially leading to delayed treatment initiation, possible emergence of drug resistance and poor compliance to monitoring treatment outcome. The current study aimed to evaluate TB patients' clinical and imaging features of CNPTB compared to CPPTB in TB endemic setting.

**Methodology:** A case-control study was conducted on 311 PTB patients, recruited from health facilities in Addis Ababa, Ethiopia. Clinical data, image finding and sputum samples were collected from all consented participants; acid-fast microscopy, geneXpert and LJ culture analyses were performed on the collected sputum samples. Data was analysed using Stata version 17.0 and a P-value <0.05 was considered statistically significant.

**Results:** Forty percent (125/311) of the TB patients were diagnosed negative on LJ culture media, where all had similar clinical and image findings with CPPTB patients except, chest pain (72% vs 62%), previous TB history (22% vs 7%).

In contrast, CNPTB patients were less likely to have cavitory lesions than CPPTB (18.7% vs 33.3%) (P – value 0.031) rather they have other imaging findings excluding infiltration and pleural effusions (51% vs 32%) (P-value < 0.033).

In multivariable analysis, culture negativity was significantly associated with chest pain, previous TB history and absence of cavitation (P-value < 0.05).

**Conclusions:** Clinical signs and symptoms of TB seem similar in both culture negative and culture positive PTB patients except chest pain, possibly suggesting the need for early initiation of anti-TB treatment, especially in patients presenting with pertinent TB sign and symptoms and TB suggestive imaging findings. This will strengthen the TB control program and further lessen TB transmission in the community.

### TBS-EP04-02 An assessment of TB among cyclone Freddy-affected people using active TB case-finding interventions in Malawi

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**Introduction:** The displaced populations are among the key populations that are at a high risk of Tuberculosis infection and disease progression due to overcrowding and poor living conditions. Cyclone Freddy has caused deaths and extensive devastation in some Southern African countries such as Malawi. As of March 2023, more than 500,000 people were displaced and over 500 died. Many people in southern parts of Malawi are living in camps due to the destruction and flooding of houses. We assessed the proportion of pulmonary Tuberculosis cases among people that were displaced due to Cyclone-Freddy and are living in camps.

**Intervention response:** A descriptive retrospective study was conducted between 01 January 2023 to 31 March 2023 in Blantyre, Zomba, Nsanje and Mangochi districts in Southern part of Malawi. The study participants were adults aged 15 years and above that were displaced by Cyclone Freddy and were living in camps. Data were extracted from Mobile Diagnostic Unit (MDU) TB screening registers for Quarter 1 2023 (January-March 2023). The study participants were screened once using chest X-ray and GeneXpert in MDU.

**Results:** Out of 2976 people screened for TB, 136 were presumptive TB cases. 22 people were diagnosed with pulmonary TB, 5 were bacteriologically confirmed using GeneXpert and 17 were clinically diagnosed using chest x-ray. The incident rate was at 739 per 100,000 population. This was high as compared to 210 estimated by World Health Organization (WHO) in 2021.

**Conclusion:** The proportion of TB cases among people displaced by Cyclone Freddy was high. Living in camps poses a risk of spread of TB. We suggest routine active TB screening using MDUs in congregate settings, such as refugee camps and prisons.

### TBS-EP04-03 Using quality improvement methods to improve TB programme: a pilot project in 10 sub-districts of South Africa

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**Background:** The 2017-2022 National TB Program's strategic plan calls for a 50% reduction in TB deaths by 2022 and a 30% reduction in TB incidence. To achieve these ambitious targets, the SA health system needs to build a reliable system to find, test, diagnose, start treatment, and retain patients in care. The National

Department of Health adopted QI methodology as an approach to close the gaps in the TB care cascade by creating learning networks of clinics, hospitals and communities in sub-districts, identify and test implementation strategies as demonstration for Phase 1 in 10 sub-districts located in South Africa.

**Methods:** The initiative was implemented using the QI approach which uses a combination of measurements, testing of ideas and standardisation of processes which is driven by District Health Management Teams (DMTs) who are capacitated to use QI methods to implement, scale up effective implementation strategies within their districts.

**Results:** The QI pilot showed variable results from 2017 baseline until 2019 in 10 pilot sub-districts. The baseline for 2017 TB screening rate was 66% and improved to 78% in 2018 and 80% in 2019. The baseline for TB symptomatic in 2017 was 4%, 2018 declined to 3% and 2019 increase to 4%

In 2017, the baseline for sputum sent to the laboratory was 74% and improved to 84% in 2018 and 89% in 2019. TB positivity rate improved from 2017 baseline figure of 7% to 9% in 2018 and 8% in 2019.

**Conclusions:** The results from the pilot have provided NDoH with key lessons to inform the implementation design for the national scale up. There is need to strengthen data analysis and reporting when implementing QI.

### TBS-EP04-04 Development of a point-of-care nano-biosensor using non-invasive urine sample from a patient with TB

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**Background:** Globally, in 2021, 1.6 million individuals (including 187,000 HIV infected individuals) died from tuberculosis (TB). TB is the second most lethal infectious disease in the world, after COVID-19. Though, it is possible to prevent and treat tuberculosis, 40% of the TB cases are missed by health system in India alone due to sophisticated mode of diagnosis.

**PROBLEM STATEMENT:** It is difficult and expensive to diagnose HIV-associated TB, multidrug-resistant TB, and other resistant forms of TB. The technical complexity of the disease diagnosis require trained professionals, sophisticated instruments and high cost laboratory facilities.

Access to tuberculosis diagnostics has been hampered by the COVID-19 pandemic. The number of reported TB cases dropped to 18% in 2020 in comparison to 2019. Globally, there were 3-7 million unreported cases of tuberculosis in 2021.

To achieve the End TB targets, the gap in TB diagnosis is to be bolted followed by assured treatment of detected cases. The currently available diagnostics in the market

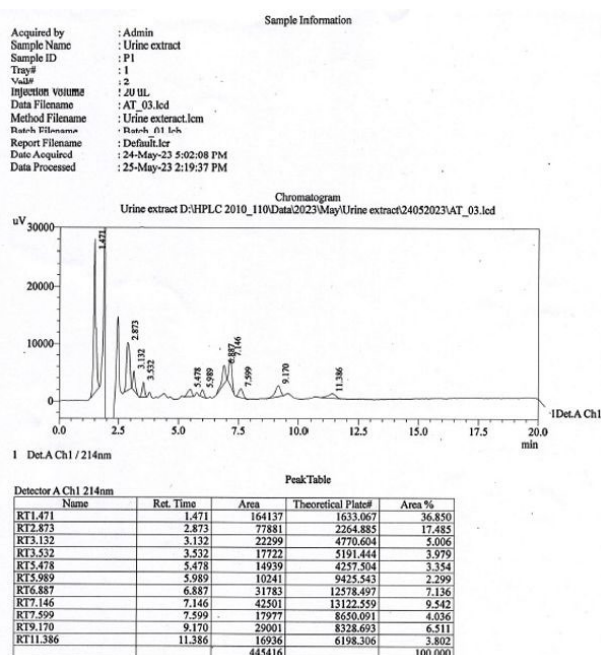
require high technical competence and sophisticated machinery under regulatory guidelines. At present, there is no point of care diagnosis accessible for use by a person alone.

**Proposed Solution:** Non-sputum-based, affordable, easy to use test with high sensitivity and specificity, particularly for PLHIV or children who are often unable to produce a sputum specimen.

**Aim:** To develop a lateral flow immunoassay for the rapid and effective diagnosis of tuberculosis.

**Method:** Biomarkers will be identified through LC-MS in the urine sample of TB patients. The potent biomarkers will be conjugated to gold nanoparticles through covalent bonding and a biosensor based enzymatic assay will be employed for the development of lateral flow assay.

**Results:** The study is currently in progress with few identified biomarkers that are expressed in the urine sample of clinically confirmed TB patients from indian cohort.



## TBS-EP04-05 Addressing TB diagnostic and treatment delays in low- and middle-income countries: insights from a study in Kampala District, Uganda

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Diagnostic and treatment delays of tuberculosis (TB) remain a significant public health challenge in many low- and middle-income countries, including Uganda. This study sought to determine the extent of diagnostic and treatment delays and their related factors among newly identified TB patients in the Kampala district, Uganda. This was a cross-sectional study conducted in all the five (5) divisions of Kampala district on newly diagnosed smear-positive, or MTB GeneXpert (high and medium) detected pulmonary tuberculosis patients. Data was entered into Epi Info v7.2, cleaned, and coded before analysis using N-vivo version 11. The level of significance was set at 95% (p value <0.05). Specific statistical tests for inferential statistics, such as Chi-square and Poisson regression, were used to test for independence or association between variables.

Results showed that TB patients in Kampala continue to suffer from diagnostic and treatment delays. The prevalence of diagnostic delay was 58.2% (53.0 – 63.1) while that of treatment delay was 20.7% (16.8 – 25.1). The median diagnostic delay was 30 days IQR (7 – 60), whereas the treatment delay was 1 day (0 – 2) days.

In a summative format to determine total delay, a proportion of 61.7% (95% CI: 56.6 – 66.5) was delayed. Peri-urban residence, current smoking and previous history of tuberculosis statistically associated with both diagnostic and treatment delays. Total delay was attributed to severe TB illness, income status, kind of health facility visited first. A combination of social, economic, and healthcare-related factors may have contributed to the significant TB diagnostic and treatment.

In conclusion, TB patients experienced diagnostic and treatment delays in the Kampala district. The study generally highlights the patient and system factors associated with diagnostic and treatment delays through strategic policy executions in order to reduce the delay in diagnosis and treatment of TB in the country.

### TBS-EP04-06 A point-of-care rapid RT-PCR diagnostic solution for *M. tuberculosis* and multidrug-resistant TB: the RAPI-Q platform

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Tuberculosis (TB) is a deadly infectious disease that can affect any organ of the body, caused by the bacteria *Mycobacterium tuberculosis*. Early diagnosis and adequate treatment of infectious pulmonary TB patients are essential to reduce the transmission of *Mycobacterium tuberculosis*. Rapid diagnostic methods offer higher sensitivity and specificity, allowing for more precise diagnoses of illnesses.

With the increasing prevalence of multiple drug resistance (MDR) cases, early detection can be critical and more effective in treating these cases. This will improve patient outcomes and reduce the cost associated with drug-resistance treatment. RT-PCR (Reverse Transcription Polymerase Chain Reaction) is a powerful tool that has revolutionized the diagnosis of infectious diseases. Rapi-Q-HT POC platform is revolutionizing the diagnosis of various diseases which is a compact, lightweight, easy-to-carry RT-PCR instrument. Rapi-Q-HT is a Dual independent block platform that can run 1-16 samples each / up to 32 samples of single or 2 different protocols at a given time. This has a unique AI-integrated POC software for interpretation and reporting results.

We have evaluated our in-house TB detect & TB find protocols in the Rapi-Q HT platform for the detection of *Mycobacterium tuberculosis* and Drug-resistant mutations against the Rifampicin and Isoniazid drugs among MDR-positive pulmonary and extrapulmonary samples. A total of 100 samples (pulmonary and extrapulmonary) were tested comprising of equal positives and negatives. Among the 50 positives, *Mycobacterium tuberculosis* was detected in all the GeneXpert Low and medium cases exception being the very low bacterial load samples (<1%).

We also successfully detected varying mutations in the 81bp rpoB gene among the MDR-resistant samples. Hence, we have found the Rapi-Q POC TB comprehensive testing solution to be a low-cost, highly specific and sensitive test with a highly throughout multiplex assay which has a shorter turnaround time.

### TBS-EP04-07 Pulmonary TB infectiousness by case-finding approach: an estimation using cough aerosols and interferon-gamma responses

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**Background:** Halting tuberculosis (TB) transmission is essential to controlling the epidemic. While active case finding (ACF, involving community screening) has been advocated, the proportion of TB transmission events from community dwellers with undiagnosed pulmonary TB (PTB) is unknown. We investigated the infectiousness of persons with PTB identified through ACF and passive case finding (PCF, persons presenting to health-care).

**Methods:** In a prospective study in Nairobi, Kenya, adults with PTB were enrolled either through PCF or ACF. All participants were GeneXpert (excluding trace) and/or culture positive and treatment naïve. Study interventions included estimating infectiousness based on cough aerosol sampling system (CASS). Household contacts (HHCs) were enrolled and underwent interferon-gamma (IFN-) release assay (IGRA) testing. We compared the characteristics of index cases by case-finding approach. Differing factors were evaluated for their association with TB transmission to HHCs. The mixed-effect logistic regression model was used to predict transmission, clustered on index participants.

**Result:** We enrolled 135 index cases median age 34 years (interquartile range [IQR] 28-45), 109 (81%) through PCF, 39% being CASS positive (CASS+) and the remainder (26, 19%) through ACF, all CASS negative (CASS-). HHCs were 201, median age 13 years (IQR 5-28), of whom 56.7% had a positive IGRA. The median IFN-levels were highest among HHC of index cases enrolled through PCF who were CASS+ (4.25 vs 0.08 and 0.03 pg/mL among PCF CASS- and ACF CASS- index cases, respectively,  $p=0.013$ ). The best predictors of a positive IGRA were C-reactive protein ( $p=0.026$ , odds ratio [OR] 1.02, 95% confidence interval [CI] 1.02, 1.03) and CASS+ ( $p=0.015$ , OR 11.34, CI 1.61, 80.03)

**Conclusion:** Our findings suggest that persons identified with TB through ACF are less infectious, as evidenced by CASS status and IGRA responses in HHCs. Investigations into the most effective and cost-effective strategies for interrupting TB transmission are needed.

Bivariate regression			Bivariate regression		
Variable <sup>a</sup>	OR (95% CI)	p-value	Variable <sup>a</sup>	OR (95% CI)	p-value
Age (years)	1.04 (1.01, 1.07)	0.013	Cavitary disease on CXR	0.20 (0.08, 0.48)	<0.001
Any symptom suggestive of TB	0.27 (0.10, 0.77)	0.014	CRP (mg/L)	0.97 (0.96, 0.99)	<0.001
Cough duration	0.89 (0.79, 0.99)	0.03	CASS positive	1.00	<0.001
Smear status $\geq$ scanty	0.23 (0.11, 0.47)	<0.001	Positive IGRA	0.41 (0.19, 0.90)	0.025

<sup>a</sup>Additional variables evaluated in models were: Gender, Body mass index, HIV status and Xpert cycle threshold.

OR – odds ratio; CI – confidence interval; CRP – C-reactive protein; CXR – Chest x-ray

*Logistic regression analyses: Factors associated with active case-finding approach (n=135)*

### TBS-EP04-08 Reconstructing constituent sequences in mixed *M. tuberculosis* infections to measure transmission

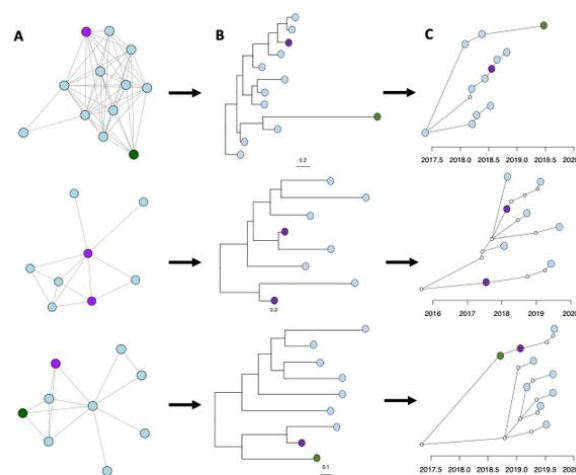
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**Background:** Mixed *Mycobacterium tuberculosis* (*Mtb*) infection, when an individual is concurrently infected with more than one TB strain, is a common occurrence in natural populations. Mixed samples are often removed prior to population analyses as inferring evolutionary relationships between hosts is complicated by the mixed signal in sequence data. Reconstructing the constituent strains of mixed samples allows us understand the dynamics of mixed *Mtb* infection and better measure TB transmission. Here, we present a novel method to estimate constituent sequences in mixed infections that leverages sequence information from other samples in the tested population. We then conduct a population-level transmission analysis using 2,220 real-world *Mtb* samples from Moldova.

**Methods:** We inferred the constituent strains of mixed samples using allele frequencies at mixed loci and pairwise sequence comparison to non-mixed strains in the study population. We validated our new approach in simulated, *in vitro*, and real-world mixed *Mtb* samples, and compared our results against existing methods for estimating mixed infection. Lastly, we identified transmission clusters in the Moldovan *Mtb* data, including the constituent strains of mixed samples, and reconstructed person-to-person transmission networks to find evidence of recent transmission involving mixed *Mtb* infection.

**Results:** Our new approach identified mixed infection in simulated and *in vitro* mixed samples, with > 95% of strains correctly classified, and the constituent strains

were accurately reconstructed. We estimated constituent sequences in mixed real-world *Mtb* samples from Moldova and found more complete sequences with fewer ambiguous sites than previously published methods. Finally, we found evidence of recent transmission in hosts with mixed *Mtb* infection, including direct transmission events (Figure 1).



**Figure 1.** Three example transmission networks containing constituent strains of mixed infections from real-world *Mtb* sequence data from Moldova. A) Transmission clusters constructed with a 12 SNP pairwise distance threshold, B) time-calibrated phylogenetic trees, and C) full transmission networks reconstructed using TransPhylo. Purple nodes represent major frequency strains in mixed infection samples, green nodes represent minor frequency strains in mixed infection samples, pale blue nodes represent non-mixed samples, and white nodes represent inferred missing intermediate hosts in transmission networks.

**Conclusions:** Here, we found evidence of transmission events involving mixed infection using a novel approach for estimating the constituent strains. This work emphasizes the value of including mixed samples in TB population analyses to accurately reconstruct transmission.

### TBS-EP04-09 Transmission signatures in within-host *M. tuberculosis* variations

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Because *M. tuberculosis* evolves slowly, transmission clusters often contain multiple individuals with identical consensus genomes, making it difficult to reconstruct transmission chains and identify settings with high transmission risk. Finding additional sources of shared *M. tuberculosis* variation could help overcome this problem.

Previous studies have reported *M. tuberculosis* diversity within infected individuals, however, whether within-host variation improves transmission inferences is unclear. To evaluate the transmission information present in within-host *M. tuberculosis* variation, we re-analyzed

publicly available sequence data from a household transmission study, using household membership as a proxy for transmission linkage between 25 donor-recipient pairs.

We found moderate levels of variation within individual isolates (median 160 intrahost single nucleotide variants, iSNVs; IQR: 129-219; >1% minor allele frequency) outside of PE/PPE genes. Household members shared more iSNVs (median: 101; IQR: 72-138) compared to pairs of isolates from different households (median: 1; IQR: 0-9), a signal which persisted when applying a 5% minor allele frequency threshold (household members shared a median of 6; IQR 1-4 iSNVs compared to a median of 0; IQR: 0-1 iSNVs among members of different households).

Shared within-host variation above a 1% minor allele frequency threshold was significantly associated with household membership (OR: 3.10; IQR: 2.46-4.03, for one standard deviation increase in shared iSNVs), and shared iSNVs predicted household membership with an AUC of 0.97.

Finally, we found that transmission bottlenecks, the size of the founding *M. tuberculosis* population in recipient hosts, varied widely across transmission pairs. The signal of shared within-host variation present in routine culture-based *M. tuberculosis* sequencing data suggests that within-host variation could augment standard, consensus-sequenced based approaches, providing greater resolution to transmission inferences.

### TBS-EP04-10 The MAGMA platform: leveraging whole-genome sequencing for identifying recent transmission events and enabling precision public health interventions

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Understanding where transmission of *Mycobacterium tuberculosis* (*Mtb*) occurs is essential to reduce transmission for TB control. Yet, source investigation is rarely performed because it is considered too resource intensive. The high discriminatory power of whole genome sequencing (WGS) could accurately guide source investigations, enabling programs to target and prioritize source- and contact investigations. These could include super-spreading events and patients whose *Mtb* is resistant to key drugs.

Using WGS to accurately determine in 'real-time' whether, when and where recent transmission events occurred however still poses technical challenges. This is in part due to the complexity of translating a phylogenetic

tree into a transmission chain and the lack of data visualization outputs that are interpretable and actionable by public health staff.

We are developing the MAGMA (Maximum Accessible Genome for *Mtb* Analysis) platform to enable precision public health interventions by TB control programs. Phylogenetic trees are generated by the MAGMA bioinformatics pipeline for real-time WGS analysis of DNA extracted from clinical primary liquid *Mtb* cultures or -in future- sputum samples. Transphylo is integrated in the MAGMA platform for the translation of phylogenetic trees into transmission chains. A case study is being performed to evaluate the impact of this functionality on the communication of transmission events to the TB control program in a low TB-burden country.

To identify transmission events of drug-resistant TB, Transphylo-DR is being developed to integrate drug-resistant variants in the assessment of phylogenetic clusters. This will identify clusters representing recent transmission events of drug-resistant TB and determine where along the transmission chain drug resistance amplification occurred.

The MAGMA platform aims to visualize transmission data in a way that enables TB control programs to undertake targeted precision public health interventions with the goal of halting transmission of TB and drug resistant TB in both low and high TB burden communities.

### TBS-EP04-11 Genotypic and spatial analysis of transmission dynamics of TB in Shanghai, China: a 10-year prospective population-based observational study

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**Background:** With improved tuberculosis (TB) control programs, the incidence of TB in China declined dramatically over the past few decades, but recently the rate of decrease has slowed, especially in large cities such as Shanghai. To investigate how to further reduce TB incidence, we performed a 10-year study in a district of Shanghai to delineate the local characteristics, transmission patterns, and dynamic changes of the local TB burden.

**Methods:** We conducted a population-based study of culture-positive pulmonary TB patients diagnosed between January 1, 2011 and December 31, 2020 in

Songjiang, Shanghai. Genomic clusters were defined with a threshold distance of 12-single-nucleotide-polymorphisms based on whole-genome sequencing. Transmission inference was performed using phybreak. The distances between the residences of patients were compared to the genomic distances of their isolates.

**Results:** Of 2212 enrolled patients, 74.7% (1652/2212) were internal migrants. The clustering rate (25.2%, 558/2212) and spatial concentrations were unchanged over the study period. Migrants had significantly higher TB rates but less clustering than residents. Clustering was highest in male migrants, younger patients and residents and migrants employed in physical labor. The 40.9% of resident TB patients > 65 had a clustering rate of just 18.3%. Only 22.1% of transmission events occurred between residents and migrants, with residents more likely to transmit to migrants. The clustering risk decreased rapidly with increasing distances between patient residences, and more than half of clustered patients pairs lived  $\geq 5$  kilometers apart. Epidemiologic links were identified for only 15.6% of clustered patients, mostly in close contacts.

**Conclusion:** Although some TB in Songjiang's migrant population is caused by strains the migrants bring with them, recent, local transmission is an important driver of TB. These results suggest that further reductions in TB incidence will require additional strategies for early TB detection to interrupt urban transmission.

### TBS-EP04-12 Phylodynamic analysis of *M. tuberculosis* in Botswana: insights from a population-based molecular study

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Whole genome sequencing of *Mycobacterium tuberculosis*-complex (Mtb) provides valuable insights into the transmission dynamics of the pathogen at a population level. Botswana is a high-burden tuberculosis country, yet detailed characterization of bacterial phylodynamics is lacking.

We investigated historical transmission patterns underlying the tuberculosis epidemic in Botswana using a population-based, molecular study conducted between

2012–2016. Of the 1,426 Mtb isolates analyzed, the predominant lineage was L4 (87.8%), followed by L1 (6.0%), L2 (5.3%), and L3 (0.8%). We identified eight circulating L4 main sublineages, with L4.3 being the most prevalent (45.6%), followed by L4.1 (24.7%), L4.4 (16.0%), and L4.8 (7.7%).

Temporally resolved phylogenies under a strict molecular clock model inferred the most recent common ancestor (MRCA) to have emerged around year 1727 (95% highest posterior density [HPD], 1607–1828) and 1900 (95% HPD 1854–1938) for L1 and L2, respectively. Time to MRCA varied among L4 sublineages; ranged from 1695 for L4.1.2/Haarlem (95% HPD 1546–1817) to 1941 for L4.3.2/LAM (95% HPD 1911–1966).

Consistent with the observed prevalence, coalescent-based analysis revealed L4.3.4/LAM experienced the largest magnitude of expansion between 1900 and early 2000s, and remained the most significant sublineage throughout our study period.

We also observed substantial growth beginning 1990s for L4.3.2/LAM3, while L1 and L4.4 exhibited large expansion between late 1970s and late 1990s. Other sublineages experienced various magnitudes of expansion and contraction during multiple time periods (Figure).

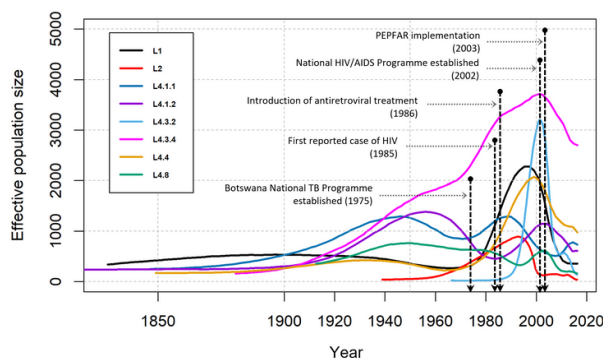


Figure.

All lineages underwent contraction after late 1990s to early 2000s, except for L4.1.1/X, which showed minimal indications of contraction. Our findings highlight the varying transmission dynamics among the Mtb lineages in Botswana. The expansion of many lineages coincided with the HIV/AIDS epidemic, while contraction aligned with the implementation of antituberculosis and antiretroviral treatment programs.

These results emphasize the importance of integrated prevention and control strategies that address HIV and TB simultaneously.



### TBS-EP04-13 MDR Lineage 4 strains have a higher case reproduction number than non-MDR Lineage 4 strains in the Republic of Moldova

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**Background:** In Moldova, nearly one third of incident TB is multidrug resistant. We recently documented that incident MDR-TB in Moldova is attributable almost entirely to local transmission of Lineage 2.2 (Beijing) and Lineage 4.2 (Ural) strains. While transmission of Beijing lineage MDR-TB has been widely documented, large-scale transmission of MDR-TB of the Ural lineage has not previously been reported.

**Study aim:** We aimed to estimate case reproduction numbers for MDR and non-MDR Ural strains to determine how differences in reproductive fitness may contribute to the high incidence of MDR-TB of this lineage.

**Data and Methods:** Whole genome sequencing was performed on all initial culture-positive clinical isolates collected from individuals diagnosed with TB in Moldova between January 1, 2018 and December 31, 2019 (n=2220). We used two complimentary approaches to estimate case reproduction numbers. Local Branching Index (LBI) is based on a maximum likelihood phylogeny and provides a quantitative measure of clade expansion.

Because LBI can be biased if strains have different serial intervals or evolutionary rates, we also fit a Multi-Type Birth Death (MTBD) Model; MTBD is a Bayesian approach to jointly estimate tree topology and the reproduction numbers of different 'types' (MDR and non-MDR) within the tree.

**Results:** Of 420 Ural strains, 255 were MDR. These MDR Ural strains accounted for 32.7% of all MDR-TB in Moldova over the study period. The LBI estimates for MDR Ural strains were higher on average than LBI estimates of non-MDR Ural strains.

Concordantly, the MTBD model estimated that the reproduction number of MDR Ural strains is 2.54 (95% CrI: 1.57, 3.77), higher on average than non-MDR Ural strains (1.07; 1.02, 1.16). Together, these results highlight the potential threat of onward spread of MDR Ural strains, and the need to better understand the factors which contribute to the reproductive success of this pathogen.

### TBS-EP04-14 Exploring TB forecasting and temporal trends by sex and age in Taiwan: the impact of the COVID-19 pandemic on the dynamics

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**Objective:** By investigate the interplay between the pandemic and TB, we can better prepare and implement the mitigating strategies.

**Methods:** This was a temporal trend analysis conducted in Taiwan with an aging population, 2011- 2022. An exploratory analysis of the monthly incidence of tuberculosis cases, smoothed according to sex and age group was performed. Subsequently, the progression of the trend and prediction of the disease were characterized.

To forecast the trends, we employed various models, including the seasonal autoregressive linear integrated moving average (ARIMA) algorithm, exponential smoothing (ETS), hybrid, and the conventional Box-Jenkins method to determine the most suitable models for the future predictions.

**Results:** There were a total of 118,747 reported tuberculosis cases, with an incidence rate from 75.4 cases per 100,000-year to 39.4 cases per 100,000 inhabitants in men and from 33.4 cases per 100,000-year to 17.7 cases per 100,000 in women of confirmed TB cases, 2011-2022, in Taiwan.

In terms of overall incidence, both sexes experienced a decreasing trend, which was also observed across different age groups. The time series analysis revealed evidence of a decreasing trend from 2011 to 2022; however with a stability in the rate of slowdown decline during the pandemics.

**Conclusions:** The study revealed a decline in tuberculosis cases, for both sexes and across different age groups, both prior to and during the Covid-19 pandemic. However, the rate of decrease during the pandemic period was relatively slower compared to the pre-pandemic period. Based on our findings, it is projected that the TB would have reached a stability of downwards trend in Taiwan in the coming years, but the pandemic might have exacerbated the situation.

These findings present compelling evidence regarding the concerning characteristics and dynamic trends of tuberculosis during epidemics, particularly emphasizing the impact of the Covid-19 pandemic and its aftermath.

### TBS-EP04-15 Non-interferon- $\gamma$ cytokines identify a high proportion of Indian infants with *M. tuberculosis* sensitisation

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**Background:** Detection of *Mycobacterium tuberculosis* (Mtb) infection among infants has been hampered by low sensitivity of interferon-gamma (IFN- $\gamma$ ) release assays (IGRAs) such as QuantiFERON-TB Gold (QFT). Recent studies have explored the use of non-IFN- $\gamma$  cytokines to detect Mtb immune responses.

We evaluated the prevalence and consistency of Mtb-specific cytokine responses over the first year of life using QFT and Luminex among Indian infants and evaluated clinical cofactors of Mtb sensitization.

**Methods:** Infants born to mothers enrolled in the PRA-CHITI observational cohort study at Byramjee Jeejeebhoy Government Medical College (BJGMC)–Sassoon General Hospital (SGH) in Pune, India were followed from birth to 1 year of life. We performed QFT at 6 months and 12 months of life and measured 17 cytokine responses in cryopreserved QFT supernatants using the Human Th9/Th17/Th22 Fixed Panel Luminex assay. Mtb sensitization by Luminex was defined by  $\geq 2$  individual cytokines meeting previously published criteria. We described the prevalence and consistency of Mtb sensitization over the first year of life and evaluated clinical cofactors of infant Mtb sensitization using univariable linear regression.

**Results:** Of 222 infants evaluated by QFT, 13 (5.9%) infants were QFT positive overall; the Luminex panel detected an additional 74 infants with Mtb sensitization (74/216, 34%) that were QFT negative. Eight (3.5%) infants had sustained Luminex positive results, and 38 (26%) had transient Mtb sensitization. Infants with weight-for-age z-score  $< -2$  were less likely to have Mtb sensitization by Luminex at 6 months (RR = 0.29, CI<sub>95%</sub>: 0.12, 0.69). There was no association of Mtb sensitization with maternal HIV exposure by Luminex or QFT.

**Conclusion:** Luminex detected additional Mtb-specific immune responses not detected by IGRA. Nutritional status may affect detection of Mtb sensitization. Future studies are needed to evaluate the prognostic value of Mtb-specific non-IFN- $\gamma$  cytokines for progression to TB disease.

### TBS-EP04-16 Alignment-free approach for inferring TB transmissions from whole-genome sequencing data

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Whole genome sequencing (WGS) can be a valuable tool in understanding the transmission dynamics of *Mycobacterium tuberculosis* (MTB), the causative agent of TB. Traditional approaches for inferring TB transmissions from MTB WGS data rely on read mapping-based algorithms, which are computationally slow and prone to systematic errors that generate substantial background noise in the estimation of genetic distances between MTB isolates.

To circumvent the limitations of the read mapping approach, novel 'alignment-free' algorithms offer a promising avenue to efficiently and accurately infer TB transmissions from MTB WGS data.

In this presentation, we will first review the advantages/disadvantages of read-mapping and alignment-free approaches.

Then, we will present a set of comparative analyses of TB transmission clusters using these two approaches, based on both simulated and real-world WGS data.

The alignment-free analyses are based on bioinformatic tools we developed and that will be briefly introduced: 'SKA2', an improved version of the popular SKA program to identify mutations based on split-kmer analyses, and 'skalo', a novel kmer-based algorithm to infer adjacent mutations and genomic insertions/deletions (indels) from SKA2 outputs.

The results show how these tools can qualitatively and quantitatively improve inferences of TB transmissions from WGS data. In particular, SKA2 generate more accurate genetic distances than the read-mapping approach and indels identified by skalo provide valuable information to decipher relationships among MTB isolates.

Finally, we will discuss implications for future TB transmission studies and TB public health programs.

## TBS-EP04-17 Measuring indirect transmission-reducing effects in TB vaccine efficacy trials: why and how?

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Tuberculosis is the leading bacterial cause of death globally. In 2021, 10.6 million people developed symptomatic tuberculosis and 1.6 million died. Seven promising vaccine candidates that aim to prevent tuberculosis disease in adolescents and adults are currently in late-stage clinical trials.

Conventional phase 3 trials provide information on the direct protection conferred against infection or disease in vaccinated individuals, but they tell us little about possible indirect (ie, transmission-reducing) effects that afford protection to unvaccinated individuals.

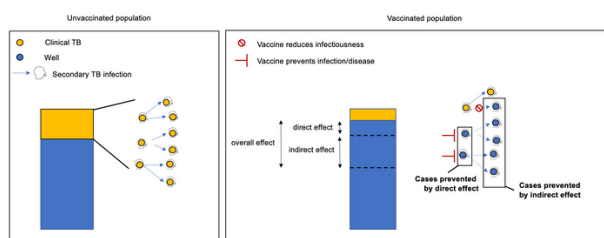


Figure. Indirect and direct effects of vaccination in vaccine trials.

Information on the potential for indirect vaccine effects can be crucial information for policymakers deciding if and how to introduce tuberculosis vaccines into immunisation programmes.

We describe the rationale for measuring indirect effects, in addition to direct effects, of tuberculosis vaccine candidates in pivotal trials and lay out several options for incorporating their measurement into phase 3 trial designs. These options include: measuring individual-level markers of infectiousness among trial participants

reaching endpoints, nesting household transmission studies within trials, and employing cluster randomised trial designs.

With any approach, incorporating subclinical TB as a secondary endpoint may provide additional insight into the transmission-reducing effects of vaccine candidates. We will discuss the pros and cons of each approach and outline the knowledge gaps that, if filled, would facilitate and further support the basis for suggested modification to pivotal trials.

## TBS-EP04-18 Fast-track follow-up of patients with detected MDR/RR-TB to limit transmission through system strengthening and coordination in Pakistan

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**Background:** The pre-enrollment lost to follow up (PLTFU) of Rifampicin Resistant (RR) TB patients is a challenge for TB Control Program Pakistan as these are known RRTB patients transmitting disease in community. The exact number of these PLTFU is however unknown as in programmatic settings, the detection cohort is taken from laboratories while the treatment numbers are taken from drug resistant TB (DRTB) sites without having case base details.

To fill this gap, current study evaluates the results of newly developed case base tracking mechanism, which has been implemented in Pakistan during 2022 with the aim to limit PLTFU and delays in treatment initiation.

**Methods:** National TB Control Program (NTP) developed a coordination mechanism for tracking and recording of RR detected cases through structured involvement of all DRTB and Xpert sites.

Under this initiative, provincial reference laboratories in coordination with Xpert sites shared online case base detection data, DRTB site staff was responsible for tracking and sharing status online, Provincial Programs monitored and validated the information before sharing with National Program. For this study, tracking results of RR TB (detection) cohort of 2022 is taken from the electronic system

**Results:** During 2022, RR TB was detected among 4441 samples, among which 563 (13%) were repeat tests. Among 3878 RR TB detected patients, 391 (10%) were not enrolled on second-line treatment (SLD).

Among these PLTFU patients, 105 (27%) had issues related to testing (already registered DRTB patients, discrepant RR results, further testing underway), 96 (25%) were untraceable, 90 (23%) died during the process of retrieval, 80 (20%) patients refused any type of treatment, whereas, 6 (2%) were still under retrieval.

	Q1 2022	Q2 2022	Q3 2022	Q4 2022	2022
Rifampicin Resistance (RR) Detected Samples	1009	1235	1243	954	4441
Repeat Tests	112	106	199	146	563
Rifampicin Resistance Detected Patients	897	1129	1044	808	3878
Enrolled among the RR Detected	814	1026	918	729	3487
Not Enrolled	83	103	126	79	391
Refusal by RR Detected Patient	19	20	20	21	80
Death of RR Detected Patient	19	25	33	13	90
Not Traceable	26	27	24	19	96
Others Not Enrolled RR Detected Patient (laboratory reasons, out of province, in process)	19	31	49	26	125

**Conclusion:** The challenge of PLTFU of RRTB may be addressed through structured coordination and system strengthening.

### TBS-EP04-19 Leveraging long-read sequencing of *M. tuberculosis* for a better resolution of isolate diversity

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Using long read sequencing, we *de novo* assembled the finished genome sequences for 55 *Mycobacterium tuberculosis* (M.tb) isolates belonging to lineage 2 and 4. These isolates were collected as part of the multinational scientific and applied medicine collaboration program TB Portals, spearheaded by the NIAID NIH. These long-read sequenced isolates were contributed to TB Portals by the member countries of Azerbaijan, Moldova, Georgia, and Kazakhstan.

We compared these genomes to each other as well as the reference sequence H37Rv through presence/absence and the synteny of orthologous genes. This comparison adds to the support that H37Rv is not an all-inclusive

reference. For example, we identified PE/PPE and virulence genes present in our sequenced isolates that are absent in H37Rv. Since PE/PPE genes and their arrangement variants, are not well resolved from short reads alone, we will use these long read sequences to assess the PE/PPE genotypes of our collection over 4,100 M.tb samples sequenced with short reads.

Additionally, we found of the 8 long-read sequenced genomes had large genomic rearrangements compared to the reference sequence. Some of these rearrangements are unique but there are four lineage 2.2.1 isolates that had the same two genomic rearrangements that were likely facilitated by nearby insertion sequence (IS) elements. These isolates all originated in one country and are part of the same clade in the ortholog based phylogeny of these 55 isolates.

The isolates with this rearrangement have more SNPs than expected for a recent transmission event, so we hypothesized that this particular rearrangement is more prevalent than expected in our whole collection and may influence the virulence and fitness of strains.

We plan to leverage the larger TB Portals short read sequencing collection to look for this rearrangement in a wide variety of isolates to determine its pervasiveness and possible correlation with clinical metadata.

### TBS-EP05 TBScience 2023 - Moderated E-poster Session V

#### TBS-EP05-01 Interrogation of an multi drug resistant tuberculosis outbreak using whole genome sequencing

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The spread of drug-resistant strains which has been reported to be attributed to primary transmission threatens TB control and prevention programmes. Previous molecular epidemiological studies have reported that the dynamics of tuberculosis transmission varies geographically.

After a reported increase in drug resistant TB cases in the West Coast region of the Western Cape Province, South Africa, the aim of this study was to identify transmission hotspots and possible outbreaks of drug-resistant tuberculosis within this region.

Spoligotyping and Sanger sequencing of first line drug resistance conferring mutations of drug resistant strains in the region over 5 years (2008-2012) identified a multi-

drug-resistant tuberculosis (MDR-TB) outbreak of the X-family, mainly located in the Northern parts of the region. Whole genome sequencing (WGS) was done on all available strains (n=177) to establish the phylogenetic relationships of this outbreak.

Through WGS and Sanger sequencing of first line drug resistance conferring mutations of drug resistance, we found identical mutations conferring resistance to the 4 first-line drugs used in tuberculosis treatment in this lineage 4.1.1.3 cluster, including a rare *katG315* double mutation. This is indicative of transmission of MDR-TB. Isolates belonging to this outbreak, but with different additional mutations conferring to resistance to second-line drugs were also identified, indicating that pre-XDR-TB are primarily acquired from this existing MDR strain genotype. XDR-TB has not yet been seen, as this outbreak peaked before the introduction of new generation anti TB drugs.

Monitoring and interrogation of drug resistant TB outbreaks plays an important part in our understanding of the drug resistant TB epidemic to ultimately eradicate TB disease worldwide.

### TBS-EP05-02 PanACEA DECODE combination dose-finding trial shows safety and efficacy results for delpazolid

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Linezolid, an oxazolidinone, is a critical component of current multi-drug resistant tuberculosis treatment, but with toxicity limiting widespread use. Delpazolid is a novel oxazolidinone with good antimicrobial activity and safety profile seen in early-phase clinical studies.

The PanACEA Delpazolid Dose-finding and Combination Development (DECODE) is a multi-center Phase IIb, Open-Label, Randomized Trial evaluating the exposure-response relationship of delpazolid in a combination potentially useful for treating drug-susceptible and drug-resistant tuberculosis with safety and tolerability profile assessment.

Participants with bacteriologically-confirmed drug-susceptible pulmonary tuberculosis were randomized among five arms: no delpazolid, or delpazolid 400mg once-daily, 800mg once-daily, 1200mg once-daily or 800mg twice-daily in combination with bedaquiline, delamanid and moxifloxacin at standard doses for 16

weeks. The primary efficacy endpoint was the slope of decline of bacterial load, measured by weekly liquid culture time-to-positivity over 16 weeks.

76 participants were enrolled in five centers in South Africa and Tanzania. No neuropathy related to oxazolidinones occurred. Adverse events of at least grade 3 with at least possible relationship to delpazolid were as follows: one event of nausea in the 1200mg arm, one event of severe anemia and one of pancreatitis, both in the 800mg twice-daily arm.

One QT interval prolongation >60ms over baseline occurred in the 800mg once-daily arm. Time-to-culture conversion was observed to be shortest in the 1200mg arm, although there was no statistical evidence of a difference between regimens. A complete pharmacokinetic-pharmacodynamic analysis is ongoing.

Delpazolid showed a good safety profile at doses up to 1200mg once-daily.

This preliminary analysis suggests a dose of 800mg once-daily or 1200mg once-daily for developing new clinical studies, but pharmacokinetic-pharmacodynamic analysis, the primary objective of this study, will provide further insight.

### TBS-EP05-03 Mixed TB infections: implications for treatment outcomes

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Mixed tuberculosis (TB) infections, characterized by presence of more than one strain of *Mycobacterium tuberculosis*, have been recognized as a significant concern in TB management.

In this study, we investigated the occurrence of mixed infections and their potential impact on treatment outcomes using samples from the TBPortals database containing patient clinical and genomics data for 4,122 isolates.

We used the tool quantTB to determine if an isolate was mixed or not, and leveraging clinical data identified several key findings. Our analysis revealed potential variations in the rates of mixed infections across different countries, although statistical significance was not achieved (Mann-Whitney p-value=0.056). It is important to note that samples from countries are clinical convenient samples and additional clinical covariates may influence analysis. Nonetheless, these findings suggest a trend deserving further investigation.

Furthermore, we observed an association between mixed infections and treatment failure (chi-square p-value = 0.0508), indicating a potential link between mixed infections and suboptimal treatment outcomes. Additionally, an association was discovered between the presence of

allele mixture in known drug-resistance conferring loci in mixed infection samples and treatment outcome (chi-square  $p$ -value=0.0005).

Several samples in our TB portals database have a mismatch between phenotypic drug resistance status and genotypic drug resistance status as called by TBprofiler. We found an association between this phenotype-genotype mismatch and mixed infection status (chi-square  $p$ -value=0.0035). This suggests that mixed infections may contribute to challenges in accurately predicting drug resistance profiles based on phenotypic and genotypic based testing.

These findings underscore the relevance of mixed TB infections and highlight their potential implications for treatment outcomes. Greater awareness and consideration of mixed infections are crucial for tailoring effective treatment regimens and improving patient care. Further studies are warranted to explore the underlying mechanisms and develop strategies to mitigate the impact of mixed infections on TB management.

#### **TBS-EP05-04 Technological innovation and TB elimination: a study by Technology Foresight**

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In the present study, tuberculosis specialists were surveyed to rate the most effective strategies to eliminate TB as a public health problem by 2050. Then were investigated the most promising emerging technologies for the prevention, diagnosis and treatment of tuberculosis (TB) expected to reach the market by 2035. This Technology Foresight study was specifically carried out by means of a web survey closed questionnaire, which was sent to 29,988 TB specialists worldwide. Of these, 2,657 answers were obtained and analysed. Respondents had demonstrated a high level of academic training (PhD), more than 10 years of professional experience, and a great diversity of both areas of knowledge and geographic reach.

In the view of experts, the strategies with the greatest potential impact on epidemic TB were

- Shorter time between diagnosis and start of treatment of DS and MDR-TB;
- Strengthening tuberculosis control actions in the most vulnerable populations;
- Shorter and less expensive regimens for drug resistant MDR/XDR-TB.

Regarding the strategies with the highest potential for eliminating TB, our data suggests that the biomedical paradigm is the strongest among the specialists.

The most promising technologies expected to reach the market by 2035 selected by the specialists were:

- New drugs of known chemical classes or new chemical classes;

- New point-of-care diagnostic tests for DS-TB, drug resistant or multidrug resistant (MDR/XDR)-TB and TB Infection (TBI).

We contribute by discussing the most promising technologies and strategies for the elimination of TB in light of social determinants of health models and forecasting studies.

We conclude by suggesting that the expected emerging technologies ongoing development will not suffice to end TB by 2050.

#### **TBS-EP05-05 A mass spectrometry approach to identifying *M. tuberculosis* antigens presenting on major histocompatibility complex classes**

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Whereas *Mycobacterium tuberculosis* (*Mtb*) is a leading cause of infectious disease mortality, no clinically licensed vaccine reliably prevents pulmonary tuberculosis (TB) in adults. Recognition of *Mtb*-infected cells by both CD4+ and CD8+ T cells contributes to protective immunity against *Mtb* infection, but not all T cells specific for *Mtb* antigens successfully recognize infected phagocytes. Defining which *Mtb* antigens are accessible for processing and presentation on major histocompatibility complexes (MHCs) on the surface of infected cells therefore may contribute to the design of effective candidate vaccines.

We previously showed that mass spectrometry (MS) could be used to identify, validate, and quantify *Mtb*-derived peptides presented on major histocompatibility complex class I (MHC-I) by primary human macrophages infected with *Mtb*, revealing potential targets for protective CD8+ T cell responses and mechanistic insights into their processing and presentation. In this new work, we extend this approach to the MHC class II (MHC-II) repertoire.

We optimized a workflow for MS analysis of MHC-II-bound peptides from samples prepared in a Biosafety Level 3 compatible manner, which can be used to identify *Mtb*-derived peptides presented on MHC-II from human dendritic cells and macrophages infected with virulent *Mtb*.

In preliminary data, we show that peptides derived from EsxB are consistently detected in the MHC-II repertoire of *Mtb*-infected dendritic cells and macrophages, which may help inform the selection of appropriate immunogens for TB vaccines designed to elicit protective CD4+

T cell responses. Our results provide a proof of concept for a technique that will help improve the field's understanding of the landscape of available targets for protective T cell responses in TB and the mechanisms by which *Mtb* antigens are processed and presented on MHCs.

### TBS-EP05-06 Phasic roll out of BPAL M / BPAL regimen in Pakistan and the preliminary findings

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**Background:** National TB Control Program Pakistan (NTP) initiated phasic roll out of BPAL/M regimen at Drug Resistant (DR) TB sites. This rollout was preceded by a revision of the training module, tools and capacity-building workshops. In this report we intend to describe the modality of phasic roll out plan and efficacy of regimen through an intermediate evaluation of available outcomes of patients

**Methods:** Programmatic rollout of BPAL/M started from ten (10) DRTB sites in October 2022, expanded to two more sites after 6 months. Future plans include expansion to 4 more sites by July 2023 and across all DRTB sites till January 2024. In this review, we have analyzed data of patients enrolled between Oct 2022 till 10<sup>th</sup> May 2023.

Culture 1 (Available results at time of assessment)	Regimen	Positive Results among Total Valid Results	Negative Results among Total Valid Results	Total Valid Results		
Culture 1	BPAL	19	70%	8	30%	27
	BPALM	31	82%	7	18%	38
	BPAL/M Regimen	50	77%	15	23%	65
Culture 2	BPAL	13	87%	2	13%	15
	BPALM	22	92%	2	8%	24
	BPAL/M Regimen	35	90%	4	10%	39
Culture 3	BPAL	10	91%	1	9%	11
	BPALM	12	100%	0	0%	12
	BPAL/M Regimen	22	96%	1	4%	23

**Result:** Out of total 263 (181 on B PaL M, 82 on BPAL) enrolled patients, at the time of review, 239 were still on BPAL/M treatment whereas 24 patient received treatment outcome; 17 patients completed the treatment successfully, 6 died and 1 patient failed the treatment.

- Amongst the patients with valid culture results of **first** month follow up, 70% enrolled on B PaL were negative whereas 82% enrolled on B PaL M were negative.
- Amongst the patients with valid culture results of **second** month follow up, 87% enrolled on B PaL were negative whereas 92% enrolled on B PaL M were negative.

- Amongst the patients with valid culture results of **third** month follow up, 91% enrolled on B PaL were negative whereas 100% enrolled on B PaL M were negative. All the patient who died during TB treatment (B PaL/M) regimen, had low BMI and their treatment days ranged from 18 days 78 days (mean = 38).

### TBS-EP05-07 Dual RNA-sequencing to understand host-pathogen interactions in *M. tuberculosis*-infected macrophages from people with diabetes mellitus

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Tuberculosis (TB) and diabetes mellitus (DM) are two co-emerging diseases that are increasingly prevalent worldwide. People with DM have a tripled risk of developing active TB and are twice as likely to succumb to the disease. We hypothesize that macrophage function in DM is altered, creating a preferred niche for *Mycobacterium tuberculosis* (*Mtb*).

Previous research primarily focused on either the host's response or the pathogen's response during infection, but not both. Simultaneous profiling of both host and pathogen mRNA, known as dual RNAseq, is necessary to uncover the crosstalk between macrophage and *Mtb*. However, performing dual RNAseq to mycobacterial infections is challenging due to low RNA yields from intracellular *Mtb*.

This study conducted a dual RNAseq approach, which overcomes the hurdles of low mycobacterial transcript numbers by applying a unique enrichment protocol. Human monocyte-derived macrophages from individuals with type 1 DM (n=4) and age-/sex-matched healthy controls (n=4) were infected with *Mtb* H37Rv strain, followed by gene expression profiling of both the host and the pathogen.

Results show that sufficient read counts and high read quality derived from the unique enrichment approach, which allows for transcriptional profiling. Additionally, the production of cytokines in response to infection and the mycobacterial load within the macrophages were assessed. By integrating the data on transcriptional changes, cytokine production, and mycobacterial growth, this study gains new insights into the interaction between macrophages and *Mtb* in the context of DM.

## TBS-EP05-08 Breast milk is enriched with functional anti-mycobacterial antibodies that decline over time

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**Background:** Breast milk plays a significant role in shaping infant respiratory tract mucosal immunity, but little is known about *Mycobacterium tuberculosis* (Mtb) humoral immunity in breast milk. We aimed to characterize the longitudinal profile of anti-mycobacterial antibodies in plasma and breast milk of lactating people living in a TB-endemic setting.

**Methods:** People of known HIV and Mtb infection status were enrolled during pregnancy in the PRACHITi observational cohort study at Byramjee Jeejeebhoy Government Medical College (BJGMC)-Sasson General Hospital (SGH) in Pune, India and followed postpartum.

We measured anti-PPD IgA and IgG levels by ELISA, and PPD-specific antibody-dependent cellular phagocytosis (ADCP) and antibody-dependent neutrophil phagocytosis (ADNP) from cryopreserved plasma and breast milk supernatant at 6 weeks and 12 weeks postpartum. Median antibody levels (OD) and phagocytosis scores in plasma and breast milk were compared using paired Wilcoxon ranksum tests.

**Results:** Of 56 study participants with available paired plasma and breast milk samples, 28 (50%) were HIV positive and 25 (44%) had Mtb infection as detected by QuantiFERON TB Gold (QFT). Overall, anti-PPD antibody levels and function were similar by HIV and IGRA status in plasma and breast milk. Anti-PPD IgA levels and antibody-dependent neutrophil phagocytosis (ADNP) were higher in breast milk compared to plasma at 6 weeks ( $p < 0.001$ ). Anti-PPD antibody-dependent cellular phagocytosis (ADCP) and neutrophil phagocytosis (ADNP) function decreased in breast milk from 6 to 12 weeks postpartum ( $p < 0.001$ ) (Figure).

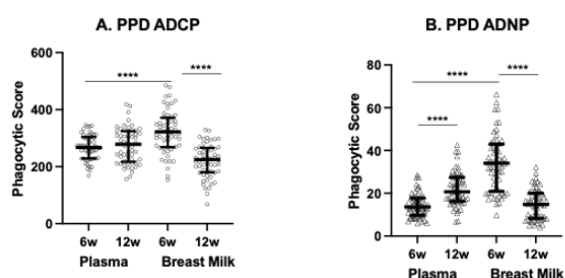


Figure:

**Conclusions:** Breast milk was enriched with functional anti-mycobacterial antibodies, which declined over time.

Future studies to evaluate the role of breast milk antibodies in infant mucosal Mtb immunity are warranted and may inform future TB vaccination strategies in pregnancy.

## TBS-EP05-10 TB-associated hemophagocytic lymphohistiocytosis: a systematic review and meta-analysis

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**Background:** Tuberculosis (TB) can induce secondary hemophagocytic lymphohistiocytosis (HLH), a severe hyperinflammatory syndrome that is often recognized late and associated with poor outcomes. As TB-HLH is rarely studied beyond case reports, we performed a systematic review and meta-analysis to better characterise the clinical features of this syndrome and to improve its diagnosis and treatment.

**Methods:** A systematic review was performed in accordance to PRISMA guidelines. We searched PubMed, Embase, and Global Index Medicus from database inception up to October 23<sup>rd</sup> 2022 for records reporting patients with TB-HLH. All records written in Roman languages reporting individual patient level data of adult, HIV-negative patients with TB associated secondary HLH were eligible.

**Results:** We included 104 records describing a total of 113 patients with TB-HLH. Seventy-five percent of patients were reported from low to moderate tuberculosis incidence countries. Patients were categorized into:

1. Those with confirmed TB that developed HLH as a paradoxical reaction while receiving anti-TB treatment and;
2. Those presenting with HLH of unknown cause and later diagnosed with TB.

Pulmonary TB involvement was present in 19 (90.5%) of patients presenting with confirmed TB, whereas pulmonary TB involvement was present in only 54 (58.7%) of patients presenting with HLH of unknown cause.

Overall, a strikingly high proportion of patients had only extrapulmonary TB (35.4%), and 50% of all patients showed microbiological or histological evidence of bone marrow involvement. In-hospital mortality



was 25% among patients who received anti-TB therapy, whereas all patients died when anti-TB therapy was not initiated.

**Conclusions:** An underlying diagnosis of TB should be considered in unexplained HLH, even in low-incidence settings. Diagnostic work-up should include multi-organ cross-sectional imaging, alongside microbiological investigation for TB in both respiratory and bone marrow samples and a low threshold to initiate anti-TB treatment may improve outcomes in TB-HLH.

### TBS-EP05-11 Harnessing digital health technology for real-time data-driven TB disease control in Uganda

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Automated data transmission from diagnostic instrument networks to a central database at the Ministries of Health has the potential of providing real-time quality data for multifaceted action. We aimed at sharing how the LabXpert Disease Surveillance (DS) platform, as a novel digital health technology, delivers actionable data from diagnostic instruments to the national dashboards for disease control in Uganda.

We developed, validated and implemented a connectivity solution for a selected diagnostic instrument network across the 15 TB zonal region in Uganda between March 2022 and May 2023. The roll out was largely characterized by configuring the server address into the host communication ports of the diagnostic platforms, as well as user trainings at designated training sites.

The LabXpertDS system was successfully configured on a selected network of multiplexing diagnostic instruments at 260 sites in Uganda, providing a layered access of data. A total of 863,535 TB results were collected from diagnostic machines, including 269 GeneXpert machines, 39 Truenat machines, and 3 digital x-ray devices. These results were then shared with various stakeholders at different levels to ensure the data's optimal utilization for their intended purposes.

The connectivity solution provided usable and actionable data to empower the government and relevant stakeholders. The successful implementation of the connectivity solution relied on key operational strategies, including sustained internet connectivity and short message services, stakeholder engagement, a robust in-country laboratory coordination network, capacity building for human resources, establishment of a diagnostic instrument network, and integration with existing health data collection tools.

However, poor bandwidth in certain locations posed a significant obstacle to the successful implementation of the connectivity solution.

LabXpertDS as a digital health technology offers the chance to collect high-quality data on a number of parameters for disease control, thereby strengthening the quality of data from the networked diagnostic sites to relevant stakeholders.

### TBS-EP05-12 Comparative whole-genome sequence analysis of *M. tuberculosis* isolated from pulmonary TB and tuberculous lymphadenitis patients in Northwest Ethiopia

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**Background:** Tuberculosis (TB), caused by the *Mycobacterium tuberculosis* complex (MTBC), is a chronic infectious disease with both pulmonary and extra pulmonary forms. This study set out to investigate and compare the genomic diversity and transmission dynamics of *Mycobacterium tuberculosis* (*Mtb*) isolates obtained from tuberculous lymphadenitis (TBLN) and pulmonary TB (PTB) cases in Northwestern Ethiopia.

**Methods:** A facility-based cross-sectional study was conducted using two groups of samples collected between February 2021 and June 2022 (Group 1) and between June 2020 and June 2022 (Group 2) in Northwestern Ethiopia.

Deoxyribonucleic acid (DNA) was extracted from 200 heat-inactivated *Mtb* isolates. Whole genome sequencing (WGS) was performed from 161 isolates having  $\geq 1\text{ng}$  DNA/ $\mu\text{L}$  using Illumina NovaSeq 6000 technology.

**Results:** From the total 161 isolates sequenced, 146 *Mtb* isolates were successfully genotyped into 3 lineages (L) and 18 sub-lineages. The Euro-American (EA, L4) lineage was the prevailing ( $n=100$ ; 68.5%) followed by Central Asian (CAS, L3,  $n=43$ ; 25.3%) and then L7 ( $n=3$ ; 2.05%). The L4.2.2.ETH sub-lineage accounted for 19.9% while Haarlem estimated at 13.7%.

The phylogenetic tree revealed distinct *Mtb* clusters between PTB and TBLN isolates even though there was no difference at lineages and sub-lineages levels. The clustering rate (CR) and recent transmission index (RTI) for PTB was 30% and 15%, respectively. Similarly, the CR and RTI for TBLN were 31.1% and 18%, respectively.

**Conclusions:** PTB and TBLN isolates showed no *Mtb* lineages and sub-lineages difference. However, at the threshold of five allelic distance *Mtb* isolates obtained from PTB and TBLN forms distinct complexes in the phylogenetic tree, which indicates the presence of *Mtb* genomic variation among the two clinical forms. Hence, the high incidence rate of TBLN in Amhara region could be the result of *Mtb* genomic diversity and rapid clinical progression from primary infection and/or short latency.

### TBS-EP05-13 Challenges and considerations in implementing an internet-dependent diagnostic connectivity solution for TB in Uganda

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The National Tuberculosis (TB) Program in Uganda has taken a strategic direction to extend a connectivity solution to all TB diagnostic sites in the country. A private-public partnership has been forged with the objective of implementing a digital health technology to facilitate an automated real time centralized reporting mechanism.

This abstract aims to share the challenges and considerations from the early implementation of the internet dependent diagnostic connectivity solution in Uganda.

This was a cross-sectional study that involved a retrospective review of field activity reports.

The field activities involved debriefs of the district and health facility administration, and configuration of the digital health technology. Selected users were then introduced to the functionality of connectivity solution at facility level.

The already created access credentials were shared with the trained authorized machine users on site. Data were then collected into developed excel sheets based on the interactions and experiences from the different sites and field reports were then made.

Internet connectivity is needed for sustained data-pick up on a daily basis, and sites, especially in the islands of Lake Victoria, suffered poor bandwidth that ultimately affected the efficiency of the digital health technology. Diagnostic system compatibility was also a challenge that was encountered at different sites, and addressed by ensuring system upgrades prior to the configurations with the digital health technology.

Machine utilization metrics using the diagnostic connectivity solution is dependent on the upload of results, making this an inefficient way to measure this indicator if internet connectivity is not reliable at a given site.

Addressing system compatibility and internet connectivity issues at some sites will therefore be crucial to ensure reliable and consistent data transmission. Since the implementation relies on automated data pick up, the need for extensive training and technical expertise is minimized, making it largely generalizable in different settings

### TBS-EP05-14 TB development in biological treatment candidates and evaluation of a screening strategy for latent TB infection based on QuantiFERON-TB Gold

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**Background:** Screening and treatment for latent tuberculosis (LTBI) is mandatory in patients receiving biological therapies (BioT). Due its higher specificity, using QuantiFERON-TB Gold (QFT) to guide preventive therapy (PT), instead of tuberculin skin test (TST), could reduce treatments without increasing the risk of TB.

**Methods:** Retrospective observational study of adults treated with BioT for immune-mediated inflammatory diseases (IMIDs) evaluated between January 2012 and June 2020 in a TB unit.

We defined two periods, according the screening strategy:

1st period (January 2012-December 2014) (PT was given if either TST or QFT were positive), and;

2nd period (January 2015-June 2020) (PT was given if QFT was positive, regardless of the TST result).

For risk estimation, patients were censored after 3 years of BioT exposition. We compared the TB incidence rates between the two different periods expressed as density of incidence.

**Results:** We included 791 individuals. Most common IMIDs were inflammatory bowel disease (34.6%), rheumatoid arthritis (18%) and psoriasis (16.2%), and 607 (76.7%) received anti-TNF $\alpha$  agents.

Overall, 133 (17.1%) individuals were diagnosed with LTBI according immunological tests results.

In addition, 2 individuals from the discordant group (TST-Positive/QFT-Negative) in the 2nd period were considered tributaries of PT. Finally, 134 completed PT (65 [48.5%] received isoniazid for 6-9 months and 58 [43.3%] rifampicin plus isoniazid for 3 months).

After an overall median exposure of 31 months to BioT (1,659.5 patient-years), 6 cases of TB were detected (3.6 cases/1,000 patient-years, IC95% 1.47-7.53). Five out of 6 occurred within the 1st year of anti-TNF $\alpha$  treatment.

Table 1 compares the two different periods. No TB cases occurred in the 42 discordant patients (TST-Positive/QFT-Negative), after a median exposure of 27 months (88 patient-years).

	1st period N= 205	2nd period N= 586	
LTBI diagnostic criteria	Positive TST and/ or QFT	Positive QFT positive regardless of the TST result	
Screening result			
QFT+	30 (%)	84 (%) <sup>a</sup>	
QFT-	156 (%)	458 (%)	
TST+/QFT-	19 (%)	44 (%) <sup>b</sup>	
PT			
Yes	49	85	
No	156	501	
Median exposure to BioT	36 months 519 p-yrs	25 months 1,141 p-yrs	
TB cases	5	1	
Density of incidence	9.6 cases/1,000 p-yrs CI95% 3.1–22.1	0.9 cases/1,000 p-yrs CI95% 0.01–4.9	p= 0.014

<sup>a</sup>One patient did not received PT.

<sup>b</sup>Two patients received PT.

Abbreviations: LTBI, latent tuberculosis infection; TST, tuberculin skin test; QFT, QuantiFERON Gold; PT, preventive therapy; BioT, biological therapies; TB, tuberculosis; p-yrs, patient-years.

Table 1. Comparison of the two periods

**Conclusions:** Our results support a screening based on the use of QFT exclusively, in the absence of increased incidence of TB cases using this strategy.

### TBS-EP05-15 Diagnostic and therapeutic dilemmas in the management of granulomatous disease in an immunocompromised patient

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A 33 year old male, non smoker, was mistakenly diagnosed with Idiopathic Inflammatory Bowel Disease (IBD) 7 years ago. Colonoscopy biopsies were performed and showed granulomatous inflammation. Corticosteroids were administered with no improvement. Anti-TNF treatment followed and led to worsening of symptoms. Mycobacterium avium extrapulmonary disease sensitive to macrolides was diagnosed through blood and tissue cultures from lymph nodes. Clarithromycin, ethambutol, rifabutin, moxifloxacin, cycloserine were administered for 2 years. Due to recurrence, the patient was checked for immunosuppression, and defects in the axis of IL12 – IFN $\gamma$  were revealed. Cycloserine, clarithromycin, moxifloxacin (without ethambutol, rifabutin for 2 months due to shortage) with IFN $\gamma$  were administered. 5 months later severe anemia (18%Ht) was diagnosed. Bone marrow biopsy was conducted and cultures showed M. avium resistant to macrolides.

An expert opinion proposed treatment with amikacin, clofazimine, bedaquiline, linezolid and later ethambutol instead of amikacin due to severe ototoxicity. One year later the patient was admitted to our hospital with high fever, epileptic seizures, pneumonia, anemia (22% Ht). Disseminated M. Avium disease (CNS, lung, bone marrow, peritoneum, lymph nodes) at least macrolide resistant, was diagnosed.

A salvage regimen with Amikacin, tedizolid, clofazimine, ceftazidime/avibactam, isoniazid, delamanide, ethambutol, antiepileptic treatment and IFN $\gamma$  was administered. The treatment led to deteriorating ototoxicity, remission of seizures, fever, dyspnea, rise of Ht and inflammatory markers near normal range.

amplicon (MAC) με τη πρότυπη μέθοδο μικροαραιώσεων σε ζυμώ (CLSI 2018 "Susceptibility testing of Mycobacteria, Nocardiae, and other Actinomyces", 3rd edition", CLSI document M24-M2, Clinical and Laboratory Standards Institute, Wayne, PA.)

ΑΠΟΤΕΛΕΣΜΑΤΑ					
ANTIBIOTIKO	MIC (μg/ml)	Όρια Ευαισθησίας			Ερμηνεία
		E	ME	A	
Clarithromycin	>64	≤8	16	≥32	A
Amikacin	8	≤16	32	≥64	E
Moxifloxacin	2	≤1	2	≥4	ME
Linezolid	16	≤8	16	≥32	ME
Ethambutol	16				
Rifabutin	0.5				
Rifampin	2				
Streptomycin	16				

Παρατηρήσεις:  
1. Για τα αντιβιοτικά μοξιφλοξασίνη και λινεζολίδη τα όρια ευαισθησίας είναι προσωρινά καθώς αναμένεται η συσσώρευση περισσότερων δεδομένων στην βιβλιογραφία.  
2. Για τα αντιβιοτικά Ethambutol, Rifabutin, Rifampin και Streptomycin δεν έχουν καθιερωθεί όρια ευαισθησίας.  
3. Στο στέλεχος εφαρμόστηκε η μοριακή δοκιμασία NTM-DR (Hain- Lifesciences) που είναι συνδυασμός PCR και ανόστρου βιβιδισμού. Με την παραπάνω δοκιμασία το στέλεχος ταυτοποιήθηκε ως Mycobacterium avium. Επίσης ανιχνεύτηκε η σημασιική μετάλλαξη A2058G ταυτοποιήθηκε ως αντοχή σε αντοχή σε μακρολίδες. Δεν ανιχνεύθηκαν μεταλλάξεις που

This case is important because NTM infections should always raise a suspicion for immunodeficiency. Granulomatous tissue should always be checked for mycobacterial infection. Drug toxicity and compliance is another important issue for NTM infections.

### TBS-EP05-16 BCG vaccination of newborns before and during the COVID-19 pandemic in Belarus

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**Introduction:** The COVID-19 pandemic has had an adverse impact on health services in the world.

The aim of the study was to research BCG vaccination of newborns before and during the COVID-19 pandemic in Belarus.

**Methods:** We used data from the state statistical report on medical care for pregnant women, women in childbirth and puerperas of Belarus for 2017-2022. We compared the first period before the COVID-19 pandemic

(2017-2019) with the second period, during the pandemic (2020-2022). The number of newborns vaccinated with BCG, the number of newborns vaccinated with BCG vaccine per 100 newborns (intensive indicator) and the average annual growth rate (AAGR) of the number of newborns vaccinated with BCG were calculated.

**Results.** In the first period, on average, 76566.7±6226.9 newborns or 80.6±3.2 newborns per 100 newborns were vaccinated with BCG per year.

In the second period, on average, 63555.0±5422.3 newborns or 82.5±1.3 newborns per 100 newborns were vaccinated with BCG vaccine per year. For 2017-2022, the AAGR of newborns vaccinated with BCG was -0.09%.

**Conclusions.** During the COVID-19 pandemic, compared with the pre-pandemic period, the number of newborns vaccinated with BCG per 100 newborns per year in Belarus remained at the same level. The AAGR of the number of newborns vaccinated with BCG was -0.09%. The COVID-19 pandemic didn't affect the BCG vaccination of newborns in Belarus.

### TBS-EP05-17 High-resolution microscopy of *M. tuberculosis* complex strains

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The development of high-resolution microscopic processes over the past 30 years has given us a fascinating insight into the curious world of microorganism and their pathobiological characteristics.

Furthermore, molecular biological techniques have revolutionized our understanding of pathogenicity and virulence associated mechanism especially in infectious diseases.

However, in many cases microscopy still remains one of the gold standard methods for staining to provide an estimation of the bacterial load in patient samples.

Exemplary, more than 100 years after discovering, classical Ziehl-Neelsen staining of the tubercle bacillus still represents one of the gold standard techniques in tuberculosis (TB) diagnostic.

However, when dealing with an aerosol-transmissible disease like TB, there is an increased biosafety risk associated with microscopy if the infectious agent is not adequately inactivated.

Therefore, heat or chemical inactivation of the TB pathogen is essential prior to microscopy. It can be assumed that these standardized methods may not always allow for high-resolution structural investigations, as

they can potentially alter or even destroy the pathogenic properties of the surface of the pathogen. To address these limitations, a new sample preparation method has been established and optimized.

This method is based on the gamma-radiation of a minimal dose, allowing for the investigation of clinical isolates of the *Mycobacterium tuberculosis* complex using Scanning Electron Microscopy (SEM) and Atomic Force Microscopy (AFM) outside of a biosafety level 3 containment.

These advanced imaging techniques can identify intricate details of mycobacteria and their interactions with host cells at high resolution. By gaining a deeper understanding of the structural characteristics and host-pathogen interactions of TB, researchers can identify potential targets for the development of new antibiotics. Overall, the optimized sample preparation method using gamma-radiation for SEM and AFM represents a valuable approach to advance our understanding of TB and ultimately combat this global health threat more effectively.

### TBS-EP05-18 Chronic hypersensitivity pneumonitis – experience in treatment with the appearance of new possibilities

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**Introduction:** Hypersensitivity pneumonitis (HP) is rare reaction to an allergen from environment, only 5% of patients with acute HP develop chronic forms. The aim was to analyze lung function in patients with chronic HP (CHP) before and after receiving treatment.

**Material and method:** 74 patients treated at the Institute for Pulmonary Diseases of Vojvodina (IPDV), Serbia, from 2012 to 2022 were included in the study.

A retrospective analysis and comparison of lung function (FVC, FEV1, PaO<sub>2</sub>) was performed before and after the applied therapy; results that altered by ≥10% represented the progression or regression of the disease; those that varied by 0-10% indicated stable disease. DLCO was introduced at IPDV in the interim and was left out of this study.

**Results:** The average age of patients was 57.61±12.60; male were 52.7%. Corticosteroid therapy was used in 67.6%, azathioprine in 9.5% and antifibrotic in 4.1% (p=0.042). 16/74 patients didn't complete the evaluation (7 died; 9 stopped being controlled).

Of the 58 patients, 56% had no significant change in FVC value; almost ¼ (24%) had significant drop and only 20% had a significant increase.

Similar values were for FEV1 (59% had no significant changes, 22.4% had significant decreases, 18.4% had significant increases), as well as for PaO<sub>2</sub> (50.90% had an unchanged status of blood oxygen levels, but almost every third (36.4%) had a fall of values).

**Conclusion:** The majority of HP responses (80%) have stable or better respiratory parameters with the most common form of treatment (corticosteroids). After the initiation of antifibrotic treatment for progressive forms of CHP, the levels of impairment are expected to decrease over time.

## COMMUNITY CONNECT SESSIONS: WEDNESDAY 15 NOVEMBER 2023

### CC-01 Communities' right to newer, safer, more effective regimens for drug-resistant TB

Chair: Archana Oinam, GCTA, India

Tuberculosis is an ancient epidemic that has marked the human experience throughout history. Despite affecting more than 10 million people every year and claiming approximately 1.4 million lives in 2021 alone - more than any other infectious disease - the progress in tuberculosis treatment has moved ahead at a glacial pace. Furthermore, the emergence and spread of drug-resistant tuberculosis, caused by Mycobacterium bacteria that are resistant to at least one first-line anti-TB drug, threatens to derail the global fight against this infectious killer.

According to WHO, among new tuberculosis incidences, an estimated 4.1% have multidrug-resistant or rifampicin-resistant tuberculosis (MDR/RR-TB). At 19%, the proportion is higher among people previously treated for tuberculosis. These might seem like negligible percentages until a deeper look is taken at the growing number of DR-TB incidences and the less-than-ideal success rate of MDR/RR-TB. For the success of the SDG UHC and UNHLM agenda to eliminate tuberculosis by 2030, it is crucial to put the community's right to newer, safer and more effective DR-TB regimen at the center of all conversations around tuberculosis.

Before recent innovations in DR-TB therapy, the conventional DR-TB treatment required more than 3,500 pills and over 85 painful, toxic injectables over a duration of up to 18 months, and sometimes longer. At less than 60% efficacy, this difficult treatment regimen with dangerous side effects cannot be the norm. The novel BPaL/BPaLM regimen, which comprises of Bedaquiline, Pretomanid, Linezolid +/- Moxifloxacin, has the potential to dramatically increase cure rates. With approximately 90% efficacy, this shorter, all oral regimen also allows broader access due to its lower cost and improves quality of life and adherence as this regimen is all-oral and significantly shorter (6-9 months) than conventional treatment regimens. BPaL/BPaLM holds promise to not only improve treatment outcomes but also experiences through the TB care cascade in groups of people with a historically difficult-to-cure illness.

The countries that have rolled out BPaL/BPaLM have seen powerful results. We have both the evidence and the WHO guidelines to support the effectiveness of this new regimen. Then, what is keeping countries, even

those with high drug resistant tuberculosis burden, from adopting this new regimen? People affected by drug resistant tuberculosis have a right to benefit from the results of scientific progress by having access to the best available regimens.

This session will focus on the clinical trials and country roll outs of BPaL/BPaLM, the activists pushing for the adoption of this new regimen and the perspective of people affected by TB on the issue.

### BPaL/BPaLM trials and their subsequent roll-out in several countries

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### BPaL roll-out in Indonesia

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### Working with a multi-country consortium to accelerate BPaL uptake

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### Communities' right to newer, safer, more effective regimens for drug-resistant TB

R Maheshwari,<sup>1</sup> <sup>1</sup>Global Coalition of TB Advocates, India.  
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### Community perspective on the shorter drug-resistant TB regimen

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## CC-02 Establishing community-centred models for integrated service delivery in rural and peri-urban Sindh, Pakistan

Chair: Uzma Khan, IRD Global, Montreal, Canada  
 Chair: Beatrice Kirubi, Stop TB Partnership, Sweden

The objective of this session is to highlight our experiences in utilizing the Community Action Groups (CAGs) model that places communities at the center of health delivery projects from design to implementation of TB activities in Pakistan. As part of the endTB clinical trials (<https://endtb.org/clinical-trial>), IRD piloted an innovative approach to foster community ownership in research in underserved areas of Sindh, Pakistan. We established CAGs, groups of volunteers from affected communities, including TB survivors, caregivers, local advocates, and trusted health providers. CAGs help empower communities with limited resources and motivate them toward active participation in decision-making. Three CAGs are presently functional and independently conduct awareness-raising and mobilize communities towards camps and service referrals. Below we outline our proposed presentations:

The opening presentation will discuss the CAG intervention as a novel approach toward community engagement in research. CAGs have proved to be an effective strategy in providing recommendations on various components of the endTB clinical trials, such as consent forms, trial procedures, and process flows. These recommendations aim to incorporate a community perspective to advance person-centered care and practices in TB research.

The presentation will also share insights gathered from community members and CAGs, revealing a lack of knowledge and expertise in TB management among local health providers. Additionally, the presentation will highlight community perspectives on how this leads to an adverse impact on health, creates misconceptions surrounding TB, and prevents women from accessing health.

The second presentation will demonstrate the expansion of our community-centered model to rural and peri-urban districts of Pakistan through an “Integrated Service Delivery” (ISD) project. We will share early findings from community insights focusing on barriers to health-seeking behavior, gender-prohibitive pathways, and the associated financial burden to the community.

We will discuss how these findings help develop care delivery models to enhance their adaptability to diverse and underrepresented communities.

We will also highlight the use of innovative art-based strategies to foster an interactive and comprehensive understanding of health-related topics within communities, emphasizing the importance of dispelling myths and reducing stigma. This includes the implementation of Theater of the Oppressed (TOs) to simulate real-life scenarios and encourage community members to delve

deeper into discussed topics, such as the diagnosis of TB, HCV, Covid-19, and common mental health conditions.

Finally, we will delve into capacity-building within existing local community-based organizations (CBO) to establish referral pathways and support networks for communities affected by chronic diseases in remote, rural areas of Pakistan. We will share the engagement process and progress made related to the selection of CBOs, their training, and oversight highlighting the effectiveness of this strategy in identification, referral linkages, and disease management.

Furthermore, we will explore how leveraging local resources provides a unique advantage by capitalizing on existing trust to cultivate self-sustained referral and support networks within under-served communities.

This approach aims to provide specific examples of gaps in identifying common mental health conditions in communities and identify potential short- and long-term health benefits using innovative approaches that include lay community members and mobile and tele-health-based counseling.

### Community action groups: Empowering communities for person-centred TB research and beyond

A Aftab,<sup>1</sup> IRD Global, Pakistan.  
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### Leveraging community-led insights and art-based strategies to enhance healthcare delivery models

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### Strengthening communities from within: A community-centred approach to effective TB management, mental health and other comorbid conditions

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### **CC-03 Think TB: Using design thinking as a framework to develop community-engaged campaigns**

Chair: Helene-Mari van der Westhuizen, TB Proof & Global Health Security Consortium, United Kingdom

**Background:** TB Proof's mission is to combine stories and science to make the world TB Proof. We involve communities affected by tuberculosis (TB) and using the latest research, we advocate for high quality TB prevention and care.

We engage communities affected by TB to ensure that interventions are sensitive to local needs, and tailored to specific populations.

**Objective:** To share lessons learned from our experience of co-designing a TB awareness campaign and increasing accountability for TB policy implementation in partnership with a local community in Cape Town, South Africa.

**Approach:** Design thinking is an iterative problem-solving approach that emphasises empathy, collaboration, and creativity to generate innovative solutions. It involves understanding user needs, prototyping ideas, and testing and refining solutions based on user feedback to address complex problems effectively. In this workshop community members were engaged to identify the best approach and messaging to engage the youth in awareness around TB. Lessons learned from this workshop were augmented by findings from 20 interviews with policy makers, health workers, community leaders and community members to inform TB policy implementation priorities.

**Results:** A total of 26 community members, including teachers, activists, and health workers, participated in the design thinking workshop. Participants were grouped to develop a persona that will represent the youth of today. The participants developed ideas for a TB awareness event that focussed around sports and artistic activities. This was used by TB Proof in delivering an event focussed on the youth at a primary school situated in a high prevalence TB community. It included soccer competitions, access to TB testing, health talks and youth advocates and was delivered with local and provincial stakeholders as part of a longitudinal Think TB campaign.

Community interviews were valuable to build consensus on TB priorities, resulting in direct engagement with policymakers through a TB advocacy letter sent to the Minister of Health.

**Lessons Learned:** Design thinking provided a good framework to think together about building an engaging campaign - its emphasis on making sure everyone participates proved particularly valuable. Although the aim of design thinking is to engage communities, this was also an opportunity for the participants to gain knowledge on design thinking and use the skill within

their own work environment. Engaging with a community on a specific challenge is not a once-off event. An iterative approach should be taken to allow for learning to take place. Selection of participants is an important factor that contributes to the success of design thinking. It was noted that certain members of the community were more difficult to approach in the workshop, e.g. school-going children and youth leaders, and could have strengthened the session.

**Conclusion:** Design thinking has proven to be an effective approach in engaging communities as it fosters a deep understanding of their needs, challenges, and aspirations. By involving community members in the design process we were able to host a successful World TB Day event focussed on creating awareness about TB in the youth, and facilitate new collaborations for sustained policy advocacy.

### **Turning empathy, creativity and ideas into TB stories that matter to people through design-thinking workshops**

P Tisile,<sup>1</sup> TB Proof, South Africa.  
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### **TB awareness in the community and the Think TB Campaign: think TB, know TB and end TB**

G Makanda,<sup>1</sup> TB Proof, South Africa.  
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### **Findings from multi-stakeholder interviews to inform TB priorities and strengthen accountability**

R Nathavitharana,<sup>1</sup> Harvard Medical School and TB Proof, Boston, United States.  
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## CC-04 Advancing rights-based and gender-sensitive TB responses in Francophone Africa through Challenge Facility for civil Society

Chair: Viorel Soltan, Stop TB Partnership, Geneva, Switzerland

At a global level there are clear targets and commitments for a rights based and gender sensitive TB response. Tools have been developed, including the TB CRG Assessment, TB CRG Action Planning Guidance, TB Stigma Assessment, TB Community Led Monitoring Framework and the TB Legal Environment and Human Rights Scorecard.

These have been implemented in over 20 countries and there have also been peer reviewed publications pertaining to relevant finding (e.g. <https://www.hhrjournal.org/2021/12/building-the-evidence-for-a-rights-based-people-centered-gender-transformative-tuberculosis-response-an-analysis-of-the-stop-tb-partnership-community-rights-and-gender-tuberculosis-assessment/>).

The Stop TB Partnership Challenge Facility for Civil Society is the leading mechanism to support communities to partner with National TB Programs to implement these tools and to operationalise human rights and gender in TB responses.

This session will share the experience of adapting, implementing and operationalising TB CRG tools and programmatic interventions in francophone africa countries - including DR Congo, Cameroon, Ivory Coast, Benin, Burkina Faso amongst others supported by Challenge Facility for Civil Society.

### Community-led TB monitoring in DR Congo

M Lunga,<sup>1</sup> <sup>1</sup>Club des Amis Damien, Kinshasa, Congo (Democratic Republic).  
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### Community, human rights and gender and TB in Burkina Faso

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### Community, human rights and gender and TB in Francophone Africa

B Kampoer,<sup>1</sup> <sup>1</sup>DRAF TB, Yaounde, Cameroon.  
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## CC-05 The power of storytelling in TB care

Chair: Blessina Kumar, Global Coalition of TB Advocates, India

Taking from SDG, UHC and UNHLM agenda to eliminate TB by 2030, it is crucial to empower communities and ensure meaningful community engagement to end TB, the world's greatest infectious killer.

However, to date, the response to TB has been largely medical; those with TB and their families have had little or no part to play in the fight against TB. Their potential role as powerful advocates, with the ability to improve public understanding of the disease, support those affected, and to destigmatize the disease has remained grossly underutilized. At large, the TB response carpets the lived experiences of TB survivors, systematically choosing to leave an essential and ready resource untapped.

It is all too common for TB survivors to feel alone and isolated, even after defeating this deadly disease. For many, hearing the stories of other survivors, and sharing their own, plays a vital role in their recovery from the trauma caused by their journey through the TB care cascade. By giving TB survivors space to share their stories, we can create safe spaces for people to confront their loss and trauma, and hopefully live better lives after recovering from TB. The sharing of these stories can also serve as important lessons for people with TB and those affected by this deadly disease.

We at the GCTA remain committed to empowering communities across the globe to sit on the same tables as all other stakeholders and make their voices heard. The lived experiences of TB matter and it is crucial that communities are meaningfully engaged to ensure a people-centred rights-based approach to TB. To further this, the GCTA has hosted a string of trainings across the globe with affected community members.

Till recently, with every subsequent training we heard the communities list stigma as one of the top barriers to accessing care and treatment. However, due to a highly medicalized response to TB, community voices were rarely heard. Stigma, while acknowledged as a great barrier to accessing TB care and treatment, remains largely unaddressed. This needs to change. The Community Connect space at the Union Conference is an ideal platform for TB survivors to share their stories. This needs to be done repeatedly and with gusto, so that these stories reach the ears of all involved stakeholders, and we buckle down to ensure a stigma and discrimination free competent TB care for all at all levels. Shame dies when stories are told in safe spaces.

With this background, the GCTA proposes the community connect session - The Power of Storytelling. The session will have five speakers come in from different walks of life to present their journey with TB.

### **Nandita's experience of the TB care cascade in India and her subsequent role as a TB advocate**

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### **Caroline's experience of the TB care cascade in Kenya and her work involving social media as a young TB advocate**

C Mrubu,<sup>1</sup> <sup>1</sup>London School of Hygiene & Tropical Medicine, Kenya.  
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### **Paran's experience of the TB care cascade in Indonesia and her extensive work to end TB since her cure**

P Sarimita,<sup>1</sup> <sup>1</sup>PETA, Indonesia.  
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### **Oxana's experience of the TB care cascade in Moldova and her subsequent work in engaging the community in TB research and development**

O Rucşineanu,<sup>1</sup> <sup>1</sup>SMIT, Moldova.  
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### **Olya's experience of the TB care cascade in Ukraine and her passionate work as a TB advocate since her cure**

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### **CC-06 Going beyond the anecdotal: Measuring TB stigma**

Chair: Vesper Boateng Fosu, Ghana National TB Voice Network, Ghana

Chair: Hyeyoung Lim, The Global Fund for AIDS Tuberculosis and Malaria, Geneva, Switzerland

Since the launch of the TB Stigma Measurement tool by the Stop TB Partnership in 2019, the Global Fund has supported the

implementation of the TB Stigma Measurement in a number of countries, across the regions. However, there has not been a forum where the outcomes were shared, lessons learnt were discussed and the solutions have been strategized using the concrete programmatic response to address human rights and gender-related barriers. Through this session, the Global Fund and country partners from Ghana, Nigeria and Bangladesh will discuss the experiences in implementing TB Stigma Assessments in different country contexts, lessons learnt and how best to address still pervasive stigma and discrimination in the context of TB through gender-responsive and transformative human rights programming. As part of its efforts to address stigma and discrimination in the context of TB, the Global Fund has included its Performance Framework, Outcome indicators related to TB Stigma to measure over the time, the impact of the human rights response on reducing TB stigma. The session will also draw attention on using concrete indicators to measure impact on human rights programming.

### **Drivers of stigma in TB care and case detection: the Ghanaian context**

G Mensah,<sup>1</sup> <sup>1</sup>Ghana National TB Voice Network, Accra, Ghana.  
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### **Ghana's TB Stigma Index Study: Outcome, lessons and key take aways**

J Amoah\_Larbi,<sup>1</sup> <sup>1</sup>Ghana National TB Voice Network, Accra, Ghana.  
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### **Community, rights and gender response to TB stigma and discrimination in Bangladesh**

S Ahmed,<sup>1</sup> <sup>1</sup>ICDDR, B (Dhaka, Bangladesh), Dhaka, Bangladesh.  
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### **Outcomes and lessons learnt from the TB stigma assessment in Nigeria**

O Chijioke-Akaniro,<sup>1</sup> <sup>1</sup>National tuberculosis Programme, Nigeria, Abuja, Nigeria.  
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## COMMUNITY CONNECT SESSIONS: THURSDAY 16 NOVEMBER 2023

### CC-07 An 'always on' approach to pandemic preparedness – building an advocacy case for dual-use global health infrastructure

Chair: Helene-Mari van der Westhuizen, TB Proof & Global Health Security Consortium, United Kingdom

**Background:** The COVID-19 pandemic had a devastating impact on lives and livelihoods, and despite this being a recent global experience, political attention is shifting away from pandemic preparedness as topic and funding priority. There is consensus that better integration between responding to health emergencies and efforts to improve routine health care services is needed.

**Objective:** To share lessons learnt from collaborating on an 'Always on' advocacy campaign that argues for dual-use global health infrastructure that can strengthen routine care and pandemic preparedness.

**Approach:** We developed 'Always on' to be the opposite of a stop-start approach to pandemic response – where infrastructure is kept in use between outbreaks. We identified areas that have dual benefit and can be hardwired into delivery systems and processes so that the solution is 'Always on'.

**Results:** We engaged global health opinion leaders, civil society representatives, political leaders, industry representatives and academics in a two-day Policy Summit that was convened by the Rhodes Trust. As deliverable from the Summit, the Global Health Security Consortium developed 'Always on' as an approach and applied it to different use cases, including pathogen surveillance, multi-disease adult vaccination infrastructure and clinical research infrastructure. Modelling by Airfinity showed how adult vaccination infrastructure that was already in use prior to a pandemic, would make a significant contribution to facilitating faster access to novel vaccines and strengthen equitable access. The media were key partners, both in discussing the importance of building trust in pandemic response policies and in engaging a wider audience.

**Lessons Learnt:** Through the proceedings of the Policy Summit, the following were identified as key directions for progress:

1. Strengthening pathogen surveillance and ensuring the widespread use of genomic surveillance is essential to combat existing and future outbreaks of infectious diseases. Important enablers for 'always on' pathogen surveillance are increased global genomic sequencing capacity, the creation of end-to-end laboratory and sur-

veillance systems alongside bioinformatic interpretation of meta data and phenotypic, clinical and epidemiological characterisation.

2. Clinical research was central to the global response to Covid-19 with rapid trial delivery resulting in the fastest development, regulatory approval and rollout of vaccines in history – which vastly outpaces the progress made on Tuberculosis vaccines. Research capacity for other infectious diseases positioned many countries to contribute to critical research for the COVID-19 pandemic, yet more needs to be done to have robust clinical research infrastructure across low and middle-income country contexts.

3. Adult vaccination infrastructure was needed to deliver novel vaccines at scale, and yet many of the innovations in vaccine delivery are being dismantled. By better utilising currently available effective adult vaccines and injectable therapies, we can develop an adult vaccination schedule that would keep this infrastructure in use and ready to roll-out novel vaccines, such as for TB, at scale.

**Conclusion:** Advocacy campaigns will play an important role to help maintain political focus on broader health priorities and leveraging investments in strengthening health systems. Through identifying synergies between a pandemic response and improving routine clinical care, the potential impact of global health interventions could be further amplified.

### An overview of the 'always on' approach to pandemic preparedness

H van der Westhuizen,<sup>1</sup> TB Proof & Global Health Security Consortium, United Kingdom.  
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### The role of civil society networks in maintaining interest in pandemic preparedness policy

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### Applying the 'always on' approach to adult TB vaccination infrastructure

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### Shared learning between advocacy campaigns for TB and COVID-19

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## **CC-08 The 2023 Roadmap towards ending TB in children and adolescents - the critical role of community and civil society organizations in reducing the policy - practice gap**

Chair: Evaline Kibuchi, Member of the WHO Civil Society Task Force, Kenya

Chair: Ben Marais, University of Sydney, Sydney, Australia

Over the last two decades, we have gained a better understanding of the burden of TB in children and adolescents as well as of their unique needs. WHO has issued evidence-based policy recommendations and implementation guidance since 2006, stakeholders exchange experiences in the Child and Adolescent TB Working Group (CAWG), child-friendly formulations of first- and second-line anti-TB drugs have become available, donors are providing support for the roll out of child- and adolescent-friendly services and global targets were included in the Political Declaration of the 2018 UN high-level meeting on TB.

There have also been many advocacy efforts to raise awareness about TB in children and adolescents including the 2011 Call to Action, World TB Day events focused on TB in children and adolescents, the 2013 Roadmap towards zero TB deaths in children and adolescents, the 2015 renewed Call to Action, and the 2018 Roadmap towards ending TB in children and adolescents. Despite these efforts, gaps still remain in translating the policy recommendations into action, in particular at primary care level. This means that many children and adolescents do not benefit from novel tools and approaches to TB prevention, diagnosis, treatment and care. In fact, based on data submitted for the Global Tuberculosis Report 2022, the world is far from reaching the global TB targets for children and adolescents and this situation was aggravated by the Covid-19 pandemic which disproportionately affected them.

In November 2023, WHO and partners united in the CAWG, including the WHO Civil Society Task Force (CSTF) for TB, will release the 2023 version of the roadmap in line with the Political Declaration of the 2023 UN high-level meeting on TB. Building on lessons learned from implementation of the previous editions and on the 2022 WHO policy guidance on the management of TB in children and adolescents, the roadmap will provide up-to-date key actions to urgently address the persistent policy-practice gaps and also draw attention to the need to improve access to TB care for pregnant and lactating women given their higher risk of developing TB.

The purpose of this session is to review and discuss the new features of the 2023 Roadmap and the critical role that affected communities, community leaders and civil society organizations can play to support the implemen-

tation of the key actions towards successful achievement of the key milestones. Proposed speakers include an adolescent TB survivor, representatives from the WHO CSTF and Child and Adolescent TB Working Group, as well as from community organizations in Mozambique and Kenya. Speakers will highlight the role of young people in advocating for TB, how the Roadmap can be used for advocacy in a high TB burden country, and how community and civil society organisations can strengthen accountability in this area.

The session will be coordinated by the WHO and the Elisabeth Glaser Pediatric AIDS Foundation and chaired by representatives from the Child and Adolescent TB Working Group and WHO CSTF on TB.

### **Experiences of an adolescent affected by TB – the role of young people in advocating for TB services**

C Goslett,<sup>1</sup> <sup>1</sup>Desmond Tutu TB Centre, Stellenbosch University, Cape Town, South Africa.  
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### **Applicability of the roadmap for TB-related advocacy in a high TB burden country**

B Kumar,<sup>1</sup> <sup>1</sup>Global Coalition of TB Advocates, India.  
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### **Community-led monitoring of the implementation of TB interventions in children and adolescents in Mozambique**

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### **Strengthening accountability in addressing TB in children and adolescents: Experience from Kenya**

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### **Strengthening community engagement to reach TB targets for children and adolescents: experience from DR Congo**

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## **CC-09 Reflecting and learning from community, academic and health professional engagement with the UN High-Level Meeting on TB for actionable next steps**

Chair: Lucica Ditiu, Stop TB Partnership, Switzerland  
 Chair: Kerry Millington, Liverpool School of Tropical Medicine, United Kingdom  
 Chair: Robyn Waite, TB Alliance, Canada

Members of the global tuberculosis (TB) community, including academics, healthcare workers, survivors, community and civil society representatives, private sector representatives and parliamentarians came together for the multistakeholder hearings on TB, Pandemic Prevention, Preparedness, and Response (PPPR) and Universal Health Coverage (UHC) at the United Nations (UN) headquarters in New York in May 2023. Together, they worked to influence negotiations of the Political Declarations of these three intersecting global health challenges ratified in September 2023. The high-level meeting process provided an essential platform for stakeholders to voice their demands, drawing on their experience, expertise, knowledge and skills.

The session will open critically reflecting on coming together as TB communities at the national, regional, and global level through the UK Academics and Professionals to end TB (UKAPT) network, civil society in the EECA region and the #2023TBHLM Affected Communities and Civil Society Coordination Hub. We will then hear from the academic and health professional experiences of engaging with this year's UNHLM process to call for change and explore how global coordination can help us mobilise around key moments, share best practice and make the most of the academic and healthcare worker voice.

The experience of Ukraine in preparing for the UNHLM on TB from the perspective of the community and civil society will also be shared. It is crucial post-UNHLM on TB, to identify key next steps for implementing commitments from the Political Declaration at country level.

Here, we emphasise the participatory approaches for the development of aligned country-level indicators and the necessary implementation of the Multisectoral Accountability Framework to end TB (MAF-TB) to hold these commitments to account. An interactive workshop will then provide a platform for community representatives, researchers, health professionals, policymakers, and others to engage in a comprehensive dialogue to exchange experiences, insights and learnings and collectively develop actionable next steps post the UNHLM on TB.

## **The coming together as TB communities at the national, regional and global levels: Reflections and learnings**

P Aiyer,<sup>1</sup> <sup>1</sup>TB HLM 2023 Affected Communities & Civil Society Coordination Hub, GFAN, India.  
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## **Using our voice to call for change – an academic and health professional's perspective**

J Potter,<sup>1</sup> <sup>1</sup>UK Academics & Professionals to end TB (UKAPT), United Kingdom.  
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## **The experience of Ukraine in preparing for the UN High-Level Meeting on TB from the perspective of the civil society and community**

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## **The development of national indicators in line with global goals and commitments as a condition for the implementation of the provisions of the UN Political Declaration on TB**

V Soltan,<sup>1</sup> <sup>1</sup>Stop TB Partnership, Geneva, Switzerland.  
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## **Multisectoral accountability framework for fulfilling commitments and achieving the goals of the UN Political Declaration on TB**

Y Kalancha,<sup>1</sup> <sup>1</sup>TB Europe Coalition, Ukraine.  
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## **Question and Answer**

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## CC-10 Experiences in engaging key and vulnerable TB populations in pandemic governance

Chair: Austin Obiefuna, University of Nigeria, Ghana  
Chair: R.D. Marte, University of Philippines, Thailand

COVID-19 has had a catastrophic impact on the most vulnerable communities around the world and threatened decades of progress in the fight against HIV, TB and malaria (HTM) and has further weakened health systems. COVID19 accentuated issues of equity across and within countries are critical determinants in access to services – with those already marginalised and vulnerable bearing the greatest burden of both the direct and indirect consequences of health threats.

In implementing the Global Plan to end TB (2023 – 2030) Stop TB Partnership (STP) prioritizes the strengthening of community TB interventions that overcome barriers to accessing quality TB services, increase community and civil society engagement and improve the impact of national TB programs at all levels. People-centred community, human rights and gender TB responses are vital towards eliminating the disease by 2030 – a commitment made by world leaders in the Political Declaration at the United Nations High-Level Meeting on Tuberculosis in 2018, and in line with the United Nations (UN) Sustainable Development Goals (SDGs).

The community engagement and leadership in pandemic governance (CELG) actions being implemented by two regional TB networks, ACT Africa and ACT Asia Pacific aims at supporting responsive health-related needs of the most neglected populations whose voices are most left out.

The main objective for the CELG initiative is to strengthen the inclusion, coordination, and engagement of TB key and vulnerable populations in the COVID19 and pandemic emergency responses. This includes identifying, testing and documenting engagement strategies, approaches and processes to enable TB networks to influence COVID19 and PPR decision-making.

The two networks would like to share the experiences they have gathered in working with the identified KVP and how they are engaging on national Pandemic Preparedness Response Platforms.

## COVID-19 response: Lessons learnt from community engagement in the ACT A Platform

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## Building agile community systems to prepare for pandemics: Community engagement in building resilient and sustainable healthcare systems

O Mumba,<sup>1</sup> <sup>1</sup>The Global Fund for AIDS Tuberculosis and Malaria, Switzerland.  
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## Community engagement and leadership in pandemic governance: Assessment results from the CELG Project, country example one

C Phorng,<sup>1</sup> <sup>1</sup>Khmer HIV/AIDS NGO Alliance (KHANA), Phnom Penh, Cambodia.  
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## Community engagement and leadership in pandemic governance: Assessment results from the CELG Project, country example two

B Kampoer,<sup>1</sup> <sup>1</sup>DRAF TB, Yaounde, Cameroon.  
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## Defining community engagement in pandemic prevention, preparedness and response: Co-creation in pandemic planning, implementation and monitoring

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## **CC-11 Community-led “test and treat” advocacy and community engagement for pandemics: lessons from India and Zimbabwe**

Chair: Karishma Saran, FIND, Switzerland

Chair: Danielle Ferris, Unitaid, Switzerland

The Diagnostics and Therapeutics Pillars of the Access to COVID-19 Tools Accelerator (ACT-Accelerator), led by FIND and Unitaid respectively (along with the Global Fund co-leading both pillars, as well as Wellcome in the Therapeutics Pillar, and with leadership and strong support from WHO), worked with over 50 global health partners across the value chain to ensure equitable access to COVID-19 diagnostic and therapeutic technologies and tools.

Diagnostics and therapeutics are essential tools to combat all diseases, especially those of pandemic potential. Modelling efforts have shown that when diagnosis is linked to timely treatment, the proportion of deaths averted increases with increasing testing rates.

Nevertheless, the alarming decline in reported COVID-19 testing rates continued throughout the COVID-19 pandemic, more so in low and middle-income countries (LMICs). Many high-risk population groups affected by tuberculosis, HIV, and other high-burden diseases in LMICs were also unable to access essential lifesaving tests and treatments in the early and mid-phases of the pandemic response.

Without sufficient use of diagnostic tools and treatments, the world risks undoing the hard-earned public health gains achieved. Therefore, ensuring equitable and affordable access to tests and treatments, and generating demand for these products, is critical to pandemic preparedness, prevention and response.

To address the challenges of COVID-19 testing and treatment, in mid-2021, the ACT-Accelerator Diagnostics Pillar identified the need to engage directly with in-country civil society and community-based organizations to drive demand generation for COVID-19 “test and treat” approaches, which led to FIND and Unitaid co-launching the COVID-19 Test and Treat Advocacy Programme in June 2022. This resulted in 21 civil society and community-based partners leading advocacy strategies in 19 countries across Africa, Asia, South America and the Middle East.

In this session, three of those civil society organizations will share their experiences, challenges and lessons learned developing and implementing test and treat advocacy strategies for COVID-19 over the last year in India and Zimbabwe. They will also reflect on how they are leveraging the insights and experiences they have gained so far from COVID-19 for other lung-related health issues like TB and HIV/AIDS.

**Session format: A live fireside chat between session co-chairs and three civil society organizations that are leading advocacy and community engagement for COVID-19 and other lung-related diseases like TB and HIV/AIDS.**

### **Community-led “test and treat” advocacy and community engagement for pandemics: lessons from India**

C Mehra,<sup>1</sup> <sup>1</sup>Survivors Against TB, India.

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### **Community-led “test and treat” advocacy and community engagement for pandemics: lessons from India**

V Panibatla,<sup>1</sup> <sup>1</sup>TB Alert India, Hyderabad, India.

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### **Community-led “test and treat” advocacy and community engagement for pandemics: lessons from Zimbabwe**

T Kujinga,<sup>1</sup> <sup>1</sup>Pan-African Treatment Access Movement (PATAM), Zimbabwe.

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## CC-12 Innovative TB community service delivery during the COVID-19 pandemic: Best practices and lessons learnt from Cambodia, India, Indonesia and Kenya

Chair: Eluid Wandalo, Global Fund, Ukraine  
 Chair: Blessina Kumar, Global Coalition of TB Advocates, India

The COVID-19 pandemic caused an unprecedented diversion of public health resources away from other disease areas. TB referrals decreased by 59% in the second and third quarters of 2020 compared with the same period in 2019,[1] and in 2021, these effects manifested in tuberculosis mortality increasing for the first time in a decade.[2] Community health workers (CHWs, sometimes known as TB champions, lay counsellors, cadres among other terms) played a crucial role in mitigating pandemic-related effects unto TB service delivery. These workers in many contexts are part of the public health workforce,[3] and CHW-led interventions have been acknowledged to contributing to improving TB treatment outcomes, psychosocial support to people affected by TB and families affected by TB, supporting household contact tracing, and facilitating access to TB services, including referral of persons with presumptive TB.[4] We conducted a qualitative study to document the community service delivery mechanisms in four high-burden countries: Cambodia, India, Indonesia, and Kenya, as well as challenges faced, human rights and gender barriers faced during the COVID-19 pandemic, and proposals for the way forward in reversing COVID-related effects on TB mortality, morbidity, and on the livelihoods of TB communities. We developed tools for information gathering which were shared with partners in all 4 countries Cambodia, India Indonesia. Data were collected through focus group discussions, in-depth discussion, key informant interviews with community health workers also known as TB champions and other stakeholders. These insights were audio-recorded and auto transcribed by Otter.ai, except for Cambodia where interviews were conducted in Khmer and manually translated by KHANA staff members. From transcriptions, responses were organised thematically into 4 major themes and further into sub themes.

- The Pandemic Begins – Multiplying Challenges in TB Detection and Treatment
- Best Practices in TB Community Service Delivery During COVID-19
- Value Add of Community-Led Interventions for TB Care
- Human Rights and Gender Barriers faced by TB Communities

This session will include presentations and findings including recommendations from the study and deliberations from different stakeholders on how community-led innovations were fundamental to sustaining the

engagement of TB communities with care services during the COVID-19 pandemic, and that without their interventions, TB detection may have stopped altogether as health systems prioritised the COVID-19 response. This will be followed by a discussion with participants on ways to expedite progress on TB elimination as countries transition out of acute COVID-19.

1. Global Fund, 'The impact of COVID-19 on HIV, TB and malaria services and systems for health' (13 April 2021)
2. World Health Organization, 'Global Tuberculosis Report 2021' (14 October 2021)
3. Public Health England, 'Community champions: A rapid scoping review of community champion approaches for the pandemic response and recovery' (August 2021)
4. World Health Organization, 'Health policy and system support to optimize community health worker programmes for HIV, TB and malaria services: an evidence guide' (2020)

### Innovative TB community service delivery during the COVID-19 pandemic: Overview and process

B Kumar,<sup>1</sup> <sup>1</sup>Global Coalition of TB Advocates, India.  
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### National TB programme perspectives on TB service delivery during the pandemic: value and contribution of cadres to the Indonesian health system

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### Healthcare workers closing the service delivery gap during the pandemic: the Indonesian experience

H Diatmo,<sup>1</sup> <sup>1</sup>Stop TB Partnership Indonesia, Jakarta, Indonesia.  
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### Contribution of TB Champions to TB care delivery during the pandemic

S Shikoli,<sup>1</sup> <sup>1</sup>Network of TB Champions Kenya, Pamoja TB Group, Kenya.  
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### TB service delivery during the pandemic: Lesson learnt and the way forward

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## CC-13 Leveraging lessons from the COVID-19 pandemic response for TB case-finding in Nigeria

Chair: Rupert Eneogu, USAID, Nicaragua

The COVID-19 pandemic resulted in very significant challenges to the health systems of countries with severe disruptions in health service delivery, including TB services. In Nigeria, there was a resulting decline in attendance of health facilities in the immediate aftermath of the outbreak, and with the availability of vaccines, the country experienced varying levels of hesitancy. This slow uptake of vaccines was fueled by mistrust of the Government, concerns about vaccine safety and low risk perception for COVID-19 infection.

With the resulting decline in hospital attendance, disease programs were forced to innovate on ways of delivering much-needed health services to the populace in their communities. It also became imperative to understand the underlying perceptions of the public regarding vaccines and the lessons were extended to other disease programs.

This session will provide some insights into how the Tuberculosis program in Nigeria benefitted from leveraging on lessons from COVID-19 pandemic response to innovate and re-strategize program implementation to achieve results. With support from the United States Agency for International Development (USAID), a pilot Telephone poll for TB knowledge and risk perception was conducted, leveraging on a commissioned COVID-19 Telephone poll to assess public perception around vaccine acceptance.

In addition, there was a significant shift in focus and targeting of TB case-finding interventions from the facilities to the communities, adopting a patient-centered integrated service delivery approach. This involved integrated community health outreaches with social behavior change communication to drive the uptake of COVID-19 vaccination, TB service delivery, and other adjunct health services in the community.

The result was a remarkable increase in the uptake of COVID-19 vaccinations and TB screening services leading to the diagnosis and treatment of missing TB patients. Integration of health service delivery maximizes access, acceptance, and quality of care that is truly patient-centered.

## Lessons learnt from the COVID-19 pandemic: Generating public insight through polling

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## Improving COVID-19 vaccine uptake through integrated social behaviour change messaging and community outreach services in Nigeria

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## Driving community access and uptake of COVID vaccines and TB services through an innovative integrated health service delivery approach

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## COMMUNITY CONNECT SESSIONS: FRIDAY 17 NOVEMBER 2023

### CC-14 From awareness to action: The role of TB survivor organisations in overcoming barriers to TB services and promoting human rights in Indonesia

Chair: Yuniar Ika Fajarini, Global Fund  
Principal Recipient Tuberculosis Community-Based  
Intervention in Indonesia, PR Konsorsium Komunitas  
Penabulu-STPI, Indonesia

Chair: Dwi Aris Subakti, PR Consortium  
Penabulu-Stop TB Partnership Indonesia (STPI),  
Indonesia

Tuberculosis (TB) remains a significant public health concern. Diagnostic tests and medications alone are insufficient to eradicate TB, it needs a supportive environment that avoids social exclusion, access to accurate information, and atmosphere without stigma and discrimination.

Therefore, it is essential to ensure that TB communities and grassroots are at the heart of the TB response. This perspective will ensure that the needs of people with TB are fully comprehended, represented, prioritized, and addressed as stated in United Nations High-Level Meeting on the Fight Against Tuberculosis. Since 2015, there has been significant growth TB Survivor Community movement in Indonesia. In 2017, the TB survivor organizations from 6 provinces united to establish the Association of Tuberculosis Patients' Organization (POP TB) Indonesia.

Currently, POP TB consists of 22 TB Survivors organization in 16 Provinces in Indonesia and has become a thematic sub-recipient for removing human rights and gender-related barriers to TB Services under Konsorsium Komunitas Penabulu-STPI as a Principal Recipient from the Global Fund which works in 190 districts in 30 Provinces in Indonesia in 2021-2023.

As a Thematic Sub-Recipient of the Global Fund for Removing Human Rights and gender-related barriers to TB Services, POP TB employs innovative and community-based interventions with all spectrums of meaningful community engagement in the TB response.

Firstly, POP TB focused on raising awareness about TB among the general population, policymakers, and healthcare providers through campaign and advocacy efforts.

Secondly, POP TB establishes community-based monitoring feedback to strengthen the service quality of the TB Program known as Laportbc.id.

Thirdly, POP TB creates hotline support for and by

people with TB with aimed at promoting well-being and human rights through the WhatsApp application. Furthermore, to monitor and respond to the negative campaign that potentially creates stigma and discrimination against people with TB and related stakeholders, POP TB establishes the TB Paralegal group and provides training and collaboration with the Legal Aid Foundation.

The interventions carried out by POP TB have had a significant impact on raising awareness and providing support for TB in Indonesia. Through a comprehensive campaign, POP TB has successfully conducted TB awareness programs across more than 100 radio networks, media briefings, and public campaigns. They have distributed information banners advocating for community support for individuals with TB, reaching over 150 healthcare facilities and Programmatic Management of Drug-Resistant TB (PMDT) hospitals in 30 provinces nationwide.

Additionally, as of April 2023, there were 153 reports from the hotline TB. Most of the respondents were male (64%) and had problems with drug side effects, followed by issues of stigma and discrimination and TB services issues.

Moreover, 34 trained paralegals have handled eight cases, providing mediation and multisectoral assistance to address TB-related challenges.

These interventions have contributed to improving awareness, access to support services, and addressing the human rights and needs of people with TB in Indonesia. These efforts have led to improved access to support services and greater recognition of the rights and needs of people with TB by people with TB.

### From awareness to action: The role of TB survivor organisations in overcoming barriers to TB services and promoting human rights in Indonesia

D Subakti,<sup>1</sup> PR Consortium Penabulu-Stop TB Partnership  
Indonesia (STPI), Indonesia.  
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### Challenges and barriers faced by TB patients in accessing services in Indonesia: Human rights implications for TB care and management

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Community-Based Intervention in Indonesia, PR  
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## How TB survivor organisations raise awareness and reduce stigma: Providing support and advocacy for TB patients through healthcare provider and government agency collaboration

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## Driving change and human rights promotion in Indonesia: Case studies of successful initiatives by TB survivor organisations and their impact on TB services

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## CC-15 Community advocates charting new paths to fund TB vaccine development

Chair: Laia Ruiz, Consultancy, Comms & Anthropology, Spain  
Chair: Priyanka Aiyer, TB HLM 2023 Affected Communities & Civil Society Coordination Hub, GFAN, India

We need new, effective, and accessible TB vaccines to reach the global goals to End TB by 2030. Yet, while the need for new TB vaccines couldn't be clearer, progress in TB vaccine research and development (R&D) is hindered by chronic underfunding and insufficient political action. New TB vaccines are within reach this decade but only with significantly scaled-up and joint investments.

Despite commitments made at the UN High Level Meeting (HLM) on TB in 2018 to invest US\$2 billion annually in TB R&D, funding for TB vaccine development has never exceeded US\$121 million per year, against an annual target of US\$613 million in the Global Plan to End TB 2018-2022. This amounts to less than 10% of the \$1.25 billion annual investment now estimated in the Global Plan to End TB 2023-2030 to advance the pipeline.

To avoid the pitfalls of the previous five years, TB vaccine development needs new funding models, based on joint financial and political action.

A second HLM on TB was held in September 2023 with world leaders endorsing a renewed set of commitments in the Political Declaration to ensure the End of TB by 2030. Civil society and affected communities will play a critical role in holding governments accountable to their commitments to support, finance, and advance TB vaccine R&D.

As expert stakeholders, affected communities and civil society possess grassroots expertise, experience, and a deep understanding of the communities affected by TB. By ensuring their equal participation in this process, we can harness the collective wisdom necessary to drive impactful, accountable, and sustainable change in TB vaccine development.

This panel discussion will bring together civil society and community advocates to discuss the urgent need for joint, increased, sustained, and accountable investments in TB vaccine development.

This session aims to inform advocacy efforts and collaboration among researchers, policymakers, public health experts, and community and civil society representatives.

During this interactive session, panelists will outline the community's demands for TB vaccine development and highlight the importance of coordinated and innovative investments in TB vaccine R&D as necessary to end TB. Further, lessons from the successes of other vaccine initiatives will be explored, while careful attention will be paid to how we can call on our countries to do their fair share and fulfill commitments made at the HLM.

## Encouraging national governments to fulfill their responsibilities in TB vaccine development

E Kibuchi,<sup>1</sup> <sup>1</sup>Stop TB Partnership-Kenya, Kenya.  
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## Securing joint financing for TB vaccine research and development

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e-mail: spalmer@iavi.org

## Learning from the successes of other vaccine initiatives

R Limaye,<sup>1</sup> <sup>1</sup>Johns Hopkins Bloomberg School of Public Health, United States.  
e-mail: rlimaye@jhu.edu

## Driving industry engagement in TB vaccine development

R Kumar Suri,<sup>1</sup> <sup>1</sup>Developing Countries Vaccine Manufacturing Network (DCVMN), India.  
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## **CC-16 Empowerment and engagement: Strengthening TB response of communities and civil society organisations through technical support and systematic data collection**

Chair: Vlada Rabinova, TB Europe Coalition, Ukraine  
Chair: Lesya Tonkonog, TB Europe Coalition, Ukraine

Civil society organizations (CSOs) play a critical role in tackling the challenges posed by TB and advancing the global health agenda. Despite their significance, they often encounter financial constraints along with the restricted availability of resources for capacity building, which hinder their ability to fully contribute.

Therefore, the provision of technical assistance (TA) offers valuable opportunities for TB-affected communities, CSOs, and civil society to enhance their capacity and implement activities that might be underfunded from other sources. This support facilitates the effective engagement of such groups in combating TB and promoting public health on a broader scale.

The session will highlight the exceptional opportunities and outcomes associated with providing short-term TA to address urgent issues, as well as long-term TA that facilitates a comprehensive approach to program planning and outcomes.

By bringing together key stakeholders, including TB-affected community representatives, technical providers, and program implementers, the session will showcase how short-term TA enhances community involvement in the design, implementation, monitoring, and evaluation of TB programs.

Real-life examples will demonstrate how CSOs have leveraged TA to strengthen their engagement in the national response to end TB, fostering community ownership and driving sustainable progress.

Long-term TA will be demonstrated through the implementation of the Algorithm of data collection for the four new WHO Europe indicators that measure the level of engagement of communities and CSOs in the National TB response. Participants will gain a comprehensive understanding of the four new indicators, their calculation, measuring, and reporting procedures, and the responsibilities of all parties involved in the data collection process.

Valuable insights and good practices from the data collection pilot in the Eastern Europe and Central Asia region will be shared, highlighting how a unified data collection tool strengthens community engagement and accountability within the TB response.

Participants will leave the session equipped with a deeper understanding of the significant contributions of CSOs in addressing TB, the value of short-term and long-term TA in strengthening their efforts, and practical examples of how TA has enhanced community engagement and ownership.

This collective learning experience will inspire participants to explore new approaches, foster partnerships, and take decisive actions to drive progress in their respective TB elimination programs, ultimately contributing to the global goal of ending TB as a public health threat by 2030.

### **Examining the role of technical support in Azerbaijan's TB response: Transitioning from obstacles to resolutions**

P Valiyeva,<sup>1</sup> <sup>1</sup>NGO "Saglamliga Khidmat" Public Union, Azerbaijan.  
e-mail: parvana.valiyeva27@gmail.com

### **Regional collaboration and knowledge sharing: creating demand for Global Fund-related technical assistance in the WHO Eastern Europe and Central Asia Region**

I Varentsov,<sup>1</sup> <sup>1</sup>Eurasian Harm Reduction Association, Lithuania.  
e-mail: ivan@harmreductioneurasia.org

### **Overview of the four new WHO Europe indicators on community engagement included in the new TB Action Plan for the WHO European Region for 2023–2030**

G Kuchukhidze,<sup>1</sup> <sup>1</sup>WHO Regional Office for Europe, Denmark.  
e-mail: kuchukhidzeg@who.int

### **Overview of the algorithm developed for data collection for the four WHO Europe indicators to measure community and civil society organisation engagement in national TB responses**

L Tonkonog,<sup>1</sup> <sup>1</sup>TB Europe Coalition, Ukraine.  
e-mail: tonkonog@tbcoalition.eu

### **Empowering the TB community in Ukraine: Lessons learnt from short and long-term technical assistance**

O Klymenko,<sup>1</sup> <sup>1</sup>TBpeople Ukraine, Ukraine.  
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## **CC-17 Driving change, the power of community-led advocacy in shaping political contexts to end TB: experience of Action 2 partners**

Chair: Zahedul Islam, Alliance for Public Health, Ukraine, Ukraine

The session will shed light on the significance of civil society organization (CSO) participation in both the Multisectoral Accountability Framework to Accelerate Progress to End TB (MAF-TB) and the United Nations High-Level Meeting (HLM) on TB/UHC/PPPR. It will feature the experiences of Cambodia, India, Ukraine and Frontline AIDS, highlighting the pivotal role of community-led advocacy in shaping political landscapes, fostering collaboration across sectors, and advancing global efforts to combat TB.

The session's primary focus will revolve around CSO involvement in initiating and implementing the MAF-TB in various countries, as well as their participation in preparing for the UN HLM on TB.

Additionally, their contributions to shaping the text of the UNHLM Political Declaration on TB will be emphasized as crucial for ensuring a comprehensive and inclusive response to TB. CSOs play a vital role in driving policy changes and accelerating progress toward ending TB by strengthening accountability, promoting community-centered approaches, and amplifying the voices of affected communities.

The session will underscore the importance of CSO engagement in the planning, implementation, and monitoring of TB programs to ensure transparency, accountability, and effectiveness. Concrete examples from Cambodia, India, Ukraine and will illustrate how CSOs advocate for increased investments, policy reforms, and enhanced accountability mechanisms.

During the Q&A session, participating countries will actively exchange valuable insights and discuss the challenges they have encountered in their pursuit of political transformation, further enriching the dialogue.

## **Transforming UNGA 78 Political Declarations on health into action: The role of the civil society in the preparatory stages and ensuring accountability**

Z Islam,<sup>1</sup> <sup>1</sup>Alliance for Public Health, Ukraine, Ukraine.  
e-mail: zislam@aph.org.ua

## **Community partnership on the road to end TB in Cambodia: Experience from Khmer HIV/AIDS NGO Alliance (KHANA)**

C Choub Sok,<sup>1</sup> <sup>1</sup>Khmer HIV/AIDS NGO Alliance (KHANA), Phnom Penh, Cambodia.  
e-mail: csokchamreun@khana.org.kh

## **Civil society as a driving force in preparing countries for the UN High-Level Meeting on TB: the Ukraine experience**

O Tsviliy,<sup>1</sup> <sup>1</sup>Alliance for Public health, Ukraine.  
e-mail: tsvilii@aph.org.ua

## **Building on what works: The TB response in future pandemic prevention, preparedness and response efforts**

E Mac Fadden,<sup>1</sup> <sup>1</sup>Frontline AIDS, United Kingdom.  
e-mail: emacfadden@frontlineaids.org

## **Integrating transgender persons into TB testing and treatment: Community-led advocacy for political change to end TB**

A Sarkar,<sup>1</sup> <sup>1</sup>Alliance India, India.  
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## CC-18 Empowering communities in TB service delivery at the primary care level: Sharing experiences from innovative projects

Chair: Ingrid Schoeman, TB Proof, Pretoria, South Africa

Despite the tremendous efforts made by tuberculosis (TB) programs worldwide to find and treat everyone with TB, a significant number of individuals, estimated to be around 3 to 4 million, continue to lack access to TB prevention and care. Many individuals seeking TB care fall through various gaps in the care cascade. To bridge this gap in TB service delivery at the primary care level, several interventions have focused on engaging the community members as well as all service providers, including private doctors, pharmacists, and lab personnel. Such a broader engagement will make TB care services accessible and closer to the people who need it. Therefore, in this symposium, we will bring the experiences of five different organizations implementing projects that involve and train people from the communities to provide TB care services in the community in a panel discussion format.

In order to set the stage for the panel discussion, we will first briefly present the findings from a literature review (to be published in 2023) that was conducted to explore existing models involving the community and various providers to deliver TB care services such as education and awareness on TB, TB screening, sputum collection, treatment follow-up, and contact tracing. Such an approach will allow the presentation of the best evidence on this topic, combining the evidence in the literature with experiences from the field. Below, we briefly summarise the projects to be included in the symposium.

**The Komesha TB program**, funded by USAID and implemented by the Kenya Conference of Catholic Bishops, operates in high-burden TB counties in Western Kenya. It involves religious leaders, community health volunteers, and support groups, successfully raising TB awareness among 2,772 religious' leaders.

**SHDEPHA+ Kahama** implemented active case finding in Tanzania's mining communities. Peer educators and community health workers were recruited and trained to provide TB education, symptom screening, and support, addressing barriers to accessing TB and HIV services.

**REACH's Nakshatra centers** in Chennai, India, involve community volunteers called TB Nanban, trained to address patients' needs, promote adherence, and provide comprehensive treatment care solutions.

These projects highlight the significance of community engagement in TB care by effectively addressing service gaps and bolstering the fight against TB. The symposium aims to provide a platform for sharing the experiences and accomplishments of these five initiatives, emphasising the importance of empowering and involv-

ing communities in comprehensive efforts to eliminate TB. By showcasing successful strategies, the symposium seeks to inspire and promote similar initiatives that can bring TB care within reach of individuals and their communities.

### Role of the community in TB service delivery

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### The Komesha TB programme

M Macharia,<sup>1</sup> <sup>1</sup>Komesha TB, Kenya.  
e-mail: michael.macharia@tb.karp.or.ke

### Mining community in Tanzania

R Abeid,<sup>1</sup> <sup>1</sup>SHDEPHA+ Kahama, Tanzania.  
e-mail: rabiabeid@gmail.com

### Community workers as 'TB Friends' in Chennai, India

R Ananthkrishnan,<sup>1</sup> <sup>1</sup>REACH, India.  
e-mail: ramyardr.reach@gmail.com

## CC-19 Upgrading the TB diagnostics toolbox – what’s needed to ensure diagnosis for all?

Chair: David Branigan, Treatment Action Group, New York, United States

*The Chair will outline the range of TB testing tools available – from point-of-care (POC) to sequencing based technologies and the role that communities and civil society (CCS) can play in championing access to diagnostics through community sensitization and demand generation activities, as well as community-led monitoring and accountability initiatives for access to quality TB screening and diagnosis.*

Every year, millions of people with TB are not diagnosed or notified to health systems – resulting in millions of preventable deaths. We are working to stop people dying from TB, a curable disease because they couldn’t access a suitable diagnostic test to inform treatment decisions. Already-stretched TB programme efforts were greatly impacted by the COVID-19 pandemic, and access to diagnostics were significantly limited in high-burden countries, delaying initiation of life-saving treatment. Current TB tests are not generally fit-for-purpose for use in LMIC primary healthcare centres, where people with TB often first seek care, or within communities where an early diagnosis is challenging to perform. This diagnostic gap has hindered TB case-finding efforts and highlighted the need to invest in development of new tools. At FIND, we are working across the TB diagnostic spectrum including technologies needed for individuals seeking care, and those required in the community to support active case finding interventions. We are conducting research on three technology classes: third generation lipoaribomannan (LAM) tests, POC molecular diagnostics, and near-POC molecular tests, all of which could potentially bridge the gap between laboratory and community health services. A number of these technologies have made advancements as a result of investments made in COVID-19 testing.

At the other end of the spectrum, we have established the utility of emerging next-generation sequencing technologies for rapid and comprehensive molecular drug-susceptibility testing for TB. The WHO END-TB strategy calls for universal access to comprehensive drug-susceptibility testing (DST) for all persons with any form of TB. This is to ensure early detection and to determine the appropriate and effective treatment for people with TB. Most available rapid molecular tests detect a few key mutations in one or more gene targets and can predict resistance mainly to a few first-line drugs and some second line drugs. Targeted next-generation sequencing solutions offer the ability to detect resistance against all existing, new, and repurposed anti-tuberculosis drugs in a single assay; this would be a paradigm shift in the

clinical care for people with drug-resistant TB and ensure preservation of new TB drug regimens for years to come.

While we have a range of promising new tools to upgrade the diagnostic toolbox, the true potential of these tools can only be realized with the direct involvement of CCS advocates by raising awareness, generating demand, and holding governments accountable to ensure uptake of these tools at all levels of the healthcare system. This session will include representatives of the Unitaid funded DriveDx4TB and Seq&Treat grants, will highlight the value of diagnostics and explore practical ways for communities to play a greater leadership role in the TB diagnostics response.

### Upgrading the TB diagnostics toolbox – what’s needed to achieve diagnosis for all?

K. Velen,<sup>1</sup> S. Uplekar,<sup>1</sup> P. Tisile,<sup>1</sup> K. Angami,<sup>1</sup>

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## **CC-20 Researchers sharing with communities: Results from the endTB trial**

Chair: Wim Vandeveld, Global Network of People living with HIV (GNP+), Cape Town, South Africa  
Chair: Rosa Herrera, Global TB Community Advisory Board (TB CAB), Malaysia

For decades researchers have sought to shorten and improve treatment regimens for drug-resistant TB. Recent advances have shortened treatment durations from 18-24 months to 6-9 months, and further optimized regimens by replacing injections with new all-oral treatments. The endTB trial, which evaluated five 9-month regimens composed of bedaquiline and/or delamanid given in combination with pyrazinamide, moxifloxacin or levofloxacin, linezolid and/or clofazimine for multidrug-resistant TB, is poised to report results during the 54th Union World Conference on Lung Health. This Community Connect session will provide a forum for researchers involved in the endTB trial to share their results with, and respond to questions from, members of TB-affected community and civil society groups. It will offer an opportunity to discuss best practice for results dissemination and next steps for: transforming evidence into practice, potential implications for the TB treatment policy and research landscapes, and how to ensure that communities are able to access the benefits of scientific progress.

## **Efficacy and safety results from the endTB Trial and what to expect with endTB-Q**

S Patil,<sup>1</sup> <sup>1</sup>ICMR-National AIDS Research Institute, India.  
e-mail: spatil@nariindia.org

## **endTB Trial results in the community context: How these results may affect the research and policy landscape for the treatment of drug-resistant TB**

C Mitnick,<sup>1</sup> <sup>1</sup>Harvard Medical School, Boston, United States.  
e-mail: carole\_mitnick@hms.harvard.edu

## **The access landscape for the medicines that make up the endTB regimens and supporting diagnostics**

C Perrin,<sup>1</sup> <sup>1</sup>Médecins Sans Frontières, France.  
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## **The endTB Trial: Community respondent #1**

A Herna Sari,<sup>1</sup> <sup>1</sup>Global TB Community Advisory Board (TB CAB), Surabaya, Indonesia.  
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## **The endTB Trial: Community respondent #2**

D Bhattacharya,<sup>1</sup> <sup>1</sup>Survivors Against TB, India, India.  
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## COMMUNITY CONNECT SESSIONS: SATURDAY 18 NOVEMBER 2023

### CC-21 From TB survivor to TB advocate: How trials and participants can work together in disseminating findings and demanding change

Chair: Lindsay McKenna, Treatment Action Group,  
New York, United States

Chair: Bern-Thomas Nyang'wa, Médecins Sans  
Frontières, United Kingdom

Lived experience of tuberculosis (TB) disease, trial participation and what its like to take these treatments is both important and impactful when reaching future people with TB and in driving policy change. New shorter, more tolerable and effective treatments mean people with TB can have an improved quality of life, reduced financial burden and social isolation and return to family more quickly, than the previous treatments.

With a growing evidence base of recently published clinical trial results, global policy change and the acceleration of the use of improved treatment regimens, the landscape for TB and multi-drug resistant TB (MDR-TB) treatment is quickly changing.

Successful communication of these pioneering TB trial results and their real-world implications is essential to ensuring wide-spread access to treatment as well as timely and effective impact for people affected by TB.

Community engagement has been a novel component of TB clinical trials and barriers such as stigma, access to services and the acceptance of research and new regimens remain a challenge.

This session aims to highlight the importance of trial participants', TB survivors' and community stakeholders' role in trial results dissemination and advocating for progress towards global adoption of new TB treatment regimens, in varying contexts.

This collaborative session between MSF, MSF Access Campaign, Treatment Action Group, Society of Moldova against Tuberculosis (SMIT), TB Patients Association in Moldova and Clinical HIV Research Unit, brings together global perspectives from TB survivors who have participated in clinical trials, TB advocates, community representatives and clinical trial health professionals. Speakers will share their lived experience and what this has meant for them supporting others affected by TB and advocating for better treatments.

Additionally, we will present results dissemination and peer support experiences from clinical trial sites of TB-PRACTECAL; a phase II/III clinical trial which found a new all-oral, six-month treatment regimen (BPALM)

which is safer and more effective at treating MDR-TB than the standard of care. Lastly, a panel discussion will discuss the civil society-led 1/4/6x24 Campaign and WHO BPALM Accelerator Platform in this context.

Collaboration with TB survivors and community stakeholders throughout the lifecycle of a TB clinical trial is essential to planning and successfully implementing communication and engagement strategies, ensuring research priorities are relevant. The accelerated rollout of new TB treatments, increasing access and paving the way for future research requires effective communication of the evidence and advocating for change, by those with first-hand experience.'

### How involvement of participants and affected communities in trial results dissemination can support programmatic scale-up

L Menghaney,<sup>1</sup> <sup>1</sup>Access Campaign, Médecins Sans  
Frontières, India.

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### Engaging communities post-trial: From last participant clinic visit to results dissemination

N Barnabas,<sup>1</sup> <sup>1</sup>Clinical HIV Research Unit (CHRU), South  
Africa.

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### Experience of a TB-PRACTECAL Trial participant

L Gumede,<sup>1</sup> <sup>1</sup>N/A, South Africa.

e-mail: lungile11gumede15@petalmail.com

### Peer support and short regimen toolkit implementation in Uzbekistan

N Salatdinova,<sup>1</sup> <sup>1</sup>Médecins Sans Frontières, Uzbekistan.

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### From TB survivor to TB advocate

O Rucsineanu,<sup>1</sup> <sup>1</sup>Global TB Community Advisory Board  
(TB CAB), Moldova National Association of TB Patients  
"SMIT", Balti, Moldova.

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## CC-22 Keeping the promise: fulfilling the commitment to develop new tools to end TB

Chair: Janika Hauser, Campaigns in Global Health, United Kingdom

Chair: Rosa Herrera, Global TB Community Advisory Board (TB CAB), Malaysia

We urgently need to develop essential new tools to reach the global End TB goals by 2030 to end the tuberculosis (TB) pandemic. We need fast, point-of-care tests that are affordable and accessible to everyone. We need universal access to World Health Organization (WHO) recommended regimens and the development of shorter, less-toxic therapies. And with only the century-old BCG vaccine available, which is largely ineffective in adolescents and adults, we need multiple new vaccines that cover all populations.

The United Nations High-Level Meeting on TB on 22 September 2023 presents a pivotal opportunity to reaffirm commitments, increase investments, and accelerate progress in TB research and development (R&D). Chronic underfunding risks further delays in the development of new TB tools and will lead to deadly yet avoidable impacts on the TB response. In 2018, governments pledged to invest \$2 billion annually in TB R&D over five years. By 2021, only 30% of the target had been invested — 49.5% for diagnostics, 19% for drugs, and only 15% for vaccines. The Global Plan now estimates that TB R&D requires \$5 billion annually from 2023 — a fraction of the more than \$100 billion spent on COVID-19 R&D by January 2021.

Product Development Partnerships (PDPs) are at the forefront of developing new TB tools. At their core is a multi-stakeholder and collaborative approach centered on the universal access and affordability of the resulting innovations to those who seek to benefit most. The experience of PDPs offers crucial lessons on innovative models for the development of biomedical interventions against poverty-related and neglected diseases, as outlined in the flagship report “Keeping the Promise: Product Development Partnerships’ Role in the New Age of Health Research and Product Development.”

Civil society and affected communities also play an essential role in demanding the resources and funding needed for TB R&D and in shaping policies and strategies to deliver TB tools that are appropriate and acceptable for the millions of people affected by TB each year. Their full and active engagement across the TB R&D continuum and all related advocacy efforts will provide invaluable insights, foster collaboration, and ensure the interests of those vulnerable to developing TB are considered. This reflects a central demand put forth by the Stop TB Partnership and its Community Delegation and Developing and Developed Countries NGO Delegations in their Key Asks for the HLM.

This session aims to foster knowledge exchange and collaboration among key stakeholders, including researchers, policymakers, public health experts, and community and civil society representatives. Panelists will showcase and discuss the latest advancements and challenges in TB R&D, while exploring how our leaders can fulfill commitments made at the UN HLM on TB through enhanced collaboration, innovation, and financing. Further, the session will be framed around the joint role of PDPs and civil society in accelerating TB R&D and facilitating the translation of research into accessible and affordable tools.

### Delivering new vaccines this decade to end TB

E Van Brakel,<sup>1</sup> IAVI, South Africa.  
e-mail: EVanBrakel@iavi.org

### New drugs to treat the deadliest forms of TB

S Seidel,<sup>1</sup> TB Alliance, United States.  
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### Bringing TB diagnostics into the 21st century

M Kohli,<sup>1</sup> FIND, Switzerland.  
e-mail: mikashmi.kohli@finddx.org

### Community and civil society action in support of new TB tools

N Venkatesan,<sup>1</sup> Independent, Mumbai, India.  
e-mail: nandita.venky@gmail.com

## **CC-23 SMART4TB: Engaging communities to enhance research and access to leading tools for TB prevention, diagnosis and treatment**

Chair: Erin McConnell, Treatment Action Group (TAG), United States  
 Chair: Patrick Agbassi, Global TB CAB, Abidjan, Cote D'Ivoire

Engaging communities in research as more than just trial participants is a human right and a critical tool to ensure that research produces social value aligned with community priorities and needs.

*Supporting, Mobilizing, and Accelerating Research for Tuberculosis Elimination* (SMART4TB) Project, a five-year cooperative agreement made possible by the United States Agency for International Development (USAID) with the assistance of the American people, has placed engagement with local, regional, and global community partners at the center of its agenda to tackle tuberculosis (TB) through research and its translation to policy and practice. Communities will help shape the SMART4TB research agenda, review study protocols, support studies and results dissemination, and lead advocacy to drive the translation of SMART4TB research into evidence-based, progressive policy and programming.

The SMART4TB Project will power the community and research collaborations needed to meet these objectives. This Community Connect session provides a forum for community and civil society groups to learn more about the SMART4TB project, ongoing and planned research activities, and the mechanisms through which community groups can engage with the project.

The session also provides an opportunity to meet the leaders of activities across the project. Communities will be able to ask questions about SMART4TB's research priorities, activities, and future opportunities to engage with SMART4TB in priority setting, research, demand generation, and policy translation.

## **Bringing diagnostics to communities: Research to advance novel sample types and TB diagnostics at the point of care**

C Denkinger,<sup>1</sup> <sup>1</sup>Heidelberg University, Heidelberg, Germany.  
 e-mail: claudia.denkinger@uni-heidelberg.de

## **TB treatment for all: Optimising TB treatment regimens for drug-susceptible and drug-resistant TB for all, including children and pregnant people**

N Salazar-Austin,<sup>1</sup> <sup>1</sup>Johns Hopkins, Baltimore, United States.  
 e-mail: nsalaza1@jhmi.edu

## **The time for TB vaccines is now: Health system and community readiness for TB vaccines**

R Limaye,<sup>1</sup> <sup>1</sup>Johns Hopkins Bloomberg School of Public Health, United States.  
 e-mail: rlimaye@jhu.edu

## **Community engagement as a core pillar of the SMART4TB programme: Generating research results that matter and ensuring communities benefit from scientific progress**

M Nash,<sup>1</sup> <sup>1</sup>Johns Hopkins and SMART4TB, Canada.  
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## **CC-24 A new approach to accelerate research and close gaps in access to new TB drugs for children**

Chair: Gloriah Kerubo, Amref Health Africa/Global TB CAB/CHEETA Taskforce, Kenya

Chair: Mandar Paradkar, Center for Infectious Diseases in India, Pune, India

We finally have new drugs and shorter regimens for TB prevention and treatment. Yet, delays between when new TB drugs are approved for adults and when they are studied and become available for children ranges from seven to thirteen or more years.

The reasons for these delays are manifold and include the historical de-prioritization of children in the global TB response, limited research resources, site capacity, and expertise, and regulatory and operational issues.

As a result of these delays, children are typically among the last populations to enjoy the benefits of scientific progress, leading to unnecessary morbidity, mortality, and suffering.

This suffering extends beyond physical health, with stigma, discrimination, and costs affecting children's education and development and the entire household and family economically. To accelerate access to the next generation of new TB drugs and regimens for the over 1 million children estimated to fall ill with TB each year, we need a new approach.

The 2023 update of the Roadmap towards ending TB in children and adolescents provides key actions on what needs to happen, including around research and development for diagnosis, prevention, and treatment.

This session will describe the global burden and key issues for children with TB; discuss the impacts of access gaps on children and their families; present key actions from the 2023 Roadmap that can be taken to better address child and adolescent TB; and propose a new approach to studying the next generation of new TB drugs in children.

### **Global burden and key issues in child TB**

M Sekadde,<sup>1</sup> <sup>1</sup>National Tuberculosis and Leprosy Programme, Uganda, Kampala, Uganda.  
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### **How gaps in the TB access landscape affect children and their families**

B Kumar,<sup>1</sup> <sup>1</sup>Global Coalition of TB Advocates, India.  
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## **2023 update of the roadmap towards ending TB in children and adolescents**

S Verkuijls,<sup>1</sup> <sup>1</sup>WHO, Global TB Programme, Geneva, Switzerland.  
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### **CHEETA: a platform to accelerate paediatric investigations of new TB drugs**

A Garcia-Prats,<sup>1</sup> <sup>1</sup>University of Wisconsin, Madison, United States.  
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## **CC-25 How migrants and refugees access HIV and TB care in Eastern Europe and Central Asia – the example of migrants from Azerbaijan**

Chair: Paul Sommerfeld, TB Europe Coalition, London, United Kingdom

Chair: Ivan Varentsov, Eurasian Harm Reduction Association, Lithuania

According to UN Migrant Stocks, at mid-year 2020 Azerbaijan had an emigration rate of 10.6% of its entire population. The Russian Federation has been and remains the country of destination hosting the largest number of migrants from Azerbaijan. Kazakhstan, Turkey, EU countries are also host countries.

According to RF's Ministry of Internal Affairs, in 2022 number of migration registration of Azerbaijan citizens is 492 839; work as a purpose of entry were indicated by 294 899 Azerbaijani.

According to UN Migrant Stocks, at mid-year 2020 Azerbaijan had an emigration rate of 10.6% of its entire population. The Russian Federation has been and remains the country of destination hosting the largest number of migrants from Azerbaijan. Kazakhstan, Turkey, EU countries are also host countries.

According to RF's Ministry of Internal Affairs, in 2022 number of migration registration of Azerbaijan citizens is 492 839; work as a purpose of entry were indicated by 294 899 Azerbaijani.

In the Russian Federation, in the structure of migrants, Azerbaijani citizens occupy the fifth largest group. Studies suggest positive trends in the socio-economic situation of Azerbaijanis in Russia — in all labor areas, there are more prosperous positions of Azerbaijanis in comparison with many other groups of international migrants. However, migrants from all countries are equally vulnerable when it comes to access to HIV and TB services because of the residence ban they face: international migrants who are diagnosed with either HIV or TB are subject to deportation or alternatively remain in illegality in Russia with documented vulnerabilities across all the social determinants of health.

Labor migration is associated with huge economic and social opportunities for the migrants. However, one area of particular concern is the growing vulnerability of migrants to HIV/TB and their lack of access to HIV/TB prevention, testing and treatment information. Migrants with HIV and TB are particularly vulnerable to discrimination and other negative factors that affect their physical and psychological well-being, as they live in conditions of legal uncertainty that deprives them of the opportunity to claim their right to health.

Taking into account the restrictions in receiving countries on access to HIV and TB services, the barriers citizens of Azerbaijan returned from migration face in accessing HIV treatment and TB care were identified.

The research identified the barriers at the legislative and law enforcement levels in access to HIV/TB services for returning migrants, assessed the burden on the national healthcare system in connection with the treatment of HIV/TB among returnees from migration of citizens of Azerbaijan, taking into account the possible interruption/late start of treatment due to the inability to receive HIV and TB services in migration. The documented results is used for advocacy that aiming design/update of both disease control strategies, evidence-based data is used to inform policy-makers on the current situation and recommend cost models for revision of policies and legislation to improve HIV and TB services for migrants.

### **Barriers to accessing HIV and TB services among migrants in Azerbaijan**

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### **Migrants' and refugees' access to HIV and TB care in Eastern Europe and Central Asia**

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