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ABSTRACT BOOK

**52nd World Conference
on Lung Health of the
International Union Against
Tuberculosis and Lung Disease (The Union)**

**VIRTUAL EVENT
19 OCTOBER – 22 OCTOBER 2021**

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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52nd World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union) Virtual event, 19 October – 22 October 2021

SYMPOSIA: TUESDAY 19 OCTOBER 2021

SP-01 Achieving UN Sustainable Development Goals through women's empowerment in TB programming

Data generation and use for gender sensitive care: Community Health Solutions

S Habib,¹ ¹Community Health Solutions, Karachi, Pakistan.
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Evidence-based gender-responsive TB programming requires a solid contextual understanding of gender dynamics, the iterative analysis and use of gender-disaggregated data along the TB care cascade, and a commitment to consistently responding to the specific barriers faced by women in access to healthcare. Community Health Solutions report on their work in Sindh Province, Pakistan, to show how a commitment to integrating data-driven, innovative and contextually acceptable interventions, such as telemedicine, women-lead community mobilization and integration with maternal, newborn and child health services can lead to streamlined and fit-to-purpose gender-responsive TB programming.

Organisational functioning: Innovators in Health and changes at the centre

D Sen,¹ ¹Innovators in Health, Patna, India.
e-mail: dsen@innovatorsinhealth.org

Ensuring a sustainable WE approach in TB programming requires that the people designing and implementing interventions understand, embody and support a WE approach. Yet TB institutions too frequently unintentionally reinforce harmful gender norms in their own practices. Innovators in Health (IIH) in Bihar, India,

addressed unequal gender norms and practices within the organisation through context-specific gender training, policy development, employment practices and increased leadership opportunities for women.

The subsequent changes have resulted in greater attention to gender equity and women's empowerment across the programmes implemented by IIH, including new reporting and protection systems put in place for female staff.

Programme delivery: Changes to the gendered landscape of TB care provision in Pakistan

S Qayyum,¹ ¹Bridge Consultants Foundation, Karachi, Pakistan. e-mail: imshahina@yahoo.com

Rights-based TB programme delivery should be gender equitable in who provides services and gender sensitive in the way that services are provided. Working in the Sindh Province, Pakistan, Bridge Consultants Foundation expanded the network of TB care providers through training female doctors, who had previously limited their work to mother and child health in TB care provision. Their work has demonstrated how capacitating previously excluded women to provide TB services has both substantively increased TB notification rates in women and children, and also expanded the areas the trained doctors work in through increases in their confidence and autonomy.

Societal perceptions: PLAN Nigeria working with leaders and men for women's empowerment

O Osude,¹ ¹PLAN Nigeria, Abuja, Nigeria.
e-mail: Obianuju.Osude@plan-international.org

Social interventions, including engagement and education of people and communities affected, are a necessary for an effective TB response. This provides a unique opportunity for undertaking some of the essential change work required for improving women's position in society – ground level engagement and sensitisation. PLAN Nigeria report on the societal shifts generated by their

work in Sokoto State, where they trained female community members in TB care provision; engaged local and religious and traditional leadership women's position in society; and worked with male champions. They further report on the ways these societal shifts have positively impacted on TB notifications.

Individual change: OGRA Foundation and investing in the women delivering TB services

M Odongo,¹ ¹OGRA foundation, Kisumu, Kenya. e-mail: millyeod@gmail.com

Women and girls often do not have access to the basic resources, autonomy, and rights that men around them have. This includes limitations on women and girls' decision-making and self-efficacy, even about their own bodies. Limits on access to education and employment undermine financial autonomy, and entrench reliance on male counterparts. In Kisumu, Kenya, the OGRA Foundation enrolled and trained 100 young women to provide TB care while also providing support for business development and finance access.

This presentation reflects on the importance and impact of an holistic investment in the women and girls providing on-the-ground TB care.

SP-02 The 'ABCs' of scaling up 3HP in children

Evidence to inform the prioritization of paediatric rifapentine formulations to ensure access and long term impact in children

A Hesseling,¹ ¹Stellenbosch University, Desmond Tutu TB Centre, Cape Town, South Africa. e-mail: annekeh@sun.ac.za

Despite global recommendations for 3HP in children, access to much-needed child-friendly formulations have limited the uptake of rifapentine for TB preventive treatment (TPT) in children. Data on the pharmacokinetics and safety of rifapentine for 3HP in children < 2 years and those living with HIV will emerge soon. A rifapentine formulation which could support the appropriate paediatric rifapentine dosing will ensure rapid access to short-course TPT (3HP and 1HP), and treatment of disease.

The evidence for the recent WHO recommendation to prioritize a standalone scored 150 mg rifapentine dispersible tablet is reviewed and further research priorities highlighted.

Setting the scene for development of child-friendly rifapentine – lessons learned from other child-friendly formulations

B Kaiser,¹ ¹Stop TB Partnership Global Drug Facility, Geneva, Switzerland. e-mail: briank@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 and suppliers to the TB market and to support early adoption and scale-up. This approach has brought more than 10 child-friendly formulations and 3 suppliers to the market to treat drug-resistant TB in children in three years.

The lessons learned from using this approach in drug-resistant TB for children are described and how this model is being applied to child-friendly formulations of rifapentine is reviewed.

Implementation of 3HP and the TPT uptake among child contacts in 73 health facilities in Ethiopia

P Mitiku,¹ ¹KNCV Tuberculosis Foundation, Addis Ababa, Ethiopia. e-mail: petros.mitiku@kncvtbc.org

In 2019 an Ethiopian national task force was established to strengthen TB prevention services and introduce 3HP. Importation of rifapentine began in 2020 with support from KNCV/ IMPAACT4TB project. 3HP implementation occurred in seventy-three health facilities from three regions and one city administration.

There were significant challenges in implementing this regimen among children 2-14 years old including acceptability, given the large pill burden, tolerability due to GI side effects, feasibility with challenges crushing tablets, and poor palatability. Due to the COVID pandemic, the full 3HP course was dispensed and phone monitoring was used. Solutions and ongoing barriers will be described.

1HP is a safe and feasible regimen for TB prevention in children and adolescents in low-resource, high-burden settings

H Hussain,¹ ¹IRD Global, Karachi, Pakistan. e-mail: hamidah.hussain@ird.global

Shorter regimens for tuberculosis prevention can improve completion rates and protection against developing active tuberculosis disease after tuberculosis exposure.

We assessed the safety and feasibility of 1 month of daily isoniazid and rifapentine (1HP) in children and adolescents in a prospective cohort study in Karachi Pakistan from December 2019 to March 2020.

We will describe facilitators and barriers to implementation of the film-coated rifapentine tablet in our programmatic setting including discussion on acceptability, tolerability, palatability and completion rates. Ultimately we conclude that 1HP can be safely and feasibly implemented as tuberculosis prevention in children and adolescents in programmatic settings.

Implementing TPT for children: experiences from the CaP TB project in nine sub-Saharan African countries

M Berset,¹ ¹EGPAF, Geneva, Switzerland.
e-mail: mberset@pedaids.org

TB preventive treatment (TPT) is a critical intervention in the global fight against TB and child contacts have been considered as one of the high priority populations to be targeted by TB prevention services. However, delivery of TPT to child contacts remains poorly implemented. The multi-country CaP TB project has implemented child contact investigation and TPT services across nine sub-Saharan African countries.

This presentation will review the experiences and lessons learned, generated by CaP TB project countries and discuss programmatic approaches as well as practical solutions that play a key role for successful implementation of TPT services for child contacts.

SP-03 Human rights, gender and tobacco

Global progress and opportunities in integrating tobacco control in human rights treaty processes

L Huber,¹ ¹Action on Smoking and Health (ASH), Washington DC, United States. e-mail: huberl@ash.org

This session will focus on how stakeholders in health can use a human rights based approach to accelerate the implementation of tobacco control measures at national level while also supporting progress towards the UN Sustainable Development Goals and promoting “the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.”

This presentation will provide practical examples of how to use Human Rights mechanisms, Human Rights treaties, as well as coordinated campaigns around national reporting obligations to Human Rights Treaties to advance health, development and human rights goals and objectives.

Women participation in decision making in global and national tobacco control efforts and initiatives

P Sudan,¹ ¹Independent Panel for Pandemic Preparedness and Response (IPPR), World Health Organization, New Delhi, India. e-mail: aspswcd@gmail.com

This session will highlight how women leaders have played a significant role in advancing global and domestic tobacco control efforts and initiatives. It will also provide an insight into the decision-making process of the WHO FCTC and its Conference of Parties in advancing tobacco control globally and how gender plays an important role in shaping these discussions and decisions.

Women's rights and tobacco control: The FCTC and beyond

E Ricafort,¹ ¹McCabe Centre for Law and Cancer, Manila, Philippines. e-mail: Evita.Ricafort@mccabecentre.org

This session will examine approaches to FCTC implementation and tobacco control to address gender gaps in tobacco control research and data and policies and programs, including evidence and options outlined by the WHO upon a request of the Conference of the Parties to the FCTC.

The session will also discuss tobacco control issues affecting women that go beyond FCTC implementation, such as the impact of COVID-19 on tobacco use and exposure among women, disingenuous ways in which the tobacco industry has continued to target women through digital marketing and entertainment media, and women's access to health care services.

Tobacco industry targets young and vulnerable women

E Dagli,¹ ¹Marmara University, Istanbul, Turkey. e-mail: elifzdagli@gmail.com

This session will present the tobacco industry tactics targeting minors and young adults especially women. While it is important to protect the young and vulnerable from exposure to tobacco use, the tobacco industry aggressively targets this age group and gender to increase its market and profitability.

This session will bring the global scenario how women are targeted by tobacco industry and the need to implement evidence based control measures to counter such industry strategies.

SP-04 Diagnosis and management of TB in children with severe pneumonia

Current evidence on TB diagnosis and management in children with severe pneumonia

S Graham,¹ ¹University of Melbourne, Melbourne, Australia. e-mail: Steve.Graham@rch.org.au

Clinical and autopsy studies, mainly from tertiary facilities in sub-Saharan Africa, have consistently shown that tuberculosis is not uncommon as a primary cause or comorbidity in children presenting with WHO-defined severe pneumonia. The challenge is for early tuberculosis diagnosis and detection, especially in infants and young children with severe pneumonia who are at risk for mortality and also have particular challenges for confirming causative pathogen.

The background epidemiology and findings of a recently updated systematic review will be presented that aimed to identify characteristics at presentation that might guide a diagnostic approach for effective and early treatment.

Microbiologically confirmed tuberculosis in children with severe pneumonia – findings from the PERCH study

D Murdoch,¹ ¹University of Otago, Christchurch, Christchurch, New Zealand. e-mail: david.murdoch@otago.ac.nz

The Pneumonia Etiology Research for Child Health (PERCH) study was a multi-country case-control study in 9 sites in 7 countries (Bangladesh, The Gambia, Kenya, Mali, South Africa, Thailand and Zambia) examining the causes of hospitalised pneumonia in children <5 years. Induced sputum and gastric aspirate samples were cultured for *Mycobacterium tuberculosis*. *M. tuberculosis* was isolated from 24 (1.5%) of 1571 HIV-negative cases with radiographic evidence of pneumonia.

Using an integrated analysis model it was estimated that *M. tuberculosis* accounted for 5% or more of the aetiological distribution and ranked among the top ten most common pathogens at all sites.

Microbiological diagnosis of TB in severely malnourished children with pneumonia

M Chisti,¹ ¹International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh. e-mail: chisti@icddr.org

A total of 405 severely malnourished children with cough and/or respiratory distress and radiological pneumonia in Dhaka Hospital between April 2011 and June 2012 sputum (one each from gastric lavage and induced sputum) collected for smear microscopy and mycobacterial culture, and Xpert MTB/RIF assay for 214 patients. Microbiological TB was confirmed in 27/396 (6.8%) children (10 culture positive, 21 Xpert MTB/RIF positive, both tests positive in 4). *M. tuberculosis* detection (culture and/or Xpert MTB/RIF) was higher from induced sputum (24/394; 6%) compared to gastric aspirate (14/396; 3.5%).

Our study provides original data on TB microbiological diagnosis in severely malnourished children.

Impact of systematic TB detection using Xpert Ultra on nasopharyngeal aspirate and stool samples on mortality of children with severe pneumonia

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

TB-Speed Pneumonia was a pragmatic stepped-wedge cluster-randomized trial aiming to assess the impact of mortality of adding systematic Xpert Ultra testing on a nasopharyngeal aspirate and 1 stool sample at hospital admission to the standard of care for aged <5 years with WHO-defined severe pneumonia in six high TB incidence countries (Côte d'Ivoire, Cameroon, Uganda, Mozambique, Zambia and Cambodia).

Children were followed-up for 12 weeks. Results on the feasibility and yield of the systematic molecular TB detection in children with severe pneumonia and impact on 12-week mortality will be presented.

SP-05 Tobacco-free generation and tobacco endgame: is COVID-19 an opportunity for the tobacco endgame?

Countering Tobacco Industry Interference for advancing tobacco free generation

E Dorotheo,¹ ¹Southeast Asia Tobacco Control Alliance (SEATCA), Manila, Philippines. e-mail: ulysses@seatca.org

This session will present the challenges of tobacco industry interference and the need to counter the same to protect the present and future generation from the scourge of tobacco use.

It will highlight the experience of monitoring and taking action against tobacco industry tactics in the Southeast Asia region.

Tobacco Control as a key to NCD Prevention, more so during COVID-19

R Perl,¹ ¹Vital Strategies, New York NY, United States. e-mail: rperl@vitalstrategies.org

The world is facing an unprecedented scale of the global public health crisis in COVID-19 pandemic. This session will highlight the need to act on the non-communicable disease burden and its risk factors like tobacco use to respond to the rising COVID-19 burden globally.

Tobacco Free Generation 2025 – Initiative by Government of Karnataka to protect the future generation

M Selvarajan,¹ ¹Government of Karnataka, Bangalore, India. e-mail: deputydirectormedical@gmail.com

This session will highlight the efforts undertaken by the Government of Karnataka through its State Tobacco Control Cell in advancing the Tobacco-Free Generation 2025 campaign in the state.

Full implementation of the FCTC and its impact on Global Tobacco Control – The Treaty and Beyond

K Lindorff,¹ ¹Cancer Council New South Wales, Melbourne, Australia. e-mail: kylie.lindorff@nswcc.org.au

The WHO FCTC played a significant role in strengthening the global response to tobacco use burden and tobacco industry tactics. However, there is still a need for full implementation of the Treaty to advance tobacco control. The Treaty provides evidence-based policy recommendations for all countries and its implementation is the first and significant step towards reducing tobacco use.

This session will highlight the role of WHO FCTC in advancing tobacco control globally and the need for its effective implementation.

Tobacco control during COVID-19 pandemic – Experiences from India

D Mishra,¹ ¹Socio Economic and Educational Development Society (SEEDS), New Delhi, India. e-mail: seedsdelhi@gmail.com

This session will highlight the efforts and initiatives taken in India to prevent COVID-19 transmission by implementing a ban on the sale and use of tobacco products and a ban on spitting in public places. Several national and sub-national efforts were undertaken during both wave-1 and wave-2 of the pandemic.

The session will highlight how efforts by civil society and government agencies resulted in rapid action against tobacco use in the country and presents a best opportunity to talk about the endgame scenario for India.

SP-06 Technical support through the Green Light Committee (GLC) mechanism to scale up programmatic management of drug-resistant TB

1. Technical support and capacity building through the GLC mechanism – priorities for the next cycle

M Yassin,¹ ¹The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland. e-mail: mohammed.yassin@theglobalfund.org

The presentation will outline the Global Fund perspectives on supporting programmatic management of drug-resistant TB including uptake and scale up of new tools and regimens via the rGLC mechanism, which is funded through the MOU between WHO and Global Fund.

Also, the modalities of the technical support, the amount of annual GLC contribution by countries as well as the importance of demand-based technical support, performance based disbursement.

2. Uptake and scale-up of updated WHO guidelines on the management of drug-resistant TB – Experience from SEA rGLC

V Bhatia,¹ WHO, Delhi, India.
e-mail: bhatiav@who.int

The presentation will summarise activities organized and coordinated by the rGLC secretariat housed in WHO SEA Regional office, focused on capacity building at the country level, scaling up the uptake of the WHO recommendations as well as the support provided for transition planning towards new DR TB regimens.

It will provide an overview of the challenges faced while implementing the rGLC MoU, as well as key achievements.

3. Operational research on modified shorter all oral regimens in the WHO European Region and rGLC support

A Yedilbayev,¹ WHO Regional Office for Europe, Copenhagen, Denmark. e-mail: yedilbayeva@who.int

The WHO European Region is on track to achieve the 2020 milestones for reductions in cases and deaths. However, the treatment success rates for MDR and XDR TB remain 57% and 39% respectively, highlighting the importance of further studies to better understand the most effective interventions.

Therefore, the research is critical to breaking the trajectory of TB epidemic in the region. The WHO RO in collaboration with partners rolled out the operational research initiative for the introduction of modified fully oral shorter treatment regimens for RR/MDR-TB in 14 countries of the WHO European region.

4. Strengthening opportunities for aDSM via rGLC mechanism: Myanmar experience

A Mohammed,¹ USAID- PHI STAR, Yangon, Myanmar.
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The presentation will focus on aDSM introduction, components, check list for countries, mechanisms of implementation, case example from Myanmar as a success story, causality assessment and benefits. aDSM challenges, aDSM strengthening and scaling up for other countries-Opportunities.

SP-07 Guideline update on rapid molecular diagnostics for extrapulmonary TB: what is new and how far are countries implementing new tools?

Xpert MTB/RIF (Ultra) for EPTB samples: WHO policy recommendations and need for future research

A Korobitsyn,¹ Global TB Programme, Genève, Switzerland. e-mail: korobitsyna@who.int

In June 2020, a WHO Consolidated guidelines on tuberculosis, Module 3: diagnosis – rapid diagnostics for tuberculosis detection, was released including number of recommendations and diagnostic tools to assist countries and TB control programs to improve diagnosis of extra pulmonary TB (EPTB). In 2021 WHO has updated above-mentioned Consolidated guidelines on tuberculosis, with inclusion, among others, the recommendations on Low complexity automated NAATs for detection of resistance to isoniazid and second-line anti-TB agents. This class of technologies provide additional opportunities to contribute to the detection of resistance to above-mentioned anti-TB agents in patients with EPTB.

Programmatic considerations for the laboratory diagnosis of EPTB by Xpert MTB/RIF Ultra – South Africa's experience in a high TB and HIV endemic setting

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Following World Health Organization endorsement, South Africa adopted Xpert MTB/RIF (Xpert) to diagnose extra-pulmonary tuberculosis (EPTB) for selected specimen types in 2014. Transition to Xpert MTB/RIF Ultra (Ultra) occurred in 2017.

This presentation considers experiences from a large laboratory diagnostic TB program, at scale, with >18.5 million Xpert/Ultra tests conducted to date. EPTB specimen types comprise ~2% of all testing.

Local laboratory processing flows and adaptations, implementation considerations, utilization patterns, positivity rate by specimen type, and programmatic considerations for Ultra and detection of 'trace' (lowest detectable amount of genetic material), in the context of EPTB, are explored.

Clinical utility of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis in Ethiopia

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The prompt diagnosis of EPTB remains challenging. In our study, 572 extra-pulmonary specimens (279 lymph nodes, 159 pleural, 80 peritoneal, 45 cerebrospinal, and 9 pericardial fluids) were analyzed.

Compared to the composite reference standard, the pooled sensitivity and specificity of Xpert were 75% and 98% respectively. The highest sensitivity (90%) was documented for lymph node specimen, moderate sensitivity (53%) for cerebrospinal fluid, and lowest sensitivity (30%) for pleural fluid.

Xpert may be used as an initial diagnostic tool for testing lymph node specimens. The added value of Xpert to diagnose pleural or peritoneal TB is limited by its poor sensitivity.

Diagnosis of EPTB in a high income country: a different epidemiological landscape

C Erkens,¹ ¹KNCV tuberculosis foundation, The Hague, Netherlands. e-mail: connie.erkens@kncvtbc.org

Low burden countries with a high proportion of TB among the foreign born population, report more than 30% of TB cases having extrapulmonary localization.

In The Netherlands, the percentage among the foreign born population with TB was 44%. Up to 54% of this population, arrived less than 5 years ago in the Netherlands, suggesting late reactivation of TB infection. 68% of EPTB diagnoses are confirmed by culture, NAAT, microscopy or histology testing.

Data will be presented on populations at risk for specific EPTB disease locations, incidence rates, case finding methods and the role of NAAT.

Lessons learned from Pakistan on EPTB Xpert testing, what is important to know?

S Tahseen,¹ ¹Pakistan National TB program, Islamabad, Pakistan. e-mail: sabira.tahseen@gmail.com

In Pakistan since 2013, Xpert® MTB/RIF is recommended as an initial test for the diagnosis of Extrapulmonary TB (EPTB) specimens. In National TB reference laboratory more than 10,000 specimens are processed annually. Among EPTB specimen (9-10%) most common are pleural fluid (33%), CSF (16%) and lymph nodes (10%). In 2018, with the introduction of Xpert Ultra, bacteriological confirmation of EPTB increased from 19.3% in 2017 to 29% and 22% in 2018 and 2019 respectively. Diagnosis of TB increased by 100% for pleural, Ascitic, synovial, and CSF fluid. In addition, Rifampicin resistance was detected among 7% of MTB-positive specimens.

SYMPOSIA: WEDNESDAY 20 OCTOBER 2021

SP-08 Rogue diagnosis: the rise of target-based next-generation sequencing (tNGS) to defeat TB

Sequencing-based surveillance of drug-resistant tuberculosis: laboratory approaches, advantages, and challenges.

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Genome sequencing represents the standard tool for anti-tuberculosis (TB) drug resistance surveillance as it can be performed with high resolution and accuracy on sputum (targeted approach), and on isolates (whole genome approach) for a wider analysis. Scaling-up of such technologies in resource-limited settings requires among others the: standardisation of procedures; establishment of quality assurance system; development of local capacity for molecular biology and bioinformatics analysis.

The support of TB Supranational Reference Laboratories and continuous mentoring will be critical, like previously done in the past for phenotypic testing, as demonstrated successfully by surveys recently conducted (Djibouti, Eritrea, Eswatini).

Deplex Myc-TB: A versatile culture-free tNGS assay to address the upgraded XDR-TB diagnostic challenge

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To combat progression of resistance to additional anti-tuberculosis (TB) drugs, the World Health Organization has recently revised the definition of (pre-)extensively drug resistant TB, based on the most potent group of drugs (group A) now available in longer second-line treatment regimens. Therefore, a scale up of diagnostic tests is urgently needed to detect fluoroquinolone-, bedaquiline- and linezolid-resistance. As a unique feature, the tNGS-based Deplex Myc-TB assay jointly detects genotypic resistance to these and 10 other drug classes directly from sputum, and simultaneously provides strain type information for epidemiological monitoring. Selected examples of impact on diagnosis and surveillance will be discussed.

Targeted Next-Generation Sequencing (tNGS) for tuberculosis drug resistance prediction in high incidence settings - challenges and chances.

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Targeted Next-Generation Sequencing (tNGS), based on pre-amplification of a set of resistance targets in a multiplex PCR followed by NGS, opens new gateways for the rapid prediction of drug resistance (DR) of clinical *Mycobacterium tuberculosis* complex (MTBC) strains. Due to the initial amplification step, tNGS can be performed even from clinical specimens e.g. sputum, and, thus, has the potential to drastically shorten the time to DR diagnosis.

Still, tNGS technology is technically demanding having special considerations for infrastructure establishment, training, and continuous mentoring support for implementation in tuberculosis high incidence settings. These considerations will be discussed in this presentation.

Variable success in implementing commercial targeted Next-Generation Sequencing (tNGS) for Mycobacterium tuberculosis drug-susceptibility testing in Benin and Rwanda

F Massou,¹ ¹Supranational Reference Laboratory for TB, Cotonou, Benin. e-mail: abenimas@gmail.com

Since 2018, the World Health Organization has recommended sequencing technologies for routine surveillance and detection of drug-resistance for TB; yet the use of the technology is still scarce in resource-constrained countries.

In the EDCTP-funded DIAMA project, the commercial Deplex®-MycTB test (GenoScreen, France) was placed in two laboratories in Africa - the Biomedical Centre of Rwanda and the SRL in Benin.

Implementation of the test required several steps: instrument installation, on/off-site training, and remote support with different outcomes at the two sites. We will discuss the steps of implementation, the challenges faced, and possible factors explaining the different outcomes.

Investigating the utility of tNGS for clinical diagnosis of DR-TB: lessons from a pilot in Mumbai

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India carries one quarter of the world's DR-TB cases with treatment success rates of 49% and 36% for MDR- and XDR-TB, respectively. Mumbai, a hot spot, has 24% MDR-TB in newly diagnosed treatment naive and 41% in previously treated patients (60% carrying fluo-

roquinolone resistance). The use of tNGS for rapid, accurate and comprehensive resistance-profiling may provide a better approach to delivering effective treatment within high DR-TB burden populations.

Our study investigated the utility tNGS as a diagnostic tool to provide well-designed individualised therapy in hopes of preventing resistance evolution and minimising transmission of highly resistant strains within communities.

SP-09 The gamechanger – traditional versus social media and commercial market strategy for social and behaviour change to end TB

Reaching the unreachable: The role of (social) communities in the fight against TB

M Koch,¹ ¹DAHW, German Leprosy and Tuberculosis Relief Association, Würzburg, Germany.
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Mr. Manuel Koch will share his insights and experiences on how various modes of communication and awareness campaigns could be used to reach out to the underprivileged who are not aware about TB. He will share approaches from various programmes and from other countries that have worked well for creating awareness about diseases and could be adapted for TB.

Explaining the key approach of DAHW's projects worldwide, the spotlight will be on socially influencing the people affected and the community as they play a key role in effectively sustaining the fight against TB.

Making health information accessible to anybody anywhere: Leveraging Audiopedia as open source tool of localized audio content and technologies

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With #SmartDevelopmentHack, the EU and BMZ called for innovative digital solutions to tackle the challenges caused by the coronavirus outbreak. GLRA and URIDU teamed up to demonstrate a way to transform community outreach, the open source technical framework 'Audiopedia' that provides expert health education using localized audio and context-relevant technology. In this session, we will discuss how Audiopedia can be an effective tool to reach especially illiterate people and share how leveraging technology has the power to change behaviour even in remote locations.

Role of cinema, theatre & art in the fight against stigmatization and discrimination amongst the TB-affected

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Communication has been playing a pivotal role in fighting against stigmatization and discrimination amongst people affected by TB. Mr Muzaffar Ali will speak on how cinema, theatre and art could become a means for reaching out to the masses and creating awareness about TB and encouraging behavioural change.

Sharing his experience on how movies and documentaries have made a lasting and positive impact on the society, he would provide some examples of how cinema has been instrumental in bringing out a change in the lives of people.

SP-10 Programmatic innovations to address challenges in TB prevention and care during the COVID-19 pandemic

Compendium of resources on TB and COVID-19

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The WHO Global TB Programme has established a compendium of resources to support countries and other stakeholders innovating on TB and COVID-19. This presentation will summarize these efforts, which comprise a collection of country case studies on programmatic innovations in TB and COVID-19, as well as, an inventory of peer-reviewed or preprint manuscripts that describe the impact of the pandemic on epidemiological, clinical and laboratory perspectives of TB and on TB disease course, treatment and prognosis.

Impact of COVID-19 on tuberculosis and HIV services: a public health surveillance project

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Disruption of TB services due to the COVID-19 pandemic affects TB detection and treatment, potentially increasing mortality from the disease.

This presentation will share results from a project assessing the impact of strengthening real-time surveillance on TB case detection and TB treatment outcomes,

during the COVID-19 pandemic. Trends during the COVID-19 pandemic (March 2020 to February 2021) will be compared with trends during the pre-COVID-19 period (March 2019 to February 2020) in selected health facilities in Nairobi (Kenya), Lilongwe (Malawi) and Harare (Zimbabwe). Innovations associated with mitigating declining trends in case detection and treatment outcomes will be highlighted.

Implementation of standard short oral regimen for drug-resistant tuberculosis during the COVID-19 pandemic in Philippines

D Gaviola,¹ ¹National TB Control Program, Department of Health, Quezon City, Metro Manila, Philippines. e-mail: atjimeyl@gmail.com

The treatment outcomes of patients with drug-resistant TB remains unsatisfactory in the Philippines. In 2018, only 65% of patients were treated successfully, mainly due to a high proportion of loss to follow-up because of adverse drug reactions. To improve the treatment outcomes of people with DR-TB, Philippines's National TB Programme adopted the shorter all-oral bedaquiline-containing regimen in March 2020, following the recommendations by the World Health Organization. At the same time, the country implemented enhanced community quarantine.

This presentation will share experiences from shifting to the short oral regimen during the COVID-19 pandemic and its impact on treatment initiation and adherence.

Multipronged approach to continue TB services during the pandemic in Pakistan

A Rashid,¹ ¹Mercy Corps, Islamabad, Pakistan. e-mail: aarashid@mercy corps.org

Districts supported by Mercy Corps in Pakistan saw a 39% reduction in TB case notifications because of public health measures implemented in response to the COVID-19 pandemic, coupled with stigma, COVID-19 infections among health care workers and fewer community referrals. Mercy Corps implemented public-private interventions to improve TB diagnostic and treatment services through targeted projects in clinics, large private hospitals and "outreach chest camps" for vulnerable populations; self-referrals through interactive voice calls; engagement of female health care workers; transport of sputum specimens by community riders; and awareness-building forums. These measures allowed for continuity of services, with 98% of TB patients able to continue their treatment.

SP-11 TB diagnosis and treatment among migrants during the COVID-19 pandemic

What do we know about COVID-19 impact on TB diagnosis and care among migrants?

D Zenner,¹ ¹Queen Mary University London, London, United Kingdom. e-mail: d.zenner@qmul.ac.uk

This talk aims to provide an overview of published and unpublished literature on TB diagnosis and care among migrants and the impact of COVID-19 control measures. The scope is global, with a focus on the global South.

Many migrants have been vulnerable to COVID-19 infection and adverse outcomes, whilst reprioritisations and non-pharmaceutical interventions may have also aggravated vulnerabilities and minimised access to care. Mitigation measures have not always proved sufficient. Barriers to healthcare access including TB diagnosis and care affecting particularly vulnerable populations could potentially result in millions of avoidable deaths, and this care gap needs to be addressed urgently.

Multi-disease platforms for integrated TB and COVID-19 testing: blessing or curse?

C Gilpin,¹ ¹International Organisation for Migration, Geneva, Switzerland. e-mail: cgilpin@iom.int

The availability of multi-disease platforms in high-TB burden settings brought the promise that the existing instrumentation could be repurposed to provide both screening for TB as well as the diagnosis COVID-19. Despite IOM's global network of well-equipped laboratories, the availability of diagnostic tests for COVID-19 was limited and alternative platforms were needed to conduct COVID-19 testing for both clinical and administrative purposes.

Newer multi-disease systems such as Molbio or TrueNat can provide an alternative platform to the GeneXpert instrument for decentralised testing for TB and COVID-19. This presentation will outline the technologies available for both TB and COVID-19 diagnosis.

Impact of the COVID-19 pandemic on TB care and treatment: A perspective from Sub-Saharan Africa

M Joloba,¹ ¹TB Supranational Reference Laboratory, Kampala, Uganda. e-mail: mlj10@case.edu

The unprecedented COVID -19 pandemic in early 2020 in Sub-Saharan Africa severely affected TB care. In Uganda, during the first wave, TB notification was reduced by 48.2% with GeneXpert use for TB being re-

duced by 51% due to travel restrictions as well as the redeployment of personnel, equipment and facilities for COVID-19 testing. Countries such as Kenya and South Africa have seen several devastating waves of COVID-19 that suggest that the worst may not yet be over for Uganda. Timely management of COVID-19, increased resources for TB and adoption of best practices is essential.

Involving communities in COVID and TB care – an experience from India

V Yeldandi,¹ ¹SHARE INDIA, Ghanpur Village, Medchal District, India. e-mail: vijayyeldandi@shareindia.org

Despite mitigation strategies, migrants in India are affected by uncertainties and health inequalities, exacerbated through COVID-19. Through community development initiatives, synergies have been found to utilise experiences from TB care, to improve care for COVID and TB.

SHARE INDIA supported the government to facilitate bi-directional TB-COVID-19 testing through intensified screening, home-based sample collection, replacement of sputum smears with rapid molecular testing, early detection and treatment initiation. Through health literacy, knowledge management and participatory approaches, communities were empowered to create awareness and promote use of Personal Protective Equipment, delivery of TB medicines, nutritional and treatment support, linkage to care and counselling.

Strategies and tools to strengthen the TB response during and after the COVID-19 pandemic.

D Falzon,¹ ¹Global TB Programme, WHO, Geneva, Switzerland. e-mail: falzond@who.int

Modelling and empirical data demonstrate the profound impact of COVID-19 on global TB control, reversing several years of continued progress. WHO data showed substantial TB notification reductions with an estimated 1.4 million (21%) fewer people receiving TB care in 2020. An additional 500,000 TB deaths are estimated, due to healthcare barriers alone, adding to increased TB transmissions, treatment interruptions, impact on comorbidities and poorer outcomes in people with TB-COVID.

Health services must ensure that TB services are maintained during an effective COVID-19 response and this presentation will highlight critical care pathway points to strengthen care efforts, using exemplary countries experiences.

SP-12 Mass screening for TB: new tools and practices

Rapid molecular tests for tuberculosis screening and case-finding

G Marks,¹ ¹University of New South Wales, Sydney, Australia. e-mail: g.marks@unsw.edu.au

Community-wide active case finding for TB requires tests that are safe, feasible, sensitive and specific for the diagnosis of pulmonary TB. Many widely used tools, including symptom screening and sputum smear microscopy, lack sensitivity for this purpose. Chest radiography has good sensitivity, but feasibility may be a problem in some setting. Testing spontaneously expectorated sputum using a molecular diagnostic (such as Xpert or TruNat) is feasible with reasonable sensitivity and excellent specificity.

Operational approaches to scale-up requires further investigation. This talk will explore the role of molecular diagnostic tests on sputum in active case finding for TB.

Community-wide systematic tuberculosis screening: Role of mass chest X-rays in the digital age in LMICs

B Mungai,¹ ¹Liverpool School of Tropical Medicine, UK, Nairobi, Kenya. e-mail: brendanyambura2013@gmail.com

Chest X-ray has an important role in early detection of TB. Historically, miniature radiography for mass TB screening activities was widely utilized in high-income countries throughout the 20th century. Now the agenda is back with WHO guidelines on systematic TB screening and the availability of newer technologies, including: more affordable and portable digital X-ray machines, and computer aided software packages.

This presentation will look at the role of CXRs in systematic TB screening in lower-and middle-income countries (LMIC) and how the new technologies are likely to shape the future of finding the missing people with TB.

Blood biomarkers for identification of people with active tuberculosis and risk of progression

T Scriba,¹ ¹University of Cape Town, Cape Town, South Africa. e-mail: thomas.scriba@uct.ac.za

This talk will discuss recent progress in the development and performance assessment of blood biomarkers, including transcriptomic signatures and T cell-based tests for identification of people with active TB and those at high risk of progression to TB.

Results of the recently completed CORTIS trial as well as those of a parallel observational study in people living with HIV will be discussed, along with insights from

studying longitudinal blood signature trajectories and the effects of respiratory infections on blood biomarkers and TB progression.

C-reactive protein in screening for tuberculosis

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C-reactive protein (CRP) is non-specific marker of inflammation whose levels rise in the setting of interleukin-6-mediated infections such as active tuberculosis (TB). Based on a growing body of evidence to support the use of CRP to screen high-risk individuals for active TB, CRP was recently endorsed by the World Health Organization as a promising TB screening test. This presentation will review the performance and operational characteristics of CRP in the context of TB screening, advantages and disadvantages relative to currently recommended tests to screen for TB and current research/knowledge gaps.

Modelling the impact of asymptomatic screening tests

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Symptom screening is only an effective tool when screening people with symptomatic TB. However a large proportion of people with TB do not present with symptoms, whilst still being infectious.

This presentation uses a cohort model to evaluate the impact that alternative screening tools can provide. This impact is measured by balancing the number of extra cases positively identified, the excess further testing needed for false positive initial screens, and an estimate of the transmission potential prevented due to treatment. This will all be compared to a baseline of symptom screening.

SP-13 Is TB elimination feasible in high TB burden countries in the foreseeable future? Reviewing progress and charting future directions

On the road to TB elimination: An overview of global guidance and tools

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In a globalized world, TB is a shared problem for all countries. In times of ever increasing population movements, TB will never be completely and sustainably eliminated in any country until it is eliminated everywhere. This interdependency calls for joint and intensified efforts on TB prevention and care in all countries. This is why the World Health Organization (WHO) developed a Global Framework for TB Elimination in conjunction with WHO's End TB Strategy. This presentation will overview progress towards TB elimination, existing guidance and tools, as well as WHO's ongoing work to launch an updated TB elimination framework in 2021.

Ethiopia's consistent decline in TB incidence as a promising trend for setting the stage for TB elimination: Data from the Eliminate TB from Ethiopia project

T Agizew,¹ ¹KNCV Tuberculosis Foundation, Addis Ababa, Ethiopia. e-mail: tefera.belachew@kncvtbc.org

Between 2010-2019, Ethiopia experienced a 5% average annual decline in TB incidence. However, with the current rate, ending the TB epidemic (<10 cases/100,000) may not be possible without intensified efforts. When we modeled the combined effects of intervention packages consisting of active community-based TB screening using the best available algorithm, TB and latent TB infection prevention and treatment among high-risk groups, the estimated annual decline of TB notification reached 16%. With this level of impact and nationwide scale-up of the interventions, Ethiopia aligns well with ending TB epidemic before 2035, and shift towards TB elimination possible in the foreseeable future.

Active case finding initiatives to reduce TB incidence: community experience in Bangladesh

A Islam,¹ BRAC, Dhaka, Bangladesh.
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Bangladesh is implementing TB control programme jointly with partners toward TB elimination. Continuous interventions of different case finding initiatives in the community, countrywide scale up of rapid/molecular testing and strengthen referral from the community to the X-pert sites are the key interventions. These interventions are largely supported by the BRAC community health workers in the community.

At the same time case holding (chemoprophylaxis, diagnosis and treatment) is also important to cut the transmission chain. BRAC identified 81% missing cases up to 2019 with more than 90% treatment success rate though case detection was hugely impacted due to COVID-19 last year.

SP-14 Tobacco endgame: is it the happily-ever-after scenario?

Tobacco and nicotine end game scenarios from Finland

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Finland was the first country in the world to enshrine the objective of ending the use of tobacco products in its Tobacco Act in 2010. In 2016, this objective was further specified to also include ending the use of other nicotine products, which is unique in international terms.

The objective of Finnish tobacco and nicotine product policy will not be achieved through a 'harm reduction' approach endorsed by some countries, which aims to reduce the consumption of cigarettes by substituting these with other nicotine products. Our experience shows that smoking reduction is possible without novel nicotine products.

Industry Goes Smoke Free - FSW activities

P Lal,¹ The Union South East Asia Office, New Delhi, India.
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Framework Convention on Tobacco Control has been an effective tool to limit the activities of tobacco industry. Tobacco industry is changing strategy and will be marketing nicotine and so called reduced risk products. This talk will discuss the tobacco endgame strategy under these circumstances.

What is in the store: Novel tobacco, nicotine, marijuana products

C Pisinger,¹ University of Copenhagen, Copenhagen, Denmark. e-mail: charlotta.pisinger@regionh.dk

Tobacco industry have been marketing e-cigarettes, heated tobacco products, non tobacco nicotine products and now starting marijuana products.

It is important to recognize the changing product platform.

SP-15 Using a family-centred approach for drug-resistant TB to promote lung health for all: experiences from Khayelitsha, South Africa

Family first: how COVID-19 led to the development of a family-centered approach to DR-TB in Khayelitsha, South Africa

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Management of DR-TB often focuses on the individual and there is a sharp divide between adult and pediatric services, which can result in fragmented care. As a result of COVID-19, MSF and the DoH implemented a home-based care program for people living with DR-TB. As a result of this program, the complex needs of families affected with DR-TB were revealed, allowing for the design of programs novel solutions.

This session will present the initial experience of home-based care for people with DR-TB in Khayelitsha and set the stage for the "family-centered" model of care developed as a result.

Finding and treating children with DR-TB in Khayelitsha using a family-centered approach

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There is a significant gap between the numbers of children estimated to be sick with DR-TB and those diagnosed and treated for DR-TB each year.

This session will present the results of a household-based, family-centered approach to identifying children with DR-TB in Khayelitsha. It will review how such children were diagnosed with DR-TB disease as well as the decentralized, community-based approach to their care.

The feasibility of using novel diagnostic and treatment strategies—such as stool Xpert testing, all-oral, shorter regimens, and pediatric formulations of second-line drugs—will also be discussed.

Preventing DR-TB in vulnerable families: post-exposure management in Khayelitsha

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The World Health Organization has recently recommended preventive therapy for vulnerable household members exposed to DR-TB, but there is limited access to this treatment. While most countries have a “watch and wait approach” to see if exposed household members will become sick with DR-TB, the increased risk of household transmission of DR-TB as a result of measures put in place to mitigate the spread of COVID-19 prompted the emergency expansion of DR-TB preventive therapy in Khayelitsha.

This session will review the experience providing DR-TB treatment of infection (i.e. “preventive therapy”) as part of a family-centered approach to DR-TB.

Addressing the socioeconomic needs of Khayelitsha households affected by DR-TB

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Households affected by DR-TB face catastrophic costs, and many of them were living in tenuous socioeconomic circumstances prior to a family member becoming sick with the disease. In Khayelitsha, COVID-19 compounded the socioeconomic stresses faced by those diagnosed with DR-TB, and the impact was readily apparent during household visits. In order to address these needs, MSF worked with partner organizations to provide additional support, including food and income supplementation. This session will review the common needs of families in which someone is diagnosed with DR-TB and present a “family-centered” roadmap for addressing them.

A family-friendly approach to counseling for DR-TB: a Khayelitsha toolkit

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Counseling is an essential part of DR-TB treatment, but most tools were developed with the narrow focus of promoting adherence in adults. There is an urgent need for tools that can address other aspects of DR-TB, such as disclosure, and for materials that can address patients of

all ages. As part of a family-centered approach to DR-TB, the patient support unit in Khayelitsha developed a family-friendly counseling toolkit focused on six key themes.

This session will present the process by which these tools were developed as well as the experience of using them and share the materials with participants.

SP-16 OBSERVA-TB: strengthening Latin America and Caribbean TB civil society through the implementation of the WHO ENGAGE-TB approach and TB social observatories

Implementing the Multi-Country Project OBSERVA-TB in 8 countries from Latin America and the Caribbean region

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OBSERVATB is an initiative of Partners In Health in partnership with the Americas TB Coalition, with financial assistance from the Global Fund.

The objective is to strengthen civil society in the LAC region to assist in the comprehensive response to TB, with a focus on human rights, gender equality, and key populations. OBSERVATB includes the implementation of the WHO Engage TB approach and the creation of TB Social Observatories at the country and regional level. In addition, the project conducts consultancies to measure the impact of TB on stigma, gender, legal context, migration, and social protection in the selected countries.

Implementation of the ENGAGE TB strategy, and the National TB Social Observatory (TBso) in Peru.

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El 3 de julio de 2020, el Observatorio Social de TB-PERÚ fue creado por 14 organizaciones de la sociedad civil y asociaciones de afectados por tuberculosis de todo el Perú. Se siguieron varios pasos para organizar las operaciones bajo toma de decisiones consensuada de todos los involucrados, la TBso seleccionó prioridades para enfocar en grupos de trabajo: monitoreo social, derechos humanos, poblaciones clave y políticas públicas en TB. Todos los meses, esos grupos de trabajo se reúnen para brindar actualizaciones sobre historias particulares y temas de seguimiento que requieren un

seguimiento cercano. El grupo ha recibido seminarios web que abordan los desafíos de la tuberculosis que enfrentan las comunidades y el en tiempos de COVID19.

Implementation of the ENGAGE TB strategy, and the National TB Social Observatory in Dominican Republic.

M Isaias,¹ ¹ADOPLAFAM, Distrito Nacional, Dominican Republic. e-mail: maximoisaias@yahoo.com

El Observatorio Social de TB - REPÚBLICA DOMINICANA fue creado por 9 organizaciones de la sociedad civil. El 14 de julio la primera asamblea, discutió y aprobó el acta constitutiva de la TBSO, el 2 de agosto durante la segunda asamblea se aprobaron los lineamientos, el 23 de septiembre durante la tercera asamblea se seleccionaron las mesas de trabajo con sus integrantes, en octubre-noviembre se realizaron asambleas de seguimiento y se desarrollaron planes para la consolidación de la OSTB. Los grupos de trabajo hijo; las poblaciones vulnerables, la vigilancia, la promoción y la investigación y el desarrollo de capacidades.

La TBSO tiene reuniones periódicas con el programa nacional de tuberculosis para proporcionar referencias y actualizaciones.

Implementation of the ENGAGE TB strategy, and the National TB Social Observatory in El Salvador

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In February 2020, an ENGAGE TB workshop was held between civil society and TB program staff. A formal meeting was held with the Global Fund CCM and the Americas TB Caucus. On May 29th several organizations were invited to formalize the TBSO, by July 9th the TBSO was formed, currently, 18 organizations are part of the observatory.

The TBSO has three working groups. public policy, community monitoring and follow-up, and vulnerable populations. Other activities include a review of the TB strategic plan 2022-2026 and the Network of para-legal volunteers in TB and HIV.

Strengthening of the Regional TB Social Observatory in Latin America and the Caribbe-an region

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The Regional TB Social Observatory (RTBSO) promotes civil society (CS) participation in order to contribute to the regional and national responses to TB. The RTBSO seeks to empower CS through 1- Communication, 2-

social monitoring and accompaniment, 3- knowledge management, 4- capacity building, 5- monitoring & evaluation, and 6- political advocacy. The RTBSO reviews and counsels on TB laws, monitors international declarations to end TB.

Since 2020, 6 national TBSO has been established, as a result of the community engagement, 2,814 TB patients have been referred to the NTPs and 4,771 have been provided social support by the community.

SP-17 The TB spectrum –consequences for surveillance, diagnosis and treatment for all

TB Surveillance: what data can and should be collected during systematic screening to define subclinical disease burden and monitor impact?

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This year WHO updated guidance on systematic screening for TB recognising and recommending several possible tools and approaches that might be adopted by national treatment programs depending on the population, priorities and objectives for screening, and resources available. Monitoring of the yield and impact of screening among people with different disease presentations will be essential to determining the contribution of screening, and the role of different screening tools, in detecting subclinical and asymptomatic disease. This talk will discuss which data should be collected and highlight how this could be used to monitor impact of systematic screening practices.

TB Diagnostics: what guides the decision process of funding bodies?

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New TB diagnostics are a pillar of the END-TB research strategy. Development and validation of new diagnostic technologies requires significant funding investment. Maximising reward against investment will be determined by the sensitivity and specificity of new tests to diagnose a range of infection and disease stages. This talk will discuss the evidence required by funding decision makers to invest in new technologies, the disease states they are aiming to diagnose and how they factor in the long-term cost-benefits of early pre-transmission and minimal disease diagnosis into such decisions.

Subclinical TB treatment: prevention or cure?

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The current binomial treatment strategy for TB ascribes curative treatment to symptomatic and/or microbiological positive active TB disease and preventative treatment to latent TB infection.

This talk will discuss whether treatment of subclinical disease should be targeted at prevention or cure, how combinations of new diagnostic tools can better inform who will benefit from curative vs preventive treatment, and the impact that diagnosing and treating subclinical disease will have on the true number needed to treat to achieve benefit from preventive therapy for latent infection.

Patient perspective: benefits and challenges of systematic screening

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The success of systematic screening is often judged through the number of people with TB identified. However early detection of disease will both impact on transmission and reduce post TB complications. However, as screening is conducted in people that feel otherwise well, they may be reluctant to take 6 months treatment highlighting the need for:

1. Early and effective community engagement,
2. Developing a greater understanding of what factors in the risk vs benefit of early treatment are important to patients, and;
3. Developing regimens that are relevant to screened populations.

SP-18 TB digital adherence technologies – implementation lessons from the field

Lessons learnt during implementation and scale-up of 99DOTS in Uganda

A Katamba,¹ ¹Department of Medicine, School of Medicine (Clinical Epidemiology & Biostatistics Unit) Makerere University, College of Health Sciences, Kampala, Uganda. e-mail: axk95@case.edu

Dr. Katamba will describe how 99DOTS was adapted and re-designed for the Ugandan context using human centered design methods and results from a stepped-wedge randomized trial of the adapted 99DOTS-based intervention.

He will then describe how the 99DOTS-based intervention was further refined to address challenges encountered during the trial and preliminary results from scaling-up the refined intervention to 30 health facilities across Uganda.

Digital monitoring of tuberculosis (TB) treatment adherence for differentiated care in Bangladesh, an implementation research project

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Studies show that irregular adherence to tuberculosis (TB) therapy is associated with disease relapse, development of drug resistance, and furthering TB transmission. Bangladesh, despite improvements, has struggled to continue to improve TB treatment success with directly observed therapy alone.

With STOP TB Partnership's TB REACH initiative, icddr,b has customized an innovative and low cost digital adherence monitoring system (99DOTS, Bangladesh) to ensure, monitor and improve medication adherence of TB patients. Since implementation in April 2018, the project has enrolled a total of 624 TB patients with an overall adherence rate of 96%.

Planning and implementation of digital adherence technologies; what steps to follow?

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Digital adherence technologies (DATs) can help persons with TB to succeed in treatment and make sure that their health and wellbeing continues to be prioritized. Based on experiences from the Unitaid funded ASCENT project, implemented across five countries, purchasing

DATs, setting up necessary infrastructure, and preparing for implementation can be accomplished through five steps.

Job van Rest (KNCV) will take participants through these steps and will provide visibility to the various planning and implementation resources that were developed which country programmes and implementing partners can utilize to plan for adoption and scale-up of DATs.

Meta-analysis of feasibility/acceptability of DATs in TB REACH-funded projects

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The University of California San Francisco and the STOP TB Partnership assessed the feasibility and acceptability of digital adherence technologies (DATs), including VOT, EvriMed, and 99DOTS, using standardized post-implementation surveys of patients and health workers using DATs for TB treatment in Kyrgyzstan, the Philippines, South Africa, Tanzania, Uganda, and Ukraine.

This meta-analysis characterized implementation feedback from participants and identified differences in the feasibility and acceptability by type of DAT and patient subgroups of interest.

SYMPOSIA: THURSDAY 21 OCTOBER 2021

SP-19 Tackling structural determinants of TB with social protection measures

Global monitoring of National surveys of costs faced by TB patients and their households

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To address the pervasive problem of catastrophic costs for TB patients and their households, reliable information is essential for effectively targeting assistance, developing interventions, and evaluating progress. WHO supports the implementation of National surveys of costs faced by TB patients and their households in countries to help build evidence for action and to monitor progress towards the End TB Strategy targets. This presentation will share survey results from selected high TB burden countries.

Improving access to social protection for TB patients in times of COVID-19 pandemic

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Countries are placing social protection measures to respond to the COVID-19 pandemic: As of January 2021, more than 1622 new and adjusted social protection measures have been introduced and/or adapted globally. This presentation will explore how Brazil is capitalizing this opportunity to make these programmes sensitive and responsive to the needs of people affected by TB.

SP-20 Advances in non-sputum biomarkers for the diagnosis of childhood TB

Pathogen-specific biomarkers for childhood tuberculosis

E Wobudeya,¹ ¹Mulago National Referral Hospital, Kampala, Uganda. e-mail: ewobudeya@gmail.com

High-sensitivity TB markers are needed in children due to their paucibacillary disease. In this presentation, we will describe a multi-country evaluation of a next generation lipoarabinomannan (Fujfilm SILVAMP TB LAM) assay for children.

In addition, we will describe ongoing efforts to use an ultra-sensitive immunoassay to identify TB-specific proteins in the plasma and urine of children with pulmonary TB, and the emerging role of cell-free DNA (cfDNA) in TB diagnosis.

Host transcriptomic biomarkers for childhood tuberculosis

M Levin,¹ ¹Imperial College London, London, United Kingdom. e-mail: m.levin@imperial.ac.uk

While host gene signatures can predict TB disease in adults, it is important to recognize that children have a different immune response to TB and are more likely to have primary rather than reactivation TB disease. To characterize the gene expression profiles for pediatric TB, RNA-seq analysis was performed on children in South Africa and the Gambia who were being evaluated for pulmonary TB.

In this presentation, we will describe the genes that were associated with TB disease in children, and preliminary data on potential child-specific gene expression signatures for TB diagnosis.

Host cytokine biomarkers for childhood tuberculosis

T Togun,¹ ¹London School of Hygiene & Tropical Medicine (MRC Unit The Gambia), Banjul, Gambia.
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A TB triage test for children would prevent delays in confirmatory testing and initiation of treatment. In the Gambia, we prospectively enrolled children with signs of pulmonary TB, performed a standard TB evaluation and collected whole blood for a multiplex cytokine assay.

In this presentation, we will describe the cytokine profiles that distinguished TB from other respiratory disease, and a promising three cytokine signature for TB triage in children.

Host proteomic biomarkers for childhood tuberculosis

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Proteins have the advantage of being more easily translated into a point-of-care assay. Proteomic analysis has the potential to comprehensively identify novel host biomarkers for children.

In this presentation, we will describe ongoing efforts to develop proteomic biosignatures for childhood TB diagnosis.

SP-21 Looking back and forward: models of community engagement in TB research and lessons learnt

Essential Principles and Practices for Good Participatory Practice (GPP)

S Hannah,¹ AVAC, New York, United States.
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The Good Participatory Practice (GPP) Guidelines were developed to provide trial funders, sponsors, and implementers with systematic guidance on how to effectively engage with all stakeholders in the design and conduct of biomedical HIV prevention trials.

This presentation will review the GPP framework, how it has been adapted and used over time, including to support community engagement in TB drug trials and vaccines research, and share lessons learned from the most recent application of GPP to COVID-19 therapeutics and vaccines research.

The Global Tuberculosis Community Advisory Board (TB CAB)

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Founded in 2011, the Global TB CAB is a group of research-literate community activists that act in an advisory capacity to product developers and institutions conducting clinical trials of new TB drugs, regimens, diagnostics and vaccines, and provide input on study design, early access, regulatory approval, post marketing, and implementation strategies.

This presentation will reflect on the evolution and impact of the TB CAB, including on clinical trials protocols, the TB research agenda, and the translation of

research into policy and access. It will also include an overview of lessons learned and future directions of the TB CAB's work.

STREAM Community Advisory Boards and Engagement

O Rucsiuanu,¹ SMIT Moldova Patients Association, Balti, Moldova. e-mail: oxana_rucs@yahoo.com

STREAM is the first large-scale, multi-country clinical trial to investigate shortened regimens for MDR-TB. The trial established a Community Engagement (CE) program that was implemented at thirteen research sites within the STREAM trial, in seven countries.

This presentation will set out a summary of the experiences of CABs in connection with the STREAM clinical trial. It will underline relevant aspects that may be useful when planning and/or engaging communities in research.

In conclusion, it will also show the experiences gained during STREAM that lead to both growing confidence in CE as a valuable process and to community participation in advocacy.

The Community Research Advisors Group (CRAG)

D Namutamba,¹ International Community of Women living with HIV Eastern Africa (ICWEA), Kampala, Uganda.
e-mail: dnamutamba@icwea.org

CRAG is an international, community-driven advisory body that works to ensure the meaningful representation and engagement of affected communities in research conducted by the Tuberculosis Trials Consortium (TBTC).

This presentation will provide an overview of the CRAG's recent experience informing the design, implementation, and dissemination of results from TBTC Study 31, a large phase III trial conducted in 13 countries that found a four-month regimen containing rifapentine and moxifloxacin non-inferior to the six-month standard of care for drug-sensitive TB, as well as a CRAG-initiated and designed sub-study of barriers to and facilitators of adolescent enrollment in TBTC Study 31.

The Brazilian National TB Community Advisory Board (CCAP)

G Israel,¹ ¹Brazilian National TB Community Advisory Board (CCAP TB Brasil), Rio de Janeiro, Brazil.
e-mail: gisrael.br@gmail.com

Founded in 2017, the Brazilian TB Community Advisory Board - CCAP TB Brasil is an advisory, information and monitoring committee formed by civil society. This presentation will cover the experience of CCAP expanding the involvement of civil society in TB research and mobilizing public authorities and community leaders to incorporate relevant technologies in the care of people affected by TB. It will also discuss how the CCAP doesn't replace other initiatives linked to specific institutions/research but plays a complementary role in seeking to promote a culture of community research monitoring and the participation of activists in shaping public policies on TB in Brazil.

SP-22 Models of care for children and adolescents affected by TB

The impact of different care models on child and adolescent TB diagnostic, treatment, and prevention outcomes – a systematic review

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We conducted a systematic review of studies assessing the impact of decentralized, integrated, or family-centered care models on TB diagnostic, treatment, or prevention outcomes for individuals 0-19 years old.

We assessed 3,265 abstracts from literature databases and 128 additional references from related reviews. We identified 26 studies that quantified the impact of a care model of interest through comparison to a control group.

Decentralized models included screening and treatment support in primary-level health facilities, communities, and patient households; integrated models included co-located TB and HIV services and TB screening in IMCI services; family-centered models included providing socioeconomic support to families.

Optimizing Care for Adolescents with Tuberculosis Infection or Disease

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Adolescents with TB infection or disease face many challenges. It is critical for healthcare providers, community leaders, and policymakers to optimize adolescents' engagement in care and minimize the harms they experience from TB infection, disease, and treatment. This presentation will share findings from a situational analysis that used published and ongoing studies to understand the experiences of adolescents with TB, best practices for engaging in care, and knowledge gaps that should be prioritized.

Specific recommendations on improving adolescent TB care, reached through consensus with key adolescent TB patients, healthcare providers and experts in the field, will be highlighted.

Perspectives from a TB meningitis survivor from Vietnam on keeping children and adolescents free of TB

P Nguy?n,¹ ¹TB Patients' Association Vietnam, Hanoi, Vietnam. e-mail: anhphuong.nguyen983@yahoo.com

I will share my experiences as an adolescent TB patient and provide perspectives on TB care in children and adolescents. I will emphasize the need for early TB screening, raising awareness of prevention, signs and symptoms of TB and the need for perseverance while on treatment.

I will also stress the need to provide psychological as well as social support, especially for adolescents with TB. I hope that I can help children and adolescents with TB to recover from their disease, and prevent disabilities. I would like to see the community join hands to improve the chances of cure.

Scaling up the experiences from the DETECT Child TB (DEcentralise TB services and Engage Communities to Transform lives of Children with TB) approach in Uganda

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The seventh key action in the global Roadmap towards ending TB in children and adolescents calls for scaling up child and adolescent TB case finding and treatment. Following successful implementation of the DETECT child TB Approach in two pilot districts in 2015, the Uganda Ministry of Health/National TB programme (NTP) recommended the scale up of the approach as part of the strategic interventions to improve child TB care and treatment.

With support from the Global Fund, the NTP Uganda scaled up the approach to 10 poorly performing districts. This presentation will highlight practical implementation experiences within a programme setting.

Closing the paediatric TB detection gap: where can we find the missing children?

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e-mail: mcasenghi@pedaids.org

Children access health-care through a variety of facility-based services. TB screening is seldomly performed during these medical encounters and presumptive TB case identification and subsequent diagnostic capacity is limited, especially at the lower levels of the health-care system. The CaP TB project has implemented across nine sub-Saharan African countries a multi-pronged case finding intervention, which included introduction of systematic TB screening in different child-health entry points as well as capacity building for paediatric TB diagnosis at lower level facilities.

This presentation will discuss the contribution to paediatric TB case detection of the integrated and decentralized approaches implemented by the project.

SP-23 Post-TB disability, sequelae, care and rehabilitation: latest evidence, and client and policy perspectives

Post-TB lung disease : what do we actually know?

B Allwood,¹ ¹Stellenbosch University, Cape Town, South Africa. e-mail: brianallwood@gmail.com

This talk will begin with the definition of post-tuberculosis lung disease (PTLD), highlighting the strengths and limitations of the currently proposed definition. It will then describe a clinical phenotypes of PTLD and explain areas of complexity which can hamper measurement of PTLD using single instruments (e.g. spirometry alone), and include new data.

The talk will use case studies of patients with PTLD as illustrations suitable for both non-clinicians and clinicians not familiar with the management of PTLD. Difficulties in clinical management of such patients will be briefly mentioned.

Life after TB treatment is completed – Does it all just end once treatment ends?

F Karmadwala,¹ ¹Liverpool School of Tropical Medicine, Preston, United Kingdom.
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This presentation will focus on the patient perspective of life after TB treatment. It will highlight the importance of post TB care and rehabilitation, focusing on the long lasting psychological, physical and socio-economic effects that a patient is forced to deal with, not only during treatment, but long after treatment is completed.

It will also illustrate the patient perspective of the sequelae of tuberculosis treatment and emphasise the importance of the patient perspective throughout the treatment process but also show how the effects of the treatment does not stop once the treatment has been completed which is often overlooked.

Socio-economic consequences and quality adjusted life years associated with post TB sequelae

D Evans,¹ ¹University of Witswatersrand, Johannesburg, South Africa. e-mail: devans@heroza.org

This presentation will feature results for over 1,500 adults with pulmonary TB who were enrolled in the TB Sequel study between 09/2017-02/2020. TB Sequel is an ongoing multi-country cohort study conducted in South Africa, Mozambique, Tanzania, and The Gambia.

The investigators will report mean summary scores for HRQOL and psychological distress, median costs from the patient perspective, and the proportion facing catastrophic costs at 6 and 18 months after TB treatment. Preliminary results have revealed that impaired HRQOL and TB's economic impact continues beyond treatment completion. This is significant because the long-term impacts of TB are often overlooked.

SP-24 Innovation in training and educational materials for TB and beyond

An overview of essential knowledge for community and public health nurses – Tuberculosis Nurse Case Management: Core Competencies

D Fortune,¹ ¹National TB Controller's Association, Santa Fe, United States. e-mail: dfortune@tbcontrollers.org

The National Tuberculosis Nurse Coalition (NTNC), a section of the National Tuberculosis Controllers Association (NTCA), developed the document Tuberculosis Nurse Case Management: Core Competencies to guide nurses seeking proficiency in the specialty of tuberculosis (TB) case management. The Core Competencies define what specific knowledge, skills, and interventions a TB NCM must master to be competent.

This document organises competencies according to overarching public health domains. The updated version will classify each competency according to a domain and one or more of the following tiers:

1. Front-line staff,
2. Middle manager or supervisor,
3. Executive, policy, or leadership role.

TB Rangers Project: Stopping TB by working within Wado, Fufutunga and Falafola

T Esau,¹ ¹Baru Conservation Alliance, Malaita, Solomon Islands. e-mail: fataiaman@gmail.com

Baru Conservation Alliance (BCA) is a well-respected community based organisation supporting remote villages and families to maintain conservation values. BCA has a holistic approach to care for plants, animals and people within mountain conservation areas. BCA has a well-trained, capable and willing ranger workforce. The rangers identified TB as an ongoing threat to the people who live within the conservation areas.

The main aim is to reduce TB by working at the grass-roots, within culture, and developing the capacity of BCA conservation rangers to identify TB in people and facilitate access to health care for people suspected of having TB.

WHO Knowledge Sharing Platform on tuberculosis

D Falzon,¹ ¹Global TB Programme, WHO, Geneva, Switzerland. e-mail: falzond@who.int

Online access to the latest WHO recommendations, implementation guidance and training catalogue on tuberculosis prevention and care, organised in five modules.

Education, one of the three pillars of The Union

M Gaye-Ayrault,¹ ¹The Union, Paris, France. e-mail: mgayeayrault@theunion.org

Union Courses provides the knowledge and skills that health professionals and programme managers need to run public health programmes that are clinically sound and administratively effective. We will share the training initiatives, tools and resources offered by The Union.

SP-25 TB contact investigation – we know it's effective, but how do we optimise its delivery for maximum impact in high-burden settings?

Updated review on effectiveness of contact investigation and TB and LTBI

K Velen,¹ ¹Foundation of Innovative New Diagnostics (FIND), Geneva, Switzerland. e-mail: Kavindhran.velen@finddx.org

The presentation will summarize evidence which informed the World Health Organization 2021 TB Screening guidelines for TB contacts – this will include updated estimates for the yield of co-prevalent TB, incident TB and LTBI prevalence in various sub-groups.

Paediatric contacts – neglected household members but how can we improve this?

L Martinez,¹ ¹Boston University School of Medicine, Boston, Massachusetts, USA, Boston, United States. e-mail: leomarti@bu.edu

The presentation will provide strategies for reaching paediatric contacts including considerations for using non-sputum-based approaches for evaluating TB. The presentation will also highlight ongoing trials aimed at improving the diagnosis of TB among this neglected group of contacts.

Point-of-care (POC) diagnostics for TB and LTBI – can POC diagnostics help optimize contact investigation?

M Ruhwald,¹ ¹Foundation for Innovative Diagnostics, Geneva, Switzerland, Geneva, Switzerland. e-mail: Morten.Ruhwald@finddx.org

Point-of-care (POC) diagnostics have the potential for overcoming known challenges with TB and TB infection diagnosis following contact investigation, enabling a di-

agnosis to be made closer to the patient. The presentation will discuss current POC tools and their potential use in contact investigation.

Simplifying algorithms for contact investigation to identify disease and scale up preventive therapy – CUT-TB trial

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

Contact investigation can be resource-intensive which for many low-resource high-burden settings presents a challenge for optimal implementation.

The CUT-TB trial proposes a universal TB testing approach among household contacts, intended to identify/exclude TB disease thereby making it simpler to scale-up TB preventive therapy.

SP-26 Tobacco industry tactics – challenges and way forward

Protecting public health policies from tobacco industry interference – Global tobacco industry interference index

M Assunta,¹ ¹Global Center for Good Governance in Tobacco Control (GGTC), Bangkok, Thailand. e-mail: mary.assunta@cancer.org.au

This session will highlight the need for strengthening tobacco control policies and protecting them from tobacco industry interference. The global TII index monitored by the Global Center for Good Governance in Tobacco Control will be shared with the participants.

This is being done in several countries now but needs further expansion. Participants will be able to see their country's position in terms of TII.

Tobacco industry interference during COVID-19 pandemic – lessons from India and beyond

P Lal,¹ ¹The Union South East Asia Office, New Delhi, India. e-mail: plal@theunion.org

Funding disaster relief has been one of the tobacco industry's key areas of corporate social responsibility. The industry has aggressively used COVID-19 Pandemic to undertake CSR activities globally.

This session will highlight the tobacco industry and its front groups CSR and other interference during COVID-19 both in India and globally. This will help par-

ticipants identify the key tactics used by the tobacco industry in gaining access to governments to influence tobacco control policies.

Building global capacity and supporting tobacco industry monitoring

P Chamberlain,¹ ¹Bath University, Bath, United Kingdom. e-mail: P.Chamberlain@exposetobacco.org

This session will present the efforts undertaken under STOP: Stopping Tobacco Organizations and Products at the University of Bath to build global capacity in tobacco industry monitoring and providing rapid support to stakeholders against TII.

The big barrier – Tobacco industry and public health policy adoption and implementation

U Bhojani,¹ ¹Institute of Public Health, Bengaluru - India, Bengaluru, India. e-mail: upendra@iphindia.org

This session will present the various dimensions of tobacco industry interference and how it delays, derails, and dilutes public health policy adoption and implementation. It will also highlight the need for presenting an appropriate response keeping with the evidence-based policy i.e. Article 5.3 of the WHO FCTC to counter any tobacco industry tactics.

SP-27 The BPAL regimen: update on clinical and operational research

Nix and ZeNix Clinical Trial results

S Foraida,¹ ¹TB Alliance, Sudbury, United States. e-mail: Salah.Foraida@tballiance.org

Nix-TB trial has shown that an all-oral, six-month BPAL-regimen has an efficacy of 90% after 24-months follow-up post-treatment completion. The main safety concern is based on side effects of linezolid i.e. neuropathy (peripheral and optic) and, myelosuppression.

The ZeNIX-study explores if a shorter duration (2 months vs 6 months) and smaller dose (600mg vs 1200mg) of linezolid in the BPAL-regimen still maintains similar efficacy but reduced safety concerns compared to NIX-TB.

TB-PRACTECAL Clinical Trial results

A Sinha,¹ ¹Manson Unit, MSF UK, London, United Kingdom. e-mail: animesh.sinha@london.msf.org

TB-PRACTECAL was terminated early after BPAL-moxifloxacin showed superiority to a locally accepted standard of care. A summary of the key results as well as plans for operational research will be shared.

BPAL Regimen for Treatment of highly-resistant tuberculosis under operational research conditions: Ukraine Experience, safety, and end of treatment outcomes

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Ukraine is the first country in the world to pilot the BPAL regimen under operational research conditions. From November 2020 till April 2021, 78 patients were screened and 65 patients were enrolled in the BPAL treatment from 18 oblasts of Ukraine. The BPAL treatment is provided at the National Institute of Phthiology and Pulmonology in Kyiv.

The pilot study aims to enroll 135 patients by the end of July 2021. We will report preliminary results on the BPAL regimen's safety, end-of-treatment outcomes, and lessons learned from the frontline of BPAL introduction under operational research conditions.

Experience, safety, and end of treatment outcomes from BPAL Clinical Access Program in South Africa

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South Africa is the second country in the world to implement BPAL and commenced treatment of patients, under the BPAL Clinical Access Programme (CAP) at five sites in March 2021. Coordinated by Wits Health Consortium, South African Department of Health's BPAL CAP aims to enroll 400 patients. We will report preliminary results from the CAP about the BPAL regimen's safety, end-of-treatment outcomes, and lessons learned so far in the treatment of XDR- and MDR-TB with BPAL.

BPAL introduction in The Philippines

I Flores,¹ ¹San Fernando, Pampanga, San Fernando, Pampanga, Philippines. e-mail: docging1003@gmail.com

Twelve sites from ten regions in the Philippines were systematically engaged for the BPAL OR following advocacy from LIFT-TB. The issuance of a Department of Health Memorandum garnered support for this new all-oral three-drug regimen for highly drug-resistant TB pa-

tients from partners and civil society. The NTP through the central Research Team provided leadership through site and laboratory needs assessments, training, supportive monitoring with periodic clinical advice from TB Medical Advisory Committees in collaboration with technical partners.

We will present lessons learned in strengthening capacity both for programmatic and clinical DR-TB patient management through the introduction of the BPAL OR.

SP-28 TB and mental health: integrating mental health into TB services for person-centred care

Mobile-based counselling support for patients on Tuberculosis treatment in South India

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Careline – a simple, cost effective, mobile technology with a human touch, with scheduled outbound calls, supports private sector patients to overcome emotional challenges and complete TB treatment. It is operated by a team of women interested in patient wellbeing, trained in counselling, fluent in 6 languages.

Careline provides TB treatment literacy, addresses anxiety, low self-esteem, loneliness, improves family support through caregiver counselling, gives feedback to the treating doctors. Careline has reached out to 18,389 patients, 10,718 patients completed treatment successfully. Careline services are preferred by, elderly and young, 31% of registered patients are either aged, 0-14 or above 60 years.

Training TB and primary care providers to deliver a brief mental health intervention in Brazil: Results from a pilot implementation study

A Sweetland,¹ ¹Columbia University, New York, United States. e-mail: annika.sweetland@gmail.com

This pilot study involved training 36 non-mental health specialists of all levels (e.g. community health workers, nurses, doctors) from three pilot sites in Brazil – two primary care clinics and a municipal TB program – to screen for and deliver a four session evidence-based treatment intervention (Interpersonal Counseling - IPC) for mild- to moderate-depression.

During the one-year implementation pilot study, providers were offered weekly in-person clinical supervision. Qualitative data includes six focus groups prior to the

one-year intervention pilot (pre-implementation, n=42) and seven focus groups after the pilot (post-implementation, n=38) with health coordinators, primary care providers, and patients.

Approaches to deliver depression care in TB services in LMICs: a systematic review

R Nava-Ruelas,¹ ¹University of York, York, United Kingdom. e-mail: rdnr500@york.ac.uk

Depression is a common comorbidity in tuberculosis (TB). However, depression care is not routinely integrated into TB services. The aim of this systematic review was to explore the approaches to the delivery of depression care for people with TB in LMICs, including barriers and facilitators for their implementation. 10,982 articles were screened and 10 articles were included in the analysis.

The interventions implemented were psychological, psychological and pharmacological, and other types including socioeconomic support and referrals. These were mainly aimed at MDR-TB patients, with the rest addressing unspecified TB patients, and one targeting healthcare providers. An analysis of barriers and facilitators will be presented.

TB-Associated Depression Risk: A Population-Based Cohort Study of Immigrants to British Columbia, Canada, 1985-2015.

C Basham,¹ ¹University of British Columbia, Vancouver, Canada. e-mail: umbashac@myumanitoba.ca

Tuberculosis (TB) has been associated with incident depression; however, studies of TB-associated depression are lacking in a low-TB-incidence setting.

This talk will present estimates of the risk of TB-associated depression and potential mediation by the length of hospital stay. A cohort study of linked healthcare claims and public health surveillance data was conducted. Multivariable Cox proportional hazards (PH) regression with causal mediation analysis was used to estimate total effect, direct effect, and indirect effect of TB on depression risk. Results are presented and interpreted in light of potential interventions in similar low-TB-incidence settings.

SP-29 Study S31/A5349 of high-dose rifapentine with/without moxifloxacin for shortening TB treatment: Month 18 efficacy results, translational science and policy implications

Final 18-month analysis of efficacy of rifapentine-based regimens

P Phillips,¹ ¹University of California San Francisco, San Francisco, United States. e-mail: Patrick.Phillips@ucsf.edu

This talk will present and discuss results for the trial's secondary efficacy endpoint of tuberculosis disease-free survival at eighteen months after study treatment assignment.

This talk will also discuss the application of whole-genome sequencing for outcomes assignment, the frequency of differing outcomes at 12- and 18-months timepoints and reasons for discrepancy, and 18-month subgroup outcomes.

Exposure-response analysis of Study 31/A5349

V Chang,¹ ¹University of California at San Francisco, San Francisco, United States. e-mail: vincent.chang@ucsf.edu

This talk will discuss the association between individual study drug pharmacokinetic (PK) parameters and TB treatment efficacy outcome of Study 31/A5349. Pharmacokinetic properties of key drugs will be presented including causes of between-patient variability and differences between HIV infected and noninfected patients.

Pharmacodynamics (PD) and patients' risk factors in Study 31/A5349 combination regimens

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

This talk will present relationships between patient phenotypes, drugs' exposure and treatment response in Study 31/5349. This will include discussion of relative effects of study drugs' pharmacokinetics in the regimen stratified for different cohorts by disease burden.

The interacting contributions of several drugs will be considered. Strategies for optimal treatment approaches in all patients will be presented.

M. tuberculosis RNA transcriptomic expression profiling in sputum of patients with active pulmonary TB

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This talk will present results of analyses exploring non-culture-based, pathogen-specific biomarkers of tuberculosis treatment effect. We will describe drug impact on *M. tuberculosis* RNA pharmacodynamic markers across S31/A5349 treatment regimens, diverse *M. tuberculosis* lineages, and diverse patient populations.

S31/A5349 results and WHO guidelines on TB treatment

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This talk will describe the process of WHO guidelines development and recent review of the new 4-month rifampentine-moxifloxacin-based regimen for drug-susceptible pulmonary tuberculosis, and will discuss implementation considerations and remaining research gaps.

SYMPOSIA: FRIDAY 22 OCTOBER 2021

SP-30 Human rights protection: enabling access to effective TB prevention and care in refugees, migrants and other displaced persons

The use of pre-existing TB infrastructure to enhance COVID control among migrants in Israel

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Israel hosts ~200,000 non-citizen migrants, who have limited access to social and healthcare services. During COVID-19 pandemic, governmental authorities and NGO's responded swiftly and provided targeted awareness campaigns, access to COVID-related testing and medical-care, food supply, housing and vaccinations. The pre-existing TB-related communication channels between the migrants and governmental authorities and the trained personnel were fundamental in formulating productive dialog to appropriate solutions to ensure access to medical and social support.

This lecture outlines the challenges in overcoming the mistrust of the migrants and re-building productive support. Additionally, how those ties can further be used for TB control among migrants.

Impact of COVID-19 on TB in the refugees and hosting population in Cox's Bazar, Bangladesh

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BRAC has been implementing TB control services in FDMN population and host community in Cox's Bazar, Bangladesh. It established peripheral laboratories and introduced 2 mobile X-ray van with Gene Xpert facility. COVID 19 pandemic has an impact on TB cases detection due to lockdown, transport restrictions, fear and stigma. Both TB presumptive identification and cases detection decreased to 16% (41,783 in 2019 vs 36,109 in 2020) and 23% (3463 in 2019 vs 2669 in 2020) respectively in FDMN population.

Efforts made to improve engagement of Rohingya and host community to increase case detection and sustain treatment success rate.

The COVID-19 pandemic and internal labour migration in India

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- Timeline of the lockdowns in India
- Impact of migration and migrant workers
- Impact on TB services and service delivery

Declaration of intent on TB care for migrants by parliamentarians of the EECA region

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Migrants may be of increased risk for the development of tuberculosis for several reasons. In the country of destination, they may have difficulties to access health-care, leading to delays in the diagnosis, initiation and/or continuation of treatment.

Migrants, who due to different reasons move between countries including the EECA Region, should have universal access to state-of-the-art diagnosis of tuberculosis and expert medical care exactly as the natives of the receiving country. Expert medical healthcare and logistics solutions for uninterrupted treatment should be provided free of charge in the country of destination and/or transit. No patient with tuberculosis should be forced to leave the country while receiving medical treatment. That is why the Declaration of intent on TB care for migrants by parliamentarians of the EECA region is now in the process of developing and during my presentation I will show you the context of it and we will briefly discuss further steps on its implementation.

Interagency field manual on tuberculosis treatment, care and prevention in refugee and displaced populations

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WHO, UNHCR and the US Centers for Disease Control and Prevention (CDC), are working towards finalising an Interagency Field Guide on tuberculosis treatment, care and prevention in refugee and displaced populations.

This operational guide provides an overview of key actions in preparing for, and delivering, effective TB prevention, treatment and care services for refugees and other populations in humanitarian emergencies. The actions are designed to be integrated fully within coherent emergency preparedness planning and response. The presentation will present an outline of the manual and next steps for its roll out.

Dismantled systems stymie infectious disease screening efforts along the US/Mexico border

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Changing immigration practices at the US/Mexico Border and an increased volume of asylum seekers approaching the border seeking admission have resulted in a loosening of long-standing infectious disease screening for individuals presenting at ports of entry. Systems changes are required to reestablish long standing infectious disease screening practices.

SP-31 Closing the gap in paediatric TB case detection: improving bacteriological diagnosis and evidence-based TB treatment decision algorithms

Diagnostic accuracy of Xpert MTB/RIF Ultra using different sample types in children: a systematic review and meta-analysis

A Kay,¹ ¹Baylor College of Medicine and Texas Children's Hospital, Houston, United States. e-mail: Alexander.Kay@bcm.edu

Dr. Kay will present the results of a comprehensive systematic review and meta-analysis on the diagnostic accuracy of Xpert Ultra for childhood pulmonary tuberculosis.

The presentation will focus on diagnostic accuracy data specific to sputum, gastric aspirate, nasopharyngeal aspirate and stool specimens in sub-populations disaggregated by age, HIV and nutritional status.

Implementing sample collection procedures for pediatric TB diagnosis under programmatic conditions : experiences from CaP TB project in Cameroon

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While clinical diagnosis is critical in pediatric TB case detection, bacteriological confirmation can play a key role in simplifying the diagnostic pathways and in allowing timely identification of drug resistance. Producing sputum is however challenging for young children.

The catalyzing pediatric tuberculosis (CaP TB) project, a multi-pronged pediatric TB case-finding intervention, has introduced and generated evidence on the imple-

mentation of collection procedures for various sample types (induced sputum, gastric aspirate, nasopharyngeal aspirate).

This presentation will discuss the feasibility of implementing various respiratory sample collection procedures in the Cameroon context and their contribution to diagnosing children with bacteriologically confirmed pulmonary TB.

Optimization of stool processing for Ultra testing: pooled data from two head to head studies comparing stool processing methods

P Nabeta,¹ ¹FIND, Geneva, Switzerland. e-mail: pamelana.nabeta@finddx.org

FIND and the TB Speed consortium are conducting two prospective, multicentric, diagnostic accuracy studies in children to assess the performance of centrifuge-free stool processing solutions for the diagnosis of pulmonary TB. Three methods are being evaluated the Stool Processing Kit (FIND), Sucrose Flotation (TB-Speed) and Simple One-Step (KNCV), in combination with Xpert Ultra.

Following-up on last year's symposium Dr Nabeta will present the preliminary results based on pooled data from these two studies.

Acceptability and feasibility of nasopharyngeal aspiration (NPA) and optimization for implementation at primary health care level: results from TB-Speed project

M Bonnet,¹ ¹French National Research Institute for Sustainable Development, Montpellier, France. e-mail: maryline.bonnet@ird.fr

Dr Bonnet will present results of the detection yield, acceptability and feasibility of using nasopharyngeal aspirate tested by Xpert Ultra for diagnosis of tuberculosis in children from the UNITAID and initiative 5% funded TB-Speed project. She will also present findings of the market screening for battery operated aspirators and the development of a manually operated aspirator pump to support the implementation of the nasopharyngeal aspirate at low level of health care facilities in resource limited countries.

Time for a paradigm shift: the role of paediatric TB Treatment Decision algorithms

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While improved microbiological diagnosis is a vital component of child TB treatment initiation, it is unlikely to be the only solution. Due to the paucibacillary nature

of disease and limited availability of microbiological tools, complementary approaches are required. Dr Seddon will present results of a large multi-study individual patient cohort that was brought together with multiple collaborators, and that was used to evaluate different treatment decision approaches as well as to develop a novel algorithm.

The future integration of clinical, radiological, microbiological and biomarker information in a data-driven manner is likely to improve child TB diagnosis.

SP-32 Leveraging existing platforms to ensure coordinated and improved diagnostics and care for HIV, TB, HPV and Covid-19

Global Fund support mechanisms to mitigate impacts of COVID-19 on TB

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COVID-19 continues to disrupt essential health services across all continents; TB notifications dropped by 21% during 2020, (WHO/2019-nCoV/EHS_continuity/survey/2021.1) due to a mix of demand and supply side factors. The Global Fund is helping address critical gaps in TB services through the COVID-19 Response Mechanism, initiated in 3/2020 with US\$988 Million, and additional >\$3.7 Billion in 2021. The 'Lab and Diagnostics' pillar will comprise investments in specimen transportation; lab information systems and digital connectivity; equipment management; biosafety; waste management; and quality management systems.

Here we present an overview of how countries have used C19RM to date and discuss anticipated impacts on TB services.

TB and multimorbidity: a systematic-review to estimate the prevalence of different clusters of co-morbidities

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Multimorbidity is a growing concern in low- and middle-income countries. We performed a meta-review and a systematic review to estimate the prevalence of different clusters of one (meta-review) or two or more (systematic review) chronic conditions in people with TB. We searched in seven different databases and included 57 systematic reviews and 89 primary studies. The most prevalent clusters of comorbidities were TB+Depression

(45.19%, 95% CI 38.04% - 52.55%, 25 studies, 4,903 subjects, I2 = 96%), TB+HIV (31.81%, 95% CI 27.83% - 36.07%, 68 studies, 62,696 subjects, I2 = 98%), and TB+DM (17.7%, 95% CI 15.1% - 20.5%, 48 studies, 48,036 subjects, I2 = 98%).

The most prevalent clusters of multimorbidity were TB+ Depression+ Anxiety (15.27%, 95% CI 10.7%-20.47%, 3 studies, 1,473 subjects, I2 = 63.81%), TB+ HIV+ PTSD (14.84%, 95% CI 13.9% - 15.8%, 2 studies, 5,400 subjects), and TB+ HIV+ Anxiety (12.72%, 95% CI 7.17% - 19.55%, 5 studies, 1,913 subjects, I2 = 93.74%). Heterogeneity was high, but these results can inform future prioritisation decisions.

Covid-19 adaptations to ensure coordinated and improved diagnostics for HIV, TB, HPV, Covid-19, Nigeria Experience

M Okoye,¹ ¹CDC Nigeria, -, Nigeria. e-mail: luo9@cdc.gov

As part of the COVID-19 pandemic response in Nigeria, we leveraged the existing HIV PCR Laboratory network and adapted it to integrate COVID-19 testing and provide testing for large volume COVID-19 samples at central and regional levels. We also leveraged the TB GeneXpert labs and adapted this for the integrated testing of TB and COVID-19 and support decentralised testing of low volume COVID-19 samples at state levels. As a result of these adaptation the lab networks, we were able to support increased access to COVID-19 testing across the entire country while sustaining HIV viral load, EID, and TB testing.

Bidirectional screening for TB and diabetes mellitus in Ethiopia as an opportunity for integrating COVID-19 care

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Ethiopia is a high TB burden country and ranks third in terms of the number of adult DM patients in sub-Saharan Africa. In 2020, we initiated a TB/DM bidirectional screening project in Addis Ababa through which we screened 732 TB patients for DM, and 843 DM patients for TB. Of 60 DM patients detected in TB patients, 42% were newly diagnosed. Among DM patients, X-ray-based screening detected three of the four TB patients identified.

In addition, we detected and managed COVID-19 patients through the routine screening approach. This highlights the potential utility of COVID-19 screening in the existing system.

Coordinated and uninterrupted diagnostics for HIV, TB in Uganda during COVID-19

C Mwangi,¹ ¹CDC, -, Uganda. e-mail: mwn0@cdc.gov

The Uganda, Ministry of Health (MoH) and its health development partners collaboratively leveraged prior investments in laboratory systems to plan, implement and monitor the COVID-19 laboratory response. The MoH used its existing coordinating structures, adapted the integrated specimen transportation network, incorporated COVID -19 into its centralised and decentralised testing and used the existing viral load and EID reporting systems as a template for the development of COVID result returns systems and ECHO zoom training for rapid competence as well as quality assurance.

Though there were initial dips in VL, EID and TB indicators during lockdown periods, the MoH policy and guidance allowed for a resurgence of these indicators to normal or above normal expectations, whilst maintaining quality of testing of TB, VL, and EID.

SP-33 Youth power to #EndTB: leading through innovation during the Covid-19 pandemic

Leading innovative efforts to galvanize young people to join the fight to end TB

A Stukalova,¹ ¹WHO, Geneva, Switzerland. e-mail: anna.stukalova@gmail.com

Today's generation of young people needs to be empowered and given the right opportunities to prove their potential as effective drivers of change. WHO has led this change and is working towards mobilizing more youth as health champions to end TB. Anna and Yi will share the progress made in engaging youth through WHO's 1+1 youth initiative to end TB and give an overview of innovative approaches and digital solutions to strengthen and empower youth in the fight against TB.

Boosting research and innovation to end TB: Young people have a role to play

P Tisile,¹ ¹University of Cape Town, Cape Town, South Africa. e-mail: ptisile@gmail.com

Despite being an old and deadly infectious disease, there is still no point-of-care test, few new drugs and no effective preventive vaccine against TB. Phumeza Tisile, who lost her hearing as a side-effect of treatment of drug-resistant TB, has a lot to say about the importance of innovation and learning experience from the COVID vaccination system.

How to succeed in enhancing TB activism among young people in the post-pandemic world

S Uakkas,¹ ¹The Moroccan federation of medical students, Kenitra, Morocco. e-mail: saaduakkas@gmail.com

The recent pandemic induced mobility restrictions, limited field access and less interactions with decision-makers for youth. This negatively affected youth advocacy and activism efforts. The session will guide participants to elevate their youth advocacy efforts and share strategies to help them do so.

Becoming a caretaker buddy – The role of young volunteers in maintaining uninterrupted TB services for patients through online peer-to-peer support community in China

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“57 Zone” is an online communication platform for the former and current TB patients, volunteers from the zone provide peer-to-peer consultation to patients with both medical and psychological difficulties, all TB patients are also encouraged to act as peer consultants to help others in the zone. During the COVID-19 pandemic, Xu cooperated with volunteers from the 57 Zone and the medical staff of hospitals to provide online medical treatment and consultation services to ensure uninterrupted treatment and care for TB Patients.

In this session, Xu will share the successful cases from China on the online peer-to-peer support mechanism.

Social Media is a Future: Fresh ideas how to encourage youth in engaging TB

S Anggita,¹ ¹TB youth movement Indonesia, Jakarta, Indonesia. e-mail: anggitasiva@gmail.com

Social Media usage has been shown to increase in situations of the global pandemic. Through social media communication, we can collaborate around the globe in a faster way. It is crucial for the Youth TB community to strengthen their capabilities and expand to a more social media-friendly network. Being active on TikTok and other Social Media platforms, Siva will share her experience and bring fresh ideas on how to encourage youth in engaging TB programs, media campaigns and raise TB Awareness through social media.

SP-34 TB-PRACTECAL: trial results and next steps

Study protocol and stage 1 results

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TB-PRACTECAL is a phase II/III study undertaken to GCP-ICH standards. The study chose an adaptive design to examine a range of 6 month regimens containing bedaquiline, linezolid and pretomanid compared to the locally approved standard of care. The phase IIB study which made up the 1st stage of the trial was used to choose the most promising regimen/s for stage 2. The study design and stage 1 results will be presented.

Stage 2 trial efficacy results

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

TB-PRACTECAL, stage 2 corresponded to a phase III trial comparing bedaquiline, linezolid and pretomanid with moxifloxacin (BPALM) to the standard of care. The interim efficacy results at end of randomisation will be presented.

Stage 2 trial safety results

K Fielding,¹ ¹London School of Hygiene and Tropical Medicine, London, United Kingdom. e-mail: katherine.fielding@lshtm.ac.uk

TB-PRACTECAL, stage 2 corresponded to a phase III trial comparing bedaquiline, linezolid and pretomanid with moxifloxacin (BPALM) to the standard of care. Patients were followed for known potential toxicities including cardiac, neurological and hepatic toxicity. The safety results at end of randomisation will be presented.

Practical aspects of implementation and care – investigator perspective

C Narasimooloo,¹ ¹TB & HIV Investigative Network – THINK, Durban, South Africa. e-mail: c.narasimooloo@think.org.za

TB-PRACTECAL was implemented during a dynamic period in drug resistant TB care with multiple changes to guidelines followed by the COVID-19 pandemic. Throughout, the team prioritised optimised care with adherence support, participant engagement and clinical care being continuously adapted to the changing needs. A provider perspective will be presented sharing the challenges, success and opportunities.

Next steps – Mobilising the TB community to scale up short regimens and live Q&A

E Kazounis,¹ ¹Médecins Sans Frontières, London, United Kingdom. e-mail: emil.kazounis@london.msf.org

Data from TB-PRACTECAL will be shared in time for the next WHO review of drug resistant TB guidelines in 2021/22. At this important juncture, we will discuss the practical implications for scaling up of these regimens and the importance of placing people with TB and TB survivors at the centre of this planning.

This session will include input from National TB programme implementers, patients, speakers from talks 1, 2, 3 and 4 and other members of the TB community.

SP-35 Alleviating the burden of non-communicable respiratory disease in low- and middle-income countries: spotlight on pulmonary rehabilitation

WHO insights: Current Global Estimates of the Need for Rehabilitation and the Rehabilitation 2030 Initiative

A Rauch,¹ ¹WHO, Geneva, Switzerland. e-mail: raucha@who.int

Rehabilitation is a priority health strategy for the 21st century. An estimated 2.4 billion people worldwide require rehabilitation at some point in their lives. These needs are spread across the lifespan and include the needs of those with pulmonary diseases. Many individuals, however, do not have access to much needed rehabilitation services, which exacerbates their condition and may lead to further complications and lifelong consequences. To date, however, perspectives on rehabilitation have been predominantly clinical.

During this session, the WHO will present both the current global estimates on the need for rehabilitation and its Rehabilitation 2030 Initiative.

Pulmonary Rehabilitation in Low- and Middle-Income Countries: State of the evidence and insights from the NIHR Global RECHARGE Group

M Orme,¹ ¹University of Leicester, Leicester, United Kingdom. e-mail: mwo4@leicester.ac.uk

Implementing clinically and cost-effective interventions to tackle chronic respiratory diseases, including post-TB lung disease, can be challenging in low-resource settings. Pulmonary Rehabilitation is a low cost, high

impact intervention that reverses CRD-related disability and is supported by the highest level of research in high income countries. Pulmonary Rehabilitation is delivered by a multidisciplinary team and has exercise training and education at its core to support effective disease management and improve people's quality of life.

This talk will explore efforts to develop, test and implement Pulmonary Rehabilitation in low resource settings, including the work of the NIHR Global RECHARGE Group.

Systematic review of clinical effectiveness, components, and delivery of pulmonary rehabilitation in low-resource settings

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Most evidence about the effectiveness and components of Pulmonary Rehabilitation (PR) is generated from high-income countries (HICs). In Low- and Middle-Income Countries (LMICs) it is under-provided and limited evidence is generated. We aimed to review the effectiveness, components and mode of delivery of PR in low-resource settings systematically. Thirteen trials were selected for the review of which two had moderate quality and others were at high risk of bias.

Despite the limitation of the trials, PR was found to be effective, deliverable, and acceptable in LMICs. Barriers and facilitators PR implementation is different from that of the HICs as well.

A development study of pulmonary rehabilitation for patients with chronic lung disease in Uganda

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We completed a pre-post intervention study of a 6-week, twice-weekly pulmonary rehabilitation (PR) for people with post TB lung disease at Mulago Hospital, Kampala, Uganda. PR was feasible and acceptable to patients and to the hospital staff at all levels. Major improvements were seen in exercise capacity and health status. In many patients, the experience was life-changing, allowing severely incapacitated patients who were entirely dependent on others to now function normally in work and social activities. This talk will present the development process of the programme in Uganda.

SP-36 TB reduction through expanded ART and TB screening (TREATS): universal screening and treatment for TB-HIV in Zambia and South Africa

Qualitative evaluation of the role of community health workers in systematic TB screening in Zambia, the HPTN 071 PopART Trial

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During the HPTN071 PopART trial, a trial cadre of community health workers called Community HIV care Providers (CHiPs) screened household participants for TB, provided TB health education and took sputum samples if necessary, alongside providing a HIV prevention package.

Towards the end of the intervention (2018), social scientists conducted 18 observations of CHiPs, 18 drop-in visits with recipient households, 9 health facility observations and in four intervention communities, held focus groups discussions with CHiPs and interviewed 48 TB patients about how they experienced the CHiPs role in TB.

This presentation will present a qualitative evaluation of this household level approach.

Did HPTN 071 (PopART) reduce the incidence of TB infection among adolescents and young people?

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There are limited studies that evaluate the impact of a combination HIV prevention package including TB screening and universal testing and treatment on transmission of TB.

We report on the impact of a community randomized HIV-prevention trial (PopART) on the incidence of TB infection measured in a cohort of adolescents and young people (15-24 years) that were initially QuantiFERON Plus negative, and followed up for 2 years. The study was done across 14 communities with high TB/HIV prevalence in Zambia and Cape town, South Africa. We present cluster level analysis using the community rates of TB infection.

Impact of population level screening for tuberculosis, combined with universal testing and treatment (UTT) for HIV on TB prevalence

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A key TREATS outcome was TB prevalence among individuals aged ≥ 15 years, compared between 14 communities randomized to receive the PopART intervention (2014-2017) and 7 communities under standard-of-care. PopART brought a combined TB/HIV intervention of population level TB symptom screening and diagnosis, combined with universal testing and treatment for HIV. TB prevalence was measured in a randomly selected sample of individuals in each community, with a total sample size of around 56,000.

Results were analysed and will be presented by trial arm and interpreted in the context of the wider impact of the intervention on TB and HIV outcomes.

Did HPTN 071 (PopART) reduce notified TB disease incidence?

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To measure the primary outcome of the HPTN 071 (PopART) trial, a randomly selected cohort of ~ 2000 adults aged 18-44 years were enrolled from each of the 21 communities. This population cohort was followed-up annually over 36 months. Using a combination of routine community-level TB notification data and population cohort data, the effect of the HPTN 071 (PopART) intervention on TB case notification rates in intervention communities compared to control communities will be reported.

What do all of these results tell us about universal TB and HIV screening?

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We will present results from modelling that gives an integrated account of TB dynamics under PopART calibrating to all of the available data, and estimates the relative contribution of different intervention components to observed effects. The TREATS model is a deterministic, compartmental TB transmission model with age-, sex-, and HIV/ART-structure that includes dynamics of population-level immunity under the UTT intervention derived from PopART HIV-modelling.

The model will be used for health-economic evaluation to estimate the cost-effectiveness of PopART, including TB, compared to standard of care, and to explore economies of scope in delivering TB screening alongside HIV UTT.

SP-37 Closing the gaps in the TB-HIV care cascade: what's new?

Global update on burden and policy

A Baddeley,¹ ¹World Health Organization, Geneva, Switzerland. e-mail: baddeleya@who.int

At the UN High-Level Meeting on ending AIDS in 2016, Member States signed up to reducing TB deaths by 75% in 2020, compared with 2010. Globally deaths have reduced by 63% in 2019 with high variability across regions and countries. COVID-19 has taken its toll on TB and HIV service delivery.

This presentation will review the burden of HIV-associated TB globally, according to latest data reported to WHO.

It will also identify the gaps in the TB/HIV care cascade and provide updates on the latest guidance and highlight opportunities to address these gaps.

Diagnostic accuracy of TB screening tools in people living with HIV: an individual patient data meta-analysis

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In 2011, WHO recommended a four-symptom rule (i.e., any of current cough, fever, weight loss, or night sweats) for screening for TB in HIV-positive people. However, it has low specificity, as well as low sensitivity in certain groups (e.g. those on ART). Ideally, according to WHO, a triage/screening test should have 90% sensitivity and 70% specificity.

This presentation will discuss the diagnostic accuracy of screening tests and approaches other than WHO four-symptom rule in all HIV-positive people and clinically important subgroups.

Optimal timing to start anti-retroviral treatment among people with HIV-associated TB

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HIV and tuberculosis are frequently diagnosed concurrently. In March 2021, World Health Organization recommended that ART should be started within two weeks of tuberculosis treatment start, regardless of CD4 count.

We will summarise evidence supporting this recommendation through systematic review and meta-analysis. All nine trials of earlier vs. later ART start for people with tuberculosis were conducted between 2004 and 2014 - before recommendations to treat HIV at any CD4 count

or to rapidly start ART in people without tuberculosis, and used legacy ART regimens. We will put the evidence in the context of tuberculosis and HIV care in 2021.

Interventions to improve linkages to testing and treatment for HIV-associated TB

A Salomon,¹ ¹McGill University, Montréal, Canada.
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Linkages between HIV and TB care are below the 2030 global targets, particularly at the points of diagnosis and treatment initiation for TB-HIV co-morbidity.

A systematic review of interventions impacting gaps at these points of the TB-HIV care cascade found co-locating services had the most consistently positive effect on TB case detection amongst PLHIV, and HIV testing and treatment initiation among PWTB. Peer support, healthcare worker training, and patient education/counselling interventions did not have consistently positive effects in isolation; instead, we found that wider health system, human resource and laboratory capacity were key to successful integration and improved outcomes.

The role of advocacy and social mobilization to address TB-HIV co-morbidities – lessons and perspectives from civil society in Asia and the Pacific

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The 2018 Political Declaration on TB committed to ensure the strong and meaningful engagement of civil society and affected communities in the TB response. While this concept of ‘meaningful engagement’ is new in the context of TB, this principle, inspired by Greater Involvement of People with HIV and AIDS (GIPA), continues to influence the advocacy and social mobilisation of TB-affected communities, including people living with HIV, especially those that have started from HIV and AIDS advocacy.

This presentation will showcase lessons from civil society from Asia and the Pacific in mobilization and advocacy in the TB response.

SP-38 Importance of early and rapid TB diagnostics: engaging private laboratories

Public in private: Challenges and solutions in engaging private laboratories in Nigeria

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This presentation outlines the complex interactions of the diagnostics processes and stakeholders in Nigeria, including the role of the private laboratories, with an emphasis on placing subsidized Xpert machines in private laboratories.

Private in public: a new model for TB laboratory collaboration in India

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World Health Partners have tried different approaches to laboratory testing for private provider engagement, including establishing their own standalone laboratory, and placing machines and technicians within a public sector facility.

Networking and sample transport to link public and private facilities

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In the absence of a true point-of-care diagnostic for TB, sample transport and networking are central elements for any TB program. Methods to apply these concepts to both public and private sector facilities will be discussed.

Expansion of the TB diagnostics market in private laboratories

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This presentation outlines opportunities and challenges for private laboratory engagement from a key vendor in the TB diagnostics field, including issues such as pricing, demand generation, and obstacles along customer journeys.

ABSTRACT PRESENTATIONS WEDNESDAY 19 OCTOBER 2021

ORAL ABSTRACT SESSION (OA)

OA-01 Road to TB elimination: scaling up TB preventive therapy in LMICs

OA01-593-19 The introduction of 3HP nearly doubled the uptake of TB preventive treatment among PLHIV newly initiated on ART in Ethiopia

P. Mitiku,¹ A. Bedru,² E. Abdissa,³ M. Gebremichael,¹ J. Hill,⁴ C. Mulder,⁴ S. Borsboom,⁴ I. Koppelaar,⁴ M. Getachew,⁵ T. Letta,⁵

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Background and challenges to implementation: Despite tuberculosis preventive treatment (TPT) being considered an effective strategy to reduce TB incidence and death among people living with HIV (PLHIV) newly enrolled on ART, the uptake in Ethiopia has been historically low.

Intervention or response: In 2019 a national task force was established for introducing a 3-month weekly administered treatment course of rifapentine with isoniazid (3HP). Since 2020 rifapentine has been imported into the country with support from KNCV/UNITAID through the IMPAACT4TB project. Seventy-three health facilities from three regions and one city administration were selected for initial 3HP implementation. We, together with technical partners, provided trainings to program officers, clinical mentors, and health care providers on the TPT care cascade, including 3HP.

Results/Impact: Following implementation of 3HP, the TPT coverage among PLHIV newly initiated on ART in the 73 facilities improved from 32.6% (1,902/5,824) prior to the implementation of 3HP (July 2019 to July 2020) to 68.9% (2,430/3,524) during August 2020 to March 2021.

However, there was a dramatic dip during the second quarter of 2020 which coincided with the beginning of the first wave of COVID-19 in the country. Occurrence

of COVID-19 and subsequent delay in delivery of supply and pill burden on clients were challenges to 3HP implementation.

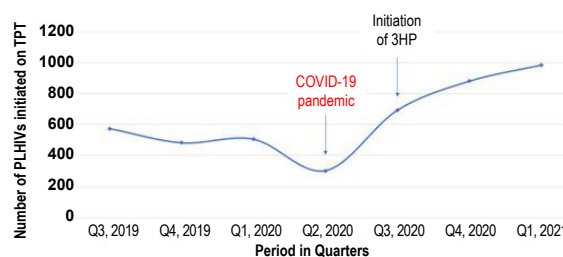


Figure: Quarterly trend of TPT uptake among PLHIV newly initiated on ART in 73 health facilities, Ethiopia, July 2019 to March 2021

Conclusions: Combining national efforts with a clear strategy for introducing 3HP showed that it is possible to nearly double the TPT uptake among PLHIV newly enrolled on ART. Yet, additional efforts to improve service delivery are required to close the gap on TPT uptake to achieve the national and global targets.

OA01-594-19 Knowledge, attitudes, beliefs and stigma among newcomers regarding TB infection and treatment

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Background: It is estimated that a quarter of the world is infected with *Mycobacterium tuberculosis*, the causative agent of tuberculosis (TB). Approximately 10 million people suffered from TB, and 1.4 million died from the disease in 2019. Current comprehensive immigration medical examinations in Canada may identify individuals with active pulmonary TB but not those with latent TB infection (LTBI). Immigrants (newcomers) from high TB-burden countries have an increased risk of LTBI with the plausible development and transmission of active TB. To improve the global prospect of eliminating TB by 2050, our TB focus must include comprehensive strategies directed toward improved LTBI surveillance,

integrated LTBI screening, and treatment. The success of LTBI screening and treatment programs requires an engaged newcomer community. This study explored the knowledge, attitudes, beliefs, and stigma of TB infection among newcomers in Atlantic Canada.

Design/Methods: This was a qualitative cross-sectional study among newcomers aged 19 years old and older in the Atlantic Canadian region of southern New Brunswick (NB). Study participants were recruited via social media and snowball sampling. Data was collected through semi-structured interviews and focus group discussions. All interviews were audio-recorded and transcribed verbatim, and the data was analyzed using thematic analysis.

Results: A total of 43 newcomers from 19 countries participated in the study. They included 14 (32.6%) male and 29 (67.4%) females with an age range of 22 - 52 years and a mean of 38.2 years.

Our findings identified four emerging themes:

- i) willingness to get tested and treated for LTBI;
- ii) desire for enhanced LTBI awareness;
- iii) importance of supporting people with an LTBI diagnosis; and,
- iv) common experience of the stigma associated with TB.

Conclusions: These findings support implementing an LTBI screening program in southern NB and highlight the need for enhanced TB awareness campaigns and support of affected individuals and reducing TB-associated stigma.

OA01-595-19 Best practices from Zambia's scale-up of TB preventive therapy amidst Covid-19

N. Kasese-Chanda,¹ M. Amin,¹ M. Kangwa,¹ ¹United States Agency for International Development, Health, Lusaka, Zambia. e-mail: pkasesechanda@usaid.gov

Background and challenges to implementation: Background: In 2020, Zambia recorded a five-fold increase in TB preventive therapy (TPT) results: 289,000 clients completed a course of TPT compared to 64,000 in 2019. The achievement was a result of a TPT surge campaign coordinated by the national TB and HIV programs. The PEPFAR/Zambia team were part of a task force that revised TPT Guidelines and assured sufficient commodities. National and site level targets were set. As the novel Coronavirus landed in March 2020, measures were put in place to mitigate its impact.

Context and challenges to implementation: Following the 1st COVID-19 cases, the government issued movement and travel restrictions. The number of clients visiting facilities reduced and some staff were redirected to work in COVID service areas. PEPFAR Zambia rose to the challenge to ensure continuity of the TPT surge campaign in its supported facilities. Here we share 2 high impact interventions.

Intervention or response:

1. Site activation activities at 24 pathfinder sites

We ensured 6 months' supply of drugs and oriented staff in revised guidelines, clinical algorithms, and the Surge M&E framework. We conducted site-driven assessment of barriers to TPT scale-up and developed action plans to address gaps.

2. Alignment of TPT with ART schedules

We provided 6 months supply of INH and Vitamin B6 synchronizing it with ART dispensation.

Results/Impact: Pathfinder site TPT initiation rate increased from 74% to 93% in 20 weeks.

20 of 24 sites recorded completion rates of above 90%; this is above programmatic average of 70%.

Conclusions: Site activation activities improved TPT initiation. Aligning TPT with ART dispensation schedules improved TPT completion.

OA01-596-19 Use of home delivery of TPT approaches among under-5-year-old household contacts (U5 HHCs) in a high TB-HIV burden, low-resource setting: lessons from Northern Uganda

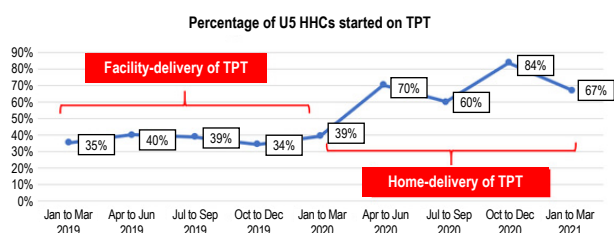
S. Muchuro,^{1,2} S. Amayo,³ E. Kizito,¹ S. Adakun Akello,⁴ H. Kizito,¹ R. Mangeni,¹ E. Laker,⁵ J.P. Otuba,¹ H. Nakato,² S. Turyahabwe,²
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Background and challenges to implementation: The World Health Organization recommends TB preventive treatment (TPT) to prevent TB among high-risk populations including under-5-year-old household contacts (U5 HHCs). Globally, only 20% of the 4 million TPT target for U5 HHCs has been achieved.¹ In Uganda a low resource high TB/HIV burden country, guidelines for TPT among U5 HHCs were first rolled out in 1992. However, national uptake remained rather low at 32.4% in Jan-Dec 2020 and 31% in Jan-Mar 2021.

Caretakers cite high travel costs as a key barrier to facility delivered TPT among U5 HHCs. We compared TPT provision at home versus that at health facilities in Acholi region in northern Uganda.

Intervention or response: From April 2020 to March 2021 we implemented a home-delivery approach to TPT. It involved line listing of index TB patients, obtaining consent to visit their homes, contact tracing, evaluation of U5 HHCs for TB symptoms, weighing of asymptomatic U5 HHCs, doze estimation & TPT initiation at home by health workers, recording in registers & reporting to the Ministry of Health, providing TPT refills

through the index patients on their follow up visit to the health facilities, and cohort monitoring & follow up including screening U5 HHCs for adverse events at home. **Results/Impact:** As shown in the graph below, there was a much higher uptake of TPT following onset of the home-delivery approach.



Conclusions: Home-delivered TPT approach increased TPT uptake among U5 HHCs. This strategy may be scaled up to increase TPT uptake among U5 HHCs in other low resource high TB/HIV burden settings.

OA01-597-19 Preparedness in West and Central Africa for implementing the new WHO guidelines on the treatment of TB infection

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Background: Tuberculosis Preventive Treatment (TPT) is strongly recommended by WHO, with new recommendations to achieve the objectives of the “End TB” strategy. This study aims to highlight challenges faced by West and Central African countries in implementing TPT.

Design/Methods: A self-administered questionnaire was developed and sent through the WARN/CARN-TB network to the 27 National TB Programmes (NTPs) following the release of the 2020 guidelines. The results were shared in a regional workshop on TPT with all NTP coordinators to discuss challenges and solutions.

Results: 22 NTPs responded to the questionnaire. Although all responding NTPs are conducting TPT activities, 2 did not have any normative documents and the 2018 WHO recommendations on TPT were only considered by 10 NTPs. More than half of the countries did not have a dedicated TPT focal person. In 14 countries, domestic funding did not include TPT activities.

The priority targets for TPT in the region remained PLHIV (22 NTPs) and children under 5 years old (20 NTPs). In addition, several NTPs (5) did not conduct home visits as part of their case investigation process. Only 3 NTPs were currently using the new shorter treat-

ment regimens proposed by WHO (3 HP and 1 HP) and 8 countries had plans to acquire rifapentine shortly. Routine NTPs activities concerning TPT and their performance are poorly documented but the survey shows that most NTPs were only able to investigate less than 50% of the estimated number of eligible contacts.

Conclusions: NTPs in both regions face significant challenges in implementing the WHO recommendations for TPT. The barriers and needs are mainly financial and related to training. It is urgent to provide support to these NTPs if we aim to reach UN declaration and End-TB goals. Synergies with COVID-19 mitigation activities should be sought.

OA01-598-19 Scaling up investigation and treatment of household contacts of TB patients in Brazil: a cost-effectiveness and budget impact analysis

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Background: Despite Brazilian guidelines recommending provision of tuberculosis preventive treatment (TPT) for all eligible household contacts (HHC) of pulmonary tuberculosis disease patients, priority continues to be given to diagnosis of tuberculosis disease. We estimated the cost-effectiveness and budget impact of scaling-up an enhanced HHC program in Brazil that would include enhanced detection of tuberculosis disease and provision of TPT.

Design/Methods: We conceptualized HHC cascades-of-care for the current HHC strategy (*status quo*) and two enhanced HHC strategies focused on: 1) tuberculosis disease detection only and 2) tuberculosis disease detection and TPT provision (full HHC management). Effectiveness outcomes were number of patients diagnosed with tuberculosis disease and number of HHC completing TPT per 100 pulmonary tuberculosis patients. Cascade-of-care data were derived from a meta-analysis. Health system costs (2019 \$USD) associated with each step of the cascades-of-care were estimated. We forecasted epidemiological and budget impacts of enhanced strategies using 2019 Brazilian data.

Results: For every 100 new pulmonary tuberculosis patients, 0.2 (95%UI: 0 to 1.5) patients with tuberculosis disease are found and 2.4 (0.1 to 18.1) HHC complete TPT for the status quo. Under a strategy to enhance tuberculosis disease detection, an additional 15.8 (3.5

to 45.2) patients would be diagnosed with tuberculosis disease. If TPT provision was also enhanced, 82.1 (20.1 to 225.1) additional HHC would complete TPT. Each additional tuberculosis disease case detected would cost USD\$300.7 and each additional HHC completing TPT would cost USD\$75.1 (table 1). Nationally, full HHC management would result in an additional 10,267 (95% UI 2,327 to 28,747) cases being detected annually, and 55,159 (95% UI 13,113 to 150,595) HHC completing TPT, utilizing 11% of the national tuberculosis program budget.

	Status quo cascade of care (95% UI)	Enhanced cascade-of-care (95% UI)	Difference [Enhanced- Status quo] (95% UI)
Effectiveness (per 100 new pulmonary TB patients)			
N TB patients prevalent at time of HHC investigation detected	0.2 (0.0 to 1.5)	16.2 (3.7 to 45.2)	15.8 (3.5 to 45.2)
N TPT completed	2.4 (0.1 to 18.1)	86.7 (20.6 to 236.8)	82.1 (20.1 to 225.1)
Costs in USD (per 100 new pulmonary TB patients)			
Investigation only for detection of HHC with active TB	\$986 (\$269 to \$2,826)	\$5,803 (\$1,521 to \$15,472)	\$4,753 (\$1218 to \$12824)
LTBI investigation and TPT provision	\$251 (\$1,718 to \$1,833)	\$6,547 (\$1,718 to \$17,864)	\$6,163 (\$1589 to \$16451)
Incremental cost per additional active TB patient detected			\$300.7
Incremental cost per additional HHC completing TPT			\$75.1

Abbreviations: HHC-Household contacts, TB-Tuberculosis, LTBI-Latent tuberculosis infection, N-Number, USD- United States Dollar UI- Uncertain interval. TPT-tuberculosis preventive therapy.

Table 1 Cost-effectiveness analyses comparing strategies for HHC management.

Conclusions: These findings suggest enhanced detection and treatment of tuberculosis disease and infection among HHC can be highly impactful at reasonable cost.

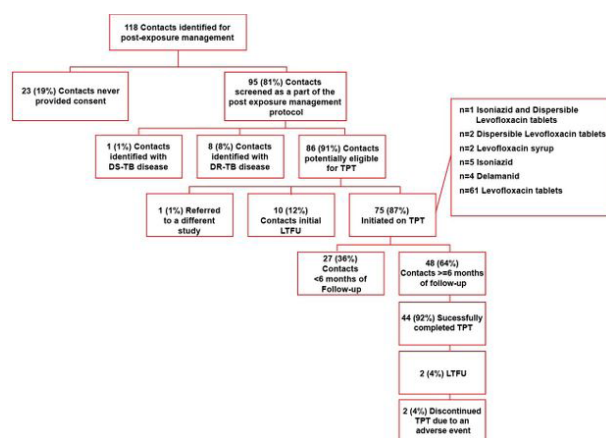
OA01-599-19 A post-exposure programme for children and adolescents exposed to rifampicin-resistant TB in their households in Khayelitsha, South Africa

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Background: One-million household contacts are exposed to rifampicin-resistant tuberculosis (RR-TB) each year. Few receive post-exposure care or tuberculosis preventative therapy (TPT).

Design/Methods: This was a prospective study of a post-exposure management programme among children/adolescents ages 0-18 years, newly exposed to RR-TB in their households in Khayelitsha, South Africa from March 2020-May 10, 2021.

Participants were assessed for active disease at baseline in the clinic or at home using a symptom screener, clinical exam, and chest X-ray where accessible. If RR-TB disease was ruled-out they were initiated on a 6-month course of TPT, determined on the basis of the index-case resistance profile.



Results: Overall, 118 child/adolescent contacts were identified and 95 (81%) consented to the study. Co-prevalent DS-TB and RR-TB disease was found in one (1%) and eight (8%) of them. Of the remaining 86 contacts, one (1%) was referred to a different study, ten (12%) were initially lost-to-follow-up (LTFU), and 75 (87%) were initiated on TPT. The median age of the treated contacts was 9 years (interquartile range [IQR] 5-13); 18 (24%), 51 (68%), and six (8%) were <5, 5-15 and >15 years of age, respectively. Forty-one (55%) were females.

The Figure displays the study flow-chart, including the regimens received and the TPT results for those with more than 6-months of follow-up.

Among the 48 child/adolescent contacts with 6-months of follow-up time, none developed TB disease and 44 (92%) successfully completed TPT. Two (2%) discontinued TPT due to grade-1 vomiting (n=1) and diarrhea (n=1).

Conclusions: We report excellent results from the implementation of a post-exposure management programme, with high rates of detection of co-prevalent RR-TB disease at baseline and very high TPT completion rates. Rollout of TPT for RR-TB needs to be urgently scaled-up as part of ongoing efforts to prevent morbidity and mortality from all forms of TB.

OA-02 TB: transmission to treatment?

OA02-600-19 Estimating the contribution of sub-clinical TB disease to transmission

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Background: Global efforts to end tuberculosis (TB) focus primarily on passive detection of individuals with clinical disease, largely overlooking those with subclinical TB (i.e. detectable bacteria in the sputum but negative on a TB symptom screen). Yet half of prevalent cases are subclinical and may contribute significantly to ongoing transmission, potentially hampering progress towards global targets. In this study we estimate the potential for infection from subclinical TB and its contribution to overall transmission.

Design/Methods: We used data from two TB infection surveys amongst household contacts of culture or Xpert confirmed cases in Vietnam, stratified by symptom and smear status at the time of diagnosis. Bayesian methods were used to fit a statistical model to this

data and estimate the potential for infection from those with subclinical TB, relative to those with clinical TB. These results were then combined with data from fifteen TB prevalence surveys to estimate the contribution of subclinical TB to transmission, both globally and at country level.

Results: We estimate that an individual with subclinical TB will typically infect 0.53 (0.05-1.97, 95% uncertainty interval (UI)) times as many people as an individual with clinical TB. As a result, we estimate that 34% (4-76%, 95% UI) of global transmission is from subclinical TB, ranging from 17% (2%-44%, 95% UI) in Nigeria to 55% (11%-83%, 95% UI) in Mongolia and Myanmar.

Conclusions: Subclinical TB likely contributes substantially to transmission, although limitations of available data led to wide uncertainty intervals. Further data are urgently needed to better understand the correlation between symptoms and infectiousness in TB. Screening for TB in target populations, regardless of symptoms, has the potential to substantially increase the proportion of infectious individuals detected, reduce transmission and accelerate progress towards TB elimination.

OA02-601-19 Clinical, mycobacteriological and radiological features of sub-clinical pulmonary TB in Canada

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Background: The burden of subclinical pulmonary tuberculosis (PTB), defined literally as a state of disease due to viable *Mycobacterium tuberculosis* that does not cause clinical TB-related symptoms but causes other abnormalities that can be detected using existing radiologic and microbiologic assays, and its clinical, mycobacteriologic and radiologic features in high-income countries, is unknown.

Design/Methods: We used a retrospective cohort study design to identify subclinical cases over a 16-year period starting January 1, 2005. We used independent reviewers to describe each case's clinical and radiologic features. Clinical features included the patients' reason for assessment, given that they were asymptomatic. Radiologic features included those on plain chest radiograph, and when available, those on computed tomographic (CT) scan.

Results: Among 1658 culture-positive PTB cases >14 years of age at diagnosis, 346 (20.9%) had subclinical disease. Ten (2.9%) were excluded from further analysis because they were HIV-positive or HIV-unknown. Most subclinical cases were young or middle-aged (77.8%), foreign-born (91.1%), and diagnosed during immigra-

tion surveillance (51.8%), during routine assessment of extrapulmonary TB (13.6%) – most of these had cervical lymph node TB –, or during investigation of positive TSTs/IGRAs (11.8%) – most of these were contacts of symptomatic cases. They were usually acid-fast bacilli smear-negative (88.8%) and had, on average, long times to liquid culture positivity (20.7 ± 8.9 days). Most (52.1%) had typical (for adult-type PTB), noncavitary and minimal PTB on chest radiograph, 18.8% had normal chest radiographs. Endobronchial spread and cavitation were more commonly seen on CT scan than on chest radiograph (21.7% versus 69.6%, and 13.0 versus 34.8%, respectively).

Conclusions: Subclinical PTB is not uncommon in Canada. It is usually diagnosed during one or other systematic screening activity. It tends to be paucibacillary and of minimal extent on chest radiograph; but more advanced on CT. Its public health importance is unknown.

OA02-602-19 Report of a TB outbreak in Kano Central Correctional Centre, Kano, Nigeria

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Background and challenges to implementation: Tuberculosis outbreak occurs when there are more TB cases than expected within a geographic area or population during a particular period with evidence of recent transmission among the cases. Movement of inmates in and out of overcrowded inadequately ventilated facilities makes correctional centers high risk environments for the transmission of TB with difficulty in implementing infection control measures.

Intervention or response: The Wellness on Wheels truck is a mobile diagnostic unit housing a digital X-ray and 2 genexpert machines. It was used to screen inmates at the Kano central correctional center. The correctional center is the biggest in the state and had a total of 2000 inmates during the time of the intervention. Presumptive TB were identified through symptom and X-ray screening using a CAD4TB cut off score of 60, sputum samples were then processed on the GeneXpert MTB/RIF for confirmation of TB cases.

Results/Impact: Over the 2 weeks intervention, 1967 (98%) of the inmates were screened, 92 were found presumptive for TB (5%); 99% of the presumptives were evaluated with a TB yield of 23%; all the 20 DSTB and 1 Pre-XDR case diagnosed were enrolled on treatment and notified. Over the preceding 1 year the correctional center only reported 7 TB cases. The results showed a marked increase above the normal reporting from the center with a high NNS and NNT of 94 and 4.3, respectively.

Conclusions: Correctional facilities are critical settings that should be focused upon for detection and treatment of TB among a vulnerable population. The findings from the intervention were communicated to the State Ministry of health and a high-level advocacy visit was made to the management of the facility to emphasize the need for mandatory TB symptom screening for all inmates and detainees at entry and periodic follow up screening to stop transmission of TB within the correctional center.

OA02-603-19 Impact of antiretroviral therapy timing on LTBI reactivation in TB-SIV non-human primate co-infection model

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Background: In this study, we aimed to identify the impact of timing of combinatorial antiretroviral therapy (cART) on components of Tuberculosis (TB) immunity that remain impaired after cART, versus those that are restored by cART.

Design/Methods: Rhesus macaques were infected with a low dose of 10 CFU *Mtb* CDC1551 via aerosol. The LTBI macaques were then co-infected with 300 TCID₅₀ SIVmac₂₃₉ via the intravenous route 9 weeks post-TB infection. 4 macaques were initiated on cART at 2 weeks post-SIV (peak viremia) and 5 macaques-initiated cART at 4 weeks post-SIV (chronic phase of SIV). Clinical and immunological parameters were studied. Statistical analysis was performed using an unpaired Student's t test, 1- or 2- way ANOVA in GraphPad Prism.

Results: We demonstrate that cART administered at peak viremia enhanced the general well-being of the study animals, controlled the viral replication, improved pathology while significantly reducing the immune activation in BAL and blood. However, cART at peak viremia failed to protect from new TB lesions post-SIV and cART, reconstitute the skewed CD4+ T effector memory responses in the lung compartment, and significantly increased cell proliferation and inflammatory CXCR3+ and CCR6+CD4+ T cells in both BAL and whole blood.

Conclusions: This is the first study to examine the impact of timing of cART on LTBI reactivation in a biologically and physiologically relevant nonhuman primate model. Though the earlier initiation of cART in this study failed to rescue from LTBI reactivation, it resulted in decreased mortality, less disease severity and improved survival. While there doesn't appear to be an impact of the timing of cART on the CD4 counts, HIV

suppression results in maintenance of CD8 responses in the primary infection site as well as in extrapulmonary organs. Further studies aiming at concurrent therapies to contain bacterial burden are needed to have an optimum translational intervention.

OA02-604-19 Spatial scale of TB transmission in Lima, Peru

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Background: Transmission is the global leading cause of tuberculosis (TB) infection. Spatial heterogeneity in the incidence of the disease combined with information of genomically linked transmission can inform spatially targeted interventions in TB prevention.

Design/Methods: We integrated whole-genome sequencing data with home geographic coordinates collected with the Global Positioning System from 2,440 TB patients in Lima, Peru. Patients and their household contacts were recruited at participating facility centers between 2009 and 2012. We calculated how the risk of infection with a nearly identical SNP-wise distance changes with increasing geographical proximity with a person with TB.

Results: We analyzed three million sequence pairs, including 191 within-household and 299 within-patient pairs. Smaller SNP pairs differences were prevalent for within-household pairs and progressively decreased at increasing distances. Consistent bimodal distributions across geographical distances suggest the presence of related and unrelated TB strains with a higher proportion of related strains at close distances.

Among the 1,015 pairs found to be genomically linked (SNP difference ≤ 1), 25% were located more than 15 minutes apart. Close genetic relatedness was more likely among pairs with 0 to 5 years of age of difference compared to pairs with more than 30 years apart (OR: 1.25, 95% CI: 1.02-1.52). Conversely, pairs with 15-20 years apart were less likely to be genomically linked than pairs with more than 30 years apart (OR: 0.71, 95% CI: 0.53-0.95).

Conclusions: TB transmission in a densely populated metropolis is spatially structured even though it does not prevent long-distance transmission. We may verify our findings using the mobile data from cell phone towers or social media to identify the unit of spatially targeted intervention.

OA02-605-19 A previous history of TB affects the performance of computer-aided detection digital chest X-ray reading technologies for active TB screening

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Background: Computer Aided Detection (CAD) technology has recently been recommended by WHO as an alternative to human interpretation of digital chest X-rays (dCXR) for TB screening and triage and may be especially useful in settings with limited availability of trained staff to interpret CXRs. CAD uses lung shape and texture analysis to determine probability of TB; however, many patients with previously treated TB have sequelae, which distorts the lung shape and texture and may affect CAD performance.

Design/Methods: We conducted a sub analysis of an active TB case finding study in which adults (≥ 15 years old) attending a primary health care facility in Lusaka, Zambia were screened for TB using symptom screening and dCXR. Those with complete data on history of TB, dCXR, and TB microbiological reference (culture, Xpert or smear) were included. dCXRs were evaluated using two CAD softwares: CAD4TB (version 7.0) and qXR (version 3.0). We determined the area under the receiver operator curves (AUROC) of both systems, overall and stratified by history of TB.

Results: Of 2,057 participants, 1,281 (62.3%) were male, mean age was 40 (sd 14.14) years, 486 (23.6%) had a history of previous TB, 759 (36.9%) were HIV positive, and 1785 (91.2%) had any TB symptom. Using CAD4TB, the overall AUROC for TB was 0.85 (95% CI: 0.82-0.87), and was 0.87 (95% CI: 0.85-0.90) and 0.75 (95% CI: 0.68-0.83) among those without and with a history of TB, respectively. Using qXR, the overall AUROC was 0.86 (95% CI: 0.83-0.88) and was 0.87 (95% CI: 0.84-0.90) and 0.80 (95% CI: 0.73-0.87) among those without and with a history of TB, respectively.

Conclusions: Both CAD4TB and qXR had excellent overall discriminatory value as screening tools for TB, however, accuracy was decreased among those previously treated for TB, especially when using CAD4TB. This suggests that different CAD threshold cutoffs are needed when screening individuals with a prior TB history in order to optimize diagnostic performance in this population.

OA02-606-19 Pulse oximeter implementation during outpatient paediatric care in rural Bangladesh: a multisite prospective observational study

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Background: Although hypoxemia (low peripheral oxygen-hemoglobin saturation (SpO₂)) measured by pulse oximeters is a risk factor for mortality among hospitalized children in Bangladesh, pulse oximeters are rarely available during outpatient care. We evaluated the outcomes of children after implementing outpatient pulse oximetry measurements in Bangladesh.

Design/Methods: We enrolled 3-35 month old children participating in a pneumococcal vaccine effectiveness study with cough and/or difficult breathing at three Upazila Health Complex outpatient clinics in Sylhet, Bangladesh between 2015-2017. At enrollment study physicians measured the SpO₂ using Masimo™ oximeters and we determined the case fatality rate (CFR) after 15 days. We used standard statistics to describe patient characteristics and fit random effects multivariable logistic regression models to examine associations between outcomes and SpO₂.

Results: The median age of 9,619 participants was 11 months (interquartile range (IQR), 6, 19) and 4,018 (42%) were female. The median SpO₂ was 97% (IQR, 96%, 98%) and 171 (1.8%) children had a SpO₂<90%, 637 (6.6%) 90-93%, and 169 (1.8%) were unsuccessfully measured. All 31 deaths occurred among <2 year olds (CFR, 0.4% (31/8,109)). Among <2 year olds, CFR differed by SpO₂ with SpO₂<90% at 2.6% CFR (4/157), 90-93% at 1.3% (7/557), 94-100% at 0.2% (15/7,254), and failed measurements at 3.6% (5/141) (p<0.001). Compared to SpO₂ 94-100%, the adjusted odds ratio for mortality of SpO₂<90% was 5.0 (95% CI, 1.5, 16.8), 90-93% was 3.1 (1.2, 8.0), and failed measurements was 8.0 (2.5, 25.2). Assuming pulse oximetry was unavailable, World Health Organization (WHO) outpatient guidelines alone identified only 8/31 fatalities (25.8%) as eligible for hospitalization. Assuming oximetry was available, SpO₂<90% and SpO₂<94% identified 17.4% (4/23) and 47.8% (11/23) more fatalities as hospitalization eligible.

Conclusions: In Bangladesh pulse oximetry implementation during outpatient care would improve the identification of children at elevated mortality risk. The WHO guidelines should revise the SpO₂ hospitalization threshold from <90% to <94%.

OA02-607-19 Achieving lung health for all through decentralised treatment for children and adolescents with rifampicin-resistant TB in South Africa

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Background: Decentralized treatment for people living with rifampicin-resistant tuberculosis (RR-TB) has been an important strategy for improving access to care. Children/adolescents, however, are still usually treated in highly centralized hospital settings, and this may contribute to low diagnosis and subsequent treatment initiation in this population.

In 2020, Médecins Sans Frontières (MSF), in collaboration with the Department of Health, started a program to diagnose and treat children/adolescents with RR-TB in 10 primary health care clinics in Khayelitsha.

Design/Methods: A prospective cohort study assessing the care cascade of all children/adolescents aged 18 years and below who were diagnosed with RR-TB in Khayelitsha between March 1, 2020 and March 31, 2021 was conducted.

Results: Fifteen children/adolescents were diagnosed with RR-TB, representing 7.1% of the RR-TB burden in the community over that period. Nine (60.0%) were female and the median age was 8 years (IQR 4-12). One (6.7%) child/adolescent had HIV and was on antiretroviral-therapy. Eight (53.3%) children had a known household contact and six (40.0%) were found through an active family screening program.

All children/adolescents were treated with oral regimens, but one later required the addition of a carbapenem when her *M. tuberculosis* strain was found to have bedaquiline resistance.

Twelve (80.0%) children/adolescents received their care entirely in the community, while two started on community treatment and had to be hospitalized (one due to a complicated social situation and one to receive an intravenous carbapenem) and one started on treatment in the hospital with RR-TB meningitis but was able to complete treatment in the community after she improved enough for discharge. Factors facilitating success can be seen in the Table.

Factors Facilitating Success

- Injectable-free regimens with child friendly formulations
- Early diagnosis of mild disease
- The presence of “champion” clinicians mentored by MSF
- A “family-centered” approach to the diagnosis and prevention of RR-TB

Conclusions: Children/adolescents with RR-TB can be successfully treated for RR-TB in decentralized settings using a “family-centered” approach. Prolonged hospitalization with its attendant developmental and family disruptions should no longer be the norm for children/adolescents living with RR-TB.

OA-03 Where are the missing millions?

OA03-608-19 Leveraging the family health team to find missing people with TB in an underserved urban population, Harar, Ethiopia

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Background and challenges to implementation: Urban dwellers are disproportionately affected by TB, due to a higher proportion of key populations living in urban centers. Ethiopia is one of the nations with fast urbanization rate (4.7% per year). Despite the increasingly challenging TB epidemic in cities, there is no Active Case Finding (ACF) strategy to address the underserved urban populations. In the reformed Urban Primary Health Care, Family Health Team (FHT) approach is introduced to carry out facility and community-based functions. The team is composed of two health officer, 2 nurses, 4-5 health extension professionals and an environmental health professional. Each health center has four to six FHTs who are responsible for both facility-based and outreach activities. This intervention leveraged FHT to find missing people with TB in Harari Regional State.

Intervention or response: USAID/Urban TB LON project supported community level interventions of four urban health centers of Harari Region. The intervention packages include training of FHT members, site level support, provision of recording tools, community

awareness creation and performance review events. The FHTs integrated community TB care activities; symptom-based TB screening and presumptive TB case identification and referral in their out-reach services for underserved community members of Urban dwellers.

Results/Impact: Between October/2020-March 2021, a total of 639 presumptive TB cases were identified and referred through FHTs out-reach activities (62% of them were males). Out of 639 Presumptive TB cases evaluated, 58 (9%) of them were diagnosed with TB. Among TB cases diagnosed 60% were males and 55% were bacteriologically confirmed PTB cases. The number of all forms of TB cases notified in the project supported health centers has increased from 82 to 130 when compared with previous year of the same period (October /2019-March 2020) showing a 37% increment.

Conclusions: Engaging FHT in ACF can be a key strategy to find missing people with TB in underserved Urban population.

OA03-609-19 Yield of TB contact tracing in high-volume health facilities in southern Nigeria

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Background and challenges to implementation: Nigeria has the highest estimated burden of Tuberculosis (TB) in Africa. The National Tuberculosis Program (NTP) since over five years has prioritized active case-finding and contact tracing is one of the strategies to achieve this. Contact tracing is poorly implemented in most low-and-middle-income countries due to many operational challenges and its attendant cost¹. Systematic review shows that contact tracing has a pooled yield of 3.1%². Nigerian NTP is grossly under-funded with a meagre 7% domestic contribution, leaving 70% of TB financing unfunded³. Until recently, NTP only funded DR-TB contact tracing.



Figure: Map of Nigeria showing states supported by GLRA

DAHW-German Leprosy and TB Relief Association (GLRA) has been supporting the NTP in southern Nigeria by funding key programmatic components that remain unfunded. From 2018, GLRA started funding DS-TB contact tracing in 3 states and scaled up to 9 states by 2020.

Intervention or response: Between January 2018-December 2020, 69 dedicated staff were recruited, trained, and paid NGN 2,000 (USD 5) transportation/call allowance per index case whose contacts were traced.-

All newly diagnosed TB patients were contacted and household visit scheduled. Upon visit, all contacts were enumerated, symptomatically screened using a 5-point screening tool, and sputum collected for GeneXpert testing. Free Chest x-ray (funded by The GF) was offered to children unable to produce sputum.

Results/Impact: From 69 high-volume facilities, 9,766 index TB cases were notified and 8,673 (89%) of them had their household contacts traced. The total number of household contacts identified was 31,416 of which 30,279 (96%) were symptomatically screened, and 10,045 presumptive cases were further evaluated for TB. A total of 1,605 TB cases (all forms) was diagnosed giving an average yield of 5.3%.

Conclusions: Contact tracing yield was much higher than anticipated and may be an overlooked opportunity for early case detection and a chance to decrease TB transmission. We recommend a cost effectiveness analysis to support policy and practice.

OA03-610-19 Intensified TB case finding in Copperbelt Province, Zambia: contribution of the mobile one-stop TB truck

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Background and challenges to implementation: Tuberculosis (TB) case notification rate for the Copperbelt Province of Zambia has remained low at around 500 per 100,000 population, compared to an estimated incidence of 1,112 per 100,000 population. There is a need for innovative intensified TB case finding (ICF) interventions to find the 'missing cases'. Here, we present the contribution of the Mobile One-stop TB Truck (MOST) to TB case finding in Copperbelt Province during the period July to December, 2020.

Intervention or response: In March 2020, USAID Eradicate TB Project deployed the MOST to support ICF in Copperbelt Province. The truck is fitted with a portable digital X-ray with artificial intelligence augmented X ray reading and a GeneXpert machine. A multi-disciplinary team of health workers and community volunteers

(CBVs), conducted monthly mobile TB clinics in 30 health facilities across the province. Prior to each clinic, CBVs sensitized communities around health facilities using public address system and door-to-door visits.

On clinic days, CBVs escorted clients for TB screening at the MOST. An algorithm used for TB case detection included screening patients by symptoms, then by CXR followed by GeneXpert sputum examination. Records were entered and analyzed in Microsoft Excel.

Results/Impact: A total of 13,135 people were screened for TB during mobile clinics in the period July – December 2020. Of these, 1,349 (10.3%) were diagnosed with TB: 182 (13.5%) bacteriologically confirmed and 1,167 (86.5%) clinically diagnosed. TB case notifications for Copperbelt Province increased by 49% in the last half of 2020, compared to the same period in 2019 (6,381 vs 4,296). Of the cases notified in the last half of 2020, 21.1% (1,349/6,381) were diagnosed using the MOST.

Conclusions: Use of MOST helped increase TB case notifications in Copperbelt Province. Scaling-up this innovation may help bridge the gap between notified TB cases and estimated incidence for Zambia.

OA03-611-19 Targeted universal testing for TB in clinics in South Africa: a cluster randomised trial

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Background: TB is under-diagnosed. We assessed if augmenting routine symptom-based sputum testing with targeted universal testing for TB (TUTT) in adults at high risk of TB would increase the total number of patients diagnosed with TB in primary care clinics.

Design/Methods: In this cluster randomised trial, 62 large clinics in three provinces in South Africa implemented either: augmentation of standard of care (SOC), symptom-based TB testing with the TUTT intervention, or to SOC. In TUTT clinics, we targeted high risk (close contacts of someone with TB in the past year; and or prior TB in the past 2 years and or HIV-infected) adults (≥ 18 years) clinic attendees, irrespective of the presence of TB symptoms. Participants provided one sputum sample, which was processed and split for Xpert Ultra and mycobacterial culture. Outcome was

the total number of TB patients diagnosed per clinic per month in each arm, assessed using counts of laboratory diagnoses of TB at all clinics in the year prior, and during the intervention.

Results: We sputum-tested 30,500 adults in TUTT intervention clinics, and overall 8% of were positive for *M. tuberculosis* on ≥ 1 assay. There was marked differences in effect of the intervention at individual clinics and by province but cluster- and province-adjusted comparison between TUTT and SOC clinics, restricted to the intervention period, showed a nonsignificant increase of 14% additional patients with TB diagnosed in TUTT clinics per month (95% CI: -6%; +38%). Difference-in-differences analyses showed TB diagnoses per clinic per month in SoC clinics declined by 8% in the study period compared to the year prior, whereas TUTT clinics diagnosed 17% (95% CI: 14%; 19%) more TB patients relative to SoC.

Conclusions: Targeted universal testing in high risk groups increased the number of TB patients diagnosed. This data was presented at CROI conference in 2021.

OA03-612-19 Active case-finding in the state of Uttar Pradesh, India: TB case-finding in the community with private sector engagement

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Background and challenges to implementation: COVID-19 affected India's national TB elimination program (NTEP) and resulted in a sharp drop in TB-notification. To identify the un-diagnosed/un-reported cases, two rounds of 'active case finding' (ACF) campaigns were conducted in Uttar Pradesh (UP). Here, we assessed the outcome of these campaigns.

Intervention or response: First round of ACF (I) was conducted in 29 districts (Nov 2-11, 2020). About 10% of the population in each district (including high-risk population/areas) was mapped for door-to-door symptom screening and sputum collection from presumptive cases. Second round of ACF (II) was conducted strategically in three phases (during Dec 26, 2020 to Jan 25, 2021) in all 75 districts of UP. First phase of ACF-II (7 days) targeted all congregate settings like orphanages, old-age home, Jail etc. Second phase of ACF-II (11 days) was carried out to target about 20% of population in the same manner as ACF-I. In third phase (13 days), private health facilities (including labs and pharmacies) were targeted, and information on un-reported cases was gathered.

Results/Impact: A total of 9.2 million cases were screened in ACF-I, with 40,289 presumptive TB cases identified. Of these, 2,906 (7.2%) were confirmed as TB using microbiological (2066; 5.1%) or radiological (848; 2.1%) methods. In second phase of ACF-II, about 44 million cases screened, with 157,684 presumptive cases. About 6.4% (10,070) presumptive TB cases were diagnosed as TB with microbiological (6,419; 4.1%) and radiological (3,651; 2.3%) tools. During third phase of ACF-II, 64,000 private health facilities (out of total 605,000 mapped facilities) were visited by NTEP teams. This activity resulted in the notification of 3,679 un-reported TB cases.

Conclusions: ACF campaign was successful in finding missed TB cases and galvanizing the public and private health systems. Since, India is currently facing resurgence of COVID-19, future rounds of ACF with strategic planning are required.

OA03-613-19 The impact of systematic TB screening in the outpatient departments of private facilities in Nigeria

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Background and challenges to implementation: Over 300,000 Tuberculosis (TB) cases are missed annually in Nigeria. It is estimated that private health care providers account for about 60% of health care seeking in the country. This high proportion of clientele provides an opportunity to finding the missing TB cases in Nigeria.

Intervention or response: The facilities were selected based on high clinic attendance with one Screening Officer (SO) each engaged to support provider-initiated screening of clients attending the Outpatient Department (OPD). SOs were trained on TB screening and given tools to document screening outcomes. Clients are screened while waiting to see the clinicians. Presumptive TB cases identified are either escorted to the TB unit to collect their sputum samples or they produce the sputum in a designated area in the OPD. Samples are tested using Xpert MTB/RIF or smear microscopy. Where client cannot produce sputum, chest X-ray with clinical diagnosis is done. Results of evaluation are returned to the TB unit and confirmed TB case are contacted and initiated on appropriate TB treatment. Relevant National TB Programme tools are used for documentation. Weekly surveillance data from intervention facilities was analyzed.

Results/Impact: Between July – December 2020, a total of 726,107 hospital attendance was recorded with 665,533 (92%) screened for TB. 30,635 (5%) presumptive TB cases were identified, 28,674 (94%) evaluated, 3,833 (13%) TB cases were diagnosed and 3,568 (93%) started on treatment. Also, 44 drug resistant TB cases were diagnosed and 34 (77%) started on treatment. Number Needed to Screen was 174 and Number Needed to Test was 7. This intervention accounted for 81% of the total TB cases notified in these facilities within the same period.

Conclusions: Systematic screening of clients attending OPD has shown the potential of finding missing TB cases in health facilities. This intervention should be integrated into facilities' routine TB case finding activities and scaled up nationwide.

OA03-614-19 Analysis of neighbourhood TB prevalence-to-notification ratios reveals underdiagnosis hotspots in Blantyre, Malawi

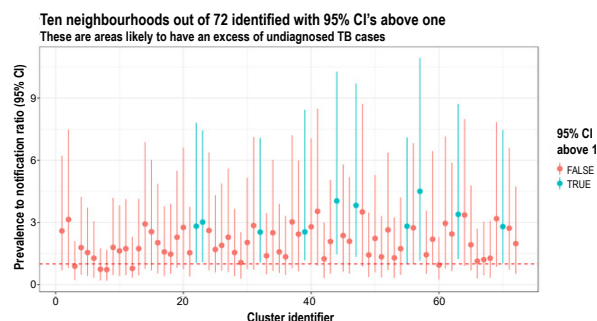
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Background: In cities, where TB epidemics in sub-Saharan Africa are concentrated, neighbourhood tuberculosis (TB) case notification rates (CNRs) are a suboptimal indicator of true disease burden. By constructing models to estimate local TB prevalence-to-notification ratios (an indicator of underdiagnosis), we sought to understand neighbourhood-level determinants of TB underdiagnosis, and to develop tools to direct targeted approaches to case finding and prevention.

Design/Methods: Through a Blantyre citywide TB surveillance system, TB notifications from 2015 to 2019 were geolocated to one of 72 neighbourhoods. In 2019, adult household members were randomly sampled and underwent symptom screening, chest X-ray, and if either was abnormal, sputum microscopy, GeneXpert and culture. We constructed Bayesian multilevel models to predict neighbourhood annual TB CNRs and prevalence; posterior draws were summarised to derive adjusted local prevalence-to-notification ratios.

Results: Between 2015 and 2019 the mean neighbourhood CNRs were 149, 187, 186, and 114 per 100,000, respectively. The prevalence of bacteriologically-confirmed TB was 214 per 100,000. Models for CNRs and

prevalence showed that completion of primary school education, distance to TB clinic, and percentage of men were important predictors of local TB burden. The mean prevalence-to-notification ratio was 2.01 (95% CrI: 0.16- 5.36), indicating substantial underdiagnosis of TB. In 10/72 neighbourhoods, the 95% credible interval for the prevalence-to-notification ratio exceeded one.



Conclusions: Using citywide enhanced surveillance data, we developed a predictive model that can prioritise neighbourhoods for TB case finding and prevention activities using readily available local data. Current untargeted active case-finding strategies are inefficient and resource-intensive; by identifying hotspots of underdiagnosis, programme managers can better direct efforts to eliminate urban TB.

OA03-615-19 Lung ultrasound for the diagnosis of paediatric pulmonary TB: interim analysis

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Background: The aim of this study was to evaluate the diagnostic accuracy of lung ultrasound (LUS) in children with pulmonary tuberculosis (PTB) and to compare this to the diagnostic accuracy of dual expert-reviewed chest X-ray (CXR).

Design/Methods: We enrolled children <13 years who presented routinely at 2 hospitals in Cape Town, South Africa, with presumptive PTB. All children were evaluated clinically and radiologically (CXR and LUS using the Butterfly IQ device) and had TB microbiological testing. Children were classified using international consensus clinical case definitions for PTB as “confirmed”, “unconfirmed” or “unlikely” PTB. LUS was performed by trained ultrasound experts. LUS features were re-

ported for 18 lung regions (≥ 3 B-lines, consolidation, pleural effusion and sub-pleural consolidations) and for “any LUS abnormality”. CXRs were classified using a consensus process after dual expert review. Microbiologically confirmed PTB was the diagnostic reference standard.

Results: Of 82 children enrolled, 56 (67%) were TB cases; 30/56 (54%) bacteriologically confirmed. The median age was 36 months; 7% were living with HIV. A total of 63/72 (88%) had any abnormality on CXR and 57/82 (70%) had any abnormality on LUS. Any abnormality on LUS had a sensitivity of 76% for confirmed TB, with 30% specificity, compared to unlikely TB. LUS and CXR had comparable sensitivity and specificity for pleural effusion and consolidation but cavities reported on CXR were not identified on LUS. CXR identified mediastinal lymphadenopathy in 16/28 (57%) children with confirmed PTB, specificity 91%, which LUS could not.

	LUS				CXR			
	Confirmed PTB	Unlikely PTB	Sensitivity (95% CI)	Specificity (95% CI)	Confirmed PTB	Unlikely PTB	Sensitivity (95% CI)	Specificity (95% CI)
Any abnormality ²	22/29	19/27	75.9% (56.5-89.7)	29.6% (13.8-50.2)	26/28	16/21	92.9% (76.5-99.1)	23.8% (8.2-47.2)
Consolidation ³	16/29	8/27	55.2% (35.7-73.6)	70.4% (49.8-86.2)	17/28	7/21	60.7% (40.6-78.5)	66.7% (43.0-85.4)
Pleural effusion	5/29	0/27	17.2% (585-35.8)	100%	4/28	1/21	14.3% (4.0-32.7)	95.2% (76.2-99.9)
Cavity	0	0			2/28	2/21	7.1% (0.8-23.5)	90.5% (69.6-98.9)
Any SPC ⁴	18/29	16/27	62.1% (42.2-79.3)	40.7% (22.4-61.2)				
≥ 3 B-lines ⁵	13/29	9/27	44.8% (26.4-64.3)	66.7% (46.05-83.5)				

LUS: lung ultrasound; CXR: chest radiograph; TB: tuberculosis; SPC: sub-pleural consolidation

¹ This diagnostic accuracy analysis was restricted to children with “unlikely” and “confirmed” PTB

² Any abnormality² on LUS was defined as the presence of any of the following in any of the lung regions: ≥ 3 B-lines, any consolidation, any pleural effusion, any sub-pleural consolidation; and on CXR was defined as the presence of any of the following: any parenchymal pathology, any pleural pathology, any enlarged mediastinal lymph nodes and any airway involvement

³ Consolidation on LUS was defined as a subpleural, echo-poor or tissue-like region ≥ 5 mm in maximum dimension, with or without sonographic air bronchograms; and on CXR as a confluent opacity, often homogeneous which may encompass an entire lobe or large segment, may erase the heart and diaphragm borders and may contain air bronchograms

⁴ SPCs on LUS were defined as well-defined echo-poor lesions < 5 mm in maximum dimension that interrupted the pleural line with or without a posterior artefact

⁵ B-lines on LUS were defined as vertical lines originating at the pleural line or from a “sub-pleural consolidation”, and were counted per intercostal space

Table: Sensitivity and specificity¹ of lung ultrasound and chest radiographic features for confirmed pulmonary tuberculosis in children

Conclusions: LUS using a handheld device can detect lung consolidation and effusion in children with PTB with similar accuracy to CXR and offers the benefit of being point-of-care. However the inability of LUS to

identify cavities and mediastinal lymphadenopathy, key radiological features of paediatric PTB, is a limitation. Its utility may be improved with the addition of the supra-sternal notch view.

OA-04 Rapid assays: focus on the target

OA04-616-19 Clinical evaluation of the non-sputum-based Xpert® TB Host Response RUO assay in a point-of-care setting

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Background: The Xpert® TB Host Response RUO (TB-HR RUO) assay (Cepheid, Sunnyvale, CA, USA) is a non-sputum based reverse transcriptase polymerase chain reaction (RT-PCR) assay measuring the expression of human genes (GBP5, DUSP3 and KLF2) in response to active disease from *Mycobacterium tuberculosis* complex (MTBC) infection. Clinical performance of the assay to identify infection with active MTBC was investigated at a primary health-care facility in Johannesburg, South Africa.

Design/Methods: 62/200 participants who met eligibility criteria were consented and enrolled in the study. Testing was performed by a health-care worker at the health care facility using 100uL of finger-stick EDTA blood in the cartridge-based test designed for the GeneXpert® instrument. Performance of TB-HR RUO’s ability to identify active disease was determined using receiver operating characteristic (ROC) and applying Youden’s index for selecting the optimal cut-off point compared to the standard-of-care Xpert MTB/RIF Ultra (Ultra) assay.

Results: Results produced by the TB-HR RUO assay demonstrates distinction between active TB disease detected by the assay and confirmed TB diagnosis using the Ultra assay (Figure 1).

The ROC plot demonstrated a sensitivity of 90% (95% CI: 68.3-98.7%), specificity of 85.7% (95% CI: 71.4-94.5%), PPV of 75.0% (95% CI: 55.6-96.3%) and NPV of 94.7% (95% CI: 81.2-98.1%) compared to the Ultra assay. The area-under-curve (AUC) was 0.923 (95% CI: 0.827-1.019).

Conclusions: The preliminary performance of the TB-HR RUO assay meets WHO’s recommended target product profile (TPP) for sensitivity ($\geq 90\%$) and specificity

($\geq 70\%$) for a rapid, biomarker-based non-sputum-based test for detecting TB. The ease of sample collection and rapid testing time (~ 50 minutes) represents added advantages of this assay.

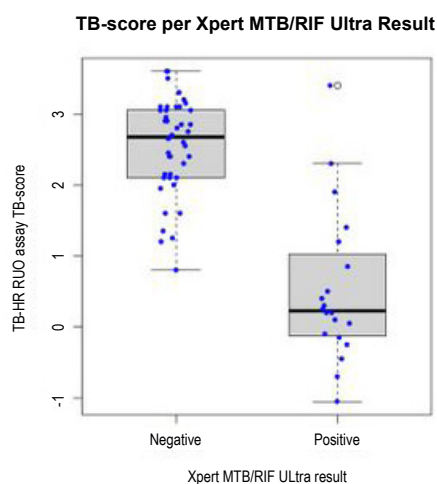


Figure 1.

OA04-617-19 Multiplex high-throughput, non-sputum-based method for the diagnosis of *M. tuberculosis* from blood samples

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Background: According to World Health Organization (WHO) report, in 2019, there were around 10 million *Mycobacterium tuberculosis* (MTB) infected cases world-wide. Early diagnosis is crucial in timely management and restricting spread. Culture based methods take long time and are labour intensive. DNA based method are more successful but expensive with possibility of false positive in case of dead bacilli. WHO negated usage of existing serological diagnostics in 2012 due to poor reliability, however suggested development of serological tests with higher sensitivity and specificity. Serological tests require processing of blood samples from TB suspects, not requiring invasive sampling or pose respiratory hazard to staff. Present study therefore highlights findings of new multiplex bead based serological diagnostic test developed by us

Design/Methods: Multiplex micro-bead-based assay is high through-put serological test, utilizing 14 different MTB specific antigens coated on the magnetic-beads. Assay detects immune response in serum samples for all 14 antigens, in single-tube format by binding of anti-

bodies against MTB followed by detection using a phycoerythrin conjugated secondary-antibody on Luminex platform. Serum samples were collected at NITRD from Microbiologically confirmed TB cases, healthy subjects and patients with diseases other than TB and subjected to this test. Results are calculated based on built in algorithm using cut off based on healthy and confirmed TB.

Results: Total of 253 blinded samples were analysed including 151 confirmed MTB cases, 49 healthy subjects and 53 disease controls. The test showed overall sensitivity and specificity of 86% and 85.7% respectively in reference to MTB and non-MTB cases. Early results in extra-pulmonary and paediatric cases showed 80% sensitivity.

Conclusions: Serological diagnostic test provides information about antibody response to pathogens in blood samples. Preliminary results with small sample size of 253 samples showed encouraging results. Study is being extended on more number of samples including extra-pulmonary, HIV for more definitive conclusion.

OA04-618-19 Diagnostic performance of the novel FujiLAM assay to detect TB in HIV-positive patients in four African countries

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Background: The novel urine-based point-of-care FujiLAM assay is a promising tool for TB diagnosis. We investigated the diagnostic performance of FujiLAM in ambulatory HIV-positive patients from fresh urine samples.

Design/Methods: Prospective multicentric diagnostic study including two groups of ambulatory adult HIV-positive patients:

- 1) with TB symptoms;
- 2) with advanced HIV disease and no TB symptoms.

The study was conducted in 4 sites: Mbarara (Uganda), Homa Bay (Kenya), Maputo (Mozambique), Eshowe (South Africa). All patients received clinical examination, FujiLAM and AlereLAM (urine), Xpert MTB/RIF Ultra (sputum or urine), culture (sputum) and chest X-

ray. A microbiological reference (Xpert or culture) was used to assess the diagnostic performance of the LAM assays.

Results: We included 1103 patients: 702 in Group 1 (with TB symptoms) and 401 in Group 2 (with advanced HIV disease and no TB symptoms). Median CD4 count was 550 cells/ μ L [IQR: 295-784] and 144 cells/ μ L [IQR: 75-189] in Group 1 and 2, respectively. In total, 82.2% and 81.8% patients in Group 1 and 2 were on ART. TB was microbiologically confirmed in 9.0% (61/677) and 4.1% (16/390) in Group 1 and 2, respectively.

Overall, FujiLAM and AlereLAM sensitivity and specificity in Group 1 and 2 are shown in the table. FujiLAM sensitivity by CD4 count in Group 1 was: 76.9% (95% CI 56.4-91.0) in CD4<200 cells/ μ L, 77.8% (95% CI 40.0-97.2) in CD4 200-349 cells/ μ L, 31.3% (95% CI 11.0-58.7) in CD4 \geq 350 cells/ μ L. AlereLAM sensitivity by CD4 count in Group 1 was: 53.6% (95% CI 33.9-72.5) in CD4<200 cells/ μ L, 40.0% (95% CI 12.2-73.8) in CD4 200-349 cells/ μ L, 13.3% (95% CI 1.7-40.5) in CD4 \geq 350 cells/ μ L.

	FujiLAM		AlereLAM	
	%	95% CI	%	95% CI
Sensitivity				
- Group 1 (TB symptoms regardless of CD4)	63.0	48.7 - 75.7	37.5	24.9 - 51.5
- Group 2 (no TB symptoms and advanced HIV)	42.9	17.7 - 71.1	7.1	0.2 - 33.9
Specificity				
- Group 1 (TB symptoms regardless of CD4)	83.8	80.6 - 86.7	84.7	81.6 - 87.5
- Group 2 (no TB symptoms and advanced HIV)	84.4	80.1 - 88.1	90.1	86.5 - 93.1

Conclusions: FujiLAM sensitivity is high in TB symptomatic HIV-positive patients with CD4<350 cells/ μ L though low in those less immunosuppressed. FujiLAM can diagnose almost half of the TB confirmed cases among patients with advanced HIV and no TB symptoms, a substantially higher proportion than AlereLAM.

OA04-619-19 A urine-based protein signature for TB triage among people living with HIV

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Background: A simple, point-of-care TB triage test for people living with HIV (PLHIV) is needed for early diagnosis and treatment. There is limited understanding of urine host proteins that could be used as biomarkers for TB screening.

Design/Methods: We conducted a proteomic analysis of urine collected from PLHIV undergoing evaluation for pulmonary TB in Kampala, Uganda. Participants provided a spontaneous void urine sample and sputum for Xpert MTB/RIF testing, and solid and liquid mycobacterial culture if Xpert negative. Urine was processed with hydrogel nanocages to remove high abundance, high molecular weight proteins and concentrate low abundant proteins, and then tandem mass spectrometry was performed.

We determined the proteins that could discriminate TB status, and performed logistic regression, lasso penalized regression, and random forests on these proteins using repeated five-fold cross-validation.

We calculated the diagnostic accuracy of the combination of candidate biomarkers in relation to the recommended minimum sensitivity (90%) and specificity (70%) for a TB triage test.

Results: We analyzed urine samples from 55 PLHIV, with median age 36 years (IQR 29.5-41), 60% male, median CD4 count 302 cells/ml (IQR 132-408) and 51% underweight. Twenty-five (45%) had microbiologically confirmed TB. Mass spectrometry analysis identified 520 proteins, of which four (A2GL, AMPN, IGL1, and IGHG2) were significantly more abundant in PLHIV with TB compared to PLHIV with non-TB respiratory disease (adjusted p-value< 0.05).

A classification algorithm based on the four proteins had high accuracy (AUROC 0.81, 95% CI 0.7-0.92), and approached the minimum sensitivity and specificity targets at 93% sensitivity (95% CI 76.8-98.3) and 68% specificity (95% CI 50.1-81.8) (Figure 1).

The addition of age, sex, underweight status and CD4 cell count did not improve performance.

Conclusions: Host urine proteins have the potential to be translated into a useful TB triage test for PLHIV. Further validation studies in larger cohorts are needed.

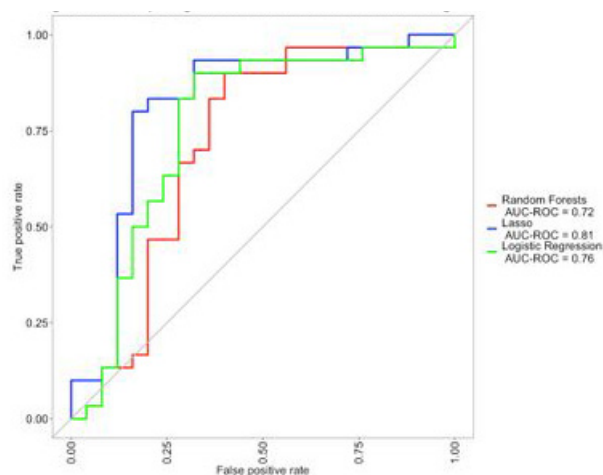


Figure 1. Receiver operating characteristic curve for four-urine protein TB signature.

OA04-620-19 Diagnostic accuracy of C-reactive protein for triaging TB diagnostic tests in a low HIV setting

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Background: C-reactive protein (CRP) is a blood-based indicator of inflammation. The World Health Organization (WHO) recently recommended it as a screening/triage test for people living with HIV. We evaluated the performance of CRP testing as a triage tool among persons with an abnormal chest X-ray (CXR) during community-based active TB case finding (ACF), in a low HIV incidence setting.

Design/Methods: CRP testing was integrated into mobile CXR screening campaigns across three provinces of Viet Nam (Ha Noi, Hai Phong and Can Tho). Individuals with an abnormal CXR were asked to provide a sputum specimen and whole blood from a finger prick. Sputum was tested with the Xpert MTB/RIF Ultra assay (Ultra), while blood was tested with the point-of-care semi-quantitative Actim CRP assay (Medix Biochemica); CRP concentrations ≥ 10 mg/L were considered a positive screen. The performance characteristics of using CRP results to triage follow-on Ultra testing were calculated. Sensitivity analyses were conducted with 'Trace Call' positive Ultra results re-classified as negatives.

Results: 367 paired CRP and Ultra test results were collected. Triaging Ultra tests using CRP would have resulted in a 73.3% reduction in Ultra testing. However, the sensitivity of CRP among persons with an abnormal

CXR was only 22/45, 48.9% (33.7-64.2%), while specificity was 246/322, 76.4% (71.4-80.9%). When 'Trace Call' positive Ultra results were re-classified as negatives, CRP triaging had similar performance.

Conclusions: Implementing the Actim CRP assay in a TB diagnostic algorithm after presumptive TB cases with an abnormal CXR did not meet the WHO's performance targets for a point-of-care triage test for TB (>95% sensitivity and >85% specificity) during community-based ACF.

This study adds to a limited body of literature indicating that CRP testing may not be a suitable triage test for TB in low HIV incidence settings.

OA04-621-19 The role of C-reactive protein for TB triage in children

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Background: C-Reactive Protein (CRP) has been endorsed by the WHO as a screening tool for tuberculosis (TB) among people living with HIV. There are limited data on its role as a triage tool in children.

Design/Methods: We prospectively enrolled children under 15 years being evaluated for pulmonary TB at outpatient clinics in Kampala, Uganda. The children underwent CRP testing using a point-of-care finger-prick assay (iChroma II, Boditech, South Korea) and a standard TB assessment, including Xpert MTB/RIF Ultra and mycobacterial culture, to classify them as having Confirmed, Unconfirmed or Unlikely TB.

We determined the sensitivity and specificity of CRP using the recommended 10 mg/L cut-off, and performed receiver operating characteristic (ROC) analysis to evaluate cut-offs at the minimum recommended sensitivity (90%) and specificity (70%) for a triage test.

Results: We enrolled 198 children, with median age 4 years (IQR 2-7), and 15 (7.7%) were HIV positive. The median CRP was higher for children with Confirmed TB (n=44, median 21.9 mg/L (IQR 2.5-66.3) compared to Unlikely TB (n=88, median 5.4 mg/L, IQR 2.5-24.5, p = 0.02). CRP had moderate accuracy with an area under ROC curve (AUROC) of 0.6 (95% CI 0.5-0.7) (Figure 1). At the cut-off of 10 mg/L, the sensitivity was 56.8% (95% CI 41-71.7) and specificity was 60.2% (95% CI 49.2-70.5). A 90% sensitivity could not be achieved, with highest sensitivity 70.5% (95% CI 54.8-83.2) at a 39.8% specificity (95% CI 29.5-50.8). At the minimum specificity (70%), sensitivity was 50% (95% CI 34.6-65.4).

The AUROC was lower (0.5, 95% CI 0.4-0.6) when Unconfirmed TB (n=66) was included in the definition of TB. Among HIV-positive children, the AUROC was 0.6 (95% CI 0.1-1), and the minimum sensitivity target could not be achieved.

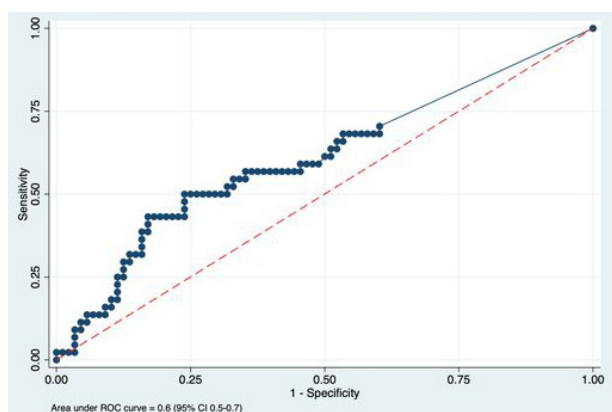


Figure 1. Receiver operating characteristic (ROC) curve for C-reactive protein to diagnose childhood TB.

Conclusions: CRP had limited utility as a TB triage test in children, highlighting the need for pediatric-specific host biomarkers for TB.

OA04-622-19 Identification of host protein biomarkers in the cerebrospinal fluid for the diagnosis of tuberculous meningitis

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Background: Tuberculous meningitis (TBM) is the most serious form of tuberculosis. Early diagnosis can improve prognosis, but the lack of sensitive methods makes it difficult in early diagnosis of TBM. Identification of TBM-specific biomarkers in cerebrospinal fluid (CSF) may help for diagnosis and improve our understanding of TBM pathogenesis.

Design/Methods: We searched PubMed for publications with the term “tuberculous meningitis”, “cerebrospinal fluid”, “proteomic” and “Mass spectrometry”, and the CSF protein biomarkers with a fold change >2 in each study, were repeatedly identified in at least two studies and presented consistent regulation patterns in TBM comparing with controls were selected. We prospectively enrolled the suspected TBM patients and evaluated the expression level the host proteins in CSF, then the logistic regression with forward stepwise analysis was used to establish the diagnostic panel. Receiver operator characteristic curves were constructed to obtain the area under the curve (AUC) and evaluate the diagnostic values of the single biomarker and the panel. Unsupervised hierarchical clustering (UHC) were performed based on the expression level of the proteins.

Results: A total of 112 suspected TBM patients were enrolled, and ELISA analyses of 8 proteins in the CSF were performed in 22 definite, 18 probable and 40 non-TBM patients. Significant differences in the expression level of 7 proteins were detected between TBM and non-TBM group ($P < 0.01$). UHC analysis revealed a disease-specific profile consisted of these 7 differentially expressed proteins for TBM diagnosis, with an accuracy of 82.5% (66/80). A panel of 3 biomarkers (APOE-APOAI-S100A8) displayed a better ability in discriminating TBM from non-TBM patients [AUC = 0.916 (0.857 – 0.976)], with a sensitivity of 95.0% (83.1% – 99.4%) and a specificity of 77.5% (61.5% – 89.2%).

	Cut-off value	AUC (95%CI)	Sensitivity% (95%CI)	Specificity% (95%CI)
Antithrombin III	>2.61	0.766 (0.658-0.854)	100.0 (91.2-100.0)	47.5 (31.5-63.9)
Apolipoprotein A-I(APOAI)	>60.67	0.753 (0.644-0.842)	75.0 (58.8-87.3)	72.5 (56.1-85.4)
Apolipoprotein B	>0.42	0.769 (0.661-0.856)	97.5 (86.8-99.9)	62.5 (45.8-77.3)
Apolipoprotein E(APOE)	>5.51	0.838 (0.739-0.911)	70.0 (53.5-83.4)	92.5 (79.6-98.4)
S100 Calcium-binding Protein A8(S100A8)	>3058.09	0.783 (0.677-0.867)	92.5 (79.6-98.4)	62.5 (45.8-77.3)
Haptoglobin	>5.27	0.712 (0.600-0.808)	85.0 (70.2-94.3)	67.5 (50.9-81.4)
Transthyretin	>33.17	0.713 (0.601-0.809)	65.0 (48.3-79.4)	77.5 (61.5-89.2)
APOE_APOAI_S100A8	> 0.2362	0.916 (0.857-0.976)	95.0 (83.1-99.4)	77.5 (61.5-89.2)

Conclusions: Our results confirmed the potential ability of CSF proteins in distinguishing TBM from non-TBM patients, and constructed a useful panel for TBM diagnosis.

OA-05 Modelling the impact of current TB control strategies

OA05-623-19 Contribution of transmission in clinics to community-wide TB disease incidence, and the impact of infection prevention and control interventions in KwaZulu-Natal, South Africa

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Background: There is a high risk of *Mycobacterium tuberculosis* (*Mtb*) transmission in healthcare facilities in high burden settings. Recent World Health Organization guidelines on tuberculosis infection prevention and control (IPC) recommend a range of measures to reduce transmission in healthcare settings, which were evaluated primarily based on their effects on transmission to healthcare workers in hospitals. To estimate the overall impact of IPC interventions, it is necessary to also consider their impact on community-wide tuberculosis incidence and mortality.

Design/Methods: We developed an individual-based model simulating *Mtb* transmission between household members, in primary healthcare (PHCs) clinics, and in other congregate settings. The model was parameterised using data from a high HIV community in KwaZulu-Natal, South Africa, including data on social contact in clinics and other settings by sex, age, and HIV/ART-status; and data on the prevalence of tuberculosis in clinic attendees. We estimated the proportion of disease that resulted from transmission in PHC clinics in 2019, and the impact of a range of IPC interventions in clinics on community-wide TB incidence and mortality.

Results: We estimate that 7.6% (plausible range 3.9-13.9%) of tuberculosis in adults resulted from transmission in PHC clinics in the study community in 2019. The proportion is higher in HIV-positive people, at

9.3% (4.8%-16.8%). We estimate that IPC interventions could reduce the number of incident TB cases in the community in 2021-2030 by 3.4-8.0%, and the number of deaths by 3.0-7.2% (Figure).

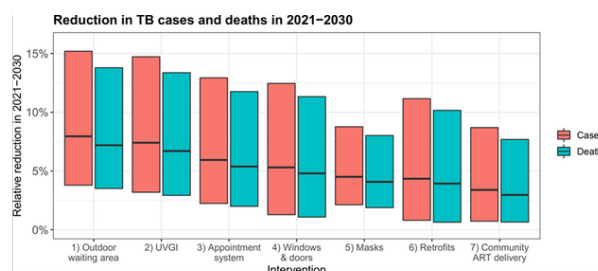


Figure. The estimated reduction in TB cases and deaths in the study population in 2021-2030 resulting from the proposed infection control interventions.

The central horizontal bar shows the best estimate, and the range of bars show the most extreme results from the sensitivity analyses. The interventions are:

- 1) Queue management systems and outdoor waiting areas;
- 2) Installing UVGI systems;
- 3) Date-time appointment systems;
- 4) Keeping windows and doors in waiting areas open;
- 5) Surgical mask wearing by patients;
- 6) Simple clinic retrofits to improve ventilation;
- 7) Increasing coverage of community-based delivery of antiretroviral therapy.

Conclusions: A non-trivial proportion of tuberculosis results from transmission in PHC clinics in the study communities, particularly in HIV-positive people. Implementing IPC interventions could lead to moderate reductions in disease burden. We recommend that IPC measures in clinics should be implemented both for their benefits to staff and patients, and for their likely effects on tuberculosis incidence and mortality in the surrounding community.

OA05-624-19 Modelling the impact of infection prevention and control interventions on TB transmission in clinics in KwaZulu-Natal, South Africa

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Background: Elevated rates of tuberculosis in health care workers demonstrate the high rate of *Mycobacterium tuberculosis* (*Mtb*) transmission in health facilities in high burden settings. In the context of a project taking a whole systems approach to tuberculosis infection prevention and control (IPC), we aimed to evaluate the potential impact of conventional and novel IPC measures on *Mtb* transmission to patients and other clinic attendees.

Design/Methods: An individual-based model of patient movements through clinics, ventilation in waiting areas, and *Mtb* transmission was developed, and parameterised using empirical data from eight clinics in two provinces in South Africa.

Seven interventions – co-developed with health professionals and policy-makers - were simulated:

1. queue management systems with outdoor waiting areas,
2. ultraviolet germicidal irradiation (UVGI) systems,
3. appointment systems,
4. opening windows and doors,
5. surgical mask wearing by clinic attendees,
6. simple clinic retrofits to improve ventilation, and
7. increased coverage of community based antiretroviral therapy (ART) delivery.

Results: In the model, 1. outdoor waiting areas reduced the transmission to clinic attendees by 83% (interquartile range [IQR] 76–88%), 2. UVGI by 77% (IQR 64–85%),

3. appointment systems by 62% (IQR 45–75%), 4. opening windows and doors by 55% (IQR 25–72%), 5. masks by 47% (IQR 42–50%), 6. clinic retrofits by 45% (IQR 16–64%), and 7. increasing coverage of community ART delivery by 22% (IQR 12–32%) (see Figure).

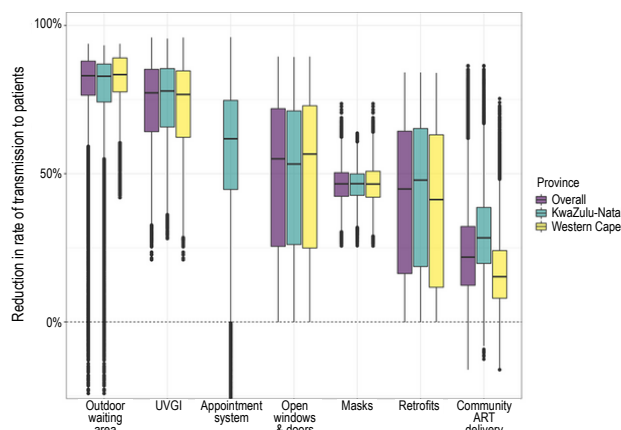


Figure. Estimated reduction in the rate of *Mycobacterium tuberculosis* transmission to patients in clinics, by province and intervention.

Conclusions: The majority of interventions achieved median reductions in the transmission rate to clinic attendees of at least 45%, suggesting that a range of effective interventions are available, that can be tailored to the local context. Measures not traditionally considered as IPC interventions, such as appointment systems, may be as effective as more traditional IPC measures, such as mask wearing.

OA05-625-19 Xpert on stool to diagnose tuberculosis in children is cost-effective in Ethiopia and Indonesia: a model-based cost-effectiveness analysis

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Background: Stool on GeneXpert MTB/Rif (Xpert) has recently been recommended by WHO as a sample type to diagnose TB in children, The SOS method is a simple method that makes it feasible to do stool testing at primary healthcare (PHC) level. We modelled the impact and cost-effectiveness of implementing the SOS stool method at PHC level for diagnosis of paediatric TB in Ethiopia and Indonesia.

Design/Methods: Tree modelling was used to represent pathways of patient care and referral. Parameters to inform the model were based on systematic review of

published literature, ongoing studies and surveillance, and expert opinion. Costing parameters were extracted from OneHealth, the global TB database, costing studies, and were obtained from in-country experts. Health outcomes were based on modelled mortality and discounted life-years lost. Comparing standard of care with the introduction of the SOS stool method at PHC level as the intervention, for every 100 children seeking care with presumptive TB in each country, we calculated a set of indicators as shown in the Table.

Results: In the context of predominantly clinical diagnosis of TB in children, particularly those aged <5 years, we found reduced mortality driven by an increase in sensitivity to detect true TB. Although the costs per child increased under intervention, projected health benefits implied the intervention would be considered cost-effective when compared against standard thresholds. Because more children could be bacteriologically diagnosed at the PHC, the number of referred children reduced while the proportion of children with a bacteriological diagnosis increased.

Quantity per 100 children with presumptive TB (unless stated):	Ethiopia			Indonesia		
	SOC	Intervention	Difference	SOC	Intervention	Difference
Children with true TB	42.8	42.8	0.0	42.8	42.8	0
Bacteriological investigations	29.3	95.2	66.0	23.5	95.3	71.9
Anti-TB treatments (ATT) irrespective of diagnosis	31.3	36.8	5.5	31.7	36.0	4.3
Percent of ATT initiated at PHC	72.9	81.0	8.1	72.1	81.2	9.1
Percent of true TB cases receiving ATT	60.0	70.4	10.4	60.6	69.0	8.3
Percent of ATT bacteriologically confirmed	14.4	33.6	19.1	11.2	33.2	22.0
Referred for receiving a diagnosis, inc. self-referrals	21.9	6.0	-15.9	23.7	6.1	-17.7
Deaths	4.7	4.0	-0.7	5.3	4.8	-0.6
Discounted life-years lost	128.9	110.1	-18.8	151.6	135.3	-16.3
Cost (2019 USD)	12084.2	12900.3	1816.1	8279.3	9488.7	1209.4
ICER		96.7			74.8	

Table. Outcomes per 100 children seeking care, unless otherwise specified*.

* Means are provided. Abbreviations: TB = tuberculosis; ATT = anti-TB treatment; PHC = primary health centre; SOC = standard of care; USD = United States Dollars; ICER = incremental cost-effective ratio.

Conclusions: In this modelling analysis, we projected that introduction of routine stool-based diagnostics at primary health care and hospital level would increase the proportion of bacteriologically confirmed TB, while reducing child mortality and life-years lost in both Ethiopia and Indonesia.

OA05-626-19 Benefits of addressing social determinants of gender disparities in TB in Vietnam: a modelling study

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Background: High prevalence of infectious tuberculosis among men suggests potential population-wide benefits from addressing gender disparities in disease burden. We assessed the potential impact of programmes to reduce tobacco smoking and alcohol consumption, both proximal determinants of tuberculosis with high rates among men. Our analysis focused on Viet Nam, where gender disparities in tuberculosis burden are among the highest globally.

Design/Methods: We developed a sex-stratified compartmental transmission model incorporating gendered programmatic and social determinants of tuberculosis. We calibrated the model to tuberculosis burden estimates for Viet Nam and modelled programmes to reduce tobacco smoking and alcohol consumption by 2025 in line with global targets. For each programme, we examined scenarios differentially targeting men and women and evaluated impact on tuberculosis morbidity and mortality in men, women, and children in 2035.

Results: When targeting men, programmes to reduce tobacco smoking and those to reduce alcohol consumption were projected to decrease overall tuberculosis incidence by 14.9% (uncertainty interval, UI, 9.7-21.8%) and 9.4% (UI 4.4-17.5%), respectively. Projected reductions were greatest for men (17.4%, UI 11.8-24.7%, and 11.0%, UI 5.4-19.4%, respectively) but still substantial for women (6.9%, UI 3.8-12.5%, and 4.4%, UI 1.9-10.6%, respectively) and children (12.7%, UI 8.4-19.0%, and 8.0%, UI 3.9-15.0%, respectively). Comparable programmes targeting women projected negligible impact, with declines in overall incidence of 0.3% (UI 0.2%-0.3%) and 0.1% (UI 0.0%-0.1%), respectively. Relative declines in tuberculosis prevalence and mortality were similar to those in incidence.

Conclusions: Addressing social determinants of tuberculosis burden in men benefits men, women, and children in Viet Nam. Population-wide impact is likely in other settings with similar gender disparities. Whilst not ignoring women, future programmes to reduce tobacco smoking and alcohol consumption should focus efforts on men to most effectively reduce tuberculosis morbidity and mortality across the population.

OA05-627-19 Health impact of novel TB vaccines in low- and middle-income countries

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Background: Tuberculosis (TB) remains a serious global health issue, particularly in low- and middle-income countries (LMICs). The introduction of novel TB vaccines is a key strategy for reaching disease elimination goals. With promising candidates in late-stage trials, a new TB vaccine may be available within the decade. Using vaccine characteristics outlined in the World Health Organization (WHO) Preferred Product Characteristics for New Tuberculosis Vaccines, we evaluated the impact of adolescent/adult vaccination in LMICs through various implementation scenarios.

Design/Methods: A novel age-structured *M.tb* transmission model was calibrated to epidemiological data in 92 countries, representing 94% of the TB incidence in LMICs, using Emulation and Approximate Bayesian Computation. The vaccine was introduced in three scenarios: 'Optimistic': routine vaccination of 9-year-olds and a single mass campaign of ages 10+ from 2028 with vaccine coverage targets reached instantly; 'Feasible': as Optimistic but with country-specific introduction years over 2028-2050, and within-country coverage targets attained over 5-years; and 'Pessimistic': as Feasible but with routine vaccination only. The vaccine was assumed to prevent progression to disease with 50% efficacy and confer 10-years protection. Impact was measured using TB incidence rate reduction in 2050 compared to no new vaccine, and cumulative treatment courses averted before 2050.

Results: Preliminary results indicated that the Optimistic, Feasible and Pessimistic scenarios reduced the TB incidence rate in 2050 by 11.0-24.0%, 10.5-17.3%, and 1.5-6.3%, respectively, with the largest reductions in the WHO African region, and Low-Income Countries. The cumulative number of TB treatment courses averted by 2050 using the Optimistic, Feasible, and Pessimistic scenarios was 32.6 million, 16.4 million, and 3.4 million respectively.

Conclusions: New TB vaccines could reduce the incidence rates of TB in LMICs by 2050, and avert large numbers of drug-sensitive and drug-resistant treatment courses, contributing to disease elimination goals and the global action plan on antimicrobial resistance.

OA05-628-19 Modelling the long-term effects of mass screening for latent and active TB in the Marshall Islands

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Background: Ambitious population-based screening programs for latent and active tuberculosis (TB) were implemented in the Republic of the Marshall Islands (RMI) in 2017 and 2018.

Design/Methods: We used a transmission dynamic model of TB informed by local data to capture the RMI epidemic's historical dynamics. We then used the model to project the future epidemic trajectory following the active screening interventions, as well as considering a counterfactual scenario with no intervention.

We also simulated future scenarios including periodic interventions similar to those previously implemented, to assess their ability to reach the End TB Strategy targets and TB pre-elimination in RMI.

Results: The screening activities conducted in 2017 and 2018 were estimated to have reduced TB incidence and mortality by more than one third in 2020, and are predicted to achieve the End TB Strategy milestone of 50% incidence reduction by 2025 compared to 2015. Screening interventions had a considerably greater impact when latent TB screening and treatment was included, compared to active case finding alone.

Such combined programs implemented at the national level could achieve TB pre-elimination around 2035 if repeated every two years, and around 2045 if repeated every five years.

Conclusions: Our model suggests that it would be possible to achieve TB pre-elimination by 2035 in RMI through periodic repetition of the same interventions as those already implemented in the country. It also highlights the importance of including latent infection testing in active screening activities.

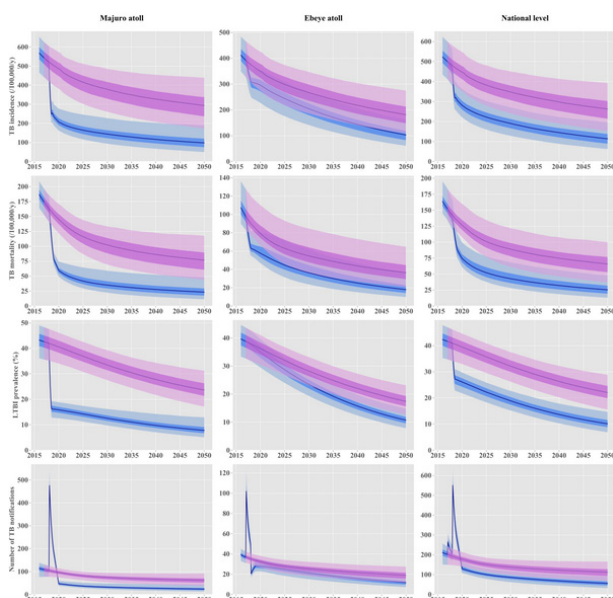


Figure. Projected effect of the active screening interventions implemented in 2017 and 2018
The solid lines represent the median estimates. The shaded areas show the interquartile ranges (dark shade) and 95% credible intervals (light shade) projected in the absence of any intervention (pink) and under a scenario including the interventions implemented in 2017–2018 in Majuro and Ebeye (blue).

OA05-629-19 The contribution of latent TB infection treatment to TB prevention in the United States: results of a transmission-dynamic model

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Background: Testing and treatment for latent tuberculosis infection (LTBI) to prevent future disease among infected individuals is a central strategy for U.S. TB elimination. We estimated how many TB cases can be averted through treatment of LTBI among 2020 U.S. residents.

Design/Methods: We used a mathematical model of TB to project impacts of a one-time targeted testing and LTBI treatment effort in 2020 U.S. resident populations recommended for testing and treatment. The model was calibrated to National TB Surveillance System (1953–2019) and other data using a Bayesian approach.

We estimated cases averted during 2020–2050 under several scenarios and reductions in prevention effectiveness through losses at each step of the LTBI care cascade.

Results: Under a base-case model representing existing TB prevention and care patterns, estimated annual TB cases declined from 8952 (2020) to 4120 (2050). Over this 30-year projection period, estimated U.S. TB cases total 180,200. 42% of these cases were attributed to LTBI and TB disease among migrants entering the country after 2020, 35% to prevalent LTBI and TB disease among U.S. residents as of 2020, and 23% to future transmission of *M. tuberculosis* within the U.S.

With an ideal LTBI care cascade, a one-time intervention among 2020 U.S. residents recommended for testing and treatment (N=132,000,000) could avert 59,200 cases by 2050. LTBI care cascade losses reduced the potential benefit of interventions by as much as 76%; testing consent had the largest reduction (29%).

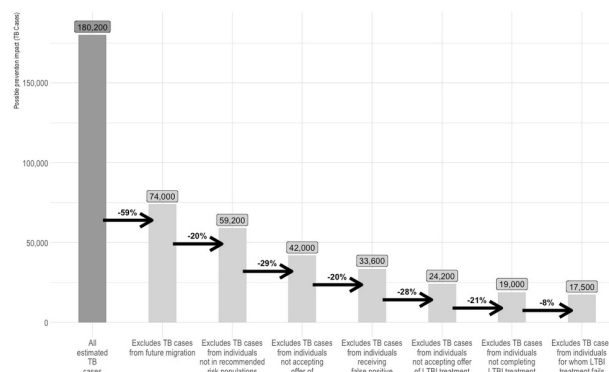


Figure. Possible prevention impact throughout the LTBI care cascade. Each bar is labelled with model-estimated cumulative cases averted between 2020–2050. The percentages between the bars represent the percent reduction in prevention impact from the previous step in the care cascade.

Conclusions: While future migration is projected as a leading source of U.S. TB cases over the next 30 years, considerable incidence reductions can be achieved through LTBI testing and treatment among current residents. Populations at risk for TB accounted for most projected TB cases among current residents. Gaps in the LTBI cascade substantially reduced the impact of LTBI testing and treatment programs.

OA-06 Quality people-centred TB care

OA06-630-19 Mapping the information technologies used by national TB programmes: an interview study across 13 countries

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Background: Despite increasing investment in digital tools throughout the tuberculosis care cascade, global coordination remains challenging. While countries often have strategic plans for the use of technology, from a global perspective, it is difficult to understand the global landscape of technology use and to facilitate the transfer of knowledge and tools across geographies.

This study sought to fill this gap by surveying information technology use across different National TB Programs, highlighting best practices, lessons learned, gaps and opportunities for improvement and increased investment.

Design/Methods: We conducted a qualitative interview study across 13 high TB burden countries. From October 2020 to February 2021, interviews were conducted via remote video calls with 44 stakeholders (3-4 participants per country), representing government programs, implementation partners, and funding organizations. Participants were recruited by way of personal introductions from the Global Fund as well as snowball sampling. Interviews were recorded (with consent), transcribed, and coded for thematic analysis using qualitative analysis software (NVivo).

Results: All countries sought to develop an integrated “backbone” system spanning management of patient cases, aggregate national reporting, and interoperability with digital tools across the care cascade. While DHIS2 provides increasing standardization in national reporting, there are still many different platforms utilized for case management, including custom solutions, e-TB Manager, and DHIS2 Tracker. Interviews revealed several unrealized opportunities to strengthen the use of technology, including market shaping for incentivizing adoption of solutions developed out-of-country and development of national and international policy guidance on cloud hosting, data security, and related areas.

Conclusions: A qualitative interview study of national TB programs revealed common patterns in the challenges, successes, and aspirations for emerging digital tools. Sharing best practices across geographies can foster improved uptake of new technologies, while also spurring global coordination and action on key areas such as standardization of platforms, shaping of markets, and development of policy guidelines.

OA06-631-19 Social protection systems for people with TB in high-burden countries: a qualitative study

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Background and challenges to implementation: To understand the availability and potential of implementation of social protection programmes for people with tuberculosis (TB) among high tuberculosis burden countries, as per the World Health Organization (WHO) classification.

Intervention or response: This is a qualitative exploratory study with primary data collection through interviews and high information power sample. Eleven high TB burden countries were included through purposive and convenience sampling strategies. One representative from each country was interviewed. They were National TB Programme managers, policymakers or researchers and were asked about their knowledge and perceptions of social protection for people with TB as well as barriers and facilitators to the implementation of such programmes in their context.

A qualitative content analysis was conducted and the Consolidated Framework for Implementation Research was used to understand the the barriers and facilitators to an effective implementation.

Results/Impact: Two themes were drawn from the qualitative data:

- i. The social protection for people with TB is a jigsaw of schemes, with no holistic coverage, and,
- ii. People with TB get support from the community and civil society.

Additionally, four major dimensions of barriers were identified: material resources; government structure and governance; social structure, social norms and values; and Covid-19; and two dimensions of facilitators: co-operation, collaboration and integration between government, civil society and research; and, engagement of politicians and policymakers and training of workers and communities.

Findings show that people with TB are indirectly and partially covered in terms of social protection, through a combination of different schemes, none of which has TB as eligibility criteria.

Conclusions: Countries are still working towards broadening the social security coverage for people with TB and are not yet focused on the type of benefit. There has to be a multi-sector approach in addressing social protection for people with TB, with collaboration between government sectors and levels, civil society and research institutions.

OA06-632-19 Acceptability of a social protection package for TB-affected families in Ho Chi Minh City, Vietnam: an exploratory qualitative study

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Background: Viet Nam's NTP has prioritized achieving universal health coverage and reducing catastrophic costs due to TB in its 2020-2025 National Strategic Plan. It has established a fund to purchase social health insurance (SHI) and provide cash transfers (CTs) for TB-affected households. However, little is known about the perceptions of these forms of social protection.

Design/Methods: We conducted key informant interviews (n=19) and focus group discussions (3 groups; 15 participants) with a wide range of relevant stakeholders to assess the acceptability of providing SHI and CTs as a form of social protection. Interviews were analyzed through thematic framework analysis and mapped back to Sekhon et al.'s *Acceptability framework of healthcare interventions*.

Results: SHI enrollment and either conditional or unconditional CTs for families affected by TB was a broadly acceptable package, according to five of seven interrelated acceptability constructs. Among all participants, SHI was viewed as a necessity, but people with TB questioned the quality of care when using it. CTs were perceived as being 'too good to be true'.

The package was considered beneficial for reducing out-of-pocket expenditure, increasing TB treatment adherence, and improving mental health and general well-being, but inadequate to fully alleviate the economic burden of the illness.

Conditions were not viewed as onerous to the participants, but the administration of tracking them increased the burden placed on patients, the health system and program staff. The package of support was viewed as improving spiritual health, TB-care and reducing stig-

ma. Dependency on the CTs and the TB program were identified as major concerns for both doctors and patients.

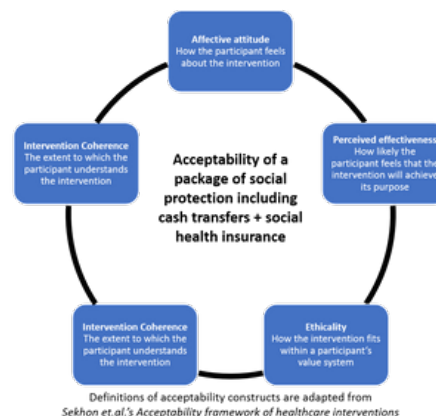


Figure. The package of support was found to be broadly acceptable according to the above five acceptability constructs.

Conclusions: We found a social protection package comprising SHI enrollment and CTs was highly acceptable in our setting by all stakeholders. Further evaluations are needed to assess its ability to reduce catastrophic costs and to measure the relative value of conditional vs unconditional CTs.

OA06-633-19 How do private practitioners manage presumptive TB patients? A standardised patient study from Indonesia

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Background: Many tuberculosis (TB) patients first present to private practitioners (PPs) in high TB burden countries. In Indonesia, few PPs are engaged in TB control organized by the National TB Programme (NTP), and quality of TB care provided by PPs is largely unknown.

Design/Methods: Randomly selected PPs were visited by standardized patients (SPs) enacting four clinical scenarios, each with classic TB-associated symptoms: (A) with no sputum test result; (B) with a negative sputum smear; (C) with a positive sputum smear; and (D) with recent history of treatment default. After medical consultation, SPs recorded their interactions on standard-

ized forms. We considered ‘concordance with the NTP guidelines’ to be referral to a DOTS facility, recommendation for chest radiograph (only for scenario B) and/or sputum testing; or prescription of anti-TB drugs (only for scenario C). We also measured use of unnecessary antibiotics and corticosteroids.

Results: We assigned 12 SPs to 254 PPs for a total of 281 visits. For scenario (A), 66% of PPs chose chest radiograph compared to sputum testing (28%) for TB diagnosis, and non-TB antibiotics were often prescribed (61%).

For smear-negative TB (B), PPs ordered chest radiograph (73%) rather than ordering Xpert or a trial of non-TB antibiotics. One-third of PPs prescribed corticosteroids. For scenario C, PPs chose chest radiograph (63%) rather than a trial of anti-TB drugs (9%), and only 1 in every 12 PPs correctly prescribed TB medication. For presumptive drug-resistant TB (D), only 3% of PPs requested sputum Xpert testing, and many PPs treated patients with non-TB antibiotics (41%) or fluoroquinolones (27%).

Conclusions: PPs prefer chest radiograph over microbiological testing, and often prescribe incorrect TB drug regimens or non-TB drugs. Better knowledge on TB management among PPs and stronger supervision from the local NTP could increase the quality of TB care in PPs in Indonesia.

OA06-634-19 Working towards patient-centred care in DR-TB-HIV: challenges faced by healthcare workers in a South African hospital

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Background: The complexities of treating and caring for people with drug-resistant tuberculosis and HIV (DR-TB HIV) require multidisciplinary health care worker (HCW) skills and support. However, few studies have examined how needed diverse categories of health care workers, with different training, orientation, value base and roles, can work towards meeting the needs of people with DR-TB HIV. This study investigated the experiences of social workers, pharmacists and nurses providing patient centered DR-TB HIV care in KwaZulu-Natal, South Africa.

Design/Methods: This qualitative study was nested within a randomized control adherence intervention trial for people with DR-TB HIV. A specially designed interview schedule was used to guide focus group discussions with 16 health care workers experienced in the care and treatment of people living with DR-TB HIV. The findings were analyzed using an inductive, content analysis approach.

Results: The participants lacked the specialized training and resources to deliver optimal patient-centered care for illnesses as complex as DR-TB HIV, were concerned for their occupational safety, and desired supplemental pay for working at a hospital where they were routinely exposed to potential infection. They emphasized secure infrastructure needs such as isolation wards, and inventory/supplies of medicines, while advocating for patient supports such as transport, food and social grants. Blurring of roles between nurses and social workers threatened to disrupt patient care, especially in the provision of counselling and feedback. Despite these challenges, participants were motivated by patient improvement.

Conclusions: Delivery of patient-centered care by multidisciplinary HCWs may be hindered by lack of staff development and job specific training, role overlap, stigma, and an overriding sense of feeling unappreciated. Multidisciplinary health care workers' roles and needs should be prioritized to improve the delivery of patient-centered care for DR-TB HIV, staff development and creating connected teams with clear roles and opportunities, and increased recognition in the workplace.

OA06-635-19 The positive impact of gender-based intervention on TB case notifications: the case study of Kano State, Nigeria

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Background and challenges to implementation: The challenges around Tuberculosis (TB) Case-Notification cannot be fully addressed without resolving issues around gender-related disparities. Understanding the unique needs and vulnerabilities of men and women, boys and girls, and other gender identities will improve service utilization, TB treatment outcomes and enhance program sustainability. We explored the role of a Gender-Based intervention in Kano state.

Intervention or response: The *Majalisa-Uwarigida* project is implemented under the TB LON project with the TB-NETWORK which is a non-profit organization, in

the fight against Tuberculosis. The intervention focuses on housewives (*Uwarigida*) who hardly go out of their homes and a group of young men (*Majalisa*) who gather in pursuit of a common goal. One of the heads of the house-wives is trained to offer symptomatic TB screening and link identified presumptive to the program for diagnostic evaluation. Within the Majalisa setup, a volunteer is trained to screen and identify presumptive during their evening gatherings. A qualitative approach was used where questionnaires were administered to both Presumptive and registered TB patients.

Results/Impact: The intervention yielded 19,160 TB clients who were screened for TB of which 3816 (20%) were presumed to have TB. Of the presumed, 3734 (98%) had their samples tested resulting in 276 (10%) TB patients diagnosed and started on TB treatment from April-December 2020. The yield is high when compared to the 47 TB cases diagnosed before the intervention kicked off. Of the diagnosed TB patients, 245(88.7%) agreed that men and women should be given equal rights and access to quality healthcare. A good percentage 31(11.3%) still maintained that decisions regarding access to health care and any other issue must be determined by the head of the family among other cultural rules.

Conclusions: The initiation of a Gender-based intervention is key to increased TB case-finding in Nigeria. This approach is recommended for scale-up within other localities in Nigeria.

OA06-636-19 Optimising active TB case-finding and treatment: a conceptual framework for performance monitoring and quality improvement

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Background and challenges to implementation: Nigeria is a high tuberculosis (TB) burden country with a treatment coverage of 27%. In recent years, the country has been recording increasing annual TB case notification, and active case finding interventions have contributed substantially to this increase. As the country scales up these interventions, maintaining quality of care remains a challenge to achieving effective and efficient programming.

Intervention or response: A conceptual framework was developed for weekly performance monitoring and quality improvement (QI) of USAID-funded TB projects.

Performance and QI indicators were used to monitor performance and quality of care along the clinical cascade (figure 1). Performance gaps were identified based on established benchmarks and corrective measures instituted for mitigation while monitoring improvement using weekly performance dashboards.

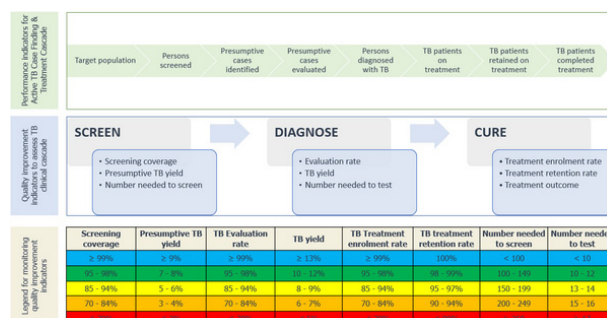


Figure 1. Conceptual framework for active TB case finding and treatment

Results/Impact: After 12 months of implementation, all performance indicators (Numbers of persons screened, presumptive cases identified and tested, TB cases diagnosed and on treatment) recorded increases in the range of 323% to 439%, when comparing the first and last quarters of implementation. Cumulatively, 9,381,005 persons were screened for TB, of which 664,416 (7%) were presumptive TB cases. Of the presumptive cases, 588,816 (89%) received diagnostic evaluation and 50,634 (9%) were diagnosed, of which 44,516 (88%) were started on treatment. Despite marked increases in the performance indicators, the QI indicators (screening coverage, presumptive TB yield, evaluation rate, TB yield, and treatment enrolment rate) remained consistent through the performance period. The average numbers needed to screen and to test to diagnose one case were 185 and 12 respectively.

Conclusions: The conceptual framework provides clear visualization that promotes discussion across the cascade, exchange of best practices and monitoring the effects of course-corrective measures to improve program performance. Its use enabled implementing partners to promptly identify and address programmatic challenges resulting in improved performance, while maintaining quality of care. It is recommended for routine program monitoring by National TB Programs.

OA-07 TPT regimens: safety first

OA07-637-19 Urticaria: a major systemic drug reaction to 1HP regimen for TB prevention in a non-HIV population

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Background: The 3HP regimen—weekly rifapentine plus isoniazid for 12 doses—improves the completion rate of latent tuberculosis infection (LTBI) treatment, but adverse reactions are common. The new 1HP regimen—daily rifapentine plus isoniazid for 28 days—has low toxicity in HIV-infected populations. However, its toxicity in non-HIV population remains unclear.

Design/Methods: This randomised, multicentre trial compared the completion rate, systemic drug reactions (SDRs), and plasma drug levels of 1HP and 3HP in ≥ 13 -year-old non-HIV subjects with LTBI from September 2019 ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04094012): NCT04094012).

The preliminary findings of this ongoing trial on the differences in SDR risk and patterns between the two regimens are described.

Results: Until August 2020, 110 and 101 individuals were randomised into 1HP and 3HP groups, respectively, with treatment completion rates of 88.2% and 83.2%, respectively.

In both groups, 10.9% experienced SDRs ($p = 0.997$): predominantly urticaria in 1HP group (92%) and flu-like syndrome in 3HP group (91%). Among participants experiencing SDRs, 83% and 55% in 1HP and 3HP groups, respectively, completed treatment ($p = 0.193$).

Cutaneous reactions were more common with 1HP (36.4% *vs.* 14.9%, $p < 0.001$). In the 1HP group, a higher plasma rifapentine level at 2 h after dosing was associated with SDR (median: 30.09 *vs.* 21.19 $\mu\text{g/mL}$; $p = 0.032$).

Conclusions: In non-HIV population, the 1HP group had a 5% higher completion rate than the 3HP group, with a similar risk of SDRs. The predominant manifestation of SDR under 1HP was urticaria, which is usually tolerable and does not cause treatment discontinuation.

OA07-638-19 Safety of short-course weekly rifapentine and isoniazid (3HP) for TB preventive treatment during pregnancy

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Background: The safety of a 3-month course of weekly rifapentine-isoniazid treatment (3HP) to prevent tuberculosis in pregnant women on antiretroviral treatment (ART) for human immunodeficiency virus infection is unknown. As part of the WHIP3TB trial, 3HP was given once or annually. We report the outcomes on women who initiated 3HP and became pregnant.

Design/Methods: Women were considered exposed to 3HP during pregnancy if their estimated conception occurred while taking study drug or within 30 days of their last 3HP dose, and unexposed if they conceived >30 days after intake of the last drug dose. Pregnant women were followed up for pregnancy outcomes (live birth, stillbirth or abortion). We present a composite adverse pregnancy outcome of stillbirth or spontaneous abortion, low birth weight ($<2500\text{g}$), preterm delivery (<37 weeks gestation), or major congenital anomalies. Analysis is restricted to each participant's first pregnancy during the trial. Outcomes were compared between exposed and unexposed pregnant women.

Results: Among 2287 women in the study, 205 pregnancies were reported, 63 (31%) among exposed women. Among pregnant women, their median age was 32 years, median months on ART 34.3, median CD4 count 525 cells/ mm^3 and median number of previous pregnancies was 2. Overall, there were 154 (75%) live births, 5 (2%) stillbirths, 27 (13%) spontaneous abortions, 16 (8%) induced abortions, and 3 (1%) unspecified abortions. The percentage of pregnancies that were spontaneous abortions were similar by group; 13% [8/63] and 13% [19/142], in the exposed and unexposed. The composite poor outcome occurred in 33% (68/205) of the pregnancies; 32% (20/63) in the 3HP exposure group and 34% (48/142) in unexposed group (Table).

	3HP exposure (n=63), n	%	Unexposed (n=142), n	%
Composite poor outcome	20	32	48	34
Still birth	1		4	
Spontaneous abortion	8		19	
Low birth weight (<2500g)	7		16	
Gestational age<37 weeks	6		12	
Major congenital anomalies in infant	0		0	

Table: Pregnancy outcomes among women of reproductive age initiating 3HP

Conclusions: The frequency of spontaneous abortion and adverse pregnancy outcomes (when analysed as a composite outcome) were similar in the 3HP exposed and unexposed groups.

OA07-639-19 Safety of the 3-month rifampicin–isoniazid TB preventive therapy in household child contacts

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Background: Short-course tuberculosis preventive treatment (TPT) may improve management of household TB child contacts. Lack of safety data can limit their introduction or implementation in some countries. We present safety data of the 3-month rifampicin-isoniazid (3RH) regimen in the cluster-randomized CONTACT Study that compares community- and facility-based interventions for child contact screening and TPT management in Cameroon and Uganda.

Design/Methods: Household child contacts <5 years old eligible for TPT were initiated by a nurse at household or at facility depending on the model of care using RH75/50. In the community-based model, TPT monitoring using symptom check list was done by trained community health-workers after 1, 2, 4, 8 and 12 weeks of TPT with referral of symptomatic children to the facility. In the facility-based model, treatment monitoring was done at 4, 8 and 12 weeks. In both models, symptomatic children were examined by a medical doctor

including specifically for identification, grading (DAIDS scale) and management of adverse events (AEs). A safety review committee reviewed all AEs.

Results: Of 418 children (median age 2.5 years, 48.6% female), 52 (12.4%) presented at least 1 AE: 34/298 (11.4%) in the community-based model and 18/120 (15.0%) in the facility-based model (p=0.31). Seventeen serious AEs were notified: 11 malaria, 2 salmonellosis, 2 urinary tract infections, 1 tonsillitis and 1 lower respiratory tract infection. None was related to the TPT. One child with salmonellosis died. Four children (1.0%) presented TPT-related AE: 1 probably related grade-2-hypersensitivity and 3 possibly related grade-1 AE (1 clinical jaundice, 1 peripheral neuropathy and 1 rash), resulting in TPT discontinuation and TPT interruption in 2 children (0.5%), respectively.

Conclusions: The 3RH TPT regimen was very well tolerated in young child contacts, supporting its routine use within decentralized, community-based contact management programs.

OA07-640-19 Factors associated with discontinuation of TB preventive treatment: analysis of two randomised trials

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Background: The effectiveness of tuberculosis preventive treatment (TPT) depends on adherence. Using data from two randomized controlled trials (RCT) comparing 4 months of daily rifampin (4R) and 9 months of daily isoniazid (9H), we assessed factors associated with early TPT discontinuation.

Design/Methods: We evaluated factors associated with discontinuation of TPT at different stages of treatment: after randomization but before starting treatment, after starting treatment but before the first follow-up visit, after first follow-up visit but before the second follow-up visit, and after second follow-up visit. We did logistic regression, using generalized linear mixed models, treating the country of randomization as the clustering variable, to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95%CI) of various factors for TPT discontinuation.

Results: In total we analyzed 6859 participants, of whom 3416 (49.8%) received 9H and 3443 (50.2%) received 4R. Median (IQR) age was 36 (IQR: 27 to 48) and the majority were female (3953, 57.6%). aOR for factors associated with discontinuation are in the Table. We found being randomized to 9H was associated with discontinuation after randomization (aOR 1.4, 95%CI 1.1 to 1.7) and after the second follow-up visit (2.4, 2.1 to 2.8). Sex and age did not appear associated with treatment discontinuation; people living with HIV had lower

odds of discontinuation early in treatment. Reporting a side effect (aOR 4.5, 95% CI 3.5 to 5.7), taking <80% of doses (6.4, 4.9 to 8.4), and rescheduling the appointment (2.3, 1.6 to 3.3) at the first follow-up visit were strongly associated with discontinuation before the second follow-up visit. These factors were also associated with discontinuation after the second follow-up visit.

Parameter	Discontinuation After Randomization but Before Starting Treatment	Discontinuation After Starting Treatment but Before First Follow-up Visit	Discontinuation After First Follow-up Visit but Before Second-Follow-up Visit	Discontinuation After Second Follow-up Visit
Randomized to 9H (ref: 4R)	1.4 (95% CI: 1.1 to 1.7)	0.8 (95% CI: 0.7 to 1.03)	1.1 (95% CI: 0.9 to 1.3)	2.4 (95% CI: 2.1 to 2.8)
Age (per year increase)	0.99 (95% CI: 0.98 to 1.01)	0.99 (95% CI: 0.98 to 1.01)	1.0 (95% CI: 0.99 to 1.01)	0.99 (95% CI: 0.98 to 1.01)
Female Sex (ref: Male Sex)	1.2 (95% CI: 0.99 to 1.5)	1.0 (95% CI: 0.8 to 1.2)	1.0 (95% CI: 0.8 to 1.2)	1.1 (95% CI: 0.9 to 1.3)
People Living with HIV (ref: HIV-Negative)	0.2 (95% CI: 0.1 to 0.7)	0.3 (95% CI: 0.2 to 0.8)	0.7 (95% CI: 0.4 to 1.4)	0.9 (95% CI: 0.6 to 1.3)
Side Effect Reported at Visit (ref: None Reported)	--	--	4.5 (95% CI: 3.5 to 5.7)	1.4 (95% CI: 1.1 to 1.7)
Had Taken <80% of Prescribed Doses Up to Time of Visit (ref: Took ≥80%)	--	--	6.4 (95% CI: 4.9 to 8.4)	6.7 (95% CI: 5.5 to 8.2)
Participant Rescheduled Appointment (ref: Did Not Reschedule) *not collected for 847 participants	--	--	2.3 (95% CI: 1.6 to 3.3)	2.1 (95% CI: 1.5 to 2.9)

Conclusions: Persons at risk for TPT discontinuation can be identified through health behaviors early in treatment follow-up, better than reliance on patient- and regimen-related factors. Early identification may allow targeted interventions to enhance adherence.

OA07-641-19 Community volunteers in Ethiopia can detect side effects and achieve high TB preventive treatment completion rate among young children exposed to infectious TB cases

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Background: Ethiopia aligned its guidelines and practices of latent TB infection (LTBI) management with the latest global recommendations. Recent data, however, showed that about 33% of eligible children were not treated for LTBI and TB preventive treatment (TPT) completion rates were either too low or unknown.

Design/Methods: Between July 2020 – March 2021, we prospectively enrolled on TPT and followed up children aged ≤ 5 years who were household contacts with pulmonary TB cases in two rural and one urban slum areas of Ethiopia. Iddirs are membership-based local associations of people who have voluntarily entered an agreement to help each other during times of adversarities. We engaged Iddir members after educating them on basics of TB and TPT and regularly supervised and mentored them. Weekly home visits and through regular phone contact, they checked for common side effects using standardized checklists. The women received monthly stipends for transportation and airtime.

Results: A total of 755, <5 year old child contacts of 365 index TB patients were initiated with TPT. Their mean age was 35.5 month (SD 17.7). Most children (92.3%) received 3RH regimen while only 6% and 1.7% received 6H and 3HP respectively. Of 323 children whose TPT completion dates were due, 99% completed successfully, three discontinued due to side effects and one was lost to follow-up.

Conclusions: Engaging volunteer women contributed to a high rate of successful TPT completion and prompt detection of side effects. This model should be considered for further scale up.

OA07-642-19 Characteristics of HIV-positive persons with TB after completing TB preventive therapy in Nairobi, Kenya, 2014–2020

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Background and challenges to implementation: TB is associated with high morbidity and mortality among persons living with HIV (PLHIV). TB preventive treatment (TPT) reduces the risk of TB and death. Kenya has been providing a 6-month course of isoniazid to eligible PLHIV since 2012. Prevalence and time to TB after TPT in Kenya is unknown.

We describe characteristics of PLHIV who develop TB after completing TPT and estimate time to TB diagnosis in 14 Nairobi clinics.

Intervention or response: We analyzed routine program data on TPT provision and TB diagnosis among PLHIV (January 2014–December 2020). Variables of interest included age, sex, World Health Organization (WHO) stage at HIV diagnosis, TPT and antiretroviral therapy (ART) adherence, opportunistic infections (OI), CD4-cell count, time to TB diagnosis post-TPT, TPT and TB treatment outcomes. TB diagnosis was based on WHO guidelines.

Using Epi-info version7, we calculated frequencies and medians with interquartile range (IQR).

Results/Impact: During the study period, of the 25,225 PLHIV who received TPT, 423 (1.7%) developed TB after completing TPT, (men, 226 [53.4%]) including 11(2.6%) not receiving ART. Median age was 39.9 years (IQR, 32.3–46.1). Median follow-up period and time to TB after TPT were 76.3 months (IQR, 44.5–109.5) and 32.9 months (IQR, 18.3–48.2), respectively (Figure).

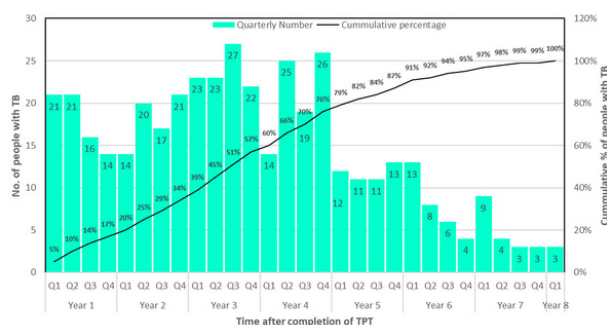


Figure. Temporal distribution of people who develop TB after TPT completion.

A total of 233(55.0%) had WHO stage 3–4 disease at HIV diagnosis. Median CD4-cell count before TB diagnosis was 259 (IQR, 111–515). Poor/inadequate adherence was reported among 241 (56.9%) for TPT and 337(81.8%) for ART. Non-TB OIs were reported among

164(38.8%) of PLHIV during TPT. Most (388 [74.6%]) completed TB treatment, but 2(0.5%) had drug-resistant TB and died.

Conclusions: TPT effectively prevents TB. The small proportion of PLHIV who developed TB had advanced HIV, suboptimal adherence to both ART and TPT, and had OIs during TPT. Identifying these patients during TPT and providing targeted support could improve health outcomes

OA07-643-19 Transcriptome-based prediction of 3HP-related systemic drug reactions in TB preventive therapy

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Background: Weekly rifapentine-based treatment (known as 3HP) is gaining popularity for its short-course and high completion rate for latent tuberculosis infection (LTBI) treatment. However, the systemic drug reaction (SDR) is a major safety concern to cause inevitable treatment discontinuation. Understanding predictors of SDR and identifying risk subjects before treatment can improve public acceptance and cost-effective implementation of the LTBI program.

Design/Methods: A total of 187 subjects receiving 3HP were prospectively recruited and randomly selected 8 cases with SDRs and 12 non-SDRs (pilot cohort) for generating whole-blood transcriptomic data. After integrating the hierarchical systems biology model (HiS-BiM) and a therapy-biomarker pathway approach, candidate genes were obtained and evaluated by RT-qPCR. We further developed interpretable machine learning models and established a universal cut-off value (Shapley additive explanations value, SHAP value) for each SDR prediction model. An independent cohort was used to evaluate the performance of these predictive models.

Results: Based on the transcriptomic profile of the pilot cohort, we identified 19 candidate genes. Six genes among them were finally selected by RT-qPCR from the training cohort. By applying the SHAP values of various combinations of the 6 gene expression signature, the best model consists of 5 genes, which had an accuracy of 0.856, sensitivity of 0.889, and specificity of 0.847 for the joint of the testing and training cohort. The predictive model also worked well across different subgroups.

Conclusions: The transcriptome-based predictive model for SDRs before 3HP treatment can guide a safe and personalized regimen to foster the implementation of the LTBI program. Additionally, it provides the potential translational value in future studies of drug-related hypersensitivity.

OA-08 Impact of COVID-19 on TB screening and detection

OA08-644-19 Impact of a public-private interface agency for TB reporting during the COVID-19 pandemic in Vietnam

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Background: Viet Nam's second prevalence survey uncovered a higher than expected burden of TB. Studies have indicated that at least half of the people with TB who are 'missed' by existing services are taking care in the private sector and not reported to the National TB Program.

Design/Methods: We established a public-private interface agency (PPIA) to engage private doctors for TB treatment reporting in 14 districts across Ho Chi Minh City (HCMC) and Hai Phong, Viet Nam. Treatment data were collected and patients missing sputum results were offered an Xpert MTB/RIF test to increase the rate of bacteriological confirmation and to identify drug resistance early. Data were cleaned and checked for duplicates prior to official entry in the government's e-reporting system (VITIMES). We collected aggregate notification data for all treatments sites in both cities to compare changes in notifications before (2019) and during (2020) our initiative

Results: 62 private providers shared treatment data for 1,746 patients with our initiative. 1,453 (83.2%) patients were then officially notified in VITIMES (1,186 in HCMC and 267 in Hai Phong). There were 19,271 notifications across the 38 districts of HCMC and Hai Phong in 2019, 16.0% of which originated at private sites. In 2020, excluding the PPIA results public-sector notifications declined by -5.1% and private notifications declined by -12.1%. However, layering the gains from the PPIA on top, notifications actually increased by +1.3%. Although we reported fewer notifications

in Hai Phong, our contribution to city-wide totals was twice as large as in HCMC (14.5% vs 6.7% of all notifications in 2020).

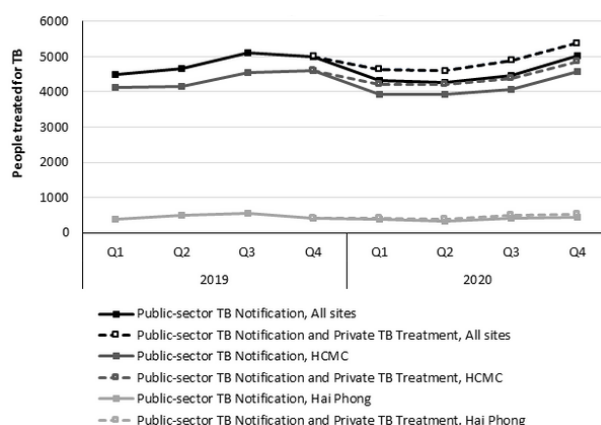


Figure. Public & private-sector TB treatment trends Ho Chi Minh City and Hai Phong, Viet Nam

Conclusions: The COVID-19 pandemic likely resulted in the large declines in routine public- and private-sector notifications, which were compensated by the PPIA results. However, further evaluations are needed to understand whether PPIA notifications displaced existing notifications or increased reach to previously 'missed' individuals.

OA08-645-19 Community contribution to TB case-finding during Covid-19: using community volunteers as cough monitors for increased case-finding in Nigeria

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Background and challenges to implementation: Despite being a high TB burden country, Nigeria has low case detection rates; only 27 percent of estimated cases were notified in 2019 (WHO World TB Report 2020). The historical focus on presumptive screening in public facilities contributes to low case identification. USAID's SHOPS Plus program in Nigeria focuses on increasing notification through the private sector using multi-cadre networks of formal clinical providers and community pharmacists alongside informal private laboratories and drug shops. However, COVID-19 and its control measures, such as lockdowns and closures, severely lowered patient attendance at formal health facilities resulting in decreased screening, testing and case finding rates.

Intervention or response: Pre-COVID-19, SHOPS Plus developed strong community connections with churches, mosques, and traditional leaders through its

provider-led social and behavior change (SBC) outreach work aimed at increasing TB awareness. The program used these connections to identify, train and equip with infection prevention control materials cough monitors able to conduct house-to-house screening, sputum collection, and referrals. Screeners, previously assigned to clinical facilities were re-assigned to “roam” between drug shops screening their clientele. This strategy contributed to closing the pandemic screening gap in formal facilities but has also identified and expanded community systems that can reach missing TB cases.

Results/Impact: The contributions of community outreach events, cough monitors, and roaming screeners to the program’s TB case detection total grew from 30% over January-March 2020 (Q1) to 47% over July-September 2020 (Q3). The program’s overall average monthly case detection grew 53% from 437 (Q1) to 669 (Q3) after a brief dip in March/April when the pandemic began.

Conclusions: Using community health systems for screening, sputum collection and referral is feasible, even in a pandemic context, making up for reduced formal sector TB service delivery. Beyond the pandemic these systems can supplement the formal private sector contribution to TB case notification in Nigeria.

OA08-646-19 Adapting and innovating TB screening during the Covid-19 pandemic: integration of TB screening to the Measles-Rubella-Oral-Polio-Vaccine Supplemental Immunisation Activity (MR-OPV-SIA) in the Philippines

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Background and challenges to implementation: The Philippines ranks 3rd among the top 30 countries with the highest TB burden. In 2019, the estimated incidence was 559,263, only 421,295 (75%) of whom were notified to the health system. The proportion of child TB among all notifications was low at 12%, versus 15-20% in other high-TB burden countries. This went further low in 2020, as the national response to the COVID-19 pandemic reduced TB notifications to 46%.

Intervention or response: USAID’s TB Platforms for Sustainable Detection, Care and Treatment Project, in collaboration with the Department of Health National Tuberculosis Program, integrated TB screening into the month-long MR-OPV-SIA in Zambales Province. The integration was an adaptation to continue TB screening among children and adults amidst the COVID-19 pandemic response. During immunization, a TB Self-Assessment Form was administered to children and adults,

for symptomatic screening and risk factor identification. All individuals presumed to have TB were sent for chest x-ray (CXR) or GeneXpert; all positives were enrolled to treatment.

Results/Impact: Within 16 days of implementation, 22,097 individuals were screened for TB. Of these, 3,058 (14%) were presumed to have TB (2,670 individuals were referred for CXR, 388 for GeneXpert). Analysis shows a potential yield of 3%, specifically, 590 TB clients diagnosed and enrolled to treatment in one month; this would allow the province to achieve 26% of its annual target for TB notifications. The strategy can also potentially increase child TB notifications in the province by 25%. The integration demonstrates good efficiency - for every 37 people screened, 1 TB client is diagnosed.

Conclusions: Integration of TB screening to widescale immunization is both an adaptation and innovation in finding TB clients. Immunization is an effective vehicle for TB services to reach more population, especially, children. It improves efficiency of TB service delivery, maximizing time and use of public health resources during a pandemic crisis.

OA08-647-19 The impact of COVID-19 lockdown on TB cascade of care in rural KwaZulu-Natal, South Africa: an interrupted time-series analysis

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Background: Effects of the COVID-19 pandemic across the TB cascade of care in high HIV-TB burden settings need to be estimated with real-world data. We describe the impact of the national lockdown in March 2020 on TB testing and treatment initiations in primary health care clinics (PHC’s) in KwaZulu-Natal, South Africa.

Design/Methods: Anonymized TB programmatic data for all ages was aggregated into monthly counts of TB tests among presumptive TB patients and TB treatment initiations, at 10 PHC’s in Eshowe/Mbongolwane area between January 1st, 2018 and December 31st, 2020. Presumptive TB cases were investigated for active TB using Xpert® MTB/RIF. In this interrupted time series analysis, we used descriptive statistics and Poisson regression models to estimate the impact of lockdown on these outcomes.

Results: During the study period, 12,922 GeneXpert tests and 3,347 TB treatment initiations were recorded among patients with presumptive TB. Average TB tests performed per month before and after lockdown were 377 (95% CI 325-429) and 312 (95% CI 254-370) respectively (Figure 1). In the Poisson regression model, lockdown was associated with 54% decrease in TB testing in April 2020 (Incidence rate ratio [IRR] 0.46, 95% CI 0.27-0.78). TB treatment initiations decreased before and after lockdown from an average of 104 (95% CI 97-110) to 65.6 (95% CI 51-81) respectively, with an estimated 50% decrease in the month of the lockdown (IRR 0.50, 95% CI 0.35 to 0.73). As restrictions eased, TB testing increased to pre-lockdown levels by a trend of 2% (95% CI 1.01-1.03) per month. However, there was no change in trend for TB treatment initiations with -1% (95% CI 0.98-1.01).

Conclusions: Lockdown severely impacted TB testing and treatment initiations. Decentralized community TB-testing sites which facilitate access to screening, testing and treatment initiation could be considered to ensure continuity of TB care in the event of future pandemics.

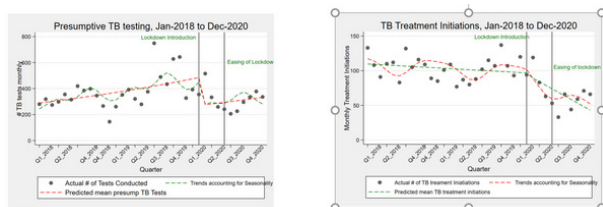


Figure 1. TB testing among patients with presumptive TB and treatment initiations before and after national lockdown, in 10 PHC's in Eshowe-Mbongolwane area, KwaZulu-Natal, South Africa.

OA08-648-19 Integrating active TB and Covid-19 screening activities: an effective strategy for increasing bacteriological confirmation of TB in the Philippines

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Background and challenges to implementation: With an incidence rate of 554 per 100,000 population, the Philippines continues to struggle with the health and socio-economic impact of TB. In 2019, it ranked 3rd among the top 30 high TB-burden countries. Notification rate was at 75%, severely reduced by the national response to the COVID-19 pandemic to 46%. To adapt to the crisis, the Department of Health published the National Tuberculosis Program (NTP) Adaptive Plan, providing guidelines on adapting TB screening during the pandemic.

Intervention or response: Guided by the plan, USAID's TB Platforms for Sustainable Detection, Care and Treatment Project integrated TB screening to active COVID-19 screening in 3 cities: Manila, San Juan and Navotas. Un-

der the initiative, populations at risk for COVID-19, including public transport operators, factory workers, vendors, government workers, senior citizens and indigents screened for COVID-19 through swab test were also screened for TB. Comparative analysis of cascade of care data between integrated TB-COVID-19 screening and TB screening alone enabled impact assessment.

Results/Impact: Within 4 months of implementation, 3,038 individuals were screened for COVID-19 and TB. Of these, 500 were presumed to have TB and tested by GeneXpert; 105 (3%) tested positive for TB. While presumptive identification rate was higher in stand-alone TB screening (19% vs 16%), integrated screening enabled 100% GeneXpert testing of all presumptives (versus the average 51% in TB screening alone). Integrated TB-COVID-19 screening also demonstrated better efficiency – for every 29 people screened, 1 TB client was diagnosed. This is considerably lower than the standard ratio of having to screen 200 people to find 1 TB client (from national prevalence survey).

Conclusions: Integrated TB-COVID-19 screening demonstrated better efficiency in finding TB clients. Mandatory prescription for COVID-19 testing was instrumental to ensuring all clients were also tested for TB, avoiding patient loss before diagnosis. Immediate availability of testing manpower and supplies were also important success drivers.

OA08-649-19 Bolstering pandemic TB case-finding: using monitoring data, patient pathways data, and community-based screening to respond to patient care-seeking behavior changes in Nigeria

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Background and challenges to implementation: Since 2017 USAID's SHOPS Plus program has supported delivery of tuberculosis (TB) services in networks of private clinics, laboratories, pharmacies, and proprietary and patent medicine vendors (PPMVs)/drug shops in Nigeria's Kano and Lagos states. These networks were developed because Nigeria misses 75% of its 400,000 annual TB cases and nearly 75% of health expenditures occur in the private sector. Within networks, PPMVs are particularly important for TB case finding because they are more financially and geographically accessible than clinical providers.

Intervention or response: COVID-19 pandemic and its associated mitigation efforts caused widespread health sector disruption: many programs anticipated negative effects on patient care-seeking behavior, screening, and ultimately suppressed TB case finding. In response, SHOPS Plus intensified case findings efforts outside of clinical settings by deploying specially trained “roaming screeners” to work with PPMVs to bolster community-level screening, sample collection, and referrals.

Results/Impact: To explore the effects of these programmatic changes, SHOPS Plus compared monitoring data before and after pandemic onset across the Kano networks’ TB cascade (including total facility attendance, screening, testing, and cases detected). Between 2019 and 2020 attendance increased by 32% in clinical facilities and decreased by 29% in PPMVs. Although clinical facility screening rates and presumptive yields fell, they increased for PPMVs leading to a 100% increase in PPMV-based case finding. Though potentially promising, the extent that increased PPMV case finding is driven by programmatic changes and/or patient behavior changes (e.g., COVID-related fear or stigma) is unclear. These trends will be further explored using additional 2021 program data as well as a patient pathways survey commenced in May 2021.

Conclusions: PPMVs play a critical role in making TB services more accessible in routine and pandemic contexts. Understanding patient care-seeking behavior will contribute to how we increase the effective use of PPMVs.

OA08-650-19 Acing the test of the COVID-19 pandemic: effective TB screening among household TB contacts in the Philippines through the TB contact centre

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Background and challenges to implementation: The Philippines ranks 3rd among the top 30 high TB-burden countries, with incidence rate of 554 per 100,000 population. In 2019, TB notification rate was at 75%, reduced by the response to COVID-19 pandemic to 46%. Rapid assessment of TB services revealed diminished screening and testing due to lockdowns, re-assignment of resources to the pandemic response, and people’s hesitation to seek care for fear of contracting COVID-19. To adapt to these, the Department of Health published the

National Tuberculosis Program (NTP) Adaptive Plan, providing guidelines on adapting TB services during the pandemic.

Intervention or response: Guided by the plan, USAID’s TB Platforms for Sustainable Detection, Care and Treatment Project assisted 14 health facilities in CALABARZON Region, Philippines, to implement the TB Contact Center (TBCC) for remote phone-based screening mainly of household contacts of index TB clients and testing referrals. TBCC was also used to monitor treatment adherence of TB clients receiving treatment. Comparative analysis of cascade of care data between TBCC and other screening strategies enabled impact assessment.

Results/Impact: Within 4 months of implementation, 1,779 clients were served through the TBCC; 732 clients were screened by symptom; 606 (83%) were presumed to have TB and referred for testing. A total of 509 (70%) clients were diagnosed and enrolled to treatment. Comparison with other strategies reveal that TBCC produced a higher yield - for every 29 people screened, 1 individual is diagnosed with TB. The ratio is considerably lower versus the standard ratio of having to screen 200 people to find 1 TB client (from national prevalence survey), demonstrating TBCC to be an efficient intervention.

Conclusions: TBCC is an effective adaptation to the pandemic response. The targeted nature of screening, focused among household TB contacts, is integral to TBCC’s success. Remote means of service delivery is effective, especially when health-seeking behavior and service delivery are compromised.

OA-09 Crucial factors in TB epidemiology

OA09-651-19 Natural history of TB among untreated patients: a review and meta-analysis

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Background: Approximately 30% of people with tuberculosis (TB) are never diagnosed and subsequently treated. Understanding their prognosis is important in practice and modeling studies and pre-chemotherapy data can provide valuable insight. For instance, these data suggest that sputum smear-positive, and smear-negative, culture-positive individuals have a 70% and 20% chance of dying within ten years, respectively. Consistent with the growing body of literature recognizing that there is

a more complex spectrum of TB disease, we aimed to use pre-chemotherapy data to quantify survival curves and natural recovery rates stratified by disease severity at presentation among untreated people with TB.

Design/Methods: We extracted data from pre-chemotherapy era papers, stratified by three categories of disease severity at presentation: “minimal”, “moderately advanced”, and “far advanced”. Each category was defined by clinical criteria primarily related to the extent of disease on chest radiography, the diagnostic standard of the time. Tuberculosis diagnostic criteria varied between studies. We used Bayesian parametric survival analysis to model the survival distribution overall and stratified by disease severity. We then used Bayesian logistic regression to estimate the severity-level specific odds of natural recovery within three years.

Results: People with minimal disease at presentation had a <0.01 (95% credible interval: 0.00-0.03) mortality probability within one year versus a 0.18 (95% credible interval: 0.05-0.41) probability for those with far advanced disease. Individuals with minimal disease had 13 times the odds (95% CI: 10.56-17.30) of natural recovery within three years of those with advanced disease.

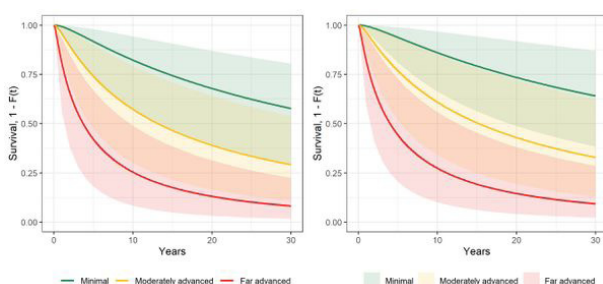


Figure. Survival for all-cause (left) and TB-specific mortality (right)

Conclusions: Mortality and natural recovery risks vary substantially by disease severity. This underscores the need for early detection, early treatment initiation, and improved diagnostics for early-stage tuberculosis disease that is not detectable through standard microbiological methods. Our findings provide valuable inputs for modeling studies to determine effective policies for TB control.

OA09-652-19 Handling missing data in serially sampled sputum specimens for mycobacterial culture conversion calculation

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Background: Missing data due to contamination, inability to produce specimens, or missed visits often occurs when serially sampling sputum to capture conversion to negative during tuberculosis treatment. Simple approaches such as ignoring missing data or carry-forward techniques are traditionally used in research protocols.

More statistically advanced multiple imputation methods potentially decrease bias and retain sample size and statistical power.

Design/Methods: We analyzed data from 224 prospective cohort participants providing weekly sputum specimens for the first 12 weeks of tuberculosis treatment. Our primary outcome was time to culture conversion, defined as two consecutive weeks with negative sputum cultures. Sputum results were missing if visits were missed or cultures were contaminated without *Mycobacterium tuberculosis* present.

We analyzed our data using:

1. Complete case analysis (CCA),
2. Last observation carry-forward (LOCF), and,
3. Multiple imputation by fully conditional specification (MIFCS).

For each method, we calculated the proportion culture converted, individual week to culture conversion, and weekly proportion with positive, negative, or missing samples.

Results: 184 (82.1%) of participants were missing at least one sample result. 70 (31.3%) participants culture converted within 12 weeks in CCA, 140 (62.5%) in LOCF, and 127 (72.0%) in MIFCS. Both MIFCS (median=8 weeks, IQR=5,9) and LOCF (median=7 weeks, IQR=4.5,9) estimated later conversion compared to CCA (median=6 weeks, IQR=3,9). The proportion of weekly positive samples was similar for all three methods.

The proportion of negative samples was larger for LOCF and MIFCS (Figure 1). MIFCS increased the negative samples, with minimal censoring and no missing samples.

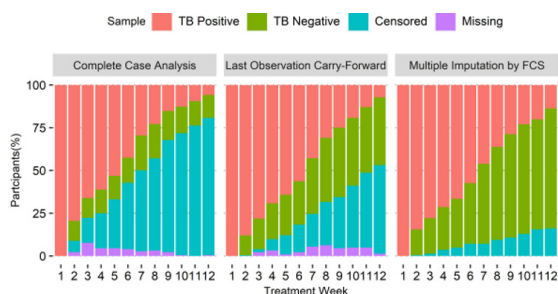


Figure 1A. Proportion of participants with TB positive, TB negative, censored or missing specimen using three methods.

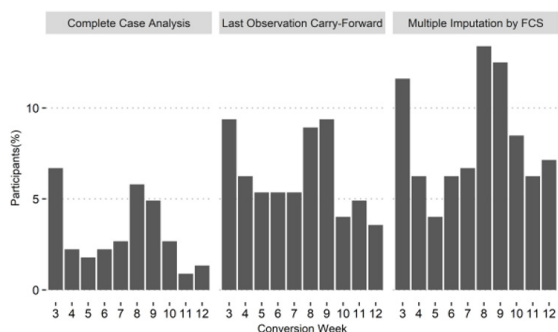


Figure 1B. Estimated week of culture conversion using three methods.

Conclusions: We show that failing to properly impute missing sputum results potentially leads to incorrect estimates of the timing and occurrence of culture conversion, when compared to approximately unbiased multiple imputation estimates. Insufficiently accounting for missing sputum data can generate incorrect understanding of the time to culture conversion with important implications in clinical trials and observational studies.

OA09-653-19 Neighbourhood risk factors of recurrent TB in Cape Town, South Africa: a cohort study using geocoded notification data

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Background: Individuals with a prior episode of tuberculosis (TB) disease are at higher risk of developing a subsequent episode than those without. Considering the role of social and environmental factors in TB, this study assessed neighbourhood-level risk factors associated with recurrent TB disease in Cape Town, South Africa.

Design/Methods: This cohort consisted of all patients who completed treatment for their first drug-sensitive TB episode between 2003 and 2015 in Cape Town, South Africa. Previously, episodes of the same patient in the Electronic TB Register were identified using probabilistic linkage.

For this analysis, addresses were geocoded at neighbourhood-level (administrative level “subplace”).

Data on neighbourhood-level risk factors were obtained from the Census 2011 (household size, population density) and the City of Cape Town (socio-economic index [SEI], five pre-defined groups by government).

The time-varying covariate neighbourhood-level TB burden was calculated annually by dividing the number of notified TB patients by the population in that neighbourhood.

Multilevel survival analysis was performed with the outcome recurrent TB, defined as having a second episode of TB, and controlling for individual level risk factors (age, gender and time since first episode in years).

Follow-up time ended at the second episode, or on 31 December 2015, whichever came first.

Results: The study included 182,670 patients from 549 neighbourhoods (Table). Very good and good SEI was associated with a lower hazard of recurrence in comparison with average SEI. An increased hazard was found for higher household size and TB burden, with an increase of 2% for every extra TB case/100 inhabitants in the neighbourhood. No association with population density was found.

Unit	Distribution	Adjusted Hazard Ratio ^a	95% confidence interval	^a Other variables in the model are age, gender and time since first episode (in years)
Socio-economic Index				
Highest	7,817 (4.3) ^b	0.69	0.55-0.87	^b n (%)
High	47,781 (26.2) ^b	0.79	0.69-0.91	
Average	41,632 (22.8) ^b	1	Ref.	
Low	64,2016 (35.2) ^b	0.97	0.81-1.16	
Lowest	21,224 (11.6) ^b	1.17	0.94-1.45	
Mean household size	Number of people 3.4 (0.7) ^c	1.23	1.13-1.34	^c mean (SD)
Population density	inhabitants/km ² 14,611.9 (6,358.1-17,637.8) ^d	1.00	1.00-1.01	^d median (IQR)
TB burden	Annual number of TB cases/ 100 inhabitants 1.2 (0.6-1.9) ^d	1.02	1.01-1.02	

Table

Conclusions: Recurrent TB was associated with increased household size and neighbourhood TB burden which suggest a role for reinfection in the underlying mechanism. However, the association with SEI independent of other neighbourhood factors suggests there are additional mechanisms at play.

OA09-654-19 Factors associated with pre-treatment loss to follow-up among TB patients in India: a systematic review

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Background: About 16% of individuals diagnosed with active TB in India do not start treatment—a problem known as pretreatment loss to follow-up (PTLFU). We conducted a systematic review to identify factors associated with PTLFU in India.

Design/Methods: We searched PubMed, Embase, and Web of Science and queried experts to find studies published between January 1, 2000 and January 10, 2020 using search terms for TB, India, and loss to follow-up, including PTLFU. Two independent reviewers identified relevant studies and extracted findings from regression

analyses and structured surveys of patients experiencing PTLFU. We report variables associated with statistically significant adjusted odds ratios of PTLFU in multivariable logistic regression analyses.

Results: Of 860 studies screened by systematic search, 24 met the inclusion criteria, of which three reported findings from multivariable regression analyses. Patient-related factors significantly associated with higher adjusted odds of PTLFU included: age >50 years (vs. age 18 to 25 years), no education or preschool only (vs. secondary education), lowest wealth tertile (vs. highest tertile), and previous TB treatment history. Health system-factors significantly associated with higher adjusted odds of PTLFU included: preference by household members for private over public health services, inability of health workers to track patients due to poor recording of contact information, and diagnosis at a private lab (vs. peripheral institute) and high-volume (vs. low-volume) microscopy center.

Study	Factor	Exposure/Independent variable	Adjusted Effect Estimate (95% CI)
Thomas 2018	Age (Years) ¹	51 and above vs. 18-35	aOR 2.94 (1.40-6.49)
Pardeshi 2018	Education ¹	No education or preschool vs. Secondary	aOR 1.82 (1.10-3.01)
Pardeshi 2018	Wealth index ¹	Poor vs. Rich	aOR 1.86 (1.01-3.34)
Ismail 2020	Type of TB ¹	Recurrent vs. New	aRR 3.2 (1.38-7.46)
Thomas 2018	Prior TB treatment history ¹	Prior TB treatment history vs. No Prior TB treatment history	aOR 3.88 (2.15-7.09)
Pardeshi 2018	Type of HCP where household members go for other illness ²	Other health services vs. Public health services	aOR 1.69 (1.26-2.26)
Thomas 2018	Trackability ²	Untrackable vs. Probably trackable	aOR 4.49 (1.29-15.1)
Ismail 2020	Type of enrollment center ²	Private lab vs. Peripheral institute	aRR 5.12 (1.38-18.92)
Thomas 2018	Site of initial microscopy test ²	High volume center vs. Moderate or low volume center	aOR 3.18 (1.69-6.32)

Table 1: Adjusted effect estimates for PTLFU of TB patients in India.

¹Patient-related factors

²Health system factors

Background and challenges to implementation: About 16% of individuals diagnosed with active TB in India do not start treatment—a problem known as pretreatment loss to follow-up (PTLFU). We conducted a systematic review to identify factors associated with PTLFU in India.

Intervention or response: We searched PubMed, Embase, and Web of Science and queried experts to find studies published between January 1, 2000 and January 10, 2020 using search terms for TB, India, and loss to follow-up, including PTLFU. Two independent reviewers identified relevant studies and extracted findings from regression analyses and structured surveys of patients experiencing

PTLFU. We report statistically significant adjusted odds ratios for variables associated with PTLFU in multivariable logistic regression analyses.

Results/Impact: Of 860 studies screened by systematic search, 24 met the inclusion criteria, of which two reported findings from multivariable regression analyses. Patient-related factors significantly associated with higher adjusted odds of PTLFU included: age >30 years (vs. age 21 to 30 years), age >50 years (vs. age 18 to 25 years), no education or preschool only (vs. secondary education), lowest wealth tertile (vs. highest tertile), seeking care in a major city while living outside the city, and previous TB treatment history. Health system-factors significantly associated with higher adjusted odds of PTLFU included: preference by household members for private rather than public health services, inability of health workers to track patients due to poor recording of contact information, and diagnosis at a high-volume (vs. low-volume) microscopy center (e.g., a tertiary hospital).

Conclusions: Challenges contributing to PTLFU in India are multifactorial. Patients who are older, of lower socioeconomic status with no education, and with recurrent TB should be a focus of efforts to reduce PTLFU. In addition, improving recording of patient contact information and facilitating navigation of patient through high-volume facilities may help reduce this critical gap in TB care.

OA09-655-19 Trends, mechanisms and ethnic differences in TB incidence in the US-born population aged ≥ 50 years in the United States

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Background: Older age is a risk factor for TB in low incidence settings. Using data from the U.S. National TB Surveillance System (NTSS), we estimated trends and racial/ethnic differences in TB incidence among US-born cohorts aged ≥ 50 years.

Design/Methods: 43,269 cases among persons ≥ 50 years were reported to NTSS during 2001–2019. We used generalized additive regression models to decompose the effects of birth cohort and age on TB incidence rates, for

the overall cohort and for sex and race/ethnicity strata. Using genotype-based estimates of recent transmission (available 2011–2019), we implemented additional models to decompose incidence trends by estimated recent (within the last two years) versus remote infection.

Results: Estimated incidence rates declined with age, for the overall cohort and most sex and race/ethnicity strata. Rates of decline flattened for older individuals, from 8.74% (95% confidence interval 8.30–9.20) per year in 51-year-olds to 4.56% (3.93–5.18) per year in 90-year-olds. Controlling for age, incidence was lower for more recent birth cohorts, dropping 8.39% (6.17–10.76) on average between successive cohort years. Incidence rates were substantially higher for racial/ethnic minorities, and these inequalities persisted across all birth cohorts. Incidence from recent infection declined at approximately 10% per year as individuals aged. Incidence from remote infection declined more slowly with age, and this rate of decline approached zero for the oldest individuals (see Figure).

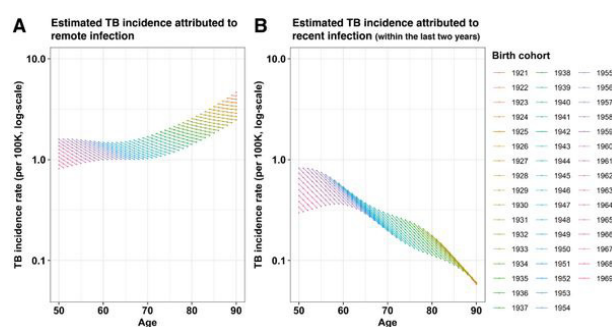


Figure.

Conclusions: Incidence was highest for racial/ethnic minorities and for the earliest birth cohorts and declined with age. For the oldest individuals, rates of decline were low, and most cases were attributed to remote infection.

OA09-656-19 Overcoming access barriers to high-quality TB services in island and mountain settings

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Background: To catalyze the country's ambitions to end tuberculosis (TB), Vietnam is scaling up active case finding (ACF) using its 'Double-X' strategy, which combines X-ray triage with Xpert-based rapid molecular

testing as the initial diagnostic test. However, there is substantial heterogeneity in X-ray infrastructure across the country and populations in hard-to-reach settings, such as islands and mountainous areas, may suffer from limited access to this new diagnostic algorithm.

Design/Methods: Between Jan-2019 and Apr-2021 we conducted mobile chest X-ray (CXR) screening campaigns on three islands and in two mountainous districts of Viet Nam. All residents age 30+ years were invited for CXR screening. Persons with parenchymal abnormalities suggestive of TB on CXR were tested with the Xpert MTB/RIF assay. We present the TB care cascade, and describe the yield and Number Needed to Screen (NNS) across all hard-to-reach areas, as well as disaggregated by islands and mountainous setting.

Results: Across all hard-to-reach areas, we screened 14,031 persons by CXR and tested 433 by Xpert according to the Double-X strategy. Another 10 sputum tests were conducted based on clinical suspicion only. We detected 64 All Forms TB patients for a yield of 456/100,000 (NNS=219). Fifty-nine persons with TB were linked to care (92.2%). The yield on islands was 417/100,000 (NNS=240) compared to 480/100,000 (NNS=208) in the mountains.

	Islands	Mountainous Areas	Total
Screened by CXR	5,274	8,757	14,032
Abnormal CXR	285 (54%)	270 (3.1%)	555 (4.0%)
Sputum test after abnormal CXR	179 (62.8%)	254 (94.1%)	433 (78.0%)
Bac(+) TB detected after abnormal CXR	18 (10.1%)	38 (15.0%)	56 (12.9%)
Sputum testing outside Double-X	7	3	10
Bac(+) TB detected outside Double-X	1	0	1
Clinically diagnosed TB	3	4	7
All forms of TB detected	22	42	64
Prevalence rate (per 100,00)	417	480	456
Linked to TB treatment	22 (100%)	37 (88.1%)	59 (92.2%)

Conclusions: While our mobile CXR screening events on islands and in mountain areas produced a similar yield, the TB burden in these hard-to-reach settings was 44%-66% higher than the national TB prevalence. To end TB the National TB Control Program must overcome access barriers to TB services in these hard-to-reach settings.

OA09-657-19 What factors should we target to reduce the delay in diagnosing pulmonary TB in Portugal? An analysis of surveillance data

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Background: The objective of the study was to identify clinical and sociodemographic factors that could influence patient, healthcare and total delays in diagnosing pulmonary tuberculosis (PTB) in Portugal.

Design/Methods: PTB patients identified through passive case finding and notified (n=11762) in the National Tuberculosis Surveillance System (2008-2017) were included in the retrospective cohort study. Mean, median and interquartile range (IQR) were used to characterize the delays. Cox regression was used to estimate the effect of clinical and sociodemographic variables on the different delays.

Results: Median time to first consultation was 37days, between first consultation and diagnosis was 8days and from symptoms onset and diagnosis was 62days (IQR:38-102). Between 2008 and 2017, median healthcare delay remained constant but median patient and total delay presented a steady increase. 17.1% of PTB cases had a total delay <1 month and 30.5% had a total delay >3 months. Being from a high TB incidence country was associated with longer patient and total delays. Age and being female were factors for longer healthcare and total delays. Alcohol abuse and unemployment were only associated with longer patient delays, while oncologic and respiratory diseases were only associated with longer healthcare delays.

Conclusions: Several authors have suggested that total delay should not exceed one month in most PTB cases. Considering this threshold, Portugal still has considerable work to do. Less than a third of the patients had a total delay <1 month, with total delay showing an increasing trend.

Older patients, patients with alcohol problems, other comorbidities, unemployed or from countries with high TB incidence would benefit from the development of public health strategies to reduce the delay in diagnosis observed in our study. This study highlights the need of increased awareness about TB in the general population and healthcare providers, in order to reduce the gap between symptoms onset and diagnosis.

OA09-658-19 Factors associated with treatment duration among TB patients possibly eligible for 4-month therapy

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Background: Shortened treatment for tuberculosis (TB) can improve quality of life, therapy completion, and reduce patient and program costs. Current guidelines recommend treatment ≥ 6 months with a regimen composed of multiple effective anti-TB drugs. Studies reported similar effectiveness of a 4-month treatment regimen for specific TB patients; however, adoption of a shorter regimen is limited. We describe factors associated with longer therapy among those potentially eligible for 4-month therapy.

Design/Methods: We used 2011–2018 US National Tuberculosis Surveillance System to characterize factors associated with 4-month therapy (111–140 days), versus therapy >140 days among adult patients who completed treatment and were potentially eligible for 4-month therapy.

We considered persons potentially eligible for 4-month therapy if they had culture-negative pulmonary-only TB; initial treatment that included pyrazinamide; no immunosuppression, miliary disease, or exposure to multidrug-resistant TB; and included in regression analyses persons who did not die, become lost to follow-up during therapy, or have therapy completion <111 days.

We used modified Poisson regression with backward elimination of main effect variables for calculating adjusted relative risks (aRR).

Results: During 2011–2018, 63,393 adults completed treatment: 5560 (8.8%) were potentially eligible for 4-month therapy; of these 5,560 patients, 79% received >4 -month therapy. Patients with diabetes were more likely to receive >4 -month therapy (aRR: 1.07; 95% CI: 1.02–1.11). Patients treated by health departments vs. private providers only (aRR: 0.96; 95% CI: 0.92–0.99), those in the South (aRR: 0.88; 95% CI: 0.84–0.91) and West (aRR: 0.94; 95% CI: 0.90–0.98) vs. Midwest, and those ages 25–64 (aRR: 0.93; 95% CI: 0.89–0.97) vs. 15–24 years were less likely to receive >4 -month therapy.

Conclusions: Most patients potentially eligible for 4-month therapy during 2011–2018 were treated with longer courses. These analyses indicate that certain patient- and program-related factors might affect treatment duration and should be explored further.

OA-10 TB and Covid-19 transmission dynamics

OA10-659-19 The long-term impact of Covid-19 pandemic on TB due to food insecurity and undernutrition in the Philippines

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Background: The COVID-19 pandemic has harshly hit the Philippines. In September 2020, the Philippines had the largest number of COVID-19 infections in East Asia and the Pacific, the largest proportion of active infections, lowest recovery rates, and the highest number of COVID-19 deaths per million. Subsequent economic collapse produced record-high unemployment rates, compromising food security and nutrition.

Given the relationship between undernutrition and Tuberculosis (TB), COVID-19's effects ripple beyond TB service availability; it extends to long-term repercussions through food insecurity-induced undernutrition, thus weakening the immune system and increasing active TB risks.

This paper aims to establish the longer-term impact of COVID-19 on TB incidence in the Philippines through food insecurity and undernutrition.

Design/Methods: We reviewed the evidence on the impact of the COVID-19 pandemic on employment, income, and food security. We conducted bivariate correlational analyses of the Philippines TB and undernutrition indicators using MS Excel and made interpretations considering how pandemic-induced food insecurity and undernutrition could impact national TB incidence and progress in achieving EndTB Strategy targets.

Results: The pandemic increased the unemployment rate to almost 20%, leading to food insecurity in $>50\%$ of the population. Correlation coefficients demonstrated slight to substantial degrees of positive correlations between undernutrition and TB indicators. Unresolved food insecurity can worsen undernutrition – currently at 14.5% of the population. Consequently, 4.3 to 8.6 million of 80% of the population estimated to have latent TB can develop active TB over the next 5 years - potentially increasing TB incidence by 8% to 16%, making it harder to achieve 2025 EndTB Strategy targets.

Conclusions: It is imperative to address the immediate impact of COVID-19 on TB service delivery. However, to catch up with EndTB strategy targets, the Philippines must also address the currently “hidden” but inevitable long-term impact of COVID-19 on TB – by acting swiftly on pandemic-induced food insecurity and undernutrition.

OA10-660-19 Overlapping burden and geographical distribution of TB and Covid-19 in Lima, Peru

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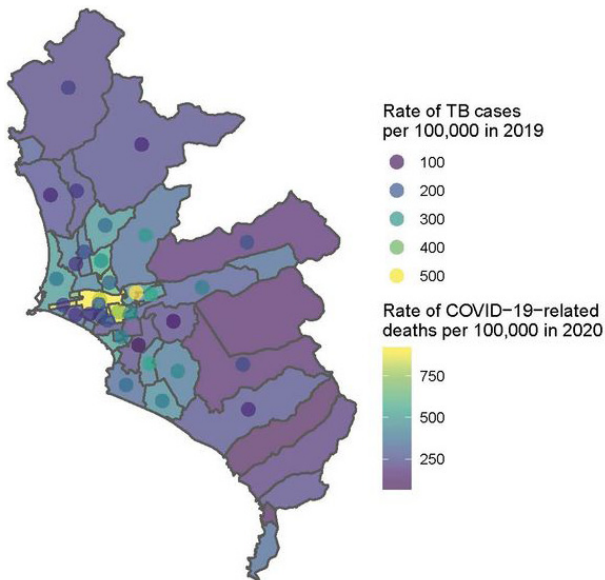
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Background: Peru has a high burden of tuberculosis (TB) and one of the highest excess mortality rates due to COVID-19 in the world. Because TB and COVID-19 share transmission mechanisms and social-environmental risk factors (linked to living conditions, lifestyle-related comorbidities and access to health care), we hypothesize that TB and COVID-19 affect similar population subgroups. We assessed TB and COVID-19 distribution in the provinces of Lima and Callao, Peru.

Design/Methods: We conducted an ecological study taking districts as unit of analysis (n=50) to evaluate the correlation between TB notification rates in 2019 and COVID-19 death rates in 2020. Data were sourced from Peruvian public registries. Incidences were calculated as cumulative counts per year divided by population projections for that year and expressed per 100,000 population. We used Spearman's rho to assess correlation and Moran's I for spatial autocorrelation.



Results: TB notifications ranged from 90 to 503/100,000 (in the 33 districts with highest rates). COVID-19 death rates ranged from 88 to 901/100,000. We found a significant positive correlation ($\rho=0.47$, $p\text{-value}=0.006$) between TB notifications and COVID-19 deaths. Districts with high TB notification rates such as Lima Center (461/100,000) and La Victoria (438/100,000), also had a high burden of COVID-19 (901 and 855/100,000, respectively), while La Molina and Santiago de Surco had low

rates of both TB and COVID-19 (115 and 90/100,000 for TB and 211 and 214/100,000 for COVID-19, respectively). Some districts did not follow this trend, e.g., Bellavista had a low TB notification rate and a very high COVID-19 death rate. The geographic distribution of COVID-19 was characterized by significant spatial autocorrelation ($p\text{-value}<0.001$); this was not the case for TB notifications ($p\text{-value}=0.2$).

Conclusions: We found overlaps in the distribution of TB and COVID-19 burden. Which factors underlie the geographical clustering of these conditions is the topic of an ongoing mixed-methods study.

OA10-661-19 The impact of Covid-19 on TB epidemiology in six high-burden countries

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Background: The COVID-19 pandemic and its restrictions have led to significant TB service disruptions. Many high-burden countries could see increases in TB incidence and mortality for the first time in a decade and suffer several years of lost progress toward TB elimination. Policy makers need to better understand the impact of disruption on the TB epidemic to design and implement targeted catch-up programs.

We projected the impact of Covid-19 restrictions on the TB epidemic in Bangladesh, Ethiopia, Nigeria, South Africa, Zambia, and Zimbabwe.

Design/Methods: We used TIME Impact, a dynamic transmission model. Calibrated models for these countries were updated to generate a counterfactual scenario of no COVID-19 related interruptions. We used hypothetical scenarios based on high-level discussions to develop 5 year projections for the best-case and worst-case impact on TB incidence, prevalence, mortality and notifications.

Results: The modelling estimates suggest that in the best-case scenario a reduction in transmission will outweigh the disruption to TB services and we will see 3.0-12% fewer TB cases and 1.8-10.7% fewer TB deaths than the counterfactual scenario of no COVID-19 related interruption.

In contrast, if we assume a limited reduction in transmission then we estimate 3.0-6.0% increase in TB cases and 0.5-10.5% increase in TB deaths. In both scenarios the total notifications over the period are lower than the counterfactual due to interruptions in case finding.

Conclusions: We used high-level estimates in this study, and the magnitude of impact on burden due to COVID-19 varied by the country's TB epidemiology. Catch-up measures are needed to detect excess prevalent cases as a result of reduced TB screening and diagnosis. As better data becomes available, countries should review their modelled scenarios to better design the catch-up campaign to have the biggest impact on reducing incidence and mortality.

Challenges due to COVID-19		Solutions to mitigate risk to trial conduct	
Themes	Specific Challenges	Themes	Specific Solutions
1. Restrictions on travel to site	<ul style="list-style-type: none"> - Public transport suspensions - Bans on non-essential travel - Repatriation of participants due to lost income - Prohibition of visits to site by non-essential personnel (including trial monitors and coordinating team) 	1. Increased provision for participant and staff transport	<ul style="list-style-type: none"> - Trial-specific vehicles utilised to bring participants and staff to site, and to facilitate home visits - Permission obtained from authorities to permit participants and trial team to travel - Increased travel reimbursement for participants who repatriate (with ethics committee (EC) oversight)
		2. Use of information and communications technology	<p>For participant follow up:</p> <ul style="list-style-type: none"> - Use of telephone visits in place of clinic visits - Remote sputum collection with video call supervision and pick-up by courier - Use of video-observed therapy, or family DOT augmented by phone support - Centralised tracking of participants at risk of loss to follow up <p>For training and monitoring:</p> <ul style="list-style-type: none"> - Trial training provided via teleconference - Remote monitoring in place of on-site visits, utilising video calls and reviews of scanned, de-identified documents for source data verification - Use of database edit checks and meta-data reports for quality control
		3. Cooperation between trial sites and with local clinics	<ul style="list-style-type: none"> - Transfer of repatriated participants to trial sites closer to their new location - Partnering with local clinics for performing routine clinical tests for participant safety - Sharing of strategies between sites at national investigator meetings via teleconference
2. COVID-19 exposure	<ul style="list-style-type: none"> - Fears of COVID-19 exposure - Acquired COVID-19 infections among participants and staff resulting in hospitalisations - Quarantine of staff and temporary site / laboratory shut downs following staff exposure and infections 	4. Enhanced communication with participants	<ul style="list-style-type: none"> - Communication strategies developed for explaining the risks and safety precautions to participants - Phone screening of participants for COVID-19 symptoms before attendance on site
		5. Strict infection prevention protocols	<ul style="list-style-type: none"> - Implementation of strict infection control measures, including social distancing, mask-wearing and hand-washing - Conducting higher risk aerosol-generating procedures (sputum collection, spirometry) in well ventilated areas with use of appropriate personal protective equipment - Restrictions on duration and number of participant visits per day - Split-team working among site and laboratory staff, or identification of adequately trained back-up team members
3. Changes in site staff work dynamics	<ul style="list-style-type: none"> - Restricted work hours for non-essential hospital services at site - Increased staff workload from COVID-19 management and testing 	6. Streamlining trial work processes	<ul style="list-style-type: none"> - Prioritisation of on-site work for participant-facing tasks and off-site work for administrative tasks - Agreement with EC for batch reporting of minor protocol deviations incurred due to COVID-19 to reduce administrative burden - Review of laboratory workflow to improve efficiency
4. Supply chain disruptions	<ul style="list-style-type: none"> - Delays in shipping of TB drugs and consumables - Reduced availability of consumable stock from vendors 	7. Prioritisation of existing resources	<ul style="list-style-type: none"> - Prioritisation of existing consumables for use at key visits and time-points - Re-distribution of TB drugs and consumables across trials and trial sites
		8. Exploring alternative supplies	<ul style="list-style-type: none"> - Approval obtained to temporarily utilise drug supply from national TB programme for trial participants - Sourcing of more readily-available alternatives for laboratory consumables (e.g. Guanidine thiocyanate (GTC) powder instead of GTC liquid) and from different vendors

OA10-662-19 Table 1: Further detail regarding COVID-19-related challenges and solutions:

OA10-662-19 Lessons learnt from running TB randomised controlled trials in Asia and Africa amidst the global Covid-19 pandemic

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Background: The COVID-19 pandemic has resulted in unprecedented disruption to the implementation of randomised controlled trials (RCTs). Here we present the challenges faced by the SPRINT-TB programme of investigator-initiated multi-national interventional RCTs conducted through an Asian/African network during this period, and describe the interventions which have enabled the safety and integrity of the trials to be maintained.

Design/Methods: Minutes recorded during coordinating team meetings, teleconferences with sites, and investigator meetings between 1st January 2020 and 31st March 2021 were reviewed. Challenges to trial implementation resulting from COVID-19 and solutions developed to overcome these barriers were extracted, qualitatively analysed and summarised by two coordinating team members.

Results: Between January 2020 and March 2021, 808 participants were under active follow-up and 357 participants were newly enrolled in trials across 19 sites (3 in Uganda, 6 in Indonesia, 5 in Philippines, 3 in Thailand, and 1 each in India and Vietnam).

Challenges encountered were grouped into four themes: restrictions on travel to site; COVID-19 exposure; changes to staff work dynamics limiting time available for trial activities; and disruptions to supply chains. Several cross-cutting solutions to these barriers were identified, including: increased provision for trial transport; use of information and communications technology to facilitate participant follow-up, training and monitoring; cooperation between trial sites and with local clinics; enhanced communication with participants; strict infection prevention protocols; streamlining of trial work processes; prioritisation of existing resources; and exploration of alternative supplies.

Despite the barriers encountered, 99% of participants have remained under follow-up, with 6.5% of clinic visits being substituted by telephone or home visits.

Conclusions: A variety of strategies were adopted across global sites that allowed trial enrolment to continue and high rates of follow-up to be maintained. These lessons learned may help ongoing and future clinical trials to be pandemic-resilient.

OA10-663-19 TB at a human–bear interface in Cambodia

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Background: Sun bears (*Helarctos malayanus*) and Asiatic black bears (*Ursus thibetanus*) are commonly found in captivity in parts of Asia, due to their exploitation by and confiscation from the illegal wildlife trade. Prolonged contact with humans is inevitable, exposing these already threatened species to human pathogens. Tuberculosis is rarely reported in bears, however 31 individuals have died with culture confirmed *Mycobacterium tuberculosis* within ten years at one bear rescue centre in Cambodia. An in-contact human developed TB within the same time frame.

Design/Methods: Culture of clinical samples was used to confirm TB in 31 bears and one human case. Drug susceptibility testing to four first line drugs was performed. 43-spacer spoligotyping and 24-locus MIRU-VNTR methods were used to genotype *M. tuberculosis* isolates. Contact data was used to model possible transmission pathways.

Results: Spoligotyping of isolates from 31 bear cases and a human case revealed two patterns. Sixty-six percent of isolates belonged to the East African-Indian (EAI) family whereas 34% belonged to the Beijing family. All Beijing lineage isolates were resistant to isoniazid and streptomycin, while the EAI isolates were pan-sensible. MIRU-VNTR typing of 20 isolates distinguished three patterns. The first cluster contained eight Beijing spoligotype isolates including the human case. The second cluster contained 11 of 12 isolates with the EAI spoligotype, with the final isolate having one locus difference. Historical records allowed inference of transmission pathways and suggested the human case linked two temporally distant bear cases.

Conclusions: We report for the first time TB susceptibility in sun bears, and illustrate how wildlife captivity in a high TB prevalence region can create the necessary conditions for pathogen exposure and disease development. Genotyping revealed two lineages of *M. tuberculosis* and confirmed involvement of a human case in this bear outbreak, with the spill-over and spill-back of *M. tuberculosis* between humans and bears suggested.

OA10-664-19 A novel compartment model for analysing and predicting Covid-19 outbreaks in Vietnam

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Background: Vietnam has successfully controlled the COVID-19 pandemic by simultaneously applying numerous strategies, including aggressive contact tracing, mandatory quarantine, routine testing, etc. To quantify the effectiveness of these measures, we developed a model multi-compartment model that integrates all of these practices to estimate impacts of possible mitigation scenarios on the COVID-19 outbreak.

Design/Methods:

We extended the SEIR model into a 9-compartment model SEIQHCDRO with S (Susceptible), E (Exposed), I (Infected), Q (Quarantined), H (Hospitalized), C (Critical), D (Death), R (Recovered), O (Other-recovered). Input data and parameters are taken from meta analysis reports globally.

Different scenarios were built, consisting of social distancing and detection capability at different levels. Outcomes include daily new and cumulative quarantined and infected cases, deaths, hospitalised patients and ICU beds needed. We run the estimation for Danang and Haiduong outbreaks in Vietnam to test the accuracy of the model in comparison to actual reported cases.

Results: The SEIQHCDRO model's outcome was less than 3% different compared to the report number of cases, and is shown in the following table.

	Danang's outbreak (July - September 2020)	Hai Duong's outbreak (January - March 2021)
Basic reproduction number (R_0)	3.25	4.4
Social distancing level	60% on day 19	60%, 40% and 80% on day 22, 34 and 41, respectively
Infected case detection capability	67%	80%
Epidemic peak	Day 29	Day 43
Total number of actual cases	385	738
Total number of predicted cases (percentage error)	396 (2.85%)	730 (1.1%)
Total number of actual deaths	35	0
Total number of predicted deaths (percentage error)	36 (2.85%)	0 (0%)

Table.

Conclusions: The SEIQHCDRO model could predict the epidemic curve with high accuracy as well as represent different scenarios for decision making, based on the capacity of the medical system.

OA10-665-19 GXAlert monitoring and rapid community-directed response to reverse the negative impact of lockdown

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Background and challenges to implementation: Nigeria is one of the high burden countries for Tuberculosis, it is placed as 6th globally and 1st in Africa. So much gains have been made by the country from 2019 when the treatment coverage increased from a previously plateaued 24% to 27%. This success was not far lived as the COVID-19 pandemic and subsequent lockdown took its toll. The similarities between TB and COVID-19 led to increased stigmatization amidst the TB presumptive and their cases. The progressive decline in presumptive TB cases accessing screening and diagnostic tests at health facilities led to rapid community-directed response to prevent a drop in annual case notification.

Intervention or response: A combination of community-directed house-to-house approach, sample transport, referral network and weekly monitoring of total Xpert MTB/Rif tests in the country using the GXAlert platform gave an insight into presumptive accessing TB diagnosis between April and June 2020. Rapid response using community approach to ensure continued TB services including diagnosis and treatment helped in minimizing excessive and reversed the progressive decline in presumptive cases screened and TB case identification.

Results/Impact: By the onset of lockdown the percentage of presumptive tested reduced by 30%. In response to this and to avoid so much decline in the country's case notification, weekly GXAlert monitoring of total number of Xpert MTB/Rif tests done in the country was instituted and subsequent increase in community activities to maintain the generation of TB presumptive within the country was carried out. At the end of quarter 2 2020, case notification decreased by only 2% (27,353) placing the country amongst those with minimal pandemic impact, as Nigeria had a 15% increase in annual case notification at the end of the year 2020.

Conclusions: Real time monitoring of presumptive flow can help inform action during movement restriction era.

OA-11 Strategies to improve TB treatment adherence

OA11-666-19 Best practices to improve telephonic adherence support for TB: a scoping review

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Background: Daily treatment regimens for tuberculosis (TB) can prove challenging for patients, yet poor adherence may increase disease severity, transmission, drug resistance, and mortality. Treatment adherence support from community health workers has been shown to improve adherence and disease outcomes, but little has been documented about telephonic TB adherence support. We conducted a scoping review to identify best practices for offering telephonic adherence support for patients with TB and/or HIV.

Design/Methods: We used the Arksey and O'Malley's framework for scoping reviews. We searched PubMed and EBSCOhost for primary research articles published in English since 2000 focusing on TB or HIV telephonic treatment adherence support. Search results were exported to and managed in RefWorks X9. Reference lists of systematic reviews were scanned for additional eligible titles. Interventions involving text-only reminders were excluded. Two reviewers independently screened titles, abstracts, and full-text articles for inclusion. Disagreements were resolved by a third reviewer. Features of successful interventions were extracted and summarised.

Results: The search yielded 523 citations from which 12 full-text articles were included. Ten articles were HIV-related and two were TB-related. In all but one study, routine telephonic adherence support resulted in significantly better adherence outcomes (range 2%-435%) compared to once-off adherence support (n=7), directly observed therapy (n=2), in-person support (n=1), or an expected proportion (n=1).

Features of successful telephonic adherence support included:

1. Individualised rapport with patients to support open communication,
2. Discussion about disease and treatment,

3. Detailed information on side effects and when to seek medical attention, and;
4. Assistance with problem-solving strategies to address adherence barriers.

Conclusions: Telephonic adherence support has proven more successful compared with other adherence support systems. Lessons from predominantly HIV-related studies suggest establishment of rapport, discussion of disease, treatment, and side effects, and problem-solving barriers with clients can contribute to improved TB treatment adherence.

OA11-667-19 Quantifying non-adherence to anti-TB treatment due to discontinuation: a systematic review of timings to loss to follow-up

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Background: Substantial investment has been made globally to improve patient adherence to TB treatment to prevent poor outcomes including relapse, microbial resistance and death. However, non-adherence is variable, ranging from sporadic doses missed to early discontinuation. The relative burden of different types of non-adherence is not known. Some forms may be both more disadvantageous than others to treatment outcomes and less responsive to current interventions.

We undertook a systematic review of timings to LFU to estimate the number of doses missed globally due to early discontinuation (PROSPERO number: CRD42021218636).

Design/Methods: Web of Science, Embase and Medline R were searched on 14 January 2021 using search-terms around default/LFU, tuberculosis and treatment. Inclusion criteria were: regimen (six-month short course), age (adult) and timing data for LFU. Quality Assessment was undertaken.

The proportion of the population LFU and the timing of LFU were extracted and used to calculate the proportion of doses missed due to discontinuation.

Results: Searches produced 7022 articles. 154 articles were selected for full text screening. 23 articles gave timings of LFU from 12 countries (low to high income) in four WHO regions, including both urban and rural settings.

Papers reported multiple measurements: 22 papers gave timing of LFU stratified by treatment phase or month, two reported the median time until LFU. Timings to LFU varied considerably, with 13 studies reporting the majority of LFU happening in the intensive phase (<2 months of treatment) and ten reporting the majority of

LFU occurring in the continuation phase (2-4 months of treatment). The proportion of doses missed due to discontinuation, estimated using the LFU data, ranged from 1.2-12.7%.

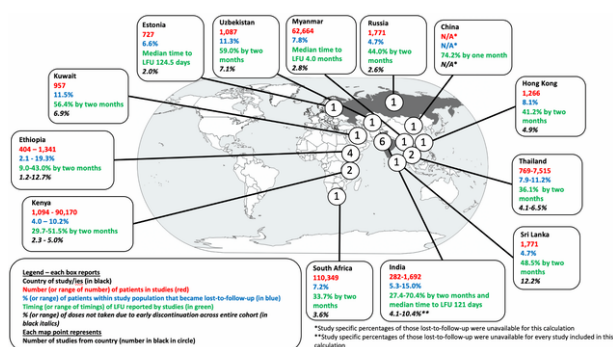


Figure. Global distribution of studies documenting timing to loss to follow-up and associated estimates of the proportion of doses missed due to discontinuation across the entire treatment cohort.

Conclusions: The proportion of doses of anti-TB medication missed due to discontinuation range widely. For effective intervention design and targeting, future studies determining how non-adherence manifests globally and the relative burden of different types of non-adherence are required.

OA11-668-19 99DOTS for TB treatment supervision: sustaining impact after trial implementation

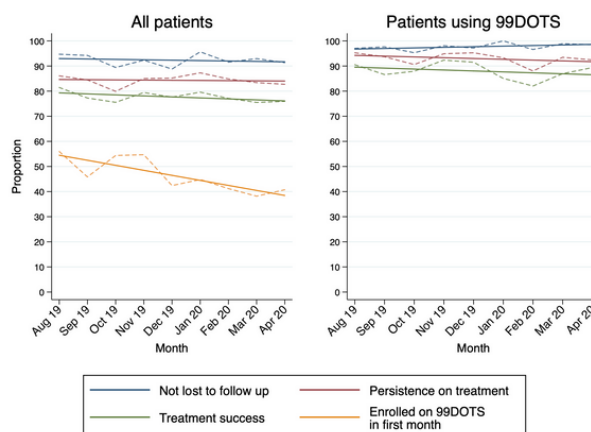
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Background: 99DOTS is a digital adherence technology (DAT) that has been implemented as an alternative to directly observed therapy (DOT). The DOT to DAT trial found that the 52.0% of patients enrolled on 99DOTS at 18 health facilities in Uganda achieved high rates of treatment completion (86.6%). Here, we report on ongoing uptake and outcomes of 99DOTS-based treatment supervision in the 9 months post trial completion.

Design/Methods: The analysis included all adults initiating treatment for drug-susceptible pulmonary TB and not transferred out during the trial (February-July 2019) and post-trial (August 2019-April 2020) periods. We compared reach (proportion enrolled on 99DOTS) and

effectiveness outcomes (proportions completing treatment, completing intensive phase and not lost to follow-up) between the two periods. Confidence intervals (CIs) were adjusted for clustering at the health facility level by bootstrapping with 1,000 repetitions.

Results: During the post-trial period, 47.0% (95% CI 39.7-54.4, n=1117/2376) of eligible patients were enrolled on 99DOTS in the first month of treatment, down from 52.0% (95% CI 45.1-58.8, n=463/891) during the trial. In a temporal trend analysis of the post-trial period, the reach of the intervention declined 2.1% (95% CI 0.7-3.4) per month, but there were no significant changes in treatment outcome trends (Figure). The proportion of patients who completed treatment significantly improved in the post-trial period (77.9%, 95% CI 73.8-81.5, n=1851/2376), compared to the trial period (72.7%, 95% CI 66.9-77.9, n=648/891). Among patients enrolled on 99DOTS, the proportion who completed treatment was similar during the post-trial (88.2%, 95% CI 86.3-90.1, n=985/1117) and trial (86.6%, 95% CI 83.5-89.7, n=401/463) periods. Similar patterns were observed for the proportion completing the intensive phase and not lost to follow-up.



Conclusions: Treatment outcomes can be maintained following initial implementation of 99DOTS, but additional interventions are needed to ensure access and achieve END TB targets.

OA11-669-19 Comparing the accuracy of multiple measures of TB drug adherence in India: data from a cohort study using urine drug metabolite testing

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Background: Poor medication adherence is associated with increased tuberculosis (TB) relapse and death. However, measuring adherence in practice is challenging. We evaluated the accuracy of different approaches for measuring TB medication adherence.

Design/Methods: We enrolled adult drug-susceptible Indian TB patients who were being monitored using 99DOTS, a cellphone-based digital adherence technology. During a one-time unannounced home visit, we assessed adherence using different measures, including collection of a urine sample that was tested for isoniazid metabolites. We estimated the area under the receiver operating characteristic curve (AUC) for four measures—99DOTS, pill count, five-day recall, and a question assessing timing of the last missed dose—in comparison to the urine test result. We compared each measure’s specificity for identifying non-adherence—i.e., the proportion of patients with negative urine test results who were correctly identified. We estimated 99DOTS’ AUC and specificity using patient-reported doses only and using both patient- and provider-reported doses, the latter reflecting how 99DOTS is implemented in practice.

Results: Out of 650 patients in the cohort, 77 (11.8%) had negative urine isoniazid test results. In comparison to the urine test, other adherence measures had the following characteristics: 99DOTS using patient-reported doses only (AUC 0.65, specificity 61%, 95% CI:48–72%), pill count (AUC 0.55, specificity 21%, 95% CI:12–32%), five-day recall (AUC 0.60, specificity 23%, 95% CI:14–34%), and last missed dose question (AUC 0.65, specificity 52%, 95% CI:40–63%). Using patient- and provider-reported doses, 99DOTS’ AUC was 0.62 and specificity was 39% (95% CI: 28–52%).

Measurement approach	Sensitivity % (95%CI)	Specificity % (95%CI)	Positive predictive value % (95%CI)	Negative predictive value % (95%CI)	Area under the receiver operating characteristic curve
99DOTS patient-reported doses	70 (66–74)	61 (48–72)	93 (91–95)	21 (18–25)	0.65
99DOTS patient- and provider-reported doses	85 (81–88)	39 (28–52)	91 (90–93)	26 (20–33)	0.62
Pill count – correctly taken vs. excess or shortage of pills	89 (86–91)	21 (12–32)	89 (86–92)	20 (12–30)	0.55
Five-day recall – no dose missed vs. any dose missed	97 (95–98)	23 (14–34)	90 (88–93)	50 (33–67)	0.60
Last missed dose – no dose missed vs. any dose missed	78 (74–81)	52 (40–63)	92 (90–95)	24 (18–31)	0.65

Conclusions: No measure identified more than three-fifths of non-adherent patients. However, a single question regarding the last missed dose had comparable AUC and identified more non-adherent patients than 99DOTS, as the technology is implemented in practice. Routine use of the last missed dose question and urine isoniazid testing may improve identification of non-adherence by TB programs.

OA11-670-19 Scale-up of a 99DOTS-based strategy for TB treatment supervision in Uganda during the Covid-19 pandemic

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Background and challenges to implementation: 99DOTS is a digital adherence technology with potential to aid medication adherence monitoring in situations when physical contact is not possible. We previously showed in a cluster-randomized trial that 52% of eligible patients were enrolled on 99DOTS when implemented by routine TB care staff. Here we describe the impact of interventions to increase reach and patient/provider engagement with 99DOTS at 30 health facilities in Uganda.

Intervention or response: Between May and June 2020, we trained 227 health workers at 30 facilities to counsel, register and monitor TB patients using 99DOTS.

We provided low cost phones to patients who needed them, task-shifted adherence monitoring and follow-up to community health workers (CHWs) and simplified daily task-lists to help CHWs identify patients with adherence challenges. We compared reach (proportion of patients enrolled on 99DOTS) and patient engagement (doses reported by phone call) during the scale-up period (July 2020-March 2021) and the intervention period (February-July 2019) of a stepped-wedge randomized trial that took place at 18 of the 30 facilities.

Month	Proportion with pulmonary TB enrolled on 99DOTS, n, (%)	Proportion of doses confirmed by patient phone calls (%)	Overall adherence (Calls + Manual doses) (%)	Support phone calls by CHWs	Support home visits by CHWs
July 2020	286 (72.4)	74.5	95.4	112	19
August 2020	318 (78.1)	77.7	96.6	371	62
September 2020	292 (76.8)	74.6	96.6	565	79
October 2020	373 (83.6)	70.7	95.5	825	83
November 2020	300 (84.5)	70.4	95.8	1008	115
December 2020	279 (84.6)	67.3	95.9	963	444
January 2021	323 (85.9)	64.1	95.3	1217	204
February 2021	327 (84.3)	65.3	95.3	1226	304
March 2021	401 (87.4)	62.6	95.0	1325	365

Results/Impact: Table 1. Monthly patient enrollment, adherence and support actions by CHWs during scale-up of 99DOTS.

The proportion of adults treated for pulmonary TB who were enrolled on 99DOTS increased from 52% (n=463/891) during the trial period to 82% (n=2899/3536) during the scale-up period, a 30% (95% CI 26.5-33.5) increase. The proportion of doses confirmed by patient phone calls increased from 54.8% to 66.2%, an 11.4% (95% CI 8.6-14.2) increase. CHWs made 7612 phone calls to 1,667 (57.5%) patients (median 2 calls per patient) and 1675 home visits to 761 (26.3%) patients (median 1 home visit per patient) during the scale-up period. Data on treatment outcomes during the scale-up period is pending.

Conclusions: Providing low-cost phones to patients, task shifting adherence monitoring to CHWs and use of daily task lists improved the reach and implementation of 99DOTS.

OA11-671-19 Risk factors for early loss to follow-up from multidrug-resistant TB treatment among people living with HIV

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Background: Early LTFU from MDR-TB is of growing interest given increasingly shorter MDR-TB treatment regimens and newer intensive-phase (IP) anti-TB drugs. We explored risk factors for early LTFU from MDR-TB care among people living with HIV (PWH).

Design/Methods: We retrospectively analyzed 270 PWH who enrolled in treatment in five South African public MDR-TB hospitals between 2014 and 2018. The relationship between time to early LTFU (i.e., missing >2 consecutive months of treatment during IP) and 16 baseline variables was analyzed using Cox regression. Variable selection was informed by Andersen's Model of Healthcare Utilization. Outcomes of early LTFU were modeled as events and other outcomes were censored at the end of IP. Death and treatment failure during IP were excluded to maximize sensitivity for early LTFU. *P*-values<0.20 in the bivariate analyses were included in the multivariable analysis, and *p*-values<0.05 were considered significant in the final model.

Results: Most patients successfully completed the IP (65.9%) and 14.4% were LTFU. After excluding early death (16.3%) and treatment failure (3.3%), 217 patients were available for analysis. Forty-eight percent of patients analyzed (48.6%) were male, 48.8% were unemployed, and 71.3% had not completed secondary school. The median age was 34 (IQR:29-40) years. The median time to early LTFU was 206 (IQR:143-275) days. In the final model, BMI <18 (HR: 3.40 [1.49, 7.82]) and history of incarceration (HR: 3.26 [1.09, 9.78]) increased risk for early LTFU, while receiving bedaquiline (HR: 0.14 [0.03, 0.79]) and a prior episode of successful TB treatment (HR: 0.18 [0.06, 0.53]) were protective against it when adjusting for employment status and financial assistance, which were not significant predictors.

	HR	<i>p</i> -value	95% CI
History of Incarceration	3.26	0.035	(1.09, 9.78)
BMI<18	3.40	0.004	(1.49, 7.82)
Treatment with BDQ	0.14	0.025	(0.03, 0.79)
Prior Episode(s) of TB			
No Prior Episodes	ref		
Previous Episode of Successful TB Treatment	0.18	0.002	(0.60, 0.53)
Previous Episode of Unsuccessful TB Treatment	0.96	0.941	(0.30, 3.09)
Previous Episode with Unknown Outcome	0.99	0.993	(0.27, 3.65)

*Employment status and receipt of financial assistance were included in the final model, but were not significantly associated with early LTFU

Table.

Conclusions: Use of bedaquiline-based MDR-TB regimens may reduce early LTFU. Considering the high rate of recidivism in South Africa and the role of incarceration in TB transmission, patients with history of incarceration may require enhanced engagement efforts.

OA11-672-19 Cost of digital technologies and family-observed DOT for the 9-month injectable-containing MDR-TB regimen

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Background: In 2017 WHO recommended the use of digital technologies, such as medication monitors and video observed treatment (VOT) for directly-observed treatment (DOT) of drug-susceptible TB, with no policy recommendations for multidrug-resistant TB (MDR-TB), which imposes considerably higher patient-costs. Given the COVID-related demand on health systems, the benefits of transitioning towards more patient-centred approaches are increasingly relevant.

Design/Methods: A decision-tree model was developed to explore the cost-effectiveness of several DOT replacement approaches including VOT, 99DOTS and family-observed DOT. Assuming a 9-month, injectable-containing regimen (as evaluated within the STREAM trial), we constructed base-case models to reflect the standard-of-care in Ethiopia, India, and Uganda. The model used STREAM data supplemented with published studies, with sensitivity analyses conducted on key parameters.

Results: Modelling suggested that standard-of-care is the most expensive strategy in India and Uganda, with considerable direct- and indirect-costs incurred by patients. In Ethiopia, implementing VOT and 99DOTS increased health-system costs by US\$402 and US\$17 respectively, but patient-costs remained lower than for standard-of-care.

These higher health-system costs were largely caused by up-front technology expenditure, with 80% of Ethiopians not owning a smartphone.

Sensitivity analyses showed costs were sensitive to both loss-to-follow-up and relapse rates. However, only the VOT strategy in Uganda exceeded standard-of-care DOT costs, by US\$70 per patient, when the relapse rate was equalled to the upper-bound of the confidence interval.

Modelling suggested each of VOT, 99DOTS, and family-observed DOT would halve patients' out-of-pocket costs. Taking a patient perspective, each strategy appeared highly cost-effective across all countries, even if implemented solely in continuation phase.

Conclusions: While data on the costs and efficacy of switching MDR-TB treatment management to new technologies are lacking, our modelling suggests alternative DOT support strategies can significantly reduce patient-costs. Health-system costs however are more country-specific, depending heavily on both internet availability and smartphone penetration within the population.

E-POSTER SESSION (EP)

Finding missing TB cases

EP-04-130 Point-of-care C-reactive protein-based TB screening may improve the efficiency of active case-finding in populations with low HIV prevalence

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Background: C-reactive protein (CRP) triage testing may facilitate ACF implementation (systematic TB screening, followed by confirmatory testing) in high TB-/low HIV-burden areas by reducing the proportion of patients with cough \geq 2 weeks requiring costly confirmatory testing and may also improve case detection if combined with more sensitive screening strategies (e.g., any TB symptom). However, the performance of CRP-based triage testing in this setting is unknown.

Design/Methods: From 3/2020-4/2021, we enrolled adults presenting to the Vietnam National Lung Hospital Pulmonary Clinic with \geq 1 TB symptom of any duration in the past month. We recorded symptom presence/duration, performed point-of-care CRP (POC-CRP) testing (normal $<$ 5 mg/L), and sputum-based TB testing (Xpert Ultra [Ultra]x1, culturex2) to determine number and proportion (diagnostic yield) of cases detected by Ultra and efficiency (number of Ultra assays used to detect one TB case) of different ACF algorithms with/without POC-CRP triage testing.

Results: Of 296 patients with any TB symptom, 140 (47%) had cough \geq 2 weeks. The number of culture-confirmed cases detected was higher among patients with any TB symptom (55/296) than those with cough \geq 2 weeks (27/140), although TB prevalence was similar (both 19%). Cough \geq 2 weeks+Ultra (current ACF algorithm) detected 26/27 cases (yield 97%) and used 5.4 Ultra assays/TB case detected while a screening strategy of any TB symptom detected more cases (43/55, yield 78%) but was less efficient (6.9 Ultra assays/TB case detected; Table). POC-CRP was elevated in 117/296 (40%)

patients with any TB symptom, including 41/55 (75%) cases, and 52/140 (37%) patients with cough \geq 2 weeks, including 23/27 (85%) cases. ACF algorithms using POC-CRP triage testing had lower yield but used half as many Ultra assays/TB case detected as algorithms without triage testing.

	Cough \geq 2 weeks (N=140)		Any TB symptom (N=296)	
	No triage testing	+ POC-CRP triage testing	No triage testing	+ POC-CRP triage testing
Xpert Ultra assays used, N (%)	140 (47%)	52 (18%)	296 (100%)	117 (40%)
TB cases detected, N (%), 95% CI)	26/27 (96%, 81-100)*	23/27 (85%, 66-96)*	43/55 (78%, 65-88)†	33/55 (60%, 46-73)†
Xpert Ultra assays used per TB case detected	5.4	2.3	6.9	3.5

Abbreviations:

Active case finding (ACF); tuberculosis (TB); point-of-care C-reactive protein (POC-CRP).

Legend:

*% Difference in TB diagnostic yield using cough \geq 2 weeks vs. cough \geq 2 weeks + POC-CRP triage testing (-11%, 95% CI: -26% to +4%; p=0.16).

†% Difference in TB diagnostic yield using any TB symptom vs. any TB symptom + POC-CRP triage testing (-18%, 95% CI: -35% to -1%; p=0.04).

Table. Yield and efficiency of ACF algorithms (symptom screening, followed by Xpert Ultra MTB/RIF testing) with and without POC-CRP triage testing.

Conclusions: POC-CRP triage testing can improve ACF efficiency but may reduce diagnostic yield. More sensitive screening strategies combined with triage testing can efficiently increase TB case detection.

EP-04-131 Community involvement in early detection of TB in the pilot areas of the USAID Eliminating TB in Central Asia Project

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Background and challenges to implementation:

Tajikistan is one of the countries with high burden of multidrug-resistant tuberculosis (MDR-TB). The WHO Global TB Report estimates that in one third of TB cases people are either not diagnosed and treated or go unreported. There were 3 760 new TB cases out of 4 317 TB notifications in Tajikistan in 2020. Despite some improvements in recent years, TB case detection rates in a traditional provider-based passive case finding system remain quite low by WHO estimates. Early detection is critical for successful TB control and treatment, however, to be effective in expanding access to diagnostic services and reaching as many infected as possible, community engagement is required.

Intervention or response: The USAID Eliminating TB in Central Asia Project is implementing an integrated continuous TB care model involving enhanced case finding (ECF) among population with high risk of TB infection and illness - contacts, labor migrants, and people living with HIV. More than 200 community workers, including volunteers and 14 outreach specialists have been trained on ECF and actively involved in its implementation across 8 pilot districts in Sughd oblast since April 2020.

Results/Impact: ECF with community participation has demonstrated not only high effectiveness in case finding, but also resilience during the COVID-19 pandemic. Between April 2020 and March 2021 case detection rates in the mentioned pilot districts increased by 18% (from 727 to 858) over the prior twelve-month period. Case detection rates in 10 non-pilot districts in the same oblast decreased by 39% (from 324 to 198) between April 2020 and March 2021 compared to prior twelve-month period.

Conclusions: Case detection in pilot districts has been 57% (18%+39%) more effective than that in non-pilot ones since the start of the COVID-19 pandemic. Community involvement in ECF demonstrated significantly superior results compared to a model relying exclusively on traditional provider-based passive TB case-detection.

EP-04-132 Paradigm shift in community outreaches for TB case-finding: health worker model vs. community-based organisation model in Northern Nigeria

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Background and challenges to implementation: KNCV TB LON project funded by USAID adopted several approaches for community-based active TB case finding, driven by community mobilization and TB awareness creation. We aim to compare the effectiveness of the health worker (HW) model versus the community-based organizations model (CBO) in conducting community Tuberculosis (TB) screening during outreaches.

Intervention or response: This intervention was a pilot, implemented in Kaduna state, Northern Nigeria. The intervention involved outreaches in selected communities with minimal/low access to the health facility or as informed by early warning outbreak response alert (EWORS) being used for identification of TB hotspots in the TB LON project. Community entry to the traditional leader(s) is followed by community mobilization in the native language, by town criers for 2 days before the scheduled days. The awareness messages included signs and symptoms of Tuberculosis, time, and venue of the outreach. The cascade involved identification of presumptive, sample collection (sputum) from all pre-

sumptive identified, prompt testing of sputum samples, the commencement of confirmed cases on treatment, and contact investigation of all cases. The HW model involved the State team, LGA TB supervisors, DOTS officers, and Community Health Workers (CHW) in 5 LGAs while the CBOs utilized engaged community TB workers (CTWs) in selected 4 LGAs. All selected LGAs were based on the burden of cases in the state, with similar demographic factors.

Results/Impact: A higher screening coverage was reported in the HW model with 609 people screened while the CBOs had 182 screened, over the same period and number of outreaches. The HW model was found more efficient in TB case finding with TB yield of 6% compared to 2% for CBOs model. See results in Fig 1.

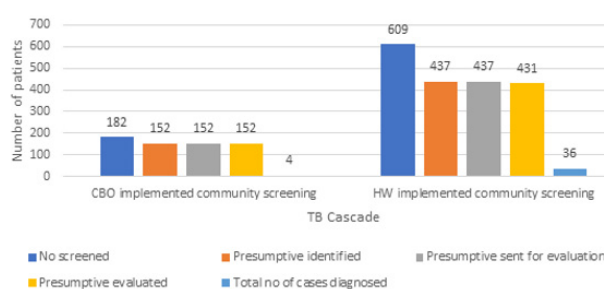


Figure 1. Comparison of TB Cascade for community screening using health workers model versus community-based organization in Kaduna State, Nigeria in March 2021.

Conclusions: The result indicates that community screening using the health worker model was more effective in Kaduna for finding the missing TB cases.

EP-04-133 Finding the missing TB cases: the value of targeted hotspots screening in a high-burden rural county in Kenya

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Background and challenges to implementation: Tuberculosis remains a disease of public health concern globally. Finding the missing people with TB in communities still remains a challenge in the path towards ending TB. The emergence of Covid-19 pandemic led to a decline in TB case notification. Field reports shared with the National Tuberculosis Program showed a 20% decline in TB case notification in the period after March 2020 compared to a similar period in the previous year in Meru County. People with TB not on appropriate treatment continue to transmit the infections especially to close contacts, notably house hold members and close communities. Targeted hotspot screening was conducted with an aim to identify people with symptoms of TB and subject them to testing and hence improve TB case notification in the County.

Intervention or response: To find the missing people with TB, targeted community TB screening in identified TB Hotspots was conducted across the county. Hotspots were defined as a small area or locality with a relatively high concentration of notified TB patients compared to surrounding areas. These were market places, alcohol dens and *Miraa* chewing centres. Symptom based screening questionnaire was done based on the national TB program TB active case finding guidelines. Presumptive TB cases were tested using Genexpert MTB RIF sputum test.

Results/Impact: Within the 9 hot spots across the county, 1131 people were screened, 560 (50%) were found to be presumptive, 100% were tested. Out of these, 27 (5%) patients were gene-xpert positive and put on treatment, a yield of 8 %. Among the 19 patients 2 had Rifampicin resistant TB.

Conclusions: From the results, targeted hotspot screening for TB using a simple symptom based screening questionnaire led to identification of missing people with TB in the community. This is a simple and cost effective way that can be adopted and scaled up.

EP-04-134 TB active case-finding in the community: community health volunteers contribution in finding missing TB cases in Tharaka Nithi County, Kenya

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Background and challenges to implementation: Tharaka Nithi County has embraced the community Health strategy for primary health care. It has engaged 1250 Community Health volunteers (CHVs) with 120 community units. These has played a major role in improving the health outcomes of the community. Covid19 presented a challenge with a significant decline in TB case finding in 2020. Patients were afraid to report cough for fear of Covid19

Intervention or response: In September of 2020, a Community TB stake holders meeting was held. It was agreed that the Community Units Lead CHVs be sensitized on the TB situation. One of the strategies adopted was scaling up Community TB active case finding with appropriate linkage and referral.

The department of Health conducted TB and Covid19 sensitizations for CHVs to help with community health education and stigma reduction. They were expected to do community symptom screening and referral of presumptives to hospital. They also supported contact tracing for both covid19 and TB disease.

The health facilities were expected to receive patients referred from the community and investigations for TB and covid19. Both CHVs and Facilities sent reports of the activity. This activity was a rapid result initiative for quarter 4 October to December 2020 to find missing TB patients

Results/Impact: 90 lead CHVs were trained on TB and Covid19. They were to sensitize their units on the same. 39 TB treatment health facilities participated and sent reports. 1370 presumptive patients were recorded in the health facilities, 76 (5.5%) of them were referred by CHVs. 24 (32.5%) of these were found with TB and started on treatment.

Conclusions: With community health strategy and availability of CHVs linked to TB treatment sites, Community TB active case finding and referral can be scaled up and thus find the missing TB cases.

EP-04-135 Finding missing TB cases: targeted community TB screening in Tharaka Nithi County, Kenya

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Background and challenges to implementation: Following the reporting of Covid19 in March 2020 in Kenya, there was significant decline in TB case finding and notification compared to the previous quarter in the county. TB is more common among men than women. In the county the data shows 72% of TB patients are men, many of them report alcohol use and smoking. Overcrowding and social places with poor ventilation increase the risk of TB transmission. This is common in rural markets and towns where alcohol drinking dens are in small poorly lit rooms, and overcrowded with revellers. As well local brews are cheap and common in this setting.

TB hotspots are defined as a small area or locality with a relatively high concentration of notified TB patients compared to surrounding areas. This could be a market, small town, village or estate. They were identified from patients' physical addresses in health facility registers.

Intervention or response: To find the missing cases and create awareness on TB disease amid the pandemic, Targeted community TB screening and testing outreaches were conducted in identified TB hot spots across the county. Use of symptoms screening questionnaire, and those presumptive offered a gene-expert sputum test. Targeted TB screening forms a basis for social contacts tracing and creating TB awareness

Results/Impact: Targeted TB screening outreaches were conducted at 11 hot spots across the county. 956 people were screened, 496 (52%) were found to be presumptive,

and 404 were tested. Out of these, 19 patients were gene-xpert positive and put on treatment, a yield of 4.7%. Among the 19 patients 17 (89%) were men.

Conclusions: From the results, undiagnosed active TB patients in the community can be found through social contacts' tracing. Targeted community TB screening is simple and cost effective with proper identification of hot spots.

EP-04-136 Implementation of intensified TB case finding (TB Surge) in health facility settings: analysis of TB yield in Ogun State, Nigeria

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Background: The World Health Organization recommended systematic TB screening and Intensified Case finding (ICF) as strategies to identify missing TB cases among at-risk populations. There is lack of sufficient evidence on the specific service delivery points (SDPs) in healthcare settings that implementers should target for such interventions. This study aimed to describe TB yield by SDPs in the first eight months of implementation of facility ICF within the USAID-funded TB LON-3 project in Ogun State, Nigeria.

Design/Methods: A cross sectional retrospective review of verbal symptomatic screening for TB across different SDPs in 31 primary, secondary and tertiary health facilities in Ogun State, Nigeria between July 2020 and February 2021. Trained screeners were strategically stationed across different hospital SDPs to ask hospital attendees for TB symptoms, demographic information and TB cascade details. Collected information was documented in recording and reporting tools and aggregated by implementing facilities. Data were analyzed using descriptive statistics like frequency and percentage.

Results: Presumptive TB yield was highest, 14% (30/213) in the in-patient ward and lowest, <1% (51/6782) at the national health insurance clinic. Tuberculosis Case yield

(all forms) was highest at the out-patient department (OPD), 13% (1,291/9,877) followed by diabetes clinic, 11% (16/148) and the least TB Case yield was from the emergency room, 0% (0/105). The lowest and highest NNS were observed from inpatient ward screening (107) and NHIS clinic (3391) respectively. NNT was also lowest in the OPD and diabetic clinics.

Indicator	ART Clinic	Inpatient ward	ANC/ Family Planning	Emergency	NHIS	Diabetes	Pediatric/ Immu/Mal-nutrition	Mental Health/ Psychiatry	OPD
Attendance	21,114	213	20,579	1,233	6,782	1,889	15,551	580	331,989
Screening	21,114	213	20,579	1,233	6,782	1,889	16,704	580	327,458
Presumptive TB cases	732	30	597	105	51	148	251	66	10,037
Presumptive TB yield	3%	14%	3%	9%	1%	8%	2%	11%	3%
Evaluated	732	30	549	105	51	148	243	66	9,877
Bacteriological Diagnosis	64	2	25	0	2	16	16	1	1,064
TB Diagnosis (all forms)	65	2	25	0	2	16	21	1	1,291
Bacteriologic Yield	9%	7%	5%	0%	4%	11%	7%	2%	11%
TB Yield (all forms)	9%	7%	5%	0%	4%	11%	9%	2%	13%

Conclusions: Tuberculosis screening among patients admitted at in-patient units of the implementing hospitals was the most efficient in terms of NNS and TB yield. There is a need to intensify TB surveillance among patient populations admitted at the wards including those who could have been missed at emergency departments. Implementers should focus human and financial resources for TB surge on the highlighted high yielding SDPs.

EP-04-137 Diagnosis of undetected TB in Peruvian prisons using active case-finding led to the: a nationwide multicentre, controlled assessment

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Background and challenges to implementation: Tuberculosis (TB) diagnosis in prisons is challenged by human and laboratory resources.

Intervention or response: Therefore, 12 prisons that reported 90% of all tuberculosis cases in prisons in Peru had a TB active case-finding intervention that included: (1) improved x-ray rooms, sputum smear areas and access to Xpert MTB/Rif testing; (2) a chest x-ray for all inmates; (3) sputum smear microscopy and clinical assessment for all inmates with an abnormal x-ray; (4) only in 5 prisons, additional Xpert MTB/Rif test for inmates who had smear-positive sputum.

To assess impact, Peruvian virtual registry of TB patients notified was analysed. Changes in TB incidence rate ratio (IRR) were performed with a stratified analysis of IRR, reporting 95% confidence intervals with STATA, with reference to data from other 57 prisons in Peru that did not receive this intervention.

Results/Impact: TB incidence increased from 4292 in the last year before intervention (2015), to 5942 in the full year of the intervention (2018). Specifically, in 12 intervention prisons (Figure), TB incidence reduced from 2014 to 2015 (IRR = 0.90 (0.84 – 0.96), $p=0.0016$) and from 2015 to 2016 (IRR=0.96 (0.90 – 1.03), $p=0.2$).

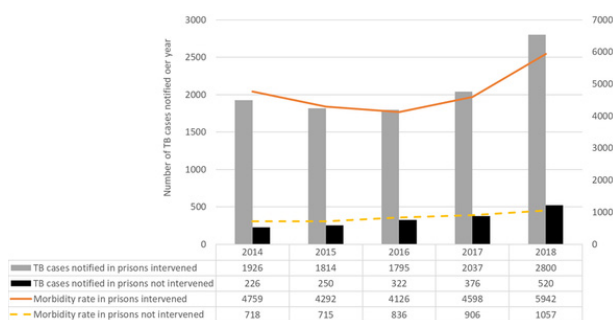


Figure.

The intervention from August 2017 to December 2018 was associated with significant increase in TB incidence (2016 to 2017 IRR=1.1 (1.0- 1.2), $p=0.0008$; 2017 to 2018 IRR=1.3 (1.2 – 1.4), $p<0.0001$; 2015 to 2017 IRR=1.1

(1.0 – 1.1), $p=0.03$). This increase in TB incidence from 2017 to 2018 in 12 intervention prisons was significantly greater than TB incidence variations in other 57 Peruvian prisons that did not receive the intervention ($p<0.0001$; Figure).

Conclusions: Implementation of TB active case-finding increased the TB incidence in Peruvian prisons by approximately 44% and the TB notification in 56% of inmates. With comprehensive resources, we improved TB detection in these vulnerable settings.

EP-04-138 Evaluating an active case-finding intervention for TB and knowledge, attitudes and practices among university students in Burundi

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Background: In 2019, 43% of estimated new tuberculosis (TB) cases were not reported in Burundi. To increase TB detection, interventions must target key populations such as university students who are at high risk of TB but who experience barriers accessing care. To improve case detection in universities, we implemented an active case finding intervention in 30 university campuses across seven provinces. In conjunction, a survey was conducted to understand student knowledge, attitudes and practices (KAP) related to TB.

Design/Methods: Student volunteers were trained to form Stop TB clubs through which they verbally screened their student peers for TB symptoms and collected sputum samples for transport to health facilities in partnership with universities for Xpert/sputum smear testing. Stop TB clubs also organised TB awareness activities on campus. To evaluate the impact, TB notifications from partnering health facilities were compared one year before and after implementation. In addition, a standardized, self-administered KAP survey was distributed to a randomized sample of students (N=380). A scoring system was used to categorize knowledge, attitudes, and practices as: poor, below average, average, above average and good.

Results: Through the intervention, 63,446 students were screened for TB and 2,864 (4.5%) had TB symptoms of whom 2,778 (97.0%) were tested. In total, 38 (1.8%) students had bacteriologically confirmed TB and all initiated treatment. After a one-year implementation, TB

notifications in partnering health facilities increased by 34%. Results from a preliminary sample of KAP surveys (N=126) indicate that 93.7% and 98.4% of students have good or above average knowledge and practices, respectively, while 73.8% have poor or below average attitudes.

Conclusions: The results presented suggest that on-campus screening and testing of university students by volunteer student clubs is a successful strategy for case finding. Further studies should explore reasons for poor attitudes towards TB in this population and how to improve them.

EP-04-139 Do community-based TB active case-finding interventions affect subsequent TB testing behaviour? A systematic review

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Background: Community-based TB active case-finding (ACF) may impact subsequent TB testing behaviour and patient-initiated diagnosis pathways. We studied the impact of ACF beyond directly diagnosed TB patients.

Design/Methods: We systematically searched for publications 01-Jan-1980 to 13-Apr-2020 that reported on community-based ACF interventions compared to a comparison group, together with review of any manuscripts reporting knowledge, attitudes, and practices (KAP) outcomes or qualitative data on TB testing behaviour. We calculated case-notification rate (CNR) ratios of routine case-notifications (i.e. excluding cases identified directly through ACF) and compared proxy behavioural outcomes of KAP, past and recent testing for TB, TB stigma, and social norms for both ACF and comparator communities.

Results: Full text manuscripts from 988 of 23,883 abstracts were screened for inclusion; 36 were included. Of these, 12 reported routine notification rates separately from ACF intervention-attributed rates, and one reported any proxy behavioural outcomes. Three further studies were identified from screening 1121 abstracts for KAP/qualitative manuscripts. 8/12 case-notification

studies were considered to be at critical or serious risk of bias. 8/11 non-randomised studies reported bacteriologically-confirmed CNR ratios between 0.47 (95% CI:0.41-0.53) and 0.96 (95% CI:0.94-0.97), with 7/11 reporting all-form CNR ratios between 0.96 (95% CI:0.88-1.05) and 1.09 (95% CI:1.02-1.16), while one high-quality randomised-controlled trial found a ratio of 1.14 (95% CI 0.94-1.40). KAP/qualitative manuscripts provided limited evidence from which impact of ACF on subsequent TB testing behaviour could not be established.

Conclusions: Though ACF has the potential to impact subsequent TB testing behaviour through an increase in TB knowledge, earlier care-seeking if TB symptoms are detected, or follow-up after a negative ACF test, data on this impact is quite scarce. Evaluation of routine TB testing and other proxy behavioural outcomes in ACF and comparator communities should be included as standard methodology in future study designs.

Find TB to stop TB

EP-06-147 Increased TB case-finding by healthcare workers at health facilities in Northern Cameroon: a controlled intervention

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Background: In Cameroon in 2019, only 53% of the estimated 46,000 people with TB were diagnosed and notified on TB treatment. Most case finding is passive, based on patients presenting to hospitals with prolonged cough.

Design/Methods: We evaluated an intervention to intensify case finding at health facilities in the North and Far North regions, the two poorest of the ten geographical regions in Cameroon. We trained 1,333 healthcare workers at 208 primary care centers and 34 hospitals to use a multi-symptom screening questionnaire combined with TB testing by either microscopy or molecular testing through a specimen referral network. Information was collected daily by facility entry point on numbers of people screened, tested and linked to treatment, by trained healthcare workers under the supervision of the project coordination team. Performance was evalu-

ated monthly against predefined targets, and healthcare workers received performance-based monetary incentives. We assessed TB case notifications in the intervention regions as compared to four control regions (Adamawa, South, East, Center) for three years prior to and one year after the start of the intervention. TB notification data were obtained from the National TB Program. This work was part of CHECK TB, a TB REACH project across six regions of Cameroon.

Results: In 2019, 28,362 people were tested for TB, as compared to 13,574 in 2018, an increase of 109%, based on preliminary data. In these two regions, there were a total of 5,955 people notified with all forms TB in 2019 as compared to 5,348 in 2018, representing an 11% increase in case notifications, as compared with a 2% increase in the control regions

Conclusions: These results suggest that the intervention enabled many people to be diagnosed and linked to care for TB at community-based primary care facilities, close to their homes, and resulted in a significant increase in people notified with TB.

EP-06-148 NGO-coordinated outreach activities to identify persons with symptoms of TB in resource-limited areas: experience from Benin

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Background: The National Tuberculosis Program (NTP) of Benin conducts mass community outreach activities through its partnership with sub-recipient Afric' Mutuality, which is responsible for monitoring and supervising the activities of the 17 contracting non-governmental organizations (NGOs) in collaboration with the NTP's Communication and Social Mobilization Department. The objective was to determine the notification rate of presumed and confirmed TB in the general population following mass outreach activities.

Design/Methods: Each quarter, outreach activities were targeted to resource-limited areas by NGO members previously trained by the NTP. Each session had a minimum of 30 participants and was conducted under the supervision of the village chief and the nurse or community liaison officer. At the end of the session, a list of people who had been coughing for at least two weeks or were known to be coughing was compiled and a referral to the nearest TB treatment center was recommended. We used data collection tools to collect the list of participants at each session, referral forms for people with TB symptoms, final TB diagnosis, and travel expenses.

Results: From August 2016 to December 2020, there were 1980 community outreach activities attended by 94,440 people. Among those attending, 2042 (2.2%)

had presumptive tuberculosis (i.e., cough of at least two weeks). Of these, 1758 (86.1%) attended follow-up screening and received either Xpert MTB/RIF or sputum smear microscopy. There were 250 (14.2%) people who were positive on either test. The notification rate for bacteriologically confirmed pulmonary tuberculosis was 264.4/100,000 persons attending outreach activities.

Conclusions: Community outreach activities appear to be an important tool to support the NTP in identifying persons with presumptive tuberculosis. Future research should consider the costs of this strategy in the context of other NTP efforts.

EP-06-149 Medical facility-based TB case detection in Anambra, Delta and Imo State Nigeria: a 6-month review

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Background and challenges to implementation: Passive case finding, detection of tuberculosis (TB) cases among persons presenting to medical facilities with symptoms suggestive of TB, has remained the principal public health approach for TB diagnosis. Missed TB cases result in delayed treatment and premature death, complications, community, and nosocomial transmission.

Intervention or response: The implementation of 100% symptomatic screening of all hospital attendees for TB have been a pivotal system in Nigeria. A six-month data from KNCV Tuberculosis Nigeria program intervention data was obtained (between June 1, 2020, and November 30, 2020) for selected health facilities in Anambra, Delta, and Imo state all in Nigeria. Information on number of attendees screened for TB, number of presumptive patients identified, and number of TB diagnosed was extracted and used for this study.

Results/Impact: A total of 225,274 attendees were screened for TB within the study area. This generated 7848 presumptive patients of which 7530 patients were further evaluated for TB. Total cases identified was 734 (9%). A total number of patients screened in Anambra, Delta and Imo was 54124, 112997 and 58153 respectively with a presumptively identified cases of 2569, 3231 and 2048 patients. Delta state had the highest number of TB diagnosed cases with 404 patients and a yield of 13% while Imo and Anambra State reported 150 and 180 patients respectively with a TB yield of 7%.

Conclusions: In the result Anambra and Imo state show an increase in its TB yield at 7%, while Delta state yielding 13% TB Cases shows a substantial missed diagnosis with only 3047 out of 3231 presumptive clients evaluated. It is evident that Delta state will yield more TB case if patients linkage to evaluation is strengthened. There is need for proper data synergy for implementation of diagnostic channels for proper detection and treatment of TB cases in Nigeria.

EP-06-150 Active TB case-finding in prison settings: experience of Harar and East Harar correction centres, Harar, Ethiopia

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Background and challenges to implementation: In Ethiopia, evidence showed that, the burden of TB disease is higher in prisons than the general population. Prison settings favor TB transmission due to their poorly ventilated environment, overcrowding, and limited access to healthcare and TB diagnostics. Harari Regional State Health Bureau in collaboration with stakeholders has initiated TB screening to 1408 inmates to find missing people with TB and provide required treatments.

Intervention or response: Project staffs, health care workers of the catchment health facility and prison's clinic health workers took part in the mass screening activity. One to one interview with symptom-based TB screening tool were done for 1408 inmates from December 18, 2020 to January 25, 2021 and sputum samples were collected from inmates having symptoms suggestive of TB and transported to Gene Xpert sites.

Results/Impact: All of the prison inmates (N=1408) were screened and 330 (22%) were found to be presumptive TB cases. Out of 330 presumptive TB cases evaluated, 30 (9%) of them were diagnosed with drug sensitive TB. Among TB cases diagnosed, 97% (N=29) were bacteriologically confirmed PTB cases and the remaining one is EPTB case. The estimated overall prevalence of diagnosed pulmonary TB cases among prison inmates was 2130/100,000. All the diagnosed TB patients were put on anti TB treatment.

Conclusions: The observed point prevalence was higher than that of reported in most previous Ethiopian prison studies. Active TB screening remains a priority intervention to find missing people with TB in prison settings. Thus, the prison administrations and prison health care

workers should screen every new arrival at entry and periodically during their stay at prison by including X-ray as one of the screening tool to improve the case detection. Besides, exit screening strategy should also be implemented to prevent spill over to the population.

EP-06-151 Repairing boundaries along pathways to TB case detection: a qualitative evidence synthesis of programme designs

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Background and challenges to implementation: To detect tuberculosis (TB) along the patient-initiated pathway, the health system has to respond appropriately to patients actively seeking care, but the appropriate response of people approached by a health system seeking TB patients, is unclear.

This review aimed to improve understanding of TB case-finding interventions by constructing a systems-based logic model of all pathways to TB case detection.

Intervention or response: We included randomized controlled trials (RCTs) aimed to improve TB case detection at community or primary care level in high TB burden countries. We searched CENTRAL, MEDLINE and EMBASE.

Analysis of included studies involved a constant comparison method. Intervention activities were coded and positioned along various patient journeys identified in the literature, visualising them as logical chains, drawing from the information contained within the studies themselves to theorise the sequence of outcomes. In collaborative virtual meetings the authors brought their combined clinical and academic experience of working with marginalised groups to develop the details of the logic model.

Results/Impact: Based on analysis of intervention activities from 17 identified RCTs, our model distinguishes two care seeking pathways: general care and specific TB care (Fig 1, dashed lines), and four TB screening pathways, initiated by services inviting people regardless of symptoms: screening offered to all people accessing care at general health services (Fig 1, green), screening at a mobile clinic or health facility with open invitation to a whole population or TB contacts (Fig 1, blue), screening personally offered to a whole population or TB contacts at home, work or school (Fig 1, orange) and screening offered to people in HIV care or other clinical risk group care (Fig 1, grey).

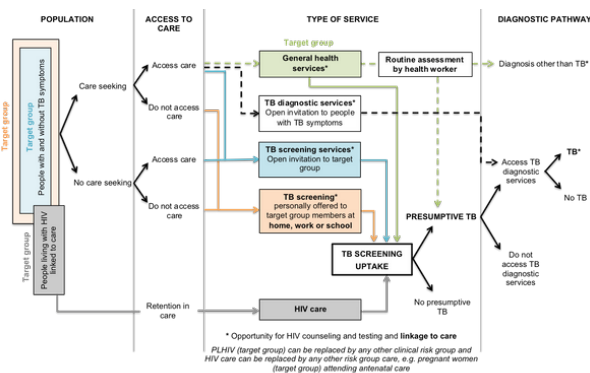


Figure 1: A system-based logic model depicting different types of services and the associated pathways to TB case detection

Figure 1. A system-based logic model depicting different types of services and the associated pathways to TB case detection.

Conclusions: This systems-based logic model may support standardized terminology, consistency, transparency and improved communication among researchers, policy makers, health workers and community members when implementing and evaluating interventions to improve TB case detection.

EP-06-152 Health screening camps for populations on the move for early identification of TB: towards a TB-free India

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Background and challenges to implementation: Eight million truck drivers and twelve million helpers criss-cross the country's highways for hours at a stretch. Truckers have been identified by the National AIDS Control Organization as a Bridge Population since they are at a higher risk and vulnerability for contracting infections like TB and HIV.

Their nomadic lifestyle poses difficulties in TB treatment, which requires a referral for diagnostics and long-term medication. Inadequate follow-ups lead to high default rates as many of them disappear from the system (TBC India: Best Practices to Eliminate TB by 2025).

Intervention or response: Health camps are organised for screening TB presumptive and raising awareness amongst the mobile population of truckers and allied who have limited knowledge and access to basic health-care services.

These health camps were organised by qualified doctors, nurses, and paramedics at different locations within the 3 Trans-shipment locations of Agra, Jaipur and Uttar Pradesh. NGO partners and corporate such as Sarthi Foundation, Cipla Drugs, Eicher Eye Van, Care 4u, provided facilities like free eye check-ups, RBS tests for

checking diabetes and respiratory illness through spirometer, HIV testing, and free sanitary pads for females in trucker's families during these camps.

Results/Impact: Health screening camps for the target population helps to identify TB patients while collaboration with other CSOs, corporates allow identification of other co-morbidities in TB patients. Through 31 health camps organized under the "Nai DISHA" project from August 2019 to March 2021 (interrupted due to lockdown to contain COVID), 2473 persons were reached, comprising 445 truckers and 2028 allied population in the trans-shipment locations. 14% (n=348) presumptive were identified during the camps. 72% (n=250) were tested and 6% (n=14) diagnosed with TB.

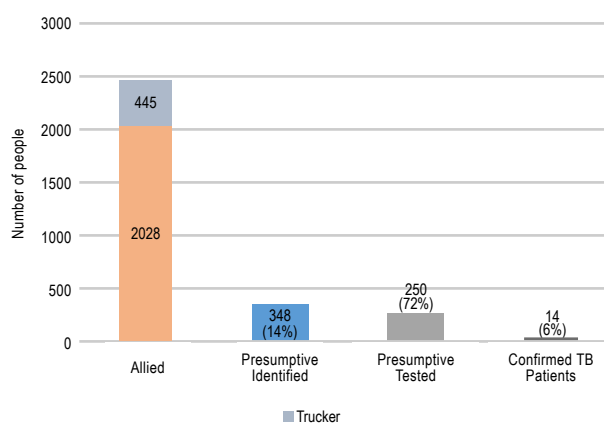


Figure. Health screening camp (Aug 2019 - Mar 2021)

Conclusions: The health screening camps organized by GLRA with the CSOs and corporate helped in identifying TB and other communicable and non-communicable diseases amongst truckers and the allied population.

EP-06-153 Provider-initiated symptomatic TB screening of accompanying caregivers of sick patients attending outpatient departments increases TB case-finding in Nigeria

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Background: Relatives and caregivers in close proximity with TB patients are at increased risk of developing active TB disease. Oftentimes, these accompanying

caregivers of sick patients are verbally screened during outpatient department (OPD) clinic visits and prior to a confirmation of TB diagnosis in the patient. However, there is a paucity of evidence on the impact of symptomatic verbal screening of accompanying caregivers on TB case finding.

Design/Methods: This is a retrospective study that evaluates outcomes of systematic TB screening among accompanying caregivers of patients visiting OPD clinics across 37 private and public health facilities in Osun State, South West Nigeria from July 2020 - March, 2021. In July 2020, the USAID-funded TB-LON 3 project implemented by Institute of Human Virology of Nigeria (IHVN). Patient responses on TB symptoms were documented in relevant tools, entered into excel for descriptive analysis.

Results: A total of 200,508 patients visited these health facilities within this period and were accompanied by 17,129 caregivers. Of the 17,129 accompanying caregivers of OPD clinic attendees, 16,897 (98.6%) were screened for TB symptoms of cough of two weeks or more, fever, weight loss and night sweats. 671 (4.0%) of the 16,897 caregivers screened were presumptive TB cases, 589 (88%) of the identified presumptive TB caregivers were evaluated, yielding only 1 (0.5%) confirmed TB cases from caregivers evaluated for TB. Number needed to screen (NNS) and Number needed to test (NNT) among accompanied relatives of TB patient was 5,632 and 193 respectively.

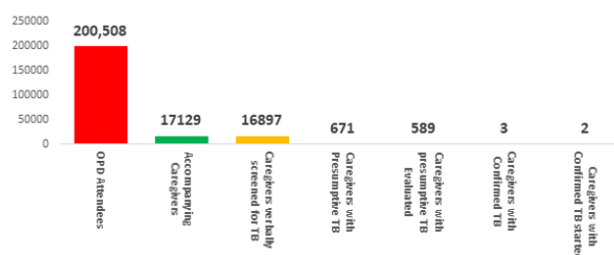


Figure. Caregiver TB screening cascade, July 2020 - March 2021

Conclusions: The current strategy of screening accompanying caregivers of sick patients attending hospital OPD clinics is not efficient enough in finding and increasing TB cases in health facility settings. Future studies should evaluate the impact of a more targeted screening strategy that focuses on caregivers of patients who have been identified as presumptive TB or confirmed TB Cases.

EP-06-154 Variations in TB yield among different health service units of health facilities

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Background and challenges to implementation: According to national Ministry of Health reports, Ethiopia is missing one third of tuberculosis (TB) patients expected to occur annually. Integrating quality TB screening activities in health facilities is a major TB case finding initiative implemented nationally. Analysis was done to assess the yield of TB among patients coming to outpatient departments (OPDs), non communicable disease (NCD) units, OPDs for children under five years of age, and other relevant service provision areas that are expected to be screened for TB.

Intervention or response: The USAID Eliminate TB Project supports the national TB program's goal of making sure that health facilities have integrated TB screening. Capacity building, availing of standard operating procedures, recording and reporting materials were provided to ensure proper screening of patients who appear at Outpatient Departments (OPDs). We analyzed data collected from 610 health facilities from October to December 2020. We calculated number needed to screen (NNS) and number needed to treat (NNT).

Results/Impact: A total of 1,480,812 patients were screened for TB with the majority (1,221,066, 82.5%) being among adults at OPDs. The overall presumptive TB rate was 0.8% (11,392/1,480,812). The highest yield of TB among TB screened was observed in adults at OPDs (0.12%) while the lowest was in children under five years of age OPDs (0.03%). Similarly, the NNS was 830 for adults at OPDs. Meanwhile, the NNT was at a minimum for those at NCD units, and children under five years of age at OPDs showed a higher yield of TB among tested in these units.

Unit	# screened	# presumptive TB	# tested	# of TB cases (%)	NNT	NNS
Adult OPDs	1,221,066	11,035 (0.9)	8,257	1,472 (0.12)	6	830
NCD	69,654	118 (0.2)	77	28 (0.04)	3	2,488
TB screening in children under five years of age OPDs	190,092	239 (0.1)	137	50 (0.03)	3	3,802
Total	1,480,812	11,392(0.8)	8,471	1,550 (0.1)	5	955

Table: TB screening and the yield in different facility service outlets, Oct– Dec 2020

Conclusions: There are variations in the yield of TB in different units of OPDs. The presumptive identification and yield of TB rate is low, which calls for improvement in the quality of TB screening.

EP-06-155 The usefulness of TB-LAMP in community outreach settings during active case-finding of TB using mobile X-ray and laboratory trucks in Zimbabwe

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Background: Targeted active screening for tuberculosis (TB) using mobile trucks in the community is implemented in high TB burden districts in Zimbabwe among high risk groups. Diagnosing TB using loop-mediated isothermal amplification (TB-LAMP) is a new manual TB detection method based on a point of care tool meant to ease challenges such as cost, ease of operation and turnover time. It can be battery-operated unlike the Xpert MTB/Rif and used in outdoor settings. A study was conducted to determine the usefulness of diagnosing TB with TB-LAMP in community outreach settings during active case finding activities using mobile X-ray trucks.

Design/Methods: A descriptive study using routinely collected project data was conducted. This study was carried out during a community outreach for TB active case finding in Kadoma and Kwekwe districts. All sputum specimens were tested using TB-LAMP and those positive were processed using the Xpert MTB/Rif and results were compared.

Results: A total of 351 TB-LAMP tests were done on presumptive TB clients that had been screened using digital chest X-ray. Of the 17 (4.8%) sputum specimens that tested positive on TB-LAMP, 16 (4.6%) also tested positive on Xpert MTB/Rif. There was one discrepancy where the sputum specimen tested positive on TB-LAMP and negative on Xpert MTB/Rif. The turnaround time for all TB-LAMP tests was 50 minutes on average as compared to the Xpert MTB/Rif which is 2 hours on average.

Conclusions: TB-LAMP can be placed in areas where there is no access to Xpert MTB/Rif or where samples have to be referred. This test can be a screening test on presumptive TB clients in remote areas to reduce turnaround time. The diagnostic method could reduce costs incurred by the healthcare system and clients in rural settings in transporting specimens to district laboratories and traveling costs for sample collection and results, respectively.

EP-06-156 Improving the efficiency of community TB active case-finding interventions using EWORS hotspot analytics

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Background and challenges to implementation: Nigeria has one of the highest burdens of TB (219/100,000) and MDR-TB (new 4.3%; retreatment 14%) in the world. However, TB treatment coverage remains low (27%) and to increase treatment coverage, innovative approaches to case-finding needs to be intensified.

Intervention or response: The USAID-funded TB LON regions 1 and 2 project led by KNCV TB Foundation Nigeria instituted TB hotspot analytics using InStrat Global Health Solutions' Early Warning Outbreak Recognition System (EWORS) to inform community screening interventions in 14 states. EWORS (built on the MediXcel platform) uses advanced surveillance mechanisms to identify TB patient's residence in clusters, enabling it to predict hotspots at Ward-level. EWORS leverages real-time data from a Commcare-based mobile app that records routine TB surveillance. An alarm is triggered when a hotspot is identified and a notification email sent to field officers to institute community outreach activities. Field officers offer TB screening during outreach activities and identified presumptive are evaluated for TB using GeneXpert MTB/Rif or Chest x-ray. Confirmed TB patients are linked to treatment and notified to the NTP. We analyzed TB yield and contribution to case-finding.

Results/Impact: From July 2020 to March 2021, 268,955 persons were screened for TB during outreach activities in 426 hotspot areas. Of 29,169 presumptive identified and evaluated for TB, 2,735 patients were detected. The number needed to screen (NNS) was 95. Similarly, 247,093 persons were screened in 385 non-hotspot areas; 23,414 presumptive were identified, and 1,327 TB patients were found. The NNS was 186. The median TB yield was higher in the hotspot compared to the non-hotspot areas ($p < 0.001$) (Figure).

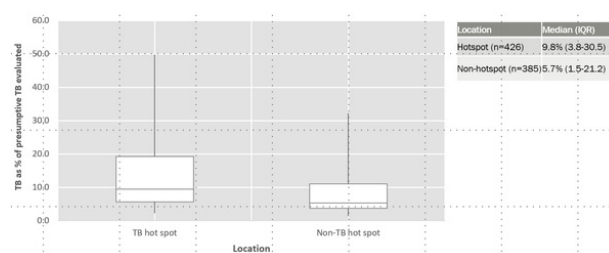


Figure. TB yield (TB positive as percent of presumptive) in hotspot vs non-hotspot areas.

Conclusions: These findings reveal the utility of prioritization based on hotspot analytics as a means of achieving a higher yield of TB from community case-finding interventions. This strategy is crucial to finding the missing TB cases and improving treatment coverage, especially in resource-constrained settings.

Effectiveness, safety and outcomes of TB treatments

EP-14-228 No adverse effects on male reproductive hormones in patients treated with pretomanid-containing regimens

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Background: In toxicology studies of pretomanid (Pa), recently approved for TB treatment, testicular toxicity was observed in rats, but not non-human-primates. Subsequent clinical studies of pretomanid-containing-regimens evaluated male hormones for potential impact on the hypothalamic-pituitary-gonadal axis and male reproductive function.

Design/Methods: 4 studies were evaluated for this analysis. SimpliciTB had 2 arms receiving 4 and 6 months of BPamZ in DS and DR-patients respectively (Pa dose-200mg). NC005 had 3 arms receiving 2 months of BPamZ +/-M in DS/DR-patients (Pa dose-200mg). The NC-002 and STAND studies evaluated PaMZ in DS/DR patients with Pa at 100 and 200mg for 2-months (NC-002) or 4 – 6 months (STAND). Studies were phase-2 except for STAND (phase-3) and all had HRZE-control arms. The male hormones measured at specific time-points in the studies included testosterone, inhibin-B, FSH, and LH (NC005 only measured FSH).

Results: This analysis is based only on data from patients who provided samples at all required visits. In SimpliciTB, 143 patients at baseline had median values for testosterone, inhibin-B, FSH, and LH within their reference ranges (albeit low within the range for testosterone) and similar across arms. After 4-6 months of treatment plus 3-5 months of recovery, all hormones remained within their reference ranges and were similar across arms with median testosterone and inhibin-B higher and median FSH and LH lower, indicating treatment-related amelioration of the relative hypogonadal state at baseline.

In NC-002 (88 patients), NC005 (24 patients), and STAND (113 patients), hormone levels analyzed behaved similarly to SimpliciTB, across the HRZE and Pa-containing-regimens (100-and-200mg) arms.

Conclusions: Treatment regimens with either 100 or 200 mg/d pretomanid administered for up to 6 months and standard of care (HRZE) similarly improved male hypogonadism present at baseline in DS- and DR-TB patients in four studies, indicating a lack of adverse effects of pretomanid on male reproductive function.

EP-14-229 Initial data on treatment outcomes and cardiotoxicity of the all-oral, 9-month treatment regimen for rifampicin-resistant TB in Belarus

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Background: Patients with rifampicin-resistant tuberculosis (RR-TB) historically have had poor treatment outcomes. Key drugs recommended for RR-TB treatment (such as fluoroquinolones, clofazimine, bedaquiline and delamanid), have been reported to be associated with prolonged QTcF interval.

Design/Methods: Operational study of standardized regimen containing levofloxacin, linezolid, clofazimine and cycloserine for 9 months and bedaquiline for 5,5 months for laboratory-confirmed rifampicin resistant and fluoroquinolone sensitive TB patients was performed in Belarus. Regular ECG monitoring was used at baseline and monthly throughout therapy. Initial treatment outcomes at the end of treatment were assessed. Sustained treatment success will be assessed after 2 years of follow-up.

Results: 222 patients were successively enrolled in treatment from 2018 to 2019. Out of 222, 90,1% had bacteriologically favourable outcome (3 consecutive negative cultures taken 30 days apart at the end of treatment), 4,1% died, 1,3% failed and 4,5% were lost to follow-up. QTcF prolongation developed in 30% of patients: 29,7% - grade 1, 3,1% - grade 2, 0,4% - grade 3-4, as per CTCAE v.4.03 severity grading scale. QTcF mean interval increased from 393ms at baseline to 410ms by the end of 5th month of treatment (Table 1).

From 6th month of treatment mean QTcF interval remained mainly unchanged. Grade 2 QTcF prolongation was observed more frequently in patients with lower treatment success and among those who died during treatment (Table 2).

Treatment month	Mean (SD), ms	Grade 1	Grade 2	Grade 3	Grade 4
0	393 (22)	0.9	0.0	0.0	0.0
1	402 (23)	2.3	0.0	0.0	0.0
2	407 (25)	4.1	0.0	0.0	0.0
3	409 (27)	6.0	0.5	0.0	0.0
4	413 (27)	6.6	0.9	0.0	0.0
5	410 (30)	8.7	0.5	0.5	0.5
6	408 (27)	7.5	0.0	0.0	0.0
7	408 (27)	6.7	1.0	0.0	0.0
8	408 (30)	8.3	0.5	0.5	0.5
9	409 (29)	6.6	0.0	0.5	0.5

SD=standard deviation; ms=milliseconds; QTcF=QT interval corrected with Frederica formula

Table 1. Duration of QTcF interval segregated by treatment month and severity grading (CTCAE v.4.03)

QTcF interval prolongation	Treatment success vs. poor treatment outcome, OR (95%CI)	Death vs. other treatment outcomes, OR (95%CI)
Grade 1	0.7 (0.3-1.8)	5.1 (1.2-21.1)
Grade 2	0.1 (0.02-0.6)	11.8 (1.9-72.2)
Grade 3-4	-	-

OR=odds ratio; CI=confidence interval

Table 2. Association of QTcF interval prolongation with treatment outcomes of modified shorter all-oral 9-month treatment regimen for RR-TB

Conclusions: Modified shorter all-oral RR-TB regimen shows excellent initial treatment outcomes. QTcF prolongation is attributable to components of modified all-oral shorter treatment regimen, especially when used in combination. Careful ECG monitoring at baseline and throughout therapy is essential to timely detect and address possible additive cardiotoxicity of this drug combination and to increase chances for treatment success.

EP-14-230 The safety of prolonged delamanid-bedaquiline-containing regimen for pre-XDR-TB treatment in Arkhangelsk Region in 2019–2021

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Background: To introduce new regimen against pre-XDR-TB (WHO definitions 2020) we need to demonstrate the safety of combined prolong regimen including delamanid and bedaquiline combination and registration of adverse events (AEs).

Design/Methods: In 2019-2021 31 adult patients with pulmonary tuberculosis received delamanid-bedaquiline containing combined regimen. The pre-XDR-TB status was proved by microbiological and PCR methods. All patients had resistance to FQ and recieved the regimen: delamanid, bedaquiline, linezolid, clofazimine for 12 months. Delamanid and bedaquiline combination was more 24 weeks simultaneously.

Results: Twenty two (71%) patients had one AE at least. Totally we found 91 AEs. The main AEs included toxic hepatitis (19%), hypopotassemia, hypomagnesemia, hypocalcaemia in blood serum (18%), QTcF prolongation (12%). Others: early AEs: hepatotoxicity 17/91, electrolyte disturbance 16/91, QTcF prolongation 11/91, nephrotoxicity 9/91, allergic dermatitis with eosinophilia 8/91, gastrotoxicity 4/31, anemia 4/31, convulsion 2/91, vomiting 4/91, ophtalmotoxicity 1/91, and diarrhea 1/91. The late AEs: peripheral polyneuropathy 6/91, hypoalbuminemia 5/91, hyperamylasemia 3/91. We found 3 SAEs. The most serious was ophtalmotoxic (significant visual impairment, paralysis of the oculomotor muscles) in HIV-positive patient. Others SAEs had not correlation with anti-TB drugs. All AEs were successfully controlled without withdrawing any medication. significant visual impairment, paralysis of the oculomotor muscles

Conclusions: The finding match the data from clinical studies. Impact on QTcF is 12% that is close to 10% in international clinical trials. The QTcF prolongation is possible due to prolong combination of several cardiotoxic medicines in the regimen. The prolongation do not lead to cancelation of the combination. We believe that the safety findings allows us to administrate 12 months delamanid-bedaquiline containing regimen for pre-XDR-TB patients.

EP-14-231 Influence of previous TB treatment on time to culture conversion in patients receiving a bedaquiline-containing regimen at Sizwe Tropical Disease Hospital, South Africa

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Background: New drug regimens were needed urgently to alleviate mortality and morbidity among drug-resistant tuberculosis (TB) patients. With widespread use of bedaquiline (a newly developed diarylquinoline), information is needed on the profile of patients who require extended duration of bedaquiline therapy. We examined whether previous exposure to TB treatment influenced the time to culture conversion (compared with no previous treatment) for patients receiving a drug-resistant (DR) TB regimen containing bedaquiline.

Design/Methods: We undertook a retrospective cohort study (April 2016 to March 2019), of DR-TB patients on a bedaquiline containing regimen with documented culture conversion. Patients were categorized into “new” and “previously treated” groups based on their exposure to TB treatment. Time to initial conversion of sputum culture was analyzed using a Kaplan-Meier survival

curve, and the log-rank test was used to test the difference between the groups. Multivariable logistic regression analysis assessed independent associations with the outcome of culture conversion after six months. A p-value less than or equal to 0.05 was considered statistically significant.

Results: A total of 397 files were audited, 303 new (no previous TB treatment exposure) and 94 previously treated DR-TB patients. The two groups experienced similar rates of culture conversion up to two months, the new-patient group thereafter displayed faster times to culture conversion. The previously treated group had 4.12 times the odds of culture converting after 6 months compared to the new group. In addition, the previously treated group received a longer duration of bedaquiline ($p < 0.001$).

Conclusions: The findings of this study substantiate the potential impact of previous exposure to TB treatment on the efficacy of bedaquiline therapy. Given the extended use of bedaquiline, monitoring of susceptible bedaquiline MIC in previously treated patients, as early as two months, in the event of failure to culture convert may be warranted.

EP-14-232 CYP3A4*1G polymorphism as a predictor of hepatotoxicity during anti-TB treatment

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Background: Previously it was shown that the risk of anti-tuberculosis (TB) drug-induced liver injury could be determined by patients' genotype polymorphism of *CYP2E1*, *NAT-2* etc. The aim of presented research was the investigation of an impact of *CYP3A4*1G* polymorphism on liver function in the patients with TB during anti-tuberculosis therapy.

Design/Methods: It was enrolled 105 patients with newly diagnosed pulmonary TB at Odessa Regional TB Hospital 2012-2014 yy. We have considered their medical records at the beginning and at the end of inpatient treatment including activity of biochemical indices such as total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyltransferase (GGT). The genotype *CYP3A4*1G*, 20230G>A was detected by PCR.

Results: At the beginning of the treatment the level of studied biochemical indices was almost the same regardless of *CYP3A4*1G* genotype. After the conducted inpatient treatment in fast metabolizers the biochemical indexes insignificantly increased, while the level of bilirubin has dropped on 10,4% ($p < 0,05$). In slow metabo-

lizers after in-patient treatment the serum total bilirubin level increased on 8,0% ($p < 0,05$), the activity of ALT raised on 67,2% ($p < 0,05$), AST - on 37,4% ($p > 0,05$), also the amount of the patients with ALT and AST level beyond normal almost doubled. After completion of in-patient treatment in moderate and slow metabolizers serum GGT activity increased in 2,5 times ($p < 0,05$) and 1,3 times ($p > 0,05$) correspondently, among fast metabolizers – on the contrary, the number of the individuals with increased GGT level has dropped ($p < 0,05$).

Conclusions: Thus in slow metabolizers according to *CYP3A4*1G* genotype after completion of in-patient stage of anti-TB treatment the level of cytotoxicity and toxicity indexes was much higher than in fast metabolizers. That is why detection of *CYP3A4*1G* genotype of TB patients at the beginning of TB treatment could help to recognize a group of the individuals with increased risk of liver injury during therapy.

EP-14-233 The effectiveness of the use of inhaled isoniazid and rifampicin in patients with pulmonary TB complicated by bronchial TB leading to I and II degree stenosis

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Background: The aim of our study was to study the efficacy of inhaled isoniazid and rifampicin in patients with TB-pulmonary complicated by bronchial tuberculosis leading to grade I-II stenosis during the intensive phase of chemotherapy.

Design/Methods: Our study included 48 patients with newly diagnosed TB. All patients had TB-susceptible and received standard chemotherapy, which included first-line oral drugs. The patients were divided into two groups: 1 group - 21 patients who additionally received 0.15 g of rifampicin and 0.15 g of isoniazid by inhalation through a nebulizer using salmeterol 50 mcg and fluticasone propionate 250 mcg twice a day for 2 months; 2 group - 27 patients received standard chemotherapy.

Results: Sputum conversion: in 1 month was observed in 14 (66.7%) patients of the 1 group and in 10 (37.0%) - 2 group ($p < 0.05$); in 2 month - 19 (90.5%) - in 1 group and in 21 (77.8%) - in 2 group ($p > 0.05$). Average time of sputum conversion: 1 group - 1.4 ± 0.3 months and 2 group - 2.5 ± 0.4 months ($p < 0.05$). Cavities healing occurred af-

ter 2 months: 1 group - 13 (61.9%) patients and 2 group - 12 (44.4%) ($p > 0.05$). After additional treatment for 2 months, bronchial stenosis continued to be observed in 3 (14.3%) patients of 1 group and in 17 (63.0%) patients in 2 group ($p < 0.05$). Average terms of treatment of patients: 1 group - 2.4 ± 0.4 months and 2 group - 3.9 ± 0.5 months ($p < 0.05$).

Conclusions: The use of this inhalation therapy in patients with TB-pulmonary complicated by bronchial tuberculosis leading to stenosis of I-II degrees increases the effectiveness of chemotherapy and reduces the case of bronchial stenosis in the 2nd month of treatment in 48.7% of patients.

EP-14-234 Haemoglobin increase associated with favourable outcomes in primary multidrug-resistant TB: a prospective observational cohort study

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Background: Multidrug resistant tuberculosis (MDR-TB) is a major threat to global TB control. MDR-TB can be transmitted (primary MDR-TB) or develop during the course of treatment (secondary MDR-TB). The success treatment rates for the two types are different. However, the clinical features and predictors for treatment outcomes between two types are unclear.

Design/Methods: A prospective, observational cohort study was conducted at Shanghai Pulmonary Hospital. Univariate and multivariable logistic regression models were used to screen potential risk factors for treatment outcomes.

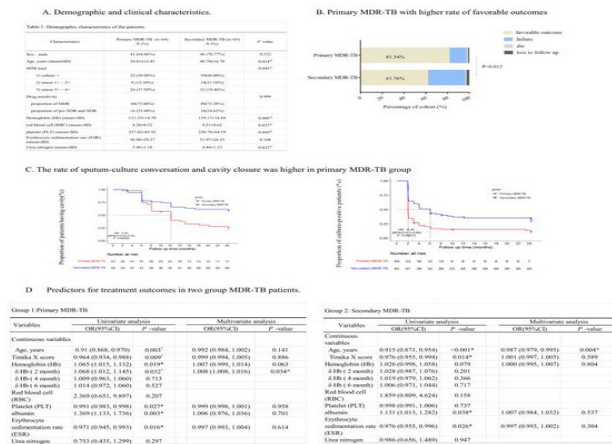
Results: Primary MDR-TB patients were younger ($P=0.014$), and with higher bacteria load ($P=0.042$) than secondary MDR-TB patients. As for the laboratory test results, primary MDR-TB patients with a lower hemoglobin levels ($P=0.008$) and red blood cell count ($P=0.023$)

The platelet count were higher ($P=0.049$) and urea nitrogen levels were lower ($P=0.025$) in primary MDR-TB group than that in secondary MDR-TB group. The rate of favorable outcome was higher in primary MDR-TB group than secondary MDR-TB group ($P=0.012$), and the rates of sputum-culture conversation and cavity closure were higher in primary MDR-TB group than secondary MDR-TB group.

During anti-MDR-TB treatment, hemoglobin level elevated significantly in primary MDR-TB group, which was not shown in secondary MDR-TB group. Further-

more, hemoglobin level elevated significantly in patients with favorable outcomes, while not in those with poor outcomes in primary MDR-TB group. We used linear regression models and multivariate regression models to assess whether hemoglobin level elevated associated with favorable outcomes in two group.

In primary MDR-TB group, hemoglobin level elevated at the end of 2 months treatment correlated with favorable outcomes in primary MDR-TB group ($P=0.034$)



Conclusions: This study found the two types of MDR-TB were different in clinical characteristics, treatment outcomes and predictor factors correlated with treatment outcomes. For primary MDR-TB group, hemoglobin level elevated at the end of 2 months treatment correlated with favorable outcomes.

EP-14-235 Twelve-month relapse-free cure among patients treated with concomitant bedaquiline and delamanid beyond 24 weeks in Mumbai, India

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Background: People treated for TB are known to have persistent health impairment and premature death even after successful completion of treatment. Since 2016, Médecins sans Frontières (MSF) in Mumbai, India has been providing bedaquiline and delamanid to drug-resistant TB (DR-TB) patients with complex resistance pattern, and for whom an effective regimen cannot be designed without these drugs. Limited evidence exists on status of patients post DR-TB treatment completion.

This study aimed to describe the post-treatment outcomes twelve months after successful completion of DR-TB treatment with concomitant bedaquiline and delamanid.

Design/Methods: This was a descriptive study of routinely collected clinical data. All patients initiated on DR-TB treatment regimens containing concomitant bedaquiline and delamanid between January 2016-July 2018 and who successfully completed their treatment were included. Post-treatment completion, all patients were followed-up clinically and bacteriologically at 3, 6 and 12 months.

Results: During the study period, 73 patients initiated on treatment; 56 (77%) successfully completed their treatment. Median age: 24 years (Interquartile range, IQR: 20-32); 34 (60.0%) were female, one HIV-positive. Twenty-six had fluoroquinolone resistance (PreXDR); 30 had XDR-TB. The median (IQR) treatment duration was 97 weeks (85-101), on Bedaquiline: 81 weeks (75-90), on Delamanid: 95 weeks (82-97.4), and 40 weeks (26.9-52.1) on imipenem (n=37).

Twelve months post-treatment completion, 48/56 (85.7%) patients were alive and culture negative. One had died and one had relapse/reinfection. Six (10.7%) were lost to follow-up. During follow-up period, 20/48 (41.7%) patients reported one or more symptoms including breathlessness, cough and generalized muscle pain while 28/48 (58.3%) reported no symptoms.

Conclusions: We report a high proportion of twelve month post-treatment relapse-free cure among patients with complex resistance patterns treated with bedaquiline and delamanid in combination. We also report high proportion with residual symptoms. Improved access to bedaquiline and delamanid, including concomitant use for an effective regimen, could help patients with complex resistance patterns attain a post treatment favourable outcome.

EP-14-236 Linezolid toxicity in patients with drug-resistant TB is exposure driven

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Background: Long-term usage of linezolid can result in adverse events such as peripheral neuropathy (PNP) or anemia. Here, the relationship between linezolid exposure as well as patient characteristics and the occurrence of PNP and anemia are investigated using a time-to-event (TTE) approach.

Design/Methods: Therapeutic drug monitoring data from 75 drug-resistant tuberculosis patients treated with linezolid for up to 20 months was analyzed. PNP and anemia data was analyzed using parametric TTE analysis. Different time-varying linezolid pharmacokinetic exposure indices ($AUC_{0-24h,ss}$, C_{av} , C_{max} , and C_{min}) and patient characteristics were investigated as risk factors.

Results: A Gompertz distribution best described the baseline hazard for both PNP and anemia.

No patient characteristics were identified to be a statistically significant predictor for either adverse event. For both PNP and anemia, an exposure/response relationship between linezolid trough concentrations (C_{min}) and the adverse event was found. At the commonly used C_{min} target of 2.0 mg/L (total concentration), the model-predicted cumulative risk after 1 year of treatment was 41.5% and 82.4% for PNP and anemia, respectively.

The cumulative risk to develop PNP within 1 year of treatment was 17.4%, 28.3%, 47.9% and 51.5% at doses of 300 mg once daily (QD), 600 mg QD, 1200 mg QD and 300 mg twice daily (corresponding to a C_{min} of 0.51 mg/L, 1.12 mg/L, 2.51 mg/L and 2.80 mg/L) in the typical patient, respectively. The cumulative risk for anemia was 50.0%, 67.9%, 87.3% and 89.6% at the same dose groups after 1 year of treatment.

Conclusions: In this work we derived an exposure/response relationship between linezolid trough concentrations and PNP as well as anemia. Increasing trough concentrations increased the risk to develop either adverse event. At the commonly applied C_{min} safety target of 2.0 mg/L, the model-predicted cumulative risk at 1 year was 41.5% and 82.4% for PNP and anemia, respectively.

EP-14-237 Factors associated with favourable outcomes among rifampicin-susceptible, isoniazid-resistant TB patients in Taiwan, 2010–2018

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Background: Isoniazid has been one of the first-line anti-TB drugs with effective early bactericidal effect. Estimated 8% of TB patients worldwide have rifampicin-susceptible, isoniazid-resistant TB (Hr-TB) with more unfavorable outcomes compared with DS-TB. In Taiwan, universal drug susceptibility test policy has been applied for culture positive TB patients for more than a decade. The aim of this study is to analyze the treatment outcomes and the associated factors among Hr-TB patients.

Design/Methods: We conducted a retrospective cohort analysis to enroll new and relapse Hr-TB patients from TB registry during 2010 to 2018. The demographic, clinical characteristics, and treatment outcomes were obtained from TB registry. Unfavorable outcomes were

defined as failure, acquired rifampicin resistance, death, loss-to-follow-up, and relapse within one year after treatment completion. Logistic regression model was applied to estimate the odds of favorable outcomes and 95% confidence interval among covariates.

Results: The Hr-Rs rate was 7.7% and 8.9% in new and relapse culture positive TB patients respectively. A total of 5011 Hr-TB patients were enrolled after excluding those with incomplete drug susceptibility results, or death before initiating anti-TB treatment, interruption of rifampin medication, and those with adding fluoroquinolone(FQ) into regimen in 120 days after initiating anti-TB treatment to avoid selection bias. The treatment success rate was 84% among Hr-TB. After adjusting age group and gender, we found using FQs (adjusting odds ratio, aOR=3.04, 95% CI:2.34-3.94), susceptible to EMB (aOR=3.49, 95% CI:2.31-5.27), classification as new patient (aOR=1.9, 95% CI:1.27-2.84), more days in using PZA (aOR=1.36 per additional 30 days, 95% CI:1.32-1.39), and using second line drugs except injectable agents and prothionamide (aOR=2.5, 95% CI:1.11-5.62) were associated with favorable outcomes.

	Favorable outcome		Univariate	Multivariate
	n	%	OR(95% CI)	aOR(95% CI)
FQ-containing regimen				
yes (n=745)	647	86.9%	1.31(1.04-1.64)	3.04(2.34-3.94)
no (n=4266)	3561	83.5%	1	1
Age group (years)				
0-29 (n=307)	299	97.4%	10.21(5.03-20.71)	8.04(3.91-16.52)
30-59 (n=1672)	1528	91.4%	2.90(2.40-3.51)	2.86(2.33-3.51)
≥60 (n=3032)	2381	78.5%	1	1
EMB resistance at baseline				
susceptible (n=4786)	4031	84.2%	1.45(1.04-2.01)	3.49(2.31-5.27)
resistant (n=225)	177	78.7%	1	1
AFB smear at baseline				
negative (n=3115)	2621	84.1%	1.03(0.89-1.21)	1.22(1.03-1.45)
Positive (n=1896)	1587	83.7%	1	1
Patient classification				
new (n=4837)	4076	84.3%	1.7(1.19-2.43)	1.9(1.27-2.84)
Relapse (n=174)	132	75.9%	1	1
Days of PZA prescription, per 30 days (n=184)				
			1.32(1.28-1.35)	1.36(1.32-1.39)
Using SLD other than injectable agents or prothionamide				
yes (n=87)	79	90.8%	1.9(0.92-3.95)	2.5(1.11-5.62)
no (n=4924)	4129	83.9%	1	1

Abbreviation: FQ: fluoroquinolone; EMB: ethambutol; SM: streptomycin; CXR: chest X-ray; PZA: pyrazinamide; AFB: acid fast bacilli; SLD: second line drug

Table 1. Factors associated with favorable outcomes among Hr-TB patients in Taiwan, 2010 - 2018

Conclusions: Fluoroquinolone-containing regimen was associated with favorable treatment outcomes on Hr-TB. Continuous surveillance of FQ resistance and monitoring treatment outcomes would help clinical management after national guideline updated Hr-TB treatment in line with WHO recommendation.

Private sector engagement for improving TB care and detection

EP-15-238 Accelerating TB elimination through sustained engagement with the private health sector in a metropolitan city in South India

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Background and challenges to implementation: Private health sector in India diagnose and treat more than half of all people with tuberculosis each year and thus have potential to make significant contributions towards TB Elimination. Global Fund aided JEET (Joint Efforts to Eliminate Tuberculosis) project is implemented in select districts to facilitate this.

We present the trends in notifications as a result of sustained private sector engagement in a metropolitan city Bangalore, India from October 2018-March 2021.

Intervention or response: JEET followed a hub-spoke model which facilitated in establishing systems for referral of patients to the public for free, rapid TB diagnostics and treatment while continuing to be followed up by the providers of their choice. Through sustained networking and creating tailor made solutions (personnel/training/linkages), JEET established systems for notification to the centralized portal NIKSHAY for variety of providers ranging from single clinics to polyclinics/speciality centres to chain pharmacies and labs to corporate hospitals.

Results/Impact: From October 2018-March 2021, 2066 private providers referred at least 1 presumptive TB patient; 1832 providers diagnosed at least one TB patient. Number of notifying providers increased from 161 in October-December 2018 to 681 in January-March 2021. Three fold increase in identifying presumptives to facilitate early diagnosis was noted while number of patients notified increased three times from 621 in October-December 2018 to 2042 in January-March 2021. Of these 53% had microbiological confirmation. In 2018, 80% patients were diagnosed by 22% facilities; by 2021 this was 28% of the notifying facilities. Due to the sustained efforts in patient tracking, follow up and adherence support, the percentage of patients successfully completing treatment went up from 59% in the baseline year 2018 to 71% in 2019.

Conclusions: Private health sectors can make substantial contribution to TB Elimination provided there is sustained efforts in building trust, establishing systems tailored to each individual facility/provider.

EP-15-239 Routine learning for adaptation prepares for shocks: maintaining private sector TB case-finding during the Covid-19 pandemic

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Background and challenges to implementation: USAID's SHOPS Plus program has supported networks of private sector clinics, community pharmacists, proprietary and patent medicine vendors (PPMV)/drug shops and laboratories in Nigeria's Kano and Lagos States since 2017. The network model was implemented because:

- Nigeria misses 75% of the 400,000 cases of TB that occur every year and,
- Nearly 75% of health expenditures occur in the private sector.

Since inception, the program has followed the principle of "learning for adaptation" using real-time data; consequently, case finding has risen every year.

Thus, we hypothesize that the program and its providers were ready to rapidly adapt and mitigate the impact of COVID-19 pandemic.

Intervention or response: The COVID-19 pandemic-related lockdowns disrupted health activities. Formal facility patient attendance decreased and there was fear that symptom similarities would limit TB screening and patient care-seeking behavior.

The Lagos program team responded immediately by switching to virtual supportive supervision, training providers through webinars on differential diagnosis of TB and COVID, and distributing personal protective equipment. Lagos State's lockdown began three weeks before Kano's, providing time to prepare PPMVs by equipping "roaming" screeners diverted from formal facilities to communities to screen, collect samples, and make referrals.

Results/Impact: Program monitoring data for 2019 and 2020 were compared across the TB cascade (facility attendance and the number of clients screened, identified as presumptive, tested, and diagnosed with TB). See Table 1.

- Network attendance decreased by 24.9% and 14.2% in Lagos and Kano but overall case finding increased by 4% (6,950 cases)
- Compared to 2019 a 5.9% reduction in total TB cases detected occurred in Lagos but a 22.3% increase occurred in Kano
- In Kano, PPMVs' contribution to TB case finding in Kano increased from 33.4% to 55.1%

Variables	Lagos 2019	Lagos 2020	Kano 2019	Kano 2020
Total OPD attendance	2,131,326	1,600,570	808,489	693,764
Screening rate	42.9%	54.4%	100.3%	133.8%
Presumptive yield	48.8%	38.7%	8.3%	10.7%
Testing rate	89.8%	90.3%	92.8%	95.9%
TB cases diagnosed	3,412	3,211	3,058	3,739
% contribution of CFs to case detection	78.2%	81.9%	62.3%	40.1%
% contribution of Labs to case detection	12.1%	10.4%	3.2%	3.4%
% contribution of PPMVs to case detection	7.4%	6.1%	33.4%	55.1%
% contribution of CPs to case detection	2.3%	1.6%	1.0%	1.4%

Table 1.

Conclusions: Private sector providers, especially PPMVs were able to rapidly respond to COVID-19, mitigating possible negative impacts.

EP-15-240 The impact of Covid-19 on TB screening and testing in the private health sector in KwaZulu Natal, South Africa

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Background: Although TB in South Africa is mainly managed in the public sector, up to 29% of people with TB symptoms first seek care in the private sector. A previous study showed that private sector General Practitioners (GPs) delay testing for TB. We describe the impact of COVID-19 on TB screening and testing in the private sector in eThekweni District, Durban, South Africa.

Design/Methods: We conducted facilitated surveys with private GPs enrolled in a larger study offering private sector patients with TB-like symptoms free TB testing in the public sector. Surveys were conducted over the period March to April 2021, querying information on patient load, consultation methods, and clinical profile of patients with suspected COVID-19.

Results: Seventy-three surveys were completed among 80 GPs enrolled. Seventy-one percent of GPs reported an overall decline in patients since the onset of COVID-19, with 23% reporting patient increases during active waves of COVID-19. While 51% and 14% of GPs reported offering telephonic and/or video consults for patients with COVID-like symptoms, respectively, 85% of GPs saw the majority of symptomatic patients in person. Twenty-five percent of GPs reported difficulty

differentiating TB and COVID-19 symptoms, among whom, 50% reported ordering concurrent COVID-19 and TB tests at least once. Cough and fever most commonly impeded differential diagnoses (89% and 61%, respectively). Other overlapping symptoms included shortness of breath and fatigue (39% each), and chest pain and weight loss (28% each).

Conclusions: Private sector patient numbers declined in eThekweni during the COVID-19 pandemic. A quarter of GPs had trouble differentiating COVID-19 and TB symptoms, yet only half of them tested for both TB and COVID-19, suggesting missed opportunities for TB testing. Ongoing clinical training about TB and COVID-19, together with concurrent COVID-19 and TB testing, could sustain and increase TB case detection in the presence of COVID-19.

EP-15-241 Factors influencing access to free TB diagnosis and anti-TB drugs: Patient perspectives from private sector, the Joint Effort for Elimination of TB project

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Background: Provisioning of quality assured and affordable diagnosis and treatment services to all Tuberculosis (TB) patients is a key priority under India - TB National Strategic Plan. However, majority of the patients seek care in the private sector despite availability of free-of-cost diagnostic and anti-TB drugs in the public sector. We aimed to explore the preferences and bottlenecks in the uptake of free and quality TB care services by patients notified through private sector providers mapped under the Joint Effort for Elimination of Tuberculosis (JEET) project implemented by Foundation for Innovative New Diagnostics India.

Design/Methods: Among TB cases notified from the private sector through project JEET between October 2019-March 2021, 940 consenting participants were recruited into the study through stratified random sampling. Information, elicited through interviews, on several variables including first point of care, diagnostics, and anti-TB medication were analyzed descriptively.

Results: Overall, 87% participants approached private sector as the first point of TB care. Among participants who underwent a microbiological test (N=578), 78% accessed private labs. Among all participants, 58% paid for anti-TB medication. Perception of better patient care (31%), test quality and accuracy (40%), and drug efficacy (39%) were the most cited reasons for preferring private sector as the first point of care, for diagnosis, and for anti-TB medication, respectively. Only 38% of those who underwent a microbiological test at private

lab were unaware of free-TB testing, while 62% of those who paid for anti-TB drugs were aware of free treatment services. The influence of private providers on patient preferences was evident throughout the TB care cascade (Figure 1).

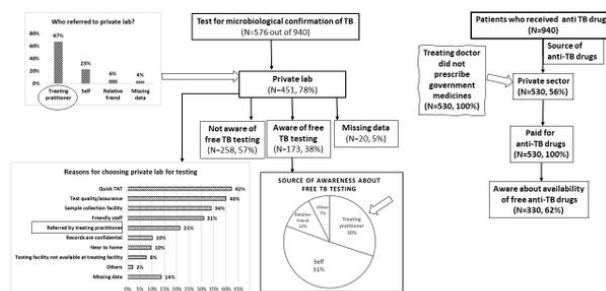


Figure 1. Influence of private sector treating partitioners on patient preferences along TB care cascade.

Conclusions: Patients' perception of better TB care services in the private sector was a major bottleneck in the uptake of quality assured free TB services available in the public sector. The treating practitioners were key influencers of care seeking preferences of TB patients.

EP-15-242 Evaluating TB diagnostic referral yields across different segments of the private sector in Vietnam

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Background: As Viet Nam's economy has grown, so has the utilization of private healthcare services. Many people with TB who are currently 'missed' by government health services are actually seeking care in the private sector. Yet few initiatives have tried to systematically engage multiple types of private providers to find and treat TB.

Design/Methods: We collected data through a private provider interface agency in 19 districts across three provinces of Viet Nam (Ha Noi, Ho Chi Minh City, and Hai Phong) from March 2020 to April 2021. Providers were categorized as either single- or multi-doctor clinics, pharmacies, hospitals, or other types. We then calculated and compared the number of providers recruited, successful chest X-ray (CXR) referrals and case detection across provider types and provinces

Results: 1,965 providers signed collaboration agreements. Pharmacies (72.9%) and single-doctor clinics (16.2%) comprised the most common provider type. Just 227 (11.6%) providers had at least one successful

CXR referral. 152,150 people were screened by CXR, with the vast majority of CXR screens occurring at hospitals (71.1%). 2,022 people were diagnosed with bacteriologically-confirmed TB (NNS=75). The largest number of diagnoses were made after referral by hospitals (n=907), other provider types (n=526) and single doctor clinics (n=345). However, yields were higher at single doctor clinics (NNS=12) and pharmacies (NNS=13) compared to hospitals (NNS=119).

Regional segmentation showed a high proportion of providers with ≥ 1 referral in Hai Phong (25.6% vs 11.6% national average), but the largest number of CXRs in Ha Noi (n=78,271) and cases detected in Ho Chi Minh City (n=1,017).

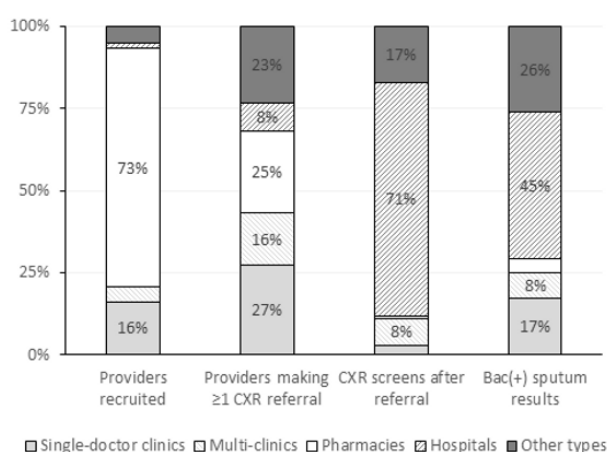


Figure. Yields by Provider type

Conclusions: This evaluation shows the variable patterns of private provider engagement and yields across types of providers and provinces. Hospitals provided the highest absolute yields of TB, but pharmacies and single-doctor clinics were most efficient in recognizing and referring persons with TB.

EP-15-243 Public-private mix intervention to increase access to TB services in rural and underserved areas: a case study from Rimi, Katsina

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Background and challenges to implementation: Rimi is a local government in katsina state with a sociocultural setting of villages and rural settlements. Of the 20 DOTS facilities in the LG, only 13 are functional to cover a large population which poses significant challenges in accessing TB Services. The absence of private facili-

ties in the LG and insufficient public facilities has consequently created underserved areas which contribute to a significant gap in accessing TB Services as evident in TB Case notification from the LG.

Intervention or response: The Public Private Mix is an intervention that is targeted to expand TB Screening and diagnostic services to private health facilities, Pharmacies, Patent Medicine Vendors and also engage and build capacity of formal and informal health sector. Implementation commenced in July 2020. In Rimi LG, a total of 39 Patent Medicine Vendors were selected across all settlements in the community and were given orientation and capacity building in TB service provision. The PMVs were linked with four Public facilities which served as referral hubs in a “Hub and Spoke Model”. The referral hub linkage of PMVs provides support and evaluation of presumptive and treatment of TB patients.

Results/Impact: Quarterly Case notification of PPM activities from July 2020 to March 2021 was reviewed as against total case notification for the LG. It was discovered that PPM contributed significantly to case notification (Q3 – 43%), (Q4 – 54%) and (Q1 – 72%) respectively. Of TB cases notified from PPM, DR-TB cases contributed was (Q3-30%), (Q4 – 7%) and (Q1 – 12%).

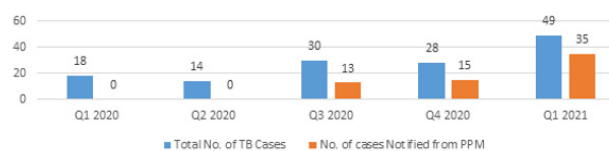


Figure. TB case notification in Rimi LG

Conclusions: PPM as an intervention has been largely successful in reaching underserved areas and rural settlements in Rimi LG through PMVs engagement in TB service provision, thus aiding in closing gaps in case detection and notification. It is believed that such strategy could also be replicated in other underserved areas.

EP-15-244 Trends in private sector notifications in India, 2017–2020: experiences from the Joint Effort for Elimination of TB project

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Background and challenges to implementation: Engaging private sector is pivotal in achieving the target of TB elimination in India by 2025. This necessitates large scale sustainable interventions focused on the private sector.

Intervention or response: Foundation for Innovative New Diagnostics India (FIND) is implementing “Joint Effort for Elimination of Tuberculosis (JEET)” in collaboration with the National TB Elimination Programme (NTEP) and funding support from The Global Fund since 2018.

The project was implemented in 101 districts across 6 states (Andhra Pradesh, Telangana State, Karnataka, Punjab, West Bengal and Himachal Pradesh) facilitating case notifications, bacteriological confirmation by Xpert MTB/RIF, and treatment adherence. Project was initiated in 2018 and by the beginning of 2019, activities were fully implemented.

Results/Impact: Government web-based portal (Nikshay) records from 2017 (baseline) to 2020 were analysed for 101 project districts in 6 states. Overall, the number of TB patients notified from the private sector increased by 77% from 2017 to 2020 (47,557 in 2017, 1,02,654 in 2019 and 84,304 in 2020).

The notification rates doubled from 21 to 42 per 100,000 population from 2017 to 2019, but dropped to 34 per 100,000 in 2020. Number of private notifiers increased by 206% (2,950 in 2017 to 9,035 in 2020). Compared with non-JEET districts within the same states, additional increase of 54% in notification rate per 100,000 population in JEET districts (91% vs 37%) was observed.

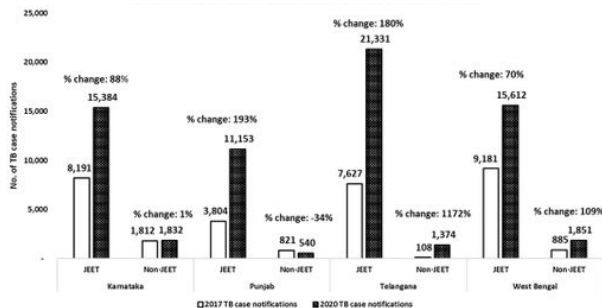


Figure 1. Trends in notifications 2017 and 2020: JEET vs Non JEET districts (except Andhra Pradesh as all districts are covered under JEET)

Conclusions: Despite notifications being adversely impacted due to the COVID-19 pandemic in 2020, it is evident that the project JEET has made significant gains in engaging the private sector in line with the NTEP’s national strategic plan. Scaling up and sustaining these interventions will be critical in order to consolidate the gains made by the project.

EP-15-245 Dynamics of home delivery of free government drugs using e-pharmacies to private sector TB patients

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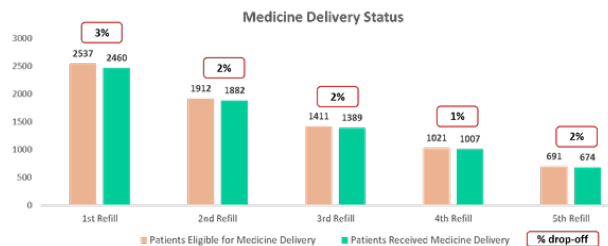
Background and challenges to implementation: In India, both public and private sector Tuberculosis patients can make use of free government drugs. Accessibility in the private sector remains a challenge due to various reasons including lack of efficient forecasting and minimal number of stocking points leading to low uptake. In 2020, the specific conditions generated due to the pandemic further increased issues with accessibility. However, a simultaneous increase in the usage of e-pharmacies was also noted, with 9 million household in 2020 from 3.5 million during the pre-Covid period.

Intervention or response: A pilot was designed by William J. Clinton Foundation (WJCF) and 1mg - a digital consumer healthcare platform, to increase access to government drugs through home-based service delivery. Patients receive telephonic reminders of upcoming provider visits and the prescriptions are collected digitally for drug delivery. This was launched in two cities of Gujarat and parts of Delhi in July’20.

Results/Impact: 2,550 patients were on-boarded till 31st March’21 and 7,307 deliveries were made with a turn-around time of 31.6 hours against the target of 48 hours. On an average 60-70% patients across geographies agreed for the pilot. Out-of-district patients, proximity to the clinic or patients not wanting to disclose their illness were some reasons for not signing-up.

On an average 41% patients came for subsequent visits, earlier than their due date which helps ensure no missed doses. 59% either visited on the last day (11%) or around 7.1 days after (48%) their due date.

The graph below showcases successful deliveries by refills. Reasons for drop-offs include change in medication by provider, patient moving out of town etc.



Conclusions: Home delivery of services can expand the reach of free government drugs and benefit patients particularly during the current scenario. It also enables better monitoring of refills and helps ensure regular visits to clinics.

EP-15-246 Contribution of public-private mix DOTS to TB case notification in Afghanistan

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Background and challenges to implementation: PPM DOTS is consistent to the Nation policy for private health sector in the aspects of accessibility, improve quality and ultimately with sustainability to implement DOTS by private sector according to the NTP policy. This will in the end improve efficiency for NTP in TB control in the country.

Therefore NTP Afghanistan has expanded the PPM DOTS to 24 province of the country with urban setup and big number of private practitioners. The aim of this assessment was to evaluate the outcomes of PPM on TB case notification.

Intervention or response: To implement PPM DOTS, NTP strengthened coordination mechanism between private and public health facilities and trained private practitioners on TB service delivery. A sustainable partnership for TB control with the private practitioners in 24 province of Afghanistan established to facilitate private practitioners in actively notifying and refer the presumptive TB patients to public diagnostic facilities. We used standard TB recording and reporting forms as data collection tool.

Results/Impact: In 2020, a total of 811 private practitioners received orientation on TB DOTS and their performances monitored through regular quarterly review meetings. The assessment team reviewed presumptive TB patients register for PPM and found that 25,322 presumptive TB patients were referred by PPM for diagnosis and among them 2010 (7.9%) diagnosed as bacteriologically confirmed and 2290 (9%) as clinically confirmed TB cases.

In total, the contribution of PPM to TB case notification were 4,300 TB cases of all forms that is 10.6% of all TB cases notified in these eight provinces. All of them registered in public health facilities and standard treatment initiated for them.

Conclusions: The above findings show that engagement of private practitioners contributed to significant improvement in TB case notification in eight provinces. PPM DOTS should be scaled up in the other provinces which have urban setup and large number of private practitioners.

EP-15-247 Experiences of private health providers in increasing TB notification in two large urban districts in Uganda

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Background: Private health providers (PHPs) engagement in tuberculosis (TB) services is a key initiative to increase TB notification. However, there is limited information on perspectives of PHPs regarding provision of TB services. We assessed PHPs' experiences on participation in a TB notification project in Kampala and Wakiso districts in Uganda.

Design/Methods: Between October 2019 and February 2021 we trained and equipped PHPs (community pharmacies and drug shops) to screen for TB using the WHO symptom screen and collect sputum. Samples were transported to public GeneXpert sites via the hub transportation system. Results were relayed by text messages and hard copies. An incentive of USD 1.5 was given per sample collected and USD 5.0 for each TB patient diagnosed. To evaluate provider experiences on TB screening, we conducted in-depth interviews using the phenomenology theory on purposively selected PHPs. Interviews were transcribed, coded and themes generated.

Results: We identified 460 PHPs, 188 accepted to participate in the project with 133 retained until project completion. Seventeen PHPs participated in the interviews. Common positive experiences shared by PHPs dwelled on satisfaction that; project training increased their competence in TB screening; screening yield increased through targeted screening based on cough or antibiotic request; ability to identify TB patients; timely sample collection and delivery of supplies (like sputum containers) and the financial incentive. TB services increased their rapport with clients, marketed their businesses and were easily incorporated in their work.

Demotivation factors identified included: occasional delay to pick samples and return of results. Regarding clients, some refused TB services due to fear of being quarantined in case found with Covid19.

Conclusions: We demonstrate that with provision of appropriate training and supplies, PHPs can readily provide TB services using the hub and spoke model. Delays in sample pick-up or result delivery may be demotivating factors.

EP-15-248 Outsourcing cartridge-based nucleic acid amplification testing to private laboratories under Project JEET in Uttar Pradesh, India

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Background and challenges to implementation: According to the National TB Elimination Program (NTEP), all TB patients, public or private, should be offered CBNAAT service to determine Rifampicin resistance. However, the Turn-Around-Time (TAT) for private-sector patients is a concern as most of the NTEP CBNAAT sites were found to be saturated. As per the NTEP Partnership guidelines, Joint Efforts for Elimination of TB (JEET), a project to extend quality TB services to private patients, proposed to procure and outsource the testing services to the private sector CBNAAT laboratories.

Intervention or response: CHRI, one of the implementers of JEET, contracted two private laboratories to work with 78 facilities catering to 170 private providers in eight districts. Laboratories were selected after a mapping and cost analysis by market survey. Health facilities were selected which faced high TAT, poor performance in CBNAAT uptake, and linked to public CBNAAT facilities with test load higher than 250 tests /month. Private providers were offered a paper voucher to prescribe CBNAAT and to track the utilization.

Results/Impact: With two phases of implementation, four districts from Sept-2020 and another four from Dec-2020 respectively, till March-2021, 7,600 samples had been processed with a detection rate of 47%. CBNAAT uptake among the engaged facilities has reached 65% as compared to 36% during the same period in the previous year, and 39% among non-engaged facilities. Microbiological confirmation improved from 22% to 43%. TAT, earlier in the range of 3-8 days, improved to 1-2 days. Though these facilities contributed 36% to the districts' total notification, their contribution to districts' CBNAAT uptake and microbiological confirmation was 48% and 49% respectively.

Conclusions: The intervention demonstrates the feasibility of outsourcing CBNAAT to private laboratories and its effect on TAT. The positive behavioral change observed among private providers towards microbiological confirmation and DST for TB diagnosis, emphasizes the need for scaling up this model for TB elimination.

Improving quality of TB care

EP-16-249 A structured assessment of infection prevention and control measures against TB and Covid-19 among healthcare workers in the Philippines

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Background and challenges to implementation: Outbreaks of diseases like TB and COVID-19 emphasize the need for robust Infection Prevention and Control (IPC). IPC measures reduce healthcare-associated infections like TB and COVID-19 by 30%. In April 2020, the proportion of healthcare workers (HCWs) in the Philippines infected with COVID-19 was higher than the average in the Western Pacific Region, 13% vs. 2%. Although TB prevalence among HCWs in the country is unknown, studies show that HCWs could account for almost 20% of the national TB incidence. High infectious disease incidence among HCWs implies high nosocomial infection rates, which may be due to poor IPC implementation.

Intervention or response: We surveyed 212 health facilities to assess WHO's IPC framework of Administrative, Environmental, and Respiratory Protection Components, including HCW TB screening and treatment. We used a composite scoring system where each survey item was scored. The sum of all scores served as the IPC composite score, and 90% was considered the passing mark. International and national IPC guidelines were used as standards to compare performance.

Results/Impact: While most facilities implement IPC, few are implementing according to recommendations. Overall, only 3 (1%) had passing scores. Ninety-four percent have TB IPC guidelines, but 43% have not conducted an annual TB risk assessment. In 35% of the facilities, HCWs are not routinely trained on TB IPC. Twenty-one percent have no HCW TB screening program in place, and in 53%, HCWs have no access to occupational health services. In 48%, ventilation systems are irregularly maintained; in 90%, no Ultraviolet Germicidal Irradiation (UVGI) units are installed. Fifty-eight percent have no respiratory protection programs.

Conclusions: IPC implementation in health facilities needs significant improvement to reduce nosocomial disease transmission among HCWs. HCW surveillance programs, including respiratory protection programs, must be institutionalized. Air ventilation systems should be installed and maintained. Data systems to track IPC implementation and outcomes must be strengthened.

EP-16-250 Evaluating the impact of developing and implementing a multi-sectoral accountability framework for TB control at the district level in Badin, Sindh Province of Pakistan

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Background and challenges to implementation: TB constitutes a major health challenge for Pakistan. The 2018 TB United Nations declaration sought establishment of Multisectoral Accountability Frameworks (MAF) at national and sub-national levels. Pakistan decentralized health to provincial level in 2011 and subsequently the Sindh province abolished all provincial programs, recognizing districts as the hub of health activity. The MAF was launched in a district of Sindh during 2019, following a consultative process.

Intervention or response: The Dopasi Foundation and Stop TB Pakistan supported by the Stop TB Partnership, engaged the provincial Health Minister, Speaker Provincial Assembly, legislators and senior functionaries of social sectors including Population Welfare, Women Development, Education Planning, Finance, Labour, Social Welfare and social safety nets in Sindh to highlight this international commitment for TB elimination.

The plan was endorsed by development partners, academicians and public health experts seeking a TB Free Sindh, with nomination of Badin as a model district. 2 day stakeholders preparatory workshop held in Badin for project launching, delineated the role of all sectors and health programs in supporting End-TB efforts, led by the Deputy Commissioner with continuous monitoring and follow up.

District Multi Sectoral Accountability Framework (2020 - 2022)										
Commitments		Actions		Who is Accountable				How these accountable are held accountable (Monitoring, reporting and review)		
Components	Targets and Timelines (Commitments)	Activities planned to be undertaken through this MSAF (Intervention Actions)	Commitments (DHQA, CDPA/WHO, FBO, Philanthropists, TB Services, District Community Representatives)	Health Service Delivery Unit (BHU, BNU, BMC/WHO, DOPASI/WHO/UNICEF, DC Office /TPI/NDCC/ ART Centre /Private Practitioners)	District Leadership (DC Office / EDO (H))	Provincial & National Institutions (PFI/ NTP /DOP / Technical / Logical / Support Units / EC /Development Partners)	MS Engagement Sections (Capacity / Population / Finance / Labour / Social Welfare / Women Empowerment / Labor, Bank of Madh, Elbas, School Subsidy)	DOPASI / STP	Monitoring & Reporting	Review

Results/Impact: After a problem analysis, reviewing critical gaps, identifying synergies, role of civil society and social security nets and mapping community services, MAF got underway in Badin. During 2020, 2,519 TB cases were notified as compared to 2,464 in 2019, depicting a nominal increase, despite an overall decline

of 17% in TB notifications owing to COVID-19, while promoting self-reliance, pooling of resources and comparative advantages of each partner

Conclusions: This extremely cost-effective exercise based on WHO principles showed promising results, although the COVID-19 related disruption rendered a program evaluation impractical. The experience underlines the imperative for establishing similar structures at provincial level to bring the social sectors closer with enhanced intersectoral action in pursuit of the SDG 2030 targets, including TB elimination

EP-16-251 Using patient pathway analysis to accelerate TB case notification and successful treatment in Tanzania

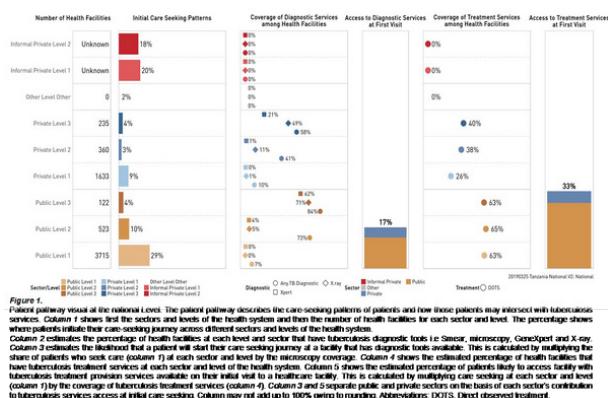
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Background and challenges to implementation: Tanzania is one of the thirty countries with a high-endemic Tuberculosis (TB) burden in the world with the TB incidence rate reported to be 253/100,000 in 2019. Only about half (53%) of new cases of TB are notified and treated annually whereas over 60,000 TB cases are missed by the TB program. Finding the missing TB patients requires information on patient's care-seeking patterns as well as the gaps in accessing TB diagnosis and treatment within the health system.

Intervention or response: A patient pathway analysis was completed at national and regional level to assess alignment between patient care initiation and the availability of diagnostic and treatment services.

Results/Impact: Less than half (43%) of all TB patient in Tanzania initiate care in the public sector even though coverage of TB diagnostic services nationally and across the health sector levels is higher in public facilities compared to private facilities. Nationally, only 17% of TB patients encountered at least one TB diagnostic technology at their point of care initiation of which, about 3% contributed by private facilities. Similarly, only 33% of patients-initiated care in facilities that had the capacity to offer tuberculosis treatment. Tuberculosis treatment was more likely to be available in public health facilities and in higher-level private sector facilities. Only 3% of patients initiating care in private sector were likely to access TB treatment on their first visit.



Conclusions: The results indicate that there is misalignment between availability of TB services and patient care-seeking behaviours in Tanzania. This could be remedied through a targeted expansion of treatment services to better meet patients where they initiate care. The PPA findings also highlight the role of private sector in TB diagnosis and treatment and therefore, it is crucial that private sector notifies TB cases so as to reduce number of missing cases in the country.

EP-16-252 Use of point-of-care haemoglobin measurement for monitoring patients receiving treatment for multidrug-resistant TB: lessons from Uganda

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Background and challenges to implementation: Uganda rolled out use of all-oral treatment regimens for the management of Multidrug resistant Tuberculosis (MDR-TB). The use of new and repurposed medicines requires rigorous clinical- and laboratory-monitoring of patients receiving treatment for MDR-TB for prompt detection and management of adverse events. However, the MDR TB treatment sites perform laboratory tests for people with MDR TB sporadically, due to machine downtime and stock out of reagents. This would in turn increase the catastrophic costs of people with MDR TB as they outsourced them privately and also suffer from severe adverse drug reactions that compromise treatment outcomes. We documented lessons from HB point of care (POC) implementation in a large MDR TB hospital in Uganda.

Intervention or response: The USAID Defeat TB project procured and supplied HB POC machines with strips to her seven directly supported sites. People with MDR TB who, according to national guidelines were due for a full

blood count test but were unable to have it had their HB done by these POC machines, results recorded in patient files and those with HB less than 10mg/dl were flagged for intervention, with hematinics and/or transfusion as per the national guidelines

Results/Impact: A total of 78 (54 male and 24 female) people with MDR TB in Mulago hospital who started all-oral treatment regimens from October 2019 to April 2021 but unable to do baseline and monitoring tests were analyzed using HB POC equipment as part of monitoring. A total of 143 tests were conducted out of which 22 (15%) patients had an HB below 10mg/dl and promptly received intervention.

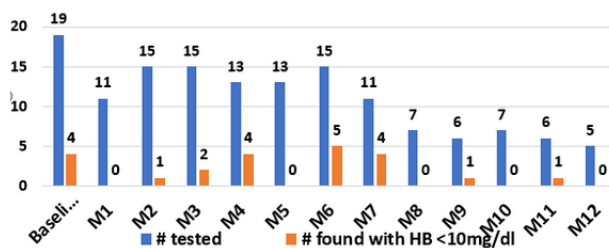


Figure. Hemoglobin level monitoring results (Oct '19 - April '21)

Conclusions: Point of care HB estimation is a critical intervention for active drug safety monitoring (aDSM) among people with MDR TB. We recommend the scale up of this intervention across all the MDR TB treatment sites to optimize aDSM and treatment outcomes.

EP-16-253 Improving access to TB services: formulation of workplace policy on TB in Jharkhand, India

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Background and challenges to implementation: Jharkhand is rich in Industry and mines. People working in mines and industries are vulnerable to occupational hazards including Tuberculosis combined with lack of awareness, access, and poor linkages. Stigma and discrimination at the workplace also play a key factor in not accessing TB services.

Improving awareness and improved uptake of services among the miners and industry workers through formulating a policy for the State will be a step closer to eliminating TB.

Intervention or response: Several advocacy and consultative meetings were conducted with twenty six industry houses and mining companies along with Departments of Industries, Mines, Labor and Health along with workers' union in the state. A draft on the Workplace policy for TB and occupational lung diseases was discussed during the state-level workshops to reach a consensus. The draft was further shared with Industries, mines, representatives of various workers' union, and departments for inputs. The workplace policy was finalized and put up with the Jharkhand cabinet for approval. The policy provides an operational framework For all stakeholders in the world of work for creating an enabling environment to prevent new TB infections, early case detection, access to free diagnosis and treatment adherence to treatment, and focus on co-morbidities.

Results/Impact: Two years of continuous advocacy with multiple stakeholders to frame a workplace policy resulted in cabinet approval and adoption of "Workplace Policy on TB and its comorbidities including occupational lung diseases". The policy was adopted by the cabinet of Jharkhand on December 23, 2020. Jharkhand is the first state in India to have adopted a workplace policy on TB.

Conclusions: The vulnerability of industry and mining workers to TB is high, as part of the TB elimination efforts, this policy and its implementation will help in spreading awareness, ensuring standard treatment, reducing stigma and discrimination, and better working conditions for the workers.

EP-16-254 Exploring the association and intersectionality of sex, race and homelessness with adverse TB treatment outcomes in Brazil: a retrospective cohort study

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Background: Brazil is one of the 30 high tuberculosis (TB) burden countries and has treatment success rates below WHO targets. Limited work has attempted to understand the overlap between risk factors for adverse treatment outcomes. We evaluated the intersection of sex, race, and experiencing homelessness in relation to adverse TB treatment outcomes in Brazil.

Design/Methods: This was a retrospective cohort with 451,998 individuals notified with TB in Brazil between 2015-2019. The outcome was adverse TB treatment outcomes. Univariable and multivariable logistic regressions were used to calculate crude and adjusted associations between the study outcome and homelessness, sex, and race/ethnicity after accounting for additional demographic and clinical covariates. Adjusted probabilities were calculated conditional on the 20 intersecting profiles of sex, race, and homelessness.

Results: Overall, 101,019 (25.22%) investigated individuals experienced unfavorable TB treatment outcomes. In multivariable regression, sex, race, and homelessness were each significantly associated with the outcome. Among people experiencing homelessness who are male, black persons showed the highest probability of having adverse TB treatment outcome, 45% (95% CI: 0.44-0.46), versus brown/mixed 43% (95% CI: 0.42-0.44); Asian 42% (95% CI: 0.39-0.44); 39% white (95% CI: 0.38-0.40); and indigenous 34% (95% CI: 0.32-0.36). Among homeless women, black persons showed the highest probability, 41% (95% CI: 0.40-0.42), versus for brown/mixed 39% (95% CI: 0.38-0.40); Asian 38% (95% CI: 0.35-0.41); white 35% (95% CI: 0.34-0.36); and indigenous 31% (95% CI: 0.29-0.33). Not experiencing homelessness was associated with lower probabilities in all sex-race overlapping groups, although black and brown/mixed men and women still showed a higher likelihood than their white counterparts.

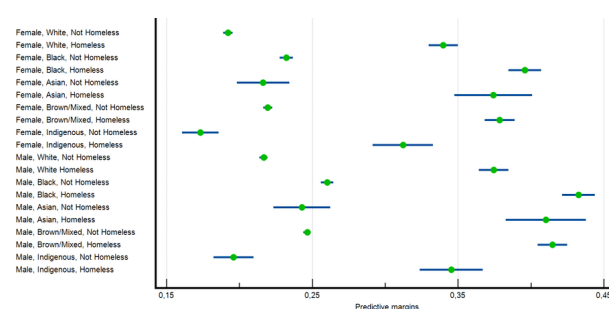


Figure. Probability of unfavorable TB treatment outcomes as per intersectional profiles of sex, race and homelessness (95% CI)

Conclusions: People experiencing homelessness, especially those of black or brown/mixed race, notably males, are at greatest risk of an adverse TB treatment outcome. Reinforcing vulnerabilities suggest the need for targeted social and adherence support for underserved people with TB in Brazil.

EP-16-255 Best practices and challenges of TB active case-finding (TB Surge) in tertiary institutions in Nasarawa State, Nigeria

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Background and challenges to implementation: TB Active Case Finding intervention (TB SURGE) was instituted in April 2020 in two high volume tertiary institutions in Nasarawa State to improve TB diagnosis. Ad-hoc Staff were engaged to screen all patients seeking care at the service delivery points, identify and ensure evaluation of presumptive TB using GeneXpert or Chest X-ray. Reporting of presumptive TB outcomes were poor with evaluation rates less than 65% due to identified gaps in the evaluation cascade reporting and feedback from the lab to the DOTS centers.

Intervention or response: The intervention to improve on the evaluation rate was instituted in July 2020 and ad-hoc staff were mandated to ensure presumptive TB clients who could provide sputum samples did so and were immediately sent for GeneXpert testing. To close the feedback gap in the evaluation cascade, the staff were mandated to indicate "SURGE" on all sample request forms. Lab staff were encouraged to prioritize samples bearing SURGE to increase turnaround time and improve reporting and feedback. Results were retrieved by the ad-hoc staff daily and documented in the National presumptive register

Results/Impact: Since the start of the period of implementation of this strategy evaluation rates rose steadily from 28% in April 2020 to 93% in March 2021. Despite a slight dip in September, the evaluation rate did not drop to the pre-intervention period of <65%. This contributed to a 20% increase in TB case finding in these two facilities.

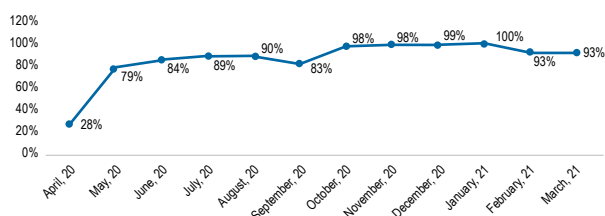


Figure. Evaluation rate trend from 2 tertiary hospitals.

Conclusions: Prioritizing TB samples in a high-volume facility based active TB case finding intervention, engagement of ad-hoc support staff and active retrieval of lab results offers best practices in improving evaluation rates especially in busy tertiary facilities

EP-16-256 Nurses' attitudes towards mental health: research to inform the integration of mental health and TB services in a South African metropolitan area

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Background: In South Africa, there is a concerted effort to integrate mental health services into existing primary healthcare (PHC) programmes such as tuberculosis (TB). As the quality of service delivery and patient treatment outcomes are partially dependent on health workers' attitudes, this study examined nurses' attitudes towards mental health patients and the field of mental healthcare.

Design/Methods: The study followed a cross-sectional design among 205 PHC nurses in a South African metropolitan. Structured self-administered questionnaires included socio-demographic questions and the Mental Illness Clinicians' Attitudes (version 4) scale. Data were subjected to descriptive and logistic regression analyses. Statistical significance was determined at 95% confidence interval (CI) and $p < 0.05$.

Results: The nurses' mean attitude score was 40.68 (± 9.70). However, over two-fifths ($n = 91$; 44.4%) of nurses scored higher than the mean score, implying negative attitudes towards mental health patients and mental healthcare. From univariate analysis, age >40 years (odds ratio [OR]: 2.3; CI: 1.20-4.33), lack of prior in-service training on mental health (OR: 1.8; CI: 1.03-3.24), being an enrolled nurse/nursing assistant (OR: 4.3; CI: 2.30-7.95), and self-reported non-referral of patients for mental health evaluation (OR: 2.2; CI: 1.14-4.23) were significantly associated with negative attitudes.

After controlling for other variables in the model, the odds of negative attitudes towards mental health patients and mental health care were 3.1 (CI: 1.48-6.28) times higher among nurses older than 40 years relative to their younger counterparts, and 4.1 (CI: 1.70-9.73) times higher among enrolled/assistant nurses compared to professional nurses.

Conclusions: Results suggest that a significant proportion of nurses harboured negative attitudes towards mental health patients and the field of mental healthcare. Successful integration of mental health into PHC programmes including the TB programme necessitates improving nurses' attitudes towards mental health patients, mental health service delivery and outcomes, particularly among older nurses and junior cadres.

EP-16-257 Contribution of active household contact screening to TB case notification in Afghanistan

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Background and challenges to implementation: National TB Programs (NTP) recommended active household contact screening for many years, but the implementation process was poor. During the implementation, some barriers and challenges identified, including lack of appropriate management structure and screening tools, lack of human resources, low community awareness, and poor adherence to Isoniazid Preventive Therapy (IPT). NTP Afghanistan implemented active contact screening in 2020. However, active household contact screening can be time consuming and expensive, and the yield needs to be carefully evaluated to determine when it is most effective. This study focuses on results of active contact screening in 2020.

Intervention or response: NTP agreed that healthcare workers contacted and permission is requested to visit households of index cases. Household contacts investigated for TB sign and symptoms, followed by sputum microscopy examination. The intervention strategies included training of health care staffs, conducting supervision, collecting data, providing feedback, and contacting a random sample of 20% of TB index case contacts for cross check. All household contacts of index TB cases were visited by health facility members. Household contacts with cough for more than two weeks and sputum were taken to the nearest TB diagnostic health facility for sputum examination. Children under 5 years of age were registered to the TB contact register and received IPT.

Results/Impact: About 24,229 TB index cases were registered; 145,376 household contacts identified and 31,564 presumptive TB screened. Among them, 4,931 (15.6%) TB cases identified and 25,035 (17.2%) children under 5 put on IPT (Table 1). Considering the total number of household contact for all notified TB cases, the incidence of TB among household contact is 3391/100,000 which is 12 times higher than estimated cases (189/100,000).

Conclusions: TB among household contacts is much higher than WHO estimated incidence cases. We recommend strengthening active contact screening nationwide.

EP-16-258 Household contact tracing contributes significantly to finding missing TB cases in pastoralist communities of Karamoja sub-region, North Eastern Uganda

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Background and challenges to implementation: In the Karamoja sub-region, crowded settlements and poorly ventilated households increase the risk of tuberculosis (TB) transmission. In June 2020, the USAID PACT Karamoja project started implementation of household contact tracing for patients with bacteriologically confirmed TB using both health workers (HWs) and community-owned resource persons (CORPs). We aimed to document the yield from this intervention.

Intervention or response: Every month, we line-listed household and close contacts of patients diagnosed with bacteriologically confirmed TB and screened them for TB using the WHO symptom screen. Contacts who were positive for any of the four symptoms had their sputum examined by Xpert® MTB/RIF testing. We analyzed the yield from contact screening using counts and proportions.

Results/Impact: From July to December 2020, household contact tracing was done for 699 index patients. A total of 3122 contacts were screened (2004 by HWs and 1118 by CORPs).

Out of 2004 contacts screened by HWs 43.7% (876/2004) had presumptive TB and of these, 86.4% (757/876) were tested with GeneXpert testing and 8.5% (64/757) diagnosed with TB.

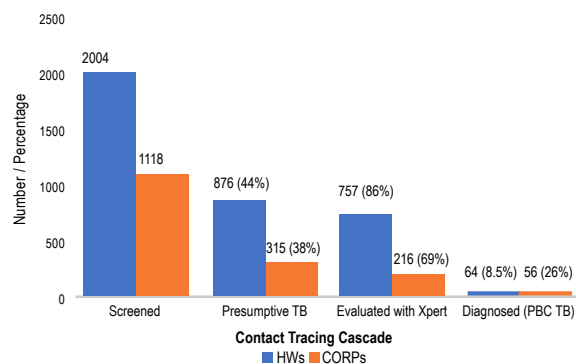


Figure 1. TB Contact Tracing Cascade for healthcare workers and CORPs in the Karamoja sub-region.

Additionally, 39(4.5%) of the contacts were clinically diagnosed with TB were initiated on treatment. In comparison, 28.2% (315/1118) of household contacts

screened by CORPs had presumptive TB and of these, 68.6% (216/315) were tested with GeneXpert testing and 25.9% (56/216) diagnosed with TB. Contact tracing contribution to TB cases notified by the sub-region increased from 3.8% in April to June 2020 to 7.4% which was much higher than the national average of 4.5% over the same period.

Conclusions: Household contact tracing contributed significantly to finding missing TB patients in rural hard to reach populations. Additional interventions to improve retention along the cascade of care for patients evaluated by the CORPs have been instituted to improve the yield from this model of care.

EP-17 Challenges and solutions for TB care in the time of COVID-19

EP-17-259 Sustaining performance gains in TB programming in the era of Covid-19: USAID Eradicate TB Project strategies in Zambia

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Background and challenges to implementation: The outbreak of the coronavirus disease 2019 (COVID-19) has disrupted TB service delivery world over due to movement restrictions and diversion of resources to the COVID response. Consequently, performance indicators such as TB case notification, have gone down in most countries. Zambia reported its first case of COVID-19 on March 18, 2020. Sustaining good performance has since been a priority for the Zambian TB program.

Here, we describe strategies employed by USAID Eradicate TB (ETB) Project to sustain performance gains in six provinces of Zambia.

Intervention or response: In the period March 2020 to March 2021, (COVID-19 period) Community Based Volunteers (CBVs) were airtime to remind patients of appointments, conduct contact tracing and treatment monitoring.

At health facility level, health care workers were regularly mentored virtually, and provided with PPEs, a 'patient tracking trigger form' that reminded them of patients due for follow-up, airtime to call patients missing appointments, and data bundles to attend monthly virtual data collection, reporting and review meetings.

Data on performance indicators were entered in District Health Information System, and exported Microsoft Excel for analysis.

Results/Impact: Compared to project targets, monthly coverages for TB testing for the period March 2020 to March 2021 remained above 100% (median =178.0%; IQR = 145.0,187.0). Total TB case notifications reduced from 88.5% in March 2020 to 63% in January and February 2021, but increased to 92% in March 2021 (median =74.0%; IQR = 71.0,93.0). Treatment success rate remained at around 90% (median =92%; IQR = 91.0,92.0). Lost-to-follow-up and mortality remained below 5%: medians of 3.2% (IQR = 3.0,3.5) and 3.7% (IQR = 3.3,4.1), respectively

Conclusions: In a COVID-19 pandemic situation, use of virtual and mobile platforms, and a 'patient tracking trigger form' helped sustain performance gains in the TB program in ETB supported provinces. We recommend adoption of these strategies by other TB programs.

EP-17-260 Empowered women groups lead TB screening and diagnosis in rural Karnataka, India, during the Covid-19 pandemic

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Background and challenges to implementation: From February 2020, FIND and MYRADA, through TB REACH Wave-7 supported project, worked through empowered women-led Self-Affinity-Groups (SAGs) to reduce diagnostic access barriers for rural communities, especially, women. Active case finding (ACF) activities were planned in over 700 villages of Bellary, Gulbarga and Yadgir districts of Karnataka, India. However, towards the end of March 2020, India went into complete lockdown to contain COVID-19 pandemic threatening the project success

Intervention or response: 1200 experienced SAG women were identified, trained and engaged in TB service provision. ACF interventions between February 2020 and March 2021 included household visits for 323,493 households; special drives in 299 TB hotspots; 1905 awareness campaigns; 36 health camps and screening are done in registration and waiting areas at 10 public hospitals.

TB patients were linked to social support schemes. The project faced disruption of services including transportation during Apr-Jun'2020 due to COVID-19 pandemic and subsequently streamlined TB testing with help of NTP officials. Despite transportation challenges, SAG women assisted in specimen collection and transportation (SCT) from patients' homes to diagnostic labs.

Results/Impact: SAG women used their experience, leadership qualities, local knowledge and community engagement skills and adapted to the situation. They were able to bring the project back on track as situation started normalizing during the COVID-19 pandemic in their areas. SAG women identified 16,774 presumptive TB cases. Of these, 85% (14,324/16,774) were tested. 1,187 TB cases i.e. 8% of tested, were diagnosed and initiated on treatment. Through SAG women lead SCT, 79% (13,233/16,774) cases got tested.

919 patients were linked to social support schemes. 127 women TB patients and 696 SAG women became active TB advocates in their villages.

Conclusions: By engaging empowered SAG women and strengthening access to TB services, this TB REACH project showcased the role of local networks of empowered women in improving access and reducing TB burden.

EP-17-261 Outstanding multidrug-resistant TB outcomes with patient support during civil unrest and the Covid-19 pandemic in Haiti

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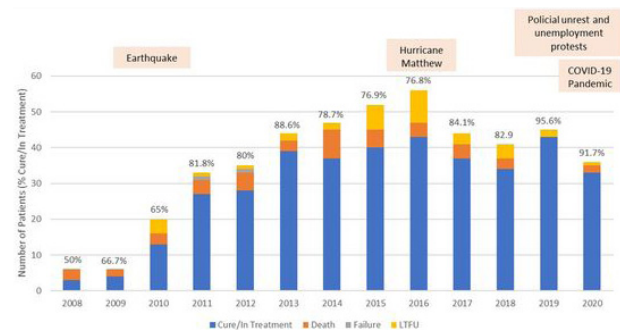
Background and challenges to implementation: MDR-TB treatment is associated with high rates of attrition worldwide. In Haiti, the COVID-19 pandemic and major civil unrest continue to create barriers for MDR-TB treatment continuation.

Intervention or response: GHESKIO in Port-au-Prince, Haiti has developed an intensive MDR-TB treatment program with directly observed treatment (DOT) and extensive patient support. Community health workers (CHW) provide daily home directly observed treatment (DOT), assess symptoms and vital signs, and photograph the patient swallowing their medications.

The CHWs activities are monitoring by mobile phones equipped with GPS. Patients who miss doses and/or visits meet with the treatment team to identify and address specific barriers to adherence. Patients are offered psychosocial support through individual counseling ses-

sions and monthly group support meetings which they attend with a treatment supporter (family member or friend). Dry food rations are provided for nutritional support, with additional enablers and incentives, including mobile phones, phone recharge cards, transportation fees, and an end-of-treatment prize (200 USD) and certificate, to reinforce adherence and increase retention. We retrospectively examined the outcomes of adults initiating MDR-TB treatment between 2008 and 2020 at GHESKIO, to assess the resilience of this system of care through the disruptions of COVID-19 and severe political unrest.

Results/Impact: The proportion of patients with successful treatment outcomes is high. In total, 381 (82%) patients have been cured or continue on treatment (338 cure, 43 on treatment), 46 (10%) have died, 36 (8%) have been LTFU and 2 (<1%) experienced treatment failure. During the peak period of disruption (2018 to 2020), 33 patients were cured (87% of those that finished treatment), which is similar to previous treatment periods ($p=0.684$).



Conclusions: GHESKIO's model of MDR-TB treatment, with extensive patient support, is associated with outstanding outcomes, in spite of the disruptions of major civil unrest and the COVID-19 pandemic.

EP-17-262 Impact of TB-Covid bidirectional screening on TB notification under the National TB Elimination Programme, India

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Background and challenges to implementation: Performance of National TB Elimination programme (NTEP), India is severely impacted by COVID 19 pandemic. NTEP initiated policy of bidirectional screening of Suspected/confirmed COVID & TB to augment case finding efforts of TB & COVID. Present study was undertaken in Maharashtra state in western India to assess status of implementation of policy and its impact on TB case notification.

Intervention or response: Prospective study in state from October 20 to March 21. NTEP staff was trained. Necessary logistics were provided from NTEP funds. NTEP officials & WHO Consultants provided monitoring support. Data was collected & analysed in excel.

Results/Impact: <10% of COVID patients were screened for TB. 12% of evaluated patients were diagnosed as TB. 9% of total TB notifications are contributed by policy of bidirectional screening. 58% of TB patients were tested for COVID. Only 2% of TB patients were diagnosed as COVID.

Conclusions: Stigma of COVID, overburdened system, suboptimal linkages are few reasons for suboptimal screening of TB amongst suspected/confirmed COVID. NTEP may strengthen linkages between COVID & TB setting. Innovations like use of same sample for COVID & TB may be considered.

Minority of suspected/confirmed COVID patients were identified as presumptive TB cases. In view of operational challenges in qualifying presumptive TB cases like stigma, unwillingness of patients for interview and intentions of NTEP to expand case finding efforts, NTEP may consider testing all suspected/ COVID patients for TB.

High yield of TB cases indicates that policy of bidirectional screening and may be strengthened further.

It indicates that establishment of COVID testing services at TB diagnostic centres is crucial to improve coverage. Study underlines effectivity of bidirectional screening specially for TB notification and captures key programme management interventions that may improve TB notification. In view of continuation of pandemic, these measures may be crucial to avert TB deaths.

EP-17-263 Impact of Covid-19 on the detection of drug-resistant TB in Ethiopia

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Background and challenges to implementation: Global tuberculosis (TB) Report 2020 estimated close to half a million Rifampicin resistant (RR) and Multi-drug resistant (MDR) TB cases in 2019. Ethiopia is one of the high DR-TB burden countries and enrolled 579 DR-TB cases to treatment in 2020. Ethiopia reported the first case of COVID-19 on March 13, 2020, since when the country has taken several mitigation and preventive measures.

Intervention or response: We evaluated the impact of COVID-19 on the detection of DR-TB in Ethiopia. We analyzed the routine national TB notification data using the district health information system from July 2019-December 2020 in Addis Ababa, Amhara, Oromia, SNNP, and Sidama regions. We described by quarter the proportions of RR/MDR-TB before and after COVID-19.

No of COVID patients reported (A)	No (%) screened for TB (B)	No (%) of presumptive TB identified (C)	No (%) of presumptive TB undergone NAAT/Microscopy (D)	No (%) micro-biologically confirmed TB cases diagnosed (E)	No (%) clinically diagnosed patients (F)	No (%) total TB cases diagnosed (G)	Total no of TB patient notified under NTEP	Total no of TB patient tested for COVID	Total no (%) of TB COVID co infected
886948	260825 (29%)	39986 (15%)	33314 (83%)	2338 (7%)	2369 (6%)	4704(12%)	54758	31632 (58%)	665 (2%)

EP-17-262 Table

Results/Impact: A total of 685 RR/MDR patients were enrolled in the five regions, of which 57% (391/685), 95% confidence interval, CI:53-61%, before and 43% (294/685), 95% CI:39%-48%, after COVID-19. The proportion of RR/MDR cases in three quarter before and after COVID-19, respectively, were: 27.4% (107/391), 34.5% (135/391), 38.1% (149/391) and 32.3% (95/294), 31.3% (92/294), 36.4% (107/294).

Quarter	N=391	n(%)	AA	Amhara	Oromia	SNNP	Sidama
Q1 (July–Sept, 2019)		107 (27.4%)	37	30	30	9	1
Q2 (Oct–Dec 2019)		135 (34.5%)	42	38	38	10	7
Q3 (Jan–Mar, 2020)		149 (38.1%)	46	37	42	14	10
	N=294	n(%)					
Q4 (Apr–Jun., 2020)		95 (32.3%)	25	22	34	5	9
Q1 (Jul–Sept, 2020)		92 (31.3%)	17	22	37	9	7
Q2 (Oct–Dec, 2020)		107 (36.4%)	33	17	34	17	6

Table. The proportion of confirmed RR/MDR TB Cases in five regions by quarter, July 2019–Dec, 2020

Conclusions: Our analysis indicates a significant declined in RR/MDR case notification following the emergence of COVID-19. To Maintain the progress TB/COVID-19 diagnostic integration needs to be strengthened and access to mWRD including using GeneXpert as a primary testing tool.

EP-17-264 Comparison of Covid-19-related TB resource reallocation in Afghanistan and Kyrgyzstan

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Background: In 2020, the COVID-19 pandemic ravaged health systems worldwide. During this time, tuberculosis (TB) programs were particularly hard hit given the overlap in medical equipment, laboratory systems, and clinical expertise needed to combat both diseases. Understanding the extent of resource reallocation will help program managers assess potential gaps in TB services and focus efforts to ensure minimal loss of progress in the fight to end TB in the post-COVID-19 era.

Design/Methods: A quality of TB services assessment (QTSA) was conducted in randomly selected health facilities in Afghanistan (N=248) and Kyrgyzstan (N=258) between November 2020 and March 2021. The tool included a module on COVID-19 designed and piloted to examine its impact on TB services and resource availability, providing a unique opportunity to document TB resource reallocations in two distinct contexts.

Results: Thirty-four percent and 16% of facilities assessed in Kyrgyzstan and Afghanistan, respectively, reported TB resources reallocated to their COVID-19 responses. Results show that while higher-level facilities appear to have borne the significant brunt of resource reallocation in both countries, primary healthcare facilities in Kyrgyzstan reported some degree of resource reallocation. Table 1 summarizes the findings for physical, financial, and human resources reallocated among the facilities in each country. Results show that among facilities reporting resource reallocations, clinic and laboratory space reallocation was more common in Afghanistan than Kyrgyzstan, while both countries reported high levels for reallocating TB service providers.

Reallocated resources*	Afghanistan	Kyrgyzstan
TB healthcare providers	67%	90%
Laboratory personnel	67%	20%
In-patient beds**	68%	50%
Clinic space	80%	45%
Laboratory space	60%	18%
Masks	97%	82%
Gloves	97%	82%
Budget originally allocated for TB		

*Results from Afghanistan based on 39 health facilities that reported TB resource reallocation to COVID-19 and results from Kyrgyzstan based on 89 health facilities that reported TB resource reallocation to COVID-19

**Only asked of facilities providing in-patient services

Table 1. Types of resource reallocation reported by facilities in Afghanistan and Kyrgyzstan.

Conclusions: The assessment highlighted the varied impact on TB resources in Afghanistan and Kyrgyzstan in the wake of the COVID-19 pandemic. Results revealed stark differences in the scope and types of TB resources reallocated in response to COVID-19, calling for tailored responses in each country. Understanding the details and context of these reallocations can assist national TB programs in prioritizing newly formed gaps that may threaten progress in the fight to end TB.

EP-17-265 Sustaining TB interventions in times of Covid-19: experiences from a TB Alert India project

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Background and challenges to implementation: COVID-19 induced lockdown had a very devastating effect on the services of TB. People with TB like symptoms (PTS) were not able to go for testing due to lockdown There was very low uptake of TB testing and treatment services, fearing contracting COVID. TB Alert India (TBAI) is implementing a project titled “RIPEND” supported by STOP TB Partnership working closely with informal providers, in slum and Semi-urban setting. Some additional activities were taken up to tackle the above mentioned COVID induced situations.

Intervention or response: RIPEND project enrolled 1586 informal health care providers across 18 Tuberculosis Units (T. Us) in Telangana state, India. Enrolled providers screen PTS and register them with a mobile-based digital application and motivate to get tested at National TB Elimination Program (NTEP) clinics.

Sample collection & Transportation (SCT) at door step, tele-counselling through call centre and free transportation services for Chest X-ray were taken up as innovative activities during lockdown, to reduce the impact.

Results/Impact: From Apr to Sept 2020, 16% (384 of 2421) of the samples transported reported TB. Among the 3723 calls attended at call centre 174 PTS were referred for testing and 6% (10) diagnosed with TB.

Around 532 PTS who utilised free transportation for Chest X-ray, 21% (110) reported lesions suggestive of TB. These activities attributed to 99% (6739 of 6790) of the PTS tested in these two quarters.

Notification of TB patients to NTP increased by 8% in Apr -Sept'20 (during COVID) in comparison to Oct 2019 to Mar 2020 (before COVID). Project contributed 28% of the total TB patients notified in T. Us during COVID, it was 15% before COVID.

Conclusions: Effective planning and strategies in times of COVID -19 will help is sustaining the efforts of TB programs.

EP-17-266 Door-to-door services improved TB case identification during the Covid-19 pandemic in Dokolo District, Uganda

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Background and challenges to implementation: In April 2020, Uganda instituted COVID-19 restrictions on public gatherings and transport. These restrictions affected community TB activities including TB hotspot mobilization and screening at a designated place and the ability of TB patients to seek treatment at healthcare facilities.

While Uganda's Ministry of Health (MOH) had declared tuberculosis an emergency, the COVID-19 measures disrupted TB case identification efforts. In June 2020, the MOH published guidelines for healthcare workers on the integration of TB and COVID-19 screening at the facility, however, TB case notification remained low due to reduced outpatient attendance and gaps in mechanisms to reach communities with TB services.

In Jan-Mar 2020, before COVID-19 restrictions Dokolo district in northern Uganda, notified 81 TB cases, during the subsequent two quarters, we noticed a gradual decline to 67 in April-June 2020 and 59 in July-September 2020.

Intervention or response: In response to these challenges, in October 2020-Mar 2021, the project scaled up efforts for targeted community door-to-door sensitization and sample collection in Dokolo district in compliance with Government COVID 19 restrictions Key support included; Register review and mapping TB hot spots by the District TB and Leprosy Supervisor, Village Health Team members and interpersonal communication (IPC) agents; use conversational story cards to sensitize on TB basic facts, prevention, care and treatment; sputum sample collection from symptomatic individuals.

Results/Impact: In October-December 2020 and Jan-March 2021, 80 and 75 TB cases respectively were identified a rise to the pre-COVID 19 period.

Conclusions: Mapping and conducting targeted door-to-door TB interpersonal communication, community sensitization and screening in the context of COVID-19 improves TB case finding and is recommended for scale up.

EP-17-267 Health worker experiences in public sector TB units responding to Covid-19 in Uganda

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Background: COVID-19 pandemic disrupted delivery of TB (Tuberculosis) services worldwide. Little is known about the effect of this on TB health workers' psychosocial and physiological well-being. To understand health worker stress and burnout, and its impact on TB services, we explored the experiences of health workers engaged in public-sector TB care in Kampala, Uganda during COVID-19.

Design/Methods: We conducted a cross-sectional qualitative study of health workers involved in TB evaluation and care at six public health centres in Kampala, Uganda between August and September 2020. All health workers currently attending to TB patients were included. Three trained interviewers contacted eligible health workers by telephone for a recorded, semi-structured interview in Luganda or English.

We probed respondents' health work setting, areas of work life, and perceived stress. Interviews were transcribed verbatim and analyzed for emergent themes using conventional content analysis.

Results: We interviewed 29 health workers, including 10 community health workers, 7 laboratory technicians, 4 TB unit in-charges, 6 nursing officers, 1 senior clinician, and 1 medical officer. The health workers described stress associated with a changing work environment and changes to routine practices. Their fear of exposure to COVID-19 was exacerbated by their perception that resources provided by the Ministry of Health to secure a safe work environment were uncoordinated. Their motivation was greatly affected by the increasing expenses associated with trying to meet the job requirements, such as transport costs to the clinic and transporting drugs to homes of patients.

However, they said they were motivated to continue delivering TB services by commitment to their patients, requests from patients, and the privilege of being an essential worker.

Conclusions: We document experiences of TB providers during onset of the COVID-19 pandemic. TB providers were sustained by a strong sense of mission and responsibility early in the pandemic, but reported unsustainable levels of work-related stress.

Providing quality care for drug-resistant TB

EP-19-278 Sustaining implementation and strengthening active drug safety monitoring and management system for drug-resistant TB in the Philippines amidst the Covid-19 pandemic

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Background and challenges to implementation: With the introduction of new drugs and regimens for multidrug-resistant tuberculosis (MDR-TB) treatment, the active drug safety monitoring and management (aDSM) framework was integrated in and implemented through the national MDR-TB treatment guidelines in 2016 to safeguard patients from drug-related harms. However, systematic and standardized data collection, analysis, and reporting, which are essential components of aDSM, were not fully implemented.

Intervention or response: In 2019, interim MDR-TB treatment guidelines were issued by the Department of Health (DOH). A pharmacovigilance focal person was appointed at the National Tuberculosis Control Program (NTP).

An interim National aDSM Taskforce (NAT) with focal persons from relevant government offices and partners was formed. Trainings were conducted for both NAT members and service providers. A mechanism to report adverse events (AE) to NTP by email was created. Reported AEs were vigilantly screened and followed-up. The NAT conducted quarterly causality analysis (CA) of reported AEs and shared feedback during NTP activities. In mid-2020, DOH issued policy and guidelines for aDSM implementation.

Results/Impact: Despite the COVID-19 pandemic in 2020, reported AEs increased substantially, 8.8 times (64 vs 563) from 2019. Regional and facility coverage of AE reporting increased to 94% and 55%, respectively in 2020 compared to 29% and 12%, respectively in 2019. Forty-seven percent (47%) of reported AEs were serious AEs.

The top three reported AEs of special interest were hepatotoxicity (33%), peripheral neuropathy (23%), and myelosuppression (14%), which have probability relationships to Pyrazinamide and Linezolid.

Through regular CA, variable quality of clinical AE management across facilities was identified. Subsequently, NTP released a memorandum outlining proper management of such AEs.

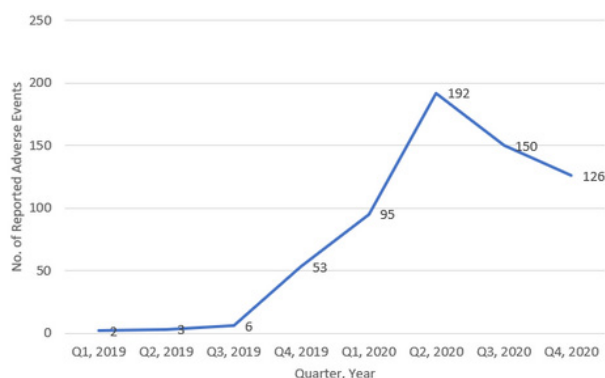


Figure 1. Frequency of quarterly reported serious adverse events and adverse events of special interest, 2019-2020, Philippines.

Conclusions: Sustaining a comprehensive aDSM system is possible amid the COVID-19 pandemic through strategic collaborative design, updated policy guidance, competent staff, and reporting and feedback mechanisms. Regular AE reporting and CA significantly contribute to properly monitoring and improving quality of MDR-TB care.

EP-19-279 Where is the gap? The rifampicin-resistant TB care cascade in a tertiary hospital in Indonesia

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Background: Management of Rifampicin-Resistant TB (RR-TB) can be challenging, both in terms of diagnosis and treatment especially in high burden TB countries. In Indonesia, many RR-TB patients remains undiagnosed and little is known about the quality of RR-TB management.

Design/Methods: We performed a retrospective cascade-of-care analysis for all presumptive RR-TB patients between 2015 and 2018 in Hasan Sadikin General Hospital, a tertiary hospital in Bandung, West-Java. We present quality of care and timeframe indicators for the cascade-of-care which consisted of presumptive RR-

TB cases and performed Xpert-MTB/RIF sputum tests, Xpert-MTB/RIF-diagnosed RR-TB, pre-treatment baseline testing, treatment initiation, appropriateness of treatment regimens, and completion of treatment. Median time between care cascade steps was measured by Kaplan Meier analysis.

Results: Through 2015-2018, we identified 9665 presumptive RR-TB cases for which Xpert-MTB/RIF results were available in 96%. Of those tested (n=9306), 10.6% were newly diagnosed RR-TB. Of those diagnosed (n=981), 90.9% went through baseline investigations, and 80.5% started second line treatment. In retrospect, of those starting treatment (n=790), 59% were supported by results from phenotypic drug-susceptibility testing (DST), and 45% were started on appropriate 2nd line treatment. Among those treated, 32.7% finalized their intensive phase and 26.6% completed the care cascade successfully on an appropriate 2nd line regimen. One in five patients starting treatment died during treatment. Major time delays were found just before baseline testing and initiation of treatment, with median time (IQR) taken of 11 (5-20) and 8 (6-11) days, respectively.

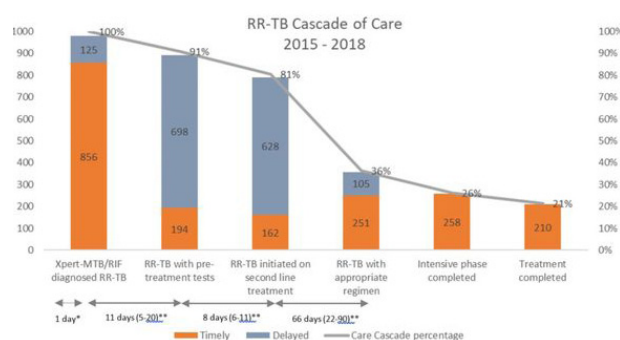


Figure.

Values in the chart indicate numbers (columns) and percentages (line). *Median time between Xpert-MTB/RIF results and sample collection, delay defined by more than 2 days. **Median time (IQR) with time delay defined by more than 4, 3 and 84 days, respectively.

Conclusions: A minority of RR-TB patients as diagnosed by Xpert-MTB/RIF in Indonesia currently receives appropriate 2nd line treatment. Major delays occur at baseline testing and treatment initiation phase. Further interventions should be focused on improving access to early case identification, culture-based DST, and treatment decentralization.

EP-19-280 Integrating care for persons with rifampicin-resistant TB and substance use disorders in Khayelitsha, South Africa

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Background: Substance use (SU) is associated with poor rifampicin-resistant tuberculosis (RR-TB) treatment outcomes. In 2017, Médecins Sans Frontières and the Department of Health integrated SU screening, a brief intervention, and referral to treatment (SBIRT) into the RR-TB treatment program in primary health care clinics. We describe SU screening and RR-TB treatment outcomes.

Design/Methods: This was an observational cohort of patients with RR-TB who were screened for SU between October 2017 and July 2020 in Khayelitsha, South Africa using the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). Patients who scored moderate or high-risk were referred to a SU support group; those with moderate or high-risk alcohol use were additionally referred for naltrexone treatment. We describe the number screened and risk categorization and the number started on naltrexone. RR-TB outcomes for those screened ≤ 2 months of starting RR-TB treatment were reported stratified by risk classification.

Results: One-hundred-and-fifty-four RR-TB patients were screened for SU; 135 (88%) patients reported SU, with 105 (78%) scoring moderate or high-risk for ≥ 1 substance. The median time from RR-TB to SU screening was 2.6-months (IQR 0.7-8.8). One-hundred-and-twenty-two (79%) patients reported alcohol use; 69 (69/122, 57%) reported moderate or high-risk use and 25 (25/122, 20%) started naltrexone.

	Overall N=67	Prescreen Negative or Low Risk N=27 (40%, row%) N (% , column)	Moderate risk N=18 (27%, row %) N (% , column)	High risk N=22 (33%, row %) N (% , column)
Success	48 (72)	19 (70)	14 (78)	15 (68)
Loss-to-follow-up	9 (13)	2 (7)	1 (5)	5 (27)
Died	7 (11)	4 (15)	3 (17)	0 (0)
Failed by treatment	1 (1)	1 (4)	0 (0)	0 (0)
Transferred out	2 (3)	1 (4)	0 (0)	1 (5)

Table.

Overall, 67 RR-TB patients were screened for SU within 2-months of treatment initiation; 72% (n=48) were successfully treated and 13% (n=9) were loss to follow-up (LTFU). Among those with high risk SU, the rates of LTFU were 27% (n=6/22) compared to 7% (n=2/27) and 5% (n=1/18) among those who prescreened negative/had low-risk SU and those with moderate-risk SU, respectively.

Conclusions: Persons with RR-TB who received the SBIRT intervention within 2-months of treatment initiation experienced high levels of treatment success and low levels of LTFU. High risk SU may predict LTFU. Holistic and integrated care for SU should be incorporated into RR-TB programs.

EP-19-281 Implementation of TB active drug safety monitoring: a cross-sectional survey in West and Central Africa

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Background: Active TB-drug safety monitoring and management (aDSM) is a key component for the wide use of new tuberculosis (TB) drugs for the treatment of drug-resistant TB (DR-TB). Harmonization and promotion of the good TB control practices is one of the goals of the West and Central Africa networks for TB control (WARN-TB and CARN-TB). As part of these network activities, an assessment of the level of implementation of aDSM in West and Central Africa was done.

Design/Methods: National Tuberculosis Programs (NTP) coordinators and staff of the countries of the West and Central Africa region completed a self-evaluation questionnaire. Topics of the questionnaire covered characteristics of the aDSM components, challenges faced by NTPs in implementing aDSM and their needs.

Results were discussed and countries' experiences shared at the WARN/CARN-TB annual meeting of NTP coordinators on February 26, 2021.

Results: All (100%) 27 countries participated in the survey. A total of 14 countries (52%) implement aDSM, 9 of which since 2015. Ten countries report serious adverse events (SAEs) and four countries also report AEs of clinical significance. Eleven countries report using standardized paper or electronic data collection tools for aDSM and 4 enter data in an electronic system at NTP central level.

All countries expressed special needs in terms of training and financial resources for implementing and/or strengthening aDSM.

Conclusions: These results indicate that half of the countries in the region have implemented aDSM. Their experience could directly benefit the 13 other countries of the region that have yet introduced aDSM. The findings reinforce the need to provide technical support and allocate resources to ensure the scaling up of aDSM in the region. This is particularly important as many countries in the region plan to start to use new TB treatment regimens such as BPaL or modified all oral shorter regimens for DR-TB patients.

EP-19-282 South African Delamanid Clinical Access Programme (DCAP) for the treatment of rifampicin-resistant TB

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Background: The South African Health Product Regulatory Authority approved a national program to treat selected Rifampicin-Resistant (RR-TB) patients with delamanid, a novel agent, among other drugs in the regimen. The DCAP was launched in March 2017 by Minister of Health and it provided delamanid to strengthen a long regimen, or for drug substitution, with strict patient safety review.

Design/Methods: From March 2017 to June 2019, eligible consenting RR-TB patients 6 years and older who had limited treatment options, or required drug substitution, were enrolled at five sites. The National TB Programme provided all assessments and treatment other than delamanid. Delamanid was donated by Otsuka. Baseline data and reportable adverse events (RAEs) were prospectively collected. RAEs included: events leading to stopping any anti-TB drug, and serious adverse events, whilst on/within one month of stopping delamanid. Other data were extracted from patients' files, the National Health Laboratory Services, and Electronic Drug-Resistant TB Register. Descriptive statistics and logistic regression modelling were employed to report baseline characteristics, safety data, treatment outcomes, and predictors of treatment success.

Results: 412 patients were analyzed: 46% female; median age 35 years (IQR: 28, 45); 2% < 15 years; 71% HIV positive; 71% fluoroquinolone-resistant RR-TB; and 93% co-administered bedaquiline. 6% had >24 weeks

of delamanid. 64% achieved Treatment Success (TS). Baseline culture positivity and previous exposure to second-line drugs independently predicted TS (aOR=0.57, 95% CI: 0.34-0.96) and (aOR=0.43, 95% CI: 0.27-0.69) respectively. HIV infection had no effect on outcome (OR=0.84 95% CI: 0.54- 1.33). 52% experienced RAEs, majority linezolid-related myelosuppression (17%), and gastro-intestinal disturbances related to PAS and/or ethionamide (12%). 9% of RAEs were delamanid-related. 8% co-administered bedaquiline, had reportable QT prolongation.

Conclusions: Delamanid, a novel agent, is a safe and effective addition for difficult-to-treat RR-TB.

Most patients received both delamanid and bedaquiline with few reported increases in QT interval

EP-19-283 Early experiences of community health workers offering multidrug-resistant TB care at the community level in Uganda: a qualitative study

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Background and challenges to implementation: Uganda currently implements a mixed model of care consisting of an initial period of hospital admission followed by an ambulatory phase where patients receive directly observed therapy (DOT) from health facilities close to their homes (HF-DOT). HF-DOT is documented to contribute to poor treatment outcomes in resource limited settings including Uganda. In 2019, Uganda introduced all oral regimens for the management of MDR-TB making the provision of community-based DOT (CB-DOT) possible.

Intervention or response: We designed a CB-DOT model for MDR-TB based on patient preferences elicited during a previous study. The model consisted of primary care giver (community health worker), place of care (home) and additional support (travel voucher). We trained community healthcare workers (CHWs) to provide CB-DOT at five tertiary hospitals in Uganda. To describe the early experiences of CHWs with this new

model of care, we conducted in-depth interviews with CHWs at two of these hospitals (in the capital and rural setting). Data collection and thematic analysis was informed by Capability, Opportunity and Motivation behavior change model (COM-B). Intervention functions were obtained using the behavioral change wheel (BCW).

Results/Impact: In April 2020, we interviewed 16 CHWs. Majority were female (12/16) and the median age 33 years (IQR 30-45). Common barriers included model alterations (psychological capability), bad weather (physical opportunity), non-disclosure and stigma at patient level (social opportunity), delays in CHW facilitation (reflective motivation). The facilitators identified were experience with community work, basic health related knowledge and proximity between the CHWs and the patient. We identified persuasion, incentivization and modelling as relevant intervention functions to alleviate these barriers to and enhance facilitators for CB-DOTs implementation by CHWs.

Conclusions: The use of the COM-B model provided insight into the early experiences of CHWs. Systematic documentation of these model alterations should be done and considered for incorporation into the final CB-DOT model for community MDR-TB care.

EP-19-284 The effect of video-observed therapy on the adherence rate of MDR-TB treatment: a pilot project

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Background: Digital adherence technology has been included in the menu of patient centred care approach in MDR-TB. We have done a pilot study on the acceptability and feasibility of VOT among patients with MDR-TB and HCWs.

Design/Methods: MDR-TB patients ≥ 13 years old were engaged to do VOT in 6 treatment centers in Cavite, Philippines. The participants were provided a smartphone with the SureAdhere mobile application to record medication intake and the Healthcare workers (HCW) monitored their adherence through the web-based platform. Good adherence was defined as intake of $>90\%$ of expected doses. Acceptability and feasibility were assessed through baseline and follow-up interviews (at 3 months and 6 months) of participants.

Results: Thirty six percent (110/307) among MDR-TB patients in Cavite preferred VOT. Among patients who have completed treatment, 87% had good adherence and 83% had good adherence among those who are still on treatment. Good adherence rate was similar in both genders. The loss to follow-up rate for the VOT cohort was only 7% with adverse drug reaction as the usual

reason. Ninety percent (9/10) of HCW had a positive perception of VOT. Ninety nine percent (89/90) of respondents mentioned benefits provided by VOT.

Conclusions: VOT is feasible and could be scaled up in the MDR-TB program in the Philippines especially during this time of restricted movement.

EP-19-285 Increasing access to healthcare services and reducing Covid-19 exposure in people with multidrug-resistant TB in Sindh, Pakistan

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Background and challenges to implementation: Limited access to health-care services for vulnerable people with multidrug-resistant tuberculosis (MDR-TB), especially those living in underserved communities is a major contributing factor towards poor clinical progress and treatment outcomes. This becomes more exposed during pandemics because of deteriorating health of patients, long distances, low resources, cultural and/or time constraints.

Our MDR-TB registry revealed that patients enrolled in the endTB clinical trials (www.endTB.org) in Sindh, Pakistan, were largely from North-East and South-West districts and would travel at least 100km to reach the clinical trial site.

Intervention or response: To address this challenge, we deployed a customized Mobile Health Van (MHV) close to homes of people with MDR-TB enrolled in the trial. The MHV was equipped with first aid, electrocardiographs, audiometry, medicines, and visual-acuity services.

We collaborated with local primary care hospitals in the identified districts to conduct patient follow up visits. Weekly clinical schedules were formalized and patients were allocated for either facility or MHV-based follow ups based on distance to trial site and patient's clinical condition. Trained medical professionals including doctors, nurses and treatment coordinator were available for routine checks.

Results/Impact: Continued services through use of MHV to improve access for people with MDR-TB ensured unhindered TB research activities during a pandemic. Approximately, thirty-five percent of patients on the trial were followed-up near their homes. This reduced distance travelled and improved access to high risk immunocompromised individuals. By avoiding

public transport, patients had reduced exposure to COVID-19 and more importantly, prevented transmission of TB. Moreover, advance scheduling of visits and coordination with patients reduced footfall and inter-patient interaction.

Conclusions: Understandably due to the COVID-19 pandemic, fewer people want to visit health-care facilities. The MHV model is a viable alternative to conventional clinics for continuity of routine health-care services and research activities for MDR-TB. Thus, resulting in greater outreach and reduced COVID-19 exposure.

EP-19-286 Relapse or re-infection? Recurrent TB in eastern China

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Background: Recurrent tuberculosis (TB) is defined by more than one TB episode per patient and is caused by re-infection with a new *Mycobacterium tuberculosis* (Mtb) strain or relapse with the previous strain. Recurrence of TB is one important obstacle for End TB strategy in the world and elucidating the triggers of recurrence is important for the current TB control strategy in China. This study aimed to analyze the sources of recurrent TB by the molecular genotyping method.

Design/Methods: A population-based surveillance was undertaken on all culture-positive TB cases in Jiangsu province, China from 2013 to 2019. Phenotypic drug susceptibility test (DST) by proportion method and mycobacterial interspersed repetitive units-variable number of tandem repeat (MIRU-VNTR) were adopted for drug resistance and genotype detection.

Results: A total of 1451 culture-positive TB patients were collected and 30 (2.06%, 30/1451) TB cases had recurrent TB episodes. Except 7 isolates were failed during subculture, 23 paired isolates were assessed. After genotyping by MIRU-VNTR, 12 (52.17%, 12/23) paired recurrence TB were demonstrated as relapse and 11 (47.83%, 11/23) paired cases were identified as re-infection. The average interval time for recurrence was 24.04 (95% CI: 19.37-28.71) months, and there was no significant difference between relapse and re-infection. For the relapsed cases, two paired isolates exhibited drug resistance shifting, while four paired isolates revealed inconsistent drug resistance among the re-infection group including two multidrug-resistant tuberculosis (MDR-TB) at the second episode.

Conclusions: Relapse and re-infection contributed equally to the current situation of recurrence TB in Jiangsu, China. Besides, more efficient treatment assessment, specific and vigorous interventions are urgently needed for MDR-TB patients, considering obvious performance among re-infection cases.

Digital tools to improve TB detection and care

EP-20-287 Implementation of an active case-finding intervention by using mobile vans equipped to reach the missing TB cases in Pakistan

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Background and challenges to implementation: TB is one of the major public health problems in Pakistan, with the country ranking fifth among high-burden TB countries worldwide. An estimated 300,000 cases remain 'missed' from the national notification system every year. To reach out to these missing TB cases, Active case finding (ACF) intervention plays an important role

Intervention or response: Mercy Corps (MC) conducts community outreach camps with the help of mobile vans equipped with digital x-rays machines, CAD4TB software, and Xpert machines (installed in four out of seven vans) in 19 intervention districts. TB patients diagnosed through these camps are registered with the nearest private/public healthcare providers. All the community members visiting the camp are screened through chest x-ray, except pediatric patients and pregnant women (who are evaluated on the spot by a trained doctor). Persons with CAD4TB scores of 70 and above are identified as presumptive TB cases. Those having a score between 50 and 70 are clinically evaluated by the doctor who follows the national diagnostic algorithm. The presumptive TB cases are tested on Xpert (where available) or their sputum is transported to the nearby Xpert testing site.

Results/Impact: A total of 1,149 x-rays screening camps were conducted during 2019-20. 78,885 individuals visited these camps, averaging 69 patients per camp, 62,656 (79%) of these individuals was screened through digital x-rays, 12,661 presumptive TB cases were identified, and further tested on Xpert. Among the total tested, 1,187 were bacteriologically positive, 1,627 were clinically diagnosed, 62 were EP and 37 patients were detected as having Rif Resistance. All form positivity of these cases was 41% and the overall yield per camp is 2.5 cases.

Conclusions: Implementation of ACF interventions in hard-to-reach areas is an effective strategy to find the missing TB cases and in early diagnosis.

EP-20-288 Factors affecting the utilisation of electronic health system in mobile van TB diagnostic units in Malawi

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Background: Electronic health (e-H) has proved to be efficient and cost-effective in improving the quality of health services. In 2019, the Malawi National TB Control Programme introduced an e-health system in all 7 Mobile Van TB diagnostic Units (MDU) in order to improve the management of patient's records. The MDUs operate in 5 major cities throughout the country. They are equipped with digital X-ray and Gene X-pert machines and are used to screen individuals for TB in the community. The aim of this study is to determine factors affecting the use of e-health system, and to investigate how the factors affect the delivery of health services.

Design/Methods: A systematic review of National TB Control Programme-Mobile Van Diagnostic Units quarterly reports from December 2019 to December 2020 was conducted and the Delphi technique was used to validate report contents.

Results: Three issues emerged from the data analysis. Firstly, e-health was found to improve data quality and efficiency in patient management as users recommended that the system is quick and reduces the time to retrieve records.

Secondly, users revealed that some technological factors of the system such as unreliable network and internet connectivity, gadgets breakdowns, frequent downtime of the server, inability to edit the data negatively affected the usage. The system was also found to be incomplete; some information that users needed for their task was missed.

Thirdly, managerial factors: inconsistency in the provision of airtime and lack of intensive e-health training compromised the system usage.

Conclusions: Findings from the study have revealed several strengths and challenges faced by users in utilizing e-health at MDU. Despite the negative factors, the overall attitude by users towards e-health usage was positive. The findings provide adequate information that could guide program management, system designers, installers, and users on measures of improving e-health usage and consequently health service delivery.

EP-20-289 Accessibility of mobile diagnostic facility for increasing TB case-finding among high-risk population in Bangladesh

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Background and challenges to implementation: In Bangladesh a huge garments workers, prisoners, people living in slums and an enormous number of Forcibly Displaced Myanmar Nationals (FDMN's) live in isolated areas with difficulties to access health care services. In addition, poverty put them at risk of falling to TB. To address these populations BRAC introduced mobile diagnostic facility comprising GeneXpert and digital X-ray in a covered van to identify missing cases among high risk groups.

Intervention or response: This new initiative in Bangladesh started in February 2020 through 2 mobile diagnostic facilities and expanded it in November 2020 adding 2 more mobile diagnostic units. Chest X-ray followed by GeneXpert test has been done among above mentioned high risk group through prior community mobilization. Due to COVID-19 pandemic situation 4 months (April-July 2020) the activity was intermittent.

Results/Impact: A total of 4069 TB presumptives were tested through these 4 facilities; 105 TB cases were diagnosed and among them 8 cases were Rifampicin Resistance (RR). Since January to March 2021 (in 3 months) a total of 6293 TB presumptives were tested there following the same algorithm while total 200 TB cases were diagnosed and among them 3 cases were Rifampicin Resistance (RR).

Conclusions: If we compare the outcome of 2021 with 2020, a significant optimistic change is sighted and an outstanding achievement we will be able to achieve in future and thus, this initiative can be a key diagnostic pillar in TB care services especially for a significant unserved high risk group. Further expansion of services in the urban slums and hard to reach areas will play a significant role in more case findings.

EP-20-290 Adoption of teleconsultation among patients and providers

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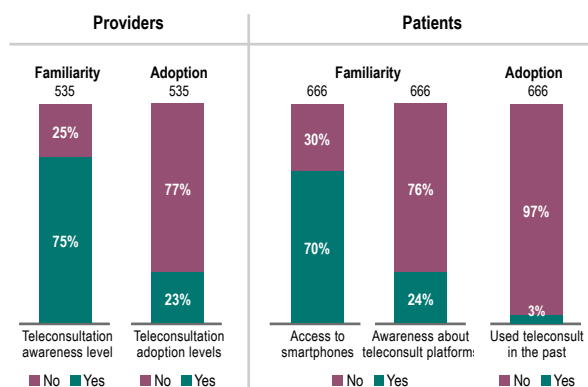
Background: The COVID-19 pandemic has disrupted healthcare services with closure of clinics/ reduced outpatient department hours, limited mobility, and stakeholders exercising precautions through limited interactions. Information and Communications Technology (ICT) enabled operational models could help bridge the gap, however reach and adoption of teleconsultation seems to be limited to specific clinical use-cases in tier-1 cities.

Design/Methods: The Joint Effort for Elimination of Tuberculosis (JEET) is a nationwide program which aims to seamlessly extend TB services to patients seeking care in the private sector. A telephonic survey was conducted with 535 providers and 666 patients in the JEET network in Q3 2020 across 9 cities.

The objective was to understand their familiarity and usage of teleconsultation platforms and online payments, which could provide valuable insights for future interventions.

Results: Providers: Around 75% of providers were familiar with teleconsultation but adoption was low at 23% and skewed towards metros. Teleconsultation usage was higher, at 34%, for providers charging more than \$7 per session as compared to 17% for providers charging lower consultation fees. 82% were aware of online payment methods and 68% had used them.

Patients: 70% had smartphone access across geographies and gender. 24% were familiar with teleconsultation, with relatively higher awareness in metros but only 3% had used it. 51% were aware of online payment methods and 38% had used these. Key challenges to usage of teleconsultation included network issues, lower confidence with online platforms as compared to in-person visits, lack of familiarity and unavailability of preferred doctor.



Background and challenges to implementation: The COVID-19 pandemic has disrupted healthcare services with closure of clinics/ reduced out-patient department hours, limited mobility, and stakeholders exercising precautions through limited interactions. Information and Communications Technology (ICT) enabled operational models could help bridge the gap, however reach and adoption of teleconsultation seems to be limited to specific clinical use-cases in tier-1 cities.

Intervention or response: The Joint Effort for Elimination of Tuberculosis (JEET) is a nationwide program which aims to seamlessly extend TB services to patients seeking care in the private sector. A telephonic survey was conducted with 535 providers and 666 patients in the JEET network in Q3 2020 across 9 cities. The objective was to understand their familiarity and usage of teleconsultation platforms and online payments, which could provide valuable insights for future interventions.

Results/Impact: Providers: Around 75% of providers were familiar with teleconsultation but adoption was low at 23% and skewed towards metros. Teleconsultation usage was higher, at 34%, for providers charging more than \$7 per session as compared to 17% for providers charging lower consultation fees. 82% were aware of online payment methods and 68% had used them.

Patients: 70% had smartphone access across geographies and gender. 24% were familiar with teleconsultation, with relatively higher awareness in metros but only 3% had used it. 51% were aware of online payment methods and 38% had used these. Key challenges to usage of teleconsultation included network issues, lower confidence with online platforms as compared to in-person visits, lack of familiarity and unavailability of preferred doctor.

Conclusions: While teleconsultation can play a critical role in service delivery, its scalability will depend upon resolving barriers to adoption and establishing effective linkages to integrate teleconsultation in existing public health service delivery models. Any intervention will have to ensure additional support to patients and providers from booking of online appointments to making online payments.

EP-20-291 Implementation bottlenecks in real time medication monitoring (evriMED) for improving drug adherence among TB patients in Kilimanjaro, Tanzania

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Background: Digital Adherence tools (DATs), which include real time medication monitoring (RTMM) and Short Message Service (SMS) reminders, have been reported to improve medication adherence among Tuberculosis (TB) patients. Recently, in limited resource settings, DATs have been described as promising tool to monitor patients medication behavior. The main objective was to assess the potential implementation bottlenecks of RTMM using the evriMED device.

Design/Methods: We conducted a mixed-method study among TB patients who participated in the REMIND-TB trial. SMS reports were created by the evriMED system. We calculated the percentage of sent and delivered SMS reminders and daily device activity status (i.e. battery "medium, low, empty"). Feedback from exit interviews was quantitatively analyzed to describe user experience. In-depth interviews investigating the TB nurses' perception on evriMED usage were thematically analyzed.

Results: A total of 266 participants received evriMED devices. A total of 99,601 SMS reminder were sent and 49,603 (50%) were delivered. Out of 266 participants who received devices, 45% (120) of devices recorded medium battery, 6.7% (18) devices recorded low battery and 2.6% (7) recorded battery empty which led to loss of data. Bottlenecks reported from in-depth interview included that nurses had experienced difficulties in accessing online adherence reports due to limited knowledge of mobile technology; participants moved away from urban to rural areas where they experienced poor network coverage; Unreliable electricity in rural areas.

Conclusions: The usage of evriMed technology provides important technical feasibility information on TB-medication intakes. However, half of SMS were not delivered. Future studies using real time monitoring devices should consider issues of network availability, improving device battery life, close monitoring of SMS sent and received and strengthening training and sensitization on mobile technology to health care provider such as TB nurses.

EP-20-292 Facility-based vs. community-based systematic screening for TB using a diagnostic algorithm of X-ray triaging for rapid molecular testing

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Background: Vietnam is scaling up its 'Double-X' strategy, which combines chest X-ray (CXR) triaging with Xpert testing. However, in this new diagnostic algorithm X-ray, most of which is facility-based, becomes a key access and convenience barrier to key vulnerable populations such as older populations or household contacts, especially if asymptomatic

Design/Methods: Between Nov-2020 and Apr-2021 we conducted a combination of home-based household contact investigation and mobile chest X-ray (CXR) screening campaigns in three provinces of Viet Nam as part of the ZTV HOPE study.

We invited all household contacts of pulmonary TB patients notified in the past year and persons aged 55+ years to present for CXR screening at the district TB unit or a mobile CXR screening event. All persons with TB-related abnormalities were tested on Xpert MTB/RIF Ultra.

We describe the yield and Number Needed to Screen (NNS) in aggregate and segmented by facility-based and community-based screening

Results: Across all provinces we screened 4,893 persons by CXR. About 442 (9.0%) CXR were abnormal with suspected TB and 89.1% was tested on Xpert with another 49 sputum tests conducted outside of the Double-X algorithm. We detected 52 All Forms TB patients for a yield of 1,063/100,000 (NNS=94). To date, 84.6% were initiated on treatment. Facility-based screening yielded only 1 case among 109 persons screened, while community-based screening produced a yield of 51 persons with TB among 4,784 participants.

	Facility-based	Community-based	Total
Summary indicators			
A People verbally screened in ACIS	350	4,863	5,213
B People screened by CXR	109 31.1%	4,784 98.4%	4,893 93.9%
C People with abnormal CXR results	15 13.8%	427 8.9%	442 9.0%
D People with sputum tests results (AFB, Xpert, TRC and/or Culture)	10 66.7%	384 89.9%	394 89.1%
E People with Bac(+) sputum test results	1 10.0%	41 10.7%	42 10.7%
Y Sputum testing outside Double-X algorithm *	0	49	49
Z Non-Double-X Bac(+) sputum test results	0 N/A	1 2.0%	1 2.0%
F People clinically diagnosed with TB	0	9	9
G All forms of TB yield (E + Z + F)	1	51	52
H All forms of TB started on treatment	0 0.0%	44 86.3%	44 84.6%

Background and challenges to implementation: Vietnam is scaling up its 'Double-X' strategy, which combines chest X-ray (CXR) triaging with Xpert testing.

However, in this new diagnostic algorithm X-ray, most of which is facility-based, becomes a key access and convenience barrier to key vulnerable populations such as older populations or household contacts, especially if asymptomatic.

Intervention or response: Between Nov-2020 and Apr-2021 we conducted a combination of home-based household contact investigation and mobile chest X-ray (CXR) screening campaigns in three provinces of Viet Nam as part of the ZTV HOPE study. We invited all household contacts of pulmonary TB patients notified in the past year and persons aged 55+ years to present for CXR screening at the district TB unit or a mobile CXR screening event. All persons with TB-related abnormalities were tested on Xpert MTB/RIF Ultra. We describe the yield and Number Needed to Screen (NNS) in aggregate and segmented by facility-based and community-based screening

Results/Impact: Across all provinces we screened 4,893 persons by CXR. About 442 (9.0%) CXR were abnormal with suspected TB and 89.1% was tested on Xpert with another 49 sputum tests conducted outside of the Double-X algorithm. We detected 52 All Forms TB patients for a yield of 1,063/100,000 (NNS=94). To date, 84.6%

were initiated on treatment. Facility-based screening yielded only 1 case among 109 persons screened, while community-based screening produced a yield of 51 persons with TB among 4,784 participants.

Conclusions: By bringing CXR screening closer to the community, we were able to successfully reduce access and convenience barriers, and found a sizeable number of people with TB. The combined rate of TB burden detected was 3.7x higher than the national TB prevalence. More active case finding efforts that focus on removing access barriers are needed to truly expand the Double-X algorithm equitably and to end TB in Vietnam

EP-20-293 Mapping potential TB transmission hotspots using artificial intelligence

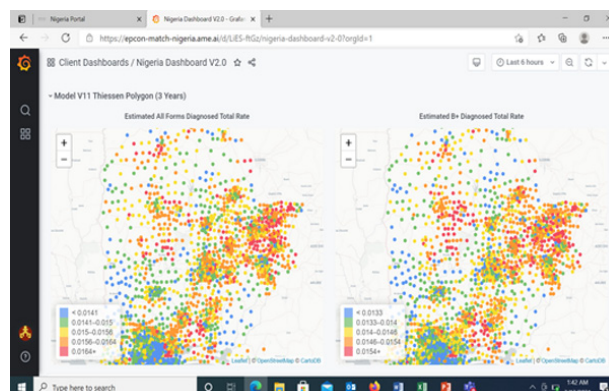
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Background and challenges to implementation: Nigeria is a high burden country for TB, TB/HIV and Drug-Resistant TB and contributed 4.4% of the global missing TB cases in 2019. The Mapping and Analysis for Tailored disease Control and Health System Strengthening (MATCH) AI is a well-recognized spatial data processing and analysis tool that allows the integration of Geographic Information Systems (GIS) with routine health surveillance data and other contextual data sources. Evidence regarding its use in modelling TB data in Nigeria is lacking.

Intervention or response: Real world program data (weekly, monthly community and facility TB cascade reports, LGA TB notification data) and contextual country data, population density, demographic information, socioeconomic indicators such as poverty, environmental and climate data, access to healthcare) were inputted into the model engine which dynamically mined, reasoned, predicted and propagated network of association and casualty (Bayesian supervised and unsupervised learning) based on conditional probability to generate twin output model (dashboard and geoportal).

Results/Impact: TB Risk quantifications covering 3,120 population clusters (Thiessen Polygons), 1,214 Wards and 103 LGAs. Field validation through targeted community TB screening activities showed that predicted/estimated TB rate (corresponding NNS as a measure of risk) significantly correlated with observed values but TB rate was estimated for a risk period of 3 years during

which TB can be developed. Presently, the 3-year model has consumed 7 months of data, hence the predicted values represent the risk over that interval. In addition, model outputs were used in facility selection and expansion strategies, recommended movement plan (in order of NNS for each community), supervision mission, resource allocation.



Conclusions: The MATCH AI is an effective tool to determine hotspots, scale and potential causes of TB under detection and under-diagnosis and when routinely applied to subnational TB surveillance data, provide valuable information required to target interventions, accounting for context specific factors causing the observed variations in TB case notifications.

EP-20-294 Mobile-based video-observed therapy, using evidence-based digital adherence technologies for TB treatment at three high-burden health facilities in Uganda

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Background: Uganda remains among the 30 HBC TB/HIV countries globally. Tuberculosis Treatment, adherence & monitoring remains a big problem in Uganda. WHO recommended DOTS is challenging in terms of implementation to both patients and the HCWs. The treatment outcomes for TB remain suboptimal at about 72-79% in 2019 with high levels of loss to follow up at over 10%. Digital evidence-based applications provide an alternative to DOT for patients on TB treatment in technology driven world.

Design/Methods: The program together with ZMQ an Indian based technology for development organization, implemented two main core intervention; 1) Mobile-phone based toolkit for TB patients to report their compliance to treatment by sending real-time evidenced video and 2) Active Community-led Supervision for TB patients, who are incapable of self-managing treatment by sending real-time video.

Results: 2000 (853F, 1147M) patients were enrolled under VOT in 3 districts. There is significant change in adherence rate which has increased 95% from 75%; treatment success rate to 83%, Cure Rate to 79% from 67% and 56% respectively. With the successful treatment completion, patient's knowledge around TB has also improved through TB learning in-built function in toolkit.

The Results shown that knowledge tools combined with adherence have increased the overall knowledge and change the attitudes towards TB.

Conclusions: It has been observed that patients who used DAT (VOT) for their adherence has shown better results in adherence rate and TSR. ACTS is a holistic System changing approach, which is a patient & community-centric model and provides secure environment for adherence, building healthy behaviors and treatment tracking of DOT as compared to top-down compliance strategy. The audio-reminders and follow-ups have improved the adherence and timely testing among patients.

In current situation, where traditional method DOTS is not achievable, innovative approaches should be there to support TB patients for adherence by programs.

EP-20-295 An online toolkit to support implementation research on digital technologies across the TB care continuum

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Background and challenges to implementation: The persistence of the TB epidemic demands innovative approaches to TB prevention and care. Digital technologies represent novel ways to improve patient-centered care or improve the use of resources by TB programmes.

However, context-specific barriers to effective implementation and scale-up of digital innovations persist and require further exploration using implementation research (IR).

Intervention or response: In 2020, the Special Programme for Research and Training in Tropical Diseases (TDR) and the WHO Global TB Programme (GTB) created the *Implementation Research for Digital Technologies for TB Toolkit (IR4DTB)*.

IR4DTB is an interactive, online tool to support the use and evaluation of digital technologies by national TB programmes (NTPs) by building their capacity to design

and conduct IR projects to trial, evaluate or scale up digital technologies under routine programmatic conditions to accelerate efforts to End TB.

IR4DTB (www.ir4dtb.org) comprises six modules covering critical steps in the IR process, includes case studies from real-life experiences to illustrate topical learning concepts, and practical activities to stimulate thinking around key research areas. Collectively, these components contribute to a comprehensive research proposal that can be used to support fundraising efforts.

Results/Impact: IR4DTB was launched in November 2020 during a five-day training workshop in Beijing with remote participation from participants from Malaysia, Pakistan and Uzbekistan. IR4DTB was used as the primary teaching tool and facilitators worked with teams to develop IR proposals addressing identified implementation challenges or research questions on the effective implementation or scale-up of digital technologies for TB in their countries.

Six proposals were developed and are currently being implemented, the results of which will provide further evidence of optimal implementation strategies for digital technologies for TB care.

Conclusions: IR4DTB is a useful tool to support NTPs to evaluate how digital technologies can help overcome challenges in TB care, and to generate evidence to guide their future introduction and scale-up.

EP-20-296 Sampark Daatha – facilitating chest X-ray in people with TB-like symptoms: experiences from a TB Alert India project

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Background and challenges to implementation: People with TB like symptoms (PTS) generally undergo sputum microscopy (SSM). If TB is not diagnosed in SSM, PTS don't show interest in getting chest X-ray done despite having symptoms, thinking that they don't have TB. However, chest X-ray is important test in the testing algorithm of National TB Elimination Program (NTEP). TB Alert India (TBAI) with funding support under TB REACH Wave 6 is implementing an innovative initiative facilitating chest X-ray to such PTS.

Intervention or response: TBAI is implementing this project in 18 Tuberculosis Units (T. Us) in the state of Telangana, India. Project facilitates free chest x-ray to PTS whose SSM report is negative for TB bacilli, through free transport facility. Seven (7) seater vehicles termed as "Sampark Daatha" hired across 18 T.Us. A route plan is designed covering villages of the T.Us, and shared with informal health care providers. Informal providers, who have referred PTS for SSM mobilize them for chest x-ray.

Four (4) PTS are transported in a trip to project enrolled private X-ray facilities following all COVID precautions, and dropped back at their respective villages. Qualified radiologist certified reports are shared with Informal providers.

Informal providers follow up those PTS, and ensure visit to NTEP for further evaluation & action. Informal providers update details in project developed mobile application.



Results/Impact: From Apr 2020 to Dec 2020, around 818 PTS utilized Sampark Daatha facility. Around 22.6% (185) reported lesions suggestive of TB, and are started on treatment at NTEP clinic as per guidelines. These TB patients constitute around 9.5% (185/1947) among the total TB patients identified and initiated on treatment during the same period. Cost for one clinically identified TB patient is USD. 2.

Conclusions: Sampark Daathas can an enabler to identify TB patients early, enhance TB notification and reduce the transmission in the community.

EP-20-297 Public-private partnership in teleradiology reduces diagnosis delays and X-ray costs to patients in rural Bihar, India

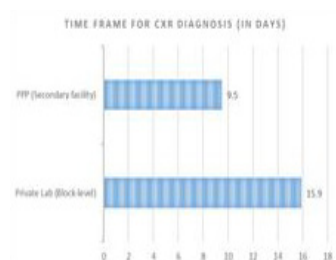
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Background and challenges to implementation: Access to quality chest radiography (CXR) at primary health facility is unavailable, private radiology services fill gaps in public. Presumptive TB patients are burdened with high out-of-pocket expense and multiple visits to private providers, leaving many un/diagnosed after long delays. Teleradiology offered through PPP mode may answer these challenges.

Intervention or response: Pilot study was held in 2 blocks (population: 426K) of Samastipur district in rural Bihar. Community Health Workers (CHWs) screened patients for TB based on active case finding approach. Those

suggestive of TB were offered a choice, either - visit a private lab at local block, if patient has reduced mobility / secondary health facility (PPP) for better physician consultation and early diagnosis. Program covered CXR cost at both facilities, travel allowance (USD 1/pt) was paid to those accessing secondary facility. Both lab facilities had digital X-ray, the secondary facility was connected to a Central Reporting System to interpret digitally transferred images by skilled radiologists and report in few hours. Each X-ray at secondary facility (PPP) cost program USD 1/pt. while the same at private lab in block came for almost USD 4/pt. All patients with abnormal CXR were advised for Genexpert (Gx) test for further diagnostic evaluation.

Results/Impact: From 16th November '20 to 15th February '21, 92 (59.7%) presumptive patients accessed secondary facility (PPP) while 62 (40.2%) others preferred a private lab locally. Patients undergoing CXR under PPP mode took 9.5 days to be diagnosed, those at private lab took 15.9 days, teleradiology reduced delays by >40%. Program saved USD 2/pt. under PPP mode even after paying travel allowance. Gx test showed 30.7% and 30.6% bacteriological confirmation for PPP mode and private lab respectively.



Conclusions: Teleradiology is cost-effective, significantly lowers diagnostic delay, in primary care settings it can enhance accessibility and quality of diagnosis while gaining trust of patients seeking care.

TB from A to Z: a mixed bag

EP-21-298 Association between latent TB infection and depressive symptoms in household contacts of TB patients: a prospective cohort study

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Background: Depression is highly prevalent among patients treated for active tuberculosis disease (TB) and is associated with unfavorable treatment outcomes. However, little is known about the role and impact of latent tuberculosis infection (LTBI) on depression. Here, we assessed the association between LTBI and development of depressive symptoms among household contacts of persons treated for active TB.

Design/Methods: Between 2016 and 2018, we enrolled and followed 1,009 household contacts (HHCs) of 307 patients being treated for culture-positive pulmonary tuberculosis in Lima, Peru. LTBI status among HHCs was assessed at enrollment using interferon gamma release assay (IGRA).

Depressive symptoms were assessed at 12 months of follow-up using the Patient Health Questionnaire-9 (PHQ-9). We defined HHCs as having depressive symptoms at 12 months of follow-up if they had PHQ-9 scores ≥ 5 (mild or more severe depressive symptoms).

We used logistic regression to estimate the odds ratio (OR) for PHQ-9 scores ≥ 5 comparing HHCs (≥ 12 years) with and without LTBI, controlling for age, sex, socioeconomic status, nutritional status, and isoniazid preventive therapy use as potential confounders.

Results: Among 921 HHCs, 378 (41.0%) tested positive for LTBI at enrollment. By the end of follow-up, 70 (12.4%) of 563 HHCs had PHQ-9 scores ≥ 5 . Compared to HHCs who were IGRA-negative at enrollment, those who were IGRA-positive were almost twice as likely to have PHQ-9 scores ≥ 5 at 12 months of follow-up even after controlling for potential confounders (adjusted OR, 1.93, 95% CI, 1.09-3.39).

We observed similar results among HHCs who had converted their IGRA status from negative to positive during follow-up compared to those who remained IGRA-negative.

Conclusions: HHCs with LTBI at enrollment had increased odds of reporting depressive symptoms 12 months later. Further research is needed to explore how LTBI may contribute to the development of depressive symptoms among close contacts of tuberculosis patients.

EP-21-299 Measuring the multi-morbidity burden during a community-based active TB case-finding event in a remote island setting

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Background: The Viet Nam National TB Program has ambitions to expand WHO's Practical Approach to Lung Health (PAL) strategy to include major public health burdens such as diabetes, hypertension and cancers in addition to the standard PAL indications and develop formal guidelines for a 'Practical Approach to Medicine' (PAM). We integrated screening for several key diseases into a community-based active tuberculosis (TB) case finding event to measure the multi-morbidity burden in persons with suspected TB.

Design/Methods: Between Jan-2019 and Apr-2021 we conducted three mobile chest X-ray (CXR) screening campaigns in Tan Hiep island, Viet Nam. All residents were invited for tuberculin skin test, CXR screening and Xpert MTB/RIF testing, if eligible. Priority groups were further screened for diabetes, hypertension, respiratory function, hepatitis B/C, breast and cervical cancer, liver function (AST/ALT) and depression. We present the rates of TB, LTBI and select co-morbidities as well as the proportion of persons with at least one and 3+ co-morbidities.

Results: We enumerated and invited 2,384 participants for screening. Among those who presented, the rate of TB was 586/100,000 (13/2,220) and LTBI was 35.6% (731/2,052). Simultaneously, about 27.8% had (pre-) diabetes and 46.7% were hypertensive. We detected asthma and COPD in 4.9% (54/1,098). Of diagnosed TB patients and persons with LTBI, 46.2% (6/13) and 52.3% (382/731) had at least one co-morbidity, respectively. The percentage of persons with at least one health issue was 46.4% (1,105/2,384), while the rate of 3+ comorbidities was 7.7% (183/2384).

	Total	M	F	0-14	15-39	40-54	≥55	No Age
1.1 Participants screening	2,384	1,404	980	308	971	528	570	7
1.2 Screened by chest X-ray (CXR)	2,220	1,313	907	280	894	501	538	7
1.3 Abnormal CXR	164	101	63	4	16	35	109	0
	7.4%	7.7%	6.9%	1.4%	1.8%	7.0%	20.3%	0.0%
1.4 Sputum test after abnormal CXR	150	88	62	4	15	32	99	0
	91.5%	87.1%	98.4%	100.0%	93.8%	91.4%	90.8%	N/A
1.7 All Forms of TB detected	13	11	2	0	2	0	11	0
TB prevalence rate (per 100,000)	586	838	221	0	224	0	2,045	0
1.8 All Forms of TB linked to treatment	13	11	2	0	2	0	11	0
	100.0%	100.0%	100.0%	N/A	100.0%	N/A	100.0%	N/A
2.1 Inoculated with tuberculin	2,247	1,308	939	302	911	493	537	4
2.2 Returned for TST reading	2,052	1,199	853	282	822	454	490	4
	91.3%	91.7%	90.8%	93.4%	90.2%	92.1%	91.2%	100.0%
2.3 TST(+)	731	451	280	36	222	231	241	1
	35.6%	37.6%	32.8%	12.8%	27.0%	59.9%	49.2%	25.0%
3.1 Tested liver enzyme	548	328	220	36	141	190	181	0
3.2 High liver enzyme	101	84	17	3	35	35	28	0
	18.4%	25.6%	7.7%	8.3%	24.8%	18.4%	15.5%	N/A
3.3 Tested hepatitis B/C	561	330	231	38	145	192	186	0
3.4 Hepatitis B/C	54	33	21	0	19	20	15	0
	9.6%	10.0%	9.1%	0.0%	13.1%	10.4%	8.1%	N/A
4.1 Measured respiratory function	149	108	41	2	19	53	75	0
4.2 COPD or Asthma	54	28	26	0	6	14	34	0
	6.2%							
5.1 Measured blood pressure	925	433	492	1	115	358	449	2
5.2 Hypertensive	433	247	186	1	20	145	265	2
	46.8%	57.0%	37.8%	100.0%	17.4%	40.5%	59.0%	100.0%
5.3 Measured blood glucose	898	419	479	2	113	344	437	2
5.4 (pre-)diabetes	250	118	132	0	12	78	159	1
	27.8%	28.2%	27.6%	0.0%	10.6%	22.7%	36.4%	50.0%
6.1 Gynecological pathology	69	0	69	0	26	38	5	0
	8.3%							
6.2 Depression	5	2	3	0	1	2	2	0
	0.2%	0.1%	0.3%	0.0%	0.1%	0.4%	0.4%	0.0%
6.3 Abnormal of Ultrasound result	153	19	134	2	23	57	71	0
	6.4%	1.4%	13.7%	0.6%	2.4%	10.8%	12.5%	0.0%

Table.

Conclusions: We detected a variety of health issues and a high rate of comorbidities among persons screened for and diagnosed with TB and LTBI. Integrating screening services for TB, LTBI and co-morbidities represents a significant effort towards more patient-centered care, while offering a model of sustaining TB case finding as we progress towards the End TB targets.

EP-21-300 The feasibility and acceptability of using treatment monitors and a differentiated care approach to improve TB treatment adherence in South Africa

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Background: Digital adherence technology (DAT) including treatment monitors overcome challenges to monitoring tuberculosis treatment adherence through remotely documenting dosing patterns of people with

tuberculosis (PWTB). We evaluated feasibility and acceptability of the Wisepill evriMED DAT triggering a differentiated care approach (DCA; short message service - sms, phone calls, home visits) in South Africa.

Design/Methods: Between June 2020 to January 2021, we conducted 87 in-depth interviews in local languages across three provinces. Interviews were audio recorded, transcribed verbatim and translated. Preliminary transcripts available for analysis included 6 PWTB (3 female and 3 male aged 31-37 years) and 4 stakeholders (2 facility, 1 research, 1 district-level staff). Saturation was assessed during data collection and thematic analysis was used.

Results: Feasibility: PWTB appreciated being able to safely store their medication in the device. The reminders were helpful, although the features of the device such as the size, alarm and flashing lights created stigma as it was difficult to take treatment discreetly; especially for those who had not disclosed their TB diagnosis. Stakeholders were supportive of the intervention being integrated into the TB programme and were eager to be trained on the device as it helped monitor treatment adherence. However, there was distrust amongst stakeholders about pill intake even when device was opened, and device set-up was considered time consuming. Acceptability: PWTB attributed low value to sms but appreciated phone calls and had mixed views about home visits due to stigma. Stakeholders did not perceive any stigma created by the device but felt awareness on use of the device could be improved.

Conclusions: Monitoring tuberculosis treatment adherence using the evriMED device and DCA was both feasible and acceptable to PWTB and stakeholders. However, the features of the device that caused stigma need to be addressed as they could potentially act as a barrier to scale-up.

EP-21-301 International migration and TB in the state of São Paulo, Brazil

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Background: To describe the demographic and clinical characteristics of international migrants with tuberculosis (TB) and to investigate factors associated with loss to follow-up among them.

Design/Methods: We conducted a retrospective-cohort of all TB patients notified to the São Paulo State TB Control Program between 1st January 2014 to 31st December 2017. The São Paulo State contain 44.1 million people (~21% of Brazilian population) and notifies 14,977 new TB patients per year (~24% Brazilian

TB patients in 2017). We extracted demographic and clinical data of TB patients from the São Paulo State TB electronic registration system (TBWEB). We compared the demographic and clinical characteristics of TB patients that occurred in international migrants and non-migrants using Pearson's chi-square or Mann-Whitney tests. We used logistic regression to investigate the factors associated with loss to follow-up among new pulmonary TB patients aged ≥ 15 years without resistance to anti-TB drugs.

Results: We included 62,839 TB patients, of which 1,180 (1.9%) were international migrants and 900/1,180 (76.3%) were from other South American countries. In relation to non-migrants, international migrants had a lower mean age (33.0 vs 39.6; $p < 0.001$), higher percentage of individuals with ≥ 8 years of study (68.2% vs 50.3%; $p < 0.001$) and higher TB treatment loss to follow-up (17.1% vs 13.3%; $p < 0.001$). Being an international migrant is associated with loss to follow-up (OR_{adj}: 1.87; 95% CI: 1.41-2.47) after adjusting for sex, age, skin color, schooling, experiencing homelessness, diagnostic health service, chest x-ray results and comorbidities (i.e., HIV, diabetes, alcoholism, and drug addiction).

Conclusions: Although international migrants with TB are younger and had more years of formal education than TB patients that are not migrants, international migrants are more likely to not complete TB treatment. International migrants should be prioritized in specific policies that respect their cultural particularities to increase adherence and completion of treatment.

EP-21-302 Effectiveness of evriMED in ensuring TB treatment adherence among TB patients in the Kilimanjaro Region: a cluster-randomised controlled two-armed trial

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Background: Tuberculosis (TB) is among the top ten causes of death globally making it the leading cause of death among all infectious diseases. In 2019, 1.4 million deaths due to TB occurred globally. Adherence to antituberculosis treatment remains a challenge. Interventions should target multiple barriers to adherence. A novel digital adherence tool (DAT), evriMED, has prov-

en effective in China, however implementation in low-income settings like Tanzania remains uncertain. The aim of this study was to investigate whether evriMED improves adherence to treatment among TB patients in Kilimanjaro.

Design/Methods: This was a two-armed cluster randomized trial with the interventional arm using evriMED and the control receiving standard TB care. The evriMED box was used to store and take patient's medication. Medication intakes were measured through box openings which sends real-time electronic signals to central server and triggers automated reminder texts through short message service (SMS). Patients were followed up for six months to determine adherence using WHO cut-off points at 80%, 90% and 100%. We calculated mean adherence based on pharmacy refill counts and self-report and conduct Student's T-test to investigate the difference in mean adherence.

Results: We recruited a total of 507 participants, 279(55%) in the intervention arm and 228(45%) in the control arm. Results from evriMED adherence reports showed that 8(2.9%) patients reached 100%, 98(35.1) reached $>90\%$ and 133(49.7) had $>80\%$. We found that mean (SD) pharmacy refill adherence for the control group was 83% (24) while for the intervention group it was 94% (14); $P < 0.01$. There was no difference in self-reported adherence between arms; 99% (1.5) in intervention group and 99% (1.6) in control group ($p = 0.86$)

Conclusions: There was little effect of evriMED on adherence as observed slightly higher in the intervention group than in control. The slight difference might be due to Hawthorne effect in the interventional group.

EP-21-303 Increased reporting of adverse drug reactions to anti-TB medication after implementation of the PAVIA Programme in Tanzania

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Background: Monitoring of adverse drug reactions (ADR) post-marketing is still limited in Sub-Saharan Africa. Interventions on improving pharmacovigilance are highly needed. In 2018, the PAVIA (Pharmacovigilance Africa) Programme started. PAVIA aimed to strengthen pharmacovigilance with a focus on medication for multi-drug resistant (MDR) Tuberculosis.

The objective of this study was to investigate trends in reporting of ADR of total medication and anti-Tuberculosis medication before and during PAVIA.

Design/Methods: We explored trends in ADR-reporting in Tanzania using data from Vigiflow, which is a web-based individual case safety report (ICSR) management system that is available for use by national pharmacovigilance centres. The PAVIA program implemented blended e-learning on reporting of ADR in Tanzania and equipped the pharmacovigilance sites. The number of total reported ADR and anti-tuberculosis ADR were collected for 2014 to April 2021. We analyzed frequencies of ADR-reports for all drugs and for anti-TB-drugs.

Results: Data showed that the total number of ADR reported was 21,747 since 2014 to April 2021 of which 561 (2.1%) were related to anti-TB medication. In the first year 2015, the number of reports was 276 with 10 (4%) anti-TB-medication related.

In the first year of PAVIA, the number of reports increased to 1,363 with 199 (15%) anti-TB-medication related and in the second year it increased to 15,024 with 133 (1%) anti-TB-medication related. Overall, ADR-reporting for anti-TB-medication during the PAVIA programme (2019-2021) is 431/19933 (2%).

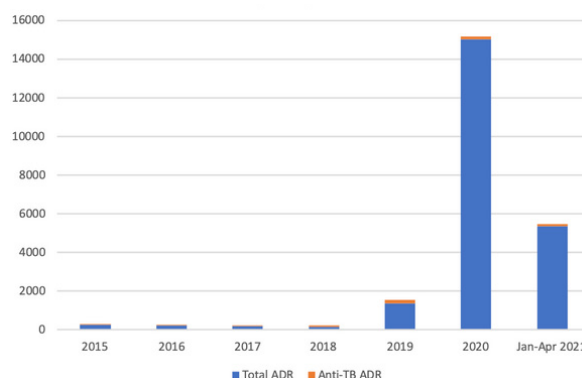


Figure. ADR reporting in Tanzania.

Conclusions: Data from Vigiflow show a clear increase in the trend of total reported ADR since PAVIA has been implemented. The number of anti-TB-medication related ADR increased as well, though they contributed less to the total number of ADR.

As Tanzania, has implemented other programmes as well, including a national campaign on ADR-reporting through clinical meetings, Television and other media, the actual effect of PAVIA should be further investigated.

EP-21-304 A multidisciplinary approach to understanding the safe and effective use of medicines in HIV-TB co-infection

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Background: Completion of tuberculosis (TB) treatment presents several challenges to patients, including long treatment duration, medication side-effects and heavy pill burden. These challenges can be greatest for people who are also living with HIV. WHO have emphasised the critical need for patient centred TB care, but such approaches can only be delivered if patient experiences are sought and understood.

Design/Methods: In 2020, we nested a qualitative study within the SAEFRIF trial, recruiting HIV-TB co-infected adults in Kampala to receive high- or standard-dose rifampicin-based TB treatment, alongside anti-retroviral therapy. A purposively selected sample of trial participants contributed to 12 in-depth interviews and 9 focus group discussions, which were recorded with a note taker present. Sessions were transcribed verbatim and translated from local languages into English. Thematic analysis focused on drug side-effects, use of self-prescribed (including “herbal” or “traditional”) medications and barriers to TB treatment adherence.

Results: Patients disclosed more side-effects during the qualitative study than formal trial reporting. Those who remembered pre-treatment counselling advice were disinclined to manage side-effects by self-prescription, including “herbal” remedies. Those who encountered difficulty in accessing a medical practitioner did report these practices. Adherence to TB therapy was motivated by the sense that “I got better” and enhanced by peer support from prior TB patients.

Obstacles to adherence included stigma (especially from visible side-effects such as “red urine”), difficulties with pill size and number, uncertainty about social impacts of taking TB medicines (e.g. “do we have to stop having sex?”), and competing beliefs about the cause of prolonged illness (e.g. “witchcraft”).

Conclusions: Nesting qualitative studies within clinical trials enriches our understanding of patient experiences. Tailored pre-treatment counselling, improved access to clinical services, peer-support platforms, and simpler drug administration will deliver more patient-centred care.

EP-21-306 Factors to better understand zoonotic TB among nomadic pastoralists in Northern Nigeria: screening with GeneXpert and evaluating pulmonary Xpert-positives using Hain MTBC testing

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Background: Nomadic pastoralists in Nigeria are thought to be at higher risk for zoonotic tuberculosis due to close contact with livestock, consumption of unpasteurized dairy and contaminated meat as well as exposure to infected carcasses. Nigeria is a high burden TB country. GeneXpert detects *M. tb complex* (MTBC) and does not differentiate between species. *M. bovis, subspecies bovis* is naturally resistant to pyrazinamide which has implications for effective treatment. The burden of zoonotic TB is not well understood in this population.

Design/Methods: Along with intensified case-finding among nomadic pastoralists in 3 states (Adamawa, Gombe and Taraba) with TB Reach funding, we prospectively enrolled clients with sputum samples that tested positive with GeneXpert. After consent, we inter-

viewed the clients on risk factors for TB and zoonotic TB. We sent their sputum samples to a reference laboratory. They were cultured and the HAIN MTBC test was performed. This operational research was approved by a Nigerian institutional review board.

Results: Between April and May 2020, we enrolled 123 clients from the 3 states into the study. Selected risk factors among this population are elaborated:

Any farming	46 (37.4%)
Any nomadic herding	52 (42.3%)
Any meat handler/butcher/abattoir	14 (11.4%)
Consumption of unpasteurized dairy products within last 6 months	71 (57.7%)
Wear gloves when handling raw meat	2 (1.6%)
Wash hands after handling raw meat	94 (94.3%)
Ever eat visibly contaminated meat	20 (16.3%)
Sleep in same space as cattle or sheep	37 (30.1%)
Exposure to chronically coughing livestock	35 (28.5%)
Close contact with a coughing man or woman	71 (57.7%)

Table.

Further, 61 clients (49.6%) reported close contact with someone with TB.

Cultures (with solid LJ) grew in 108 specimens. 60 MTBC Hain line probe assays were successfully conducted. As a proportion all 123 specimens, 45.7% (95% CI: 36.5%, 56.8%) were *M. tb* and *M. canetti*, 2.4% (95% CI: 0.5%, 7.0%) were *M. africanum*, and 0.8% (95% CI: 0.02%, 4.4%) were *M. bovis, subspecies bovis*.

Conclusions: These results suggest that it is feasible to test for zoonotic TB in rural settings, though sensitive point-of-care testing would be ideal. The burden of *M. bovis, sub-species bovis* was likely under-detected by several fold as it is more likely to present as extra-pulmonary TB. This study was limited in sample size, mostly due to the COVID-19 pandemic.

EP-21-307 Non-tuberculous mycobacteria in cattle could be a significant cause of zoonotic tuberculosis in Ghana

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Background: In Ghana, the burden and aetiological agent of zoonotic TB are unknown because commonly used diagnostic tools do not discriminate between mycobacterial species. Zoonotic TB is often associated with *Mycobacterium bovis*, the causative agent of bovine TB in cattle.

As the most common route of transmission of *Mycobacterium bovis* to humans is through food (infected dairy products), we sought to isolate and identify mycobacteria species causing Tuberculous-like (TB-like) lesions in slaughtered cattle in Ghana.

Design/Methods: Following post slaughter examination at 4 abattoirs across the country, between December, 2019 and March, 2020, 68 bovine tissues samples showing TB-lesions were obtained. Bacteria isolates obtained from culture on Lowenstein-Jensen (L-J) media were subjected to ZN microscopy.

DNA was extracted from acid-fast bacilli (AFB)-positive isolates and mycobacteria speciation was done by Line Probe Assay (LPA) using GenoType MTBC, GenoType Mycobacterium CM (Hain LifeScience, Germany), and further with mycobacteria 16S rRNA gene sequencing.

Results: No *M. bovis* was identified, however fifty-three (53) bacteria isolates were obtained in total; forty-one (41) nontuberculous mycobacteria (NTM) strains and twelve (12) gram-positive bacteria.

The predominant NTM species was *M. fortuitum* (26.5%, 18/68). The others were, *M. novocastrense*, *M. terrae*, *M. flavescens*, *M. holsaticum*, *M. cosmeticum*, *M. virginsis*, *M. intercellulare*, *M. mageritense*, *M. minesotensis*, *M. duvalii*, *M. lehmanii*, and *M. koreense*.

Conclusions: Nontuberculous mycobacteria species are a significant cause of TB-like lesions in cattle in Ghana with *M. fortuitum* being the most predominant species.

Similarly, speciation of mycobacterial isolates from the 2014 population-based nationwide TB prevalence survey in Ghana, revealed that more than 50% were NTM with *M. fortuitum* being the most frequent (35%). A One health surveillance of NTM in Ghana is therefore rec-

ommended. Sampling from humans, animals and environmental sources such as water and soil would provide insight into zoonotic potential and clinical significance.

Tobacco control: how to succeed against industry tactics

EP-37-460 How compliant are Bengali films, TV serials and "over the top" streaming services in terms of tobacco control provisions? A case from West Bengal, India

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Background: Ministry of Health and Family Welfare, Government of India issued amendments (2011, 2012) under the Cigarettes and Other Tobacco Products Act (COTPA) also known as the 'Film Rules', which came into effect on October 2, 2012 and applicable to all Indian as well as Foreign Films and Television programmes broadcast in India (WHO, 2017).

The present study was aimed to assess the level of compliance of Film Rules in Bengali films, TV serials and OTT Platforms.

Design/Methods: The present study assessed the tobacco use, advertisement, branding regulations and compliance with tobacco-free film rules in Bengali movies (at theaters/cinema halls), web series and TV serials (using the OTT platforms: Hoichoi, Hotstar, Addatimes, Voot, Zee5, Amazon Prime Video, YouTube) from december'2018 to March'2020. Survey for movies was conducted three selected districts of West Bengal i.e., Kolkata, Siliguri and Hooghly based on maximum numbers of Bengali (or regional language) films released in the previous year, most famous city and to possibility of achievement the target sample size.

Results: A total 92 movies, 13 web series and 15 TV serials were viewed. Any tobacco imagery was observed in 71.7% movies, 92.3% web series, though none of the TV serials were found with any tobacco imagery. Moreover, none of these films and web series were found to be fully compliant with legal requirements on health spots, audiovisual disclaimers and statutory health warnings.

Conclusions: Compliance of tobacco control law in Bengali films and online entertainment medias was poor. Strict enforcement of tobacco-free film rules is urgently needed to stop the exposure of tobacco usage.

The members of India's Censor Board under the Ministry of Information & Broadcasting need to be sensitized about provisions of tobacco control law and its influence on tobacco use prevalence, especially among youth.

EP-37-461 Tobacco industry interference during Covid-19: an analysis of South Asia

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Background: According to the World Health Organisation smokers are more prone to COVID-19. Also, the Indian Council of Medical Research (ICMR), Department of Health Research, Govt. of India has issued an appeal to the General Public namely "Not to consume and spit Smokeless Tobacco in Public". Despite Article 5.3 of the Framework Convention on Tobacco Control (FCTC) recommends measures to the Parties to protect their public health policies from commercial and other vested interests of the tobacco industry and Article 13 of the FCTC proposes a comprehensive ban on tobacco advertising, promotion, and sponsorship (TAPS), tobacco industry employed their marketing tactics in COVID times to not only popularize their products but also show their concern and the efforts to fight against COVID.

Design/Methods: Doctrinal research is carried out to analyze and investigate the data collected from both, primary and secondary sources. Data collected from scientific and research publications, media stories, online portals, tobacco industry reports are analyzed qualitatively.

Results: A total of 45 incidents were identified, where tobacco companies not only tried to disseminate false information regarding positive relation between tobacco use and COVID-19 but also includes incidents when Managerial level representatives of tobacco companies met the head of State government and collaborated with the government to break the chain of COVID-19 by providing awareness and also helped the government to establish handwashing booths, funded other initiatives to control COVID.

Conclusions: Tobacco companies have used this opportunity to invest in COVID 19 research and deployed numerous marketing strategies to for giving an impression that they are equally concerned about health and safety. It is necessary that state governments adopt and adhere to Article 5.3 of FCTC to prevent any kind of tobacco industry interference which can result in fatal public health implications.

EP-37-462 Enforcement of tobacco control laws using an online surveillance system and an integrated strategy to curb interference and violations by the tobacco industry in Bangladesh

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Background and challenges to implementation: Grambangla Unnayan Committee is working with the support from The Union for tobacco control in Bangladesh. Tobacco companies are massively violating the tobacco control laws at the Point of Sales (POS) of tobacco products.

Intervention or response: Grambangla has developed an online surveillance system to conduct a census of all POS of all project areas using an android software with Global Positioning System (GPS). During online surveillance an online data collection format was filled out and taken a photo of the POS with a mobile phone. The census collected data on address and type of POS, types of incidences of violations of ban on tobacco advertisement, promotion and sponsorship (TAPS), status of having a trade license by the POS, etc. This surveillance system collects periodic data for comparative analysis of data and measuring impact of anti-tobacco interventions.

Results/Impact: First round of online surveillance data identified 6821 POS and 21480 incidences of violations of TAPS bans at 12 towns i.e. project areas. Types of violations of bans were stickers, shop signage, cash box, showcase, brand name, big dummy packet with tobacco signs etc. Grambangla prepared databases by 12 towns of surveillance data and shared those with the District and Upazila Task Force Committees (TFC) on tobacco control. District and Upazila TFCs conducted 23 mobile court operations to penalize the owners of the POS. Authorized officers i.e. Sanitary Inspectors removed 4769 advertisements from POS of 12 towns. Mayor of 12 towns issued official orders for licensing of 6821 POS and have planned to collect licensing fees and municipal tax. Mayors also prohibited selling of tobacco products in 100 meter of all education institutes.

Conclusions: Using this online surveillance system Bangladesh or any other country can monitor the interferences and incidences of violations by tobacco industry and to plan and enforce provisions of anti-tobacco laws.

EP-37-463 People Movement for Tobacco-Free Village Initiative: a unique success story from Ramanagara District of Karnataka, India

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Background and challenges to implementation: As per the Global Adult Tobacco Survey (GATS) 2016-2017, Smoking prevalence is higher in rural areas (13.3%) than urban areas (9.4%). Hence, District Tobacco Control Cell (DTCC) was approached Suggenahalli Panchayat for declaration of Tobacco Free Villages. 8614 populations of 21 villages. 67 tobacco vendors were found in this panchayat area. Poor awareness regarding ill effects of the tobacco consumption is one of the main challenges.

Intervention or response: Sensitization program was conducted with Panchayat administrator and Panchayat officials by the DTCC, Ramanagara about the ill effects of tobacco consumption and motivated the officials to put up a resolution to declare their village as Tobacco Free. Resolution was submitted by Panchayat Development officer and it was approved in District Level Coordination Committee meeting and the Grama Sabha. Mapping of tobacco vendors was conducted by the accredited social health activist (ASHA) workers. Meeting was conducted with tobacco vendors in the villages. 99% of the vendors agreed to stop sale of tobacco products. Village wise meeting was conducted by DTCC and the Panchayat members. Door to door campaign was done along with ASHA workers. School awareness program was conducted. IEC/Posters on Tobacco Free Villages were developed and distributed in the panchayat. COTPA enforcement drives were also conducted twice in a month.

Results/Impact: Total 21 villages in the Ramanagara district covering a total population of 8614 from 2502 households declared themselves Tobacco Free Villages by passing the resolution. Tobacco Free Village boards displayed at the prominent places of all the villages. No sale of tobacco products in the villages.

Conclusions: Very good initiative was taken by Suggenahalli Panchayat to control the menace of tobacco use at grass root level. It will help to create awareness about the ill effects of tobacco and improve the knowledge of people regarding the Tobacco related disease and Anti-Tobacco Law at Village level.

EP-37-464 Status of compliance assessment of the Cigarette and Other Tobacco Products Act in the Marathwada Region of Maharashtra, India

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Background: It is reveals that every fifth adult was exposed to tobacco smoke at public places. In the view of protecting non tobacco users this survey was conducted in five project districts with the key objective to assess the current level of compliance and enforcement of all the sections of COTPA 2003.

Design/Methods: This is the systematic observational study conducted with partner NGO/academic institutes from respective districts. In each district 8-10 investigators were selected and trained for data collection. The sample size for each district was 400. Inter and intra observer calibration was done to assure reliability of the data and reduce observational error. During the transect walk, a systematic observation was be made and applicable checklist was filled; relevant photographs were be taken as additional evidence. The collected data was collated, entered and analyzed.

Results: It was observed that overall among the 5 survey districts only 27% public places were compliant whereas 73% public places were not compliant with section 4 of COTPA, 15.5% point of sale were compliant and 84.5% point of sale (POS) were not compliant with section 5 of COTPA; similarly, 7.5% of the POS were compliant and 92.5% POS were not compliant with section 6a of COTPA and 19% of the educational institutes were compliant and 81% of educational institute were not compliant with section 6b of COTPA in Marathwada region of Maharashtra.

Conclusions: It is observed that tobacco control is not a priority for government officials as they feel it is an addition responsibility laid upon them; it is a generalized thought of all other departments that tobacco control is the responsibility of health department. Therefore multiple follow up sensitization meetings are required for changing this attitude and getting the work done.

EP-37-465 Prevalence and factors associated with the sale of loose cigarettes at point of sale: a cross-sectional analytical study from four Indian states

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Background: The sale of loose cigarettes is a well-established threat to public health in ways that it renders cigarettes more affordable and accessible to both adults of lower socio-economic groups and youth alike. Another important concern posed by the purchase of loose cigarettes is that the consumers are no longer exposed to the health warning labels on the cigarette packs. Therefore the sale of loose cigarettes compounds the intensity and prevalence of smoking among the general population. This study was carried out with the objective to determine the prevalence and the factors associated with the sale of loose cigarettes among the Point of Sale in the selected four Indian states.

Design/Methods: It was a community-based cross-sectional analytical study. The study was conducted among a total of 2044 PoS in the project states of Meghalaya, Odisha, Puducherry, and Telangana. The characteristics of tobacco vendors and the sale of loose cigarettes were collected using a structured and pre-tested checklist. The proportion for prevalence estimate, bivariate, and multi-variable log-binomial regression analysis was done.

Results: The prevalence of loose cigarette sales was 93.05% [95%CI: 91.89-94.1]. The sale of loose cigarettes showed a significant association with the area, type of vendor, sale of tobacco products to minors, sale of smoking aids to customers, sale of flavored chewable tobacco, and presence of pack warning.

Conclusions: The study provides evidence for the alarming extent of loose cigarette sales in the country and the predictors for the same. The necessity for prompt implementation of the tobacco control laws is highlighted.

EP-37-466 Enhanced implementation and enforcement of tobacco products advertisement, promotion and sponsorship (TAPS) ban in Rio de Janeiro, Brazil

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Background and challenges to implementation: This is a successful case study on TAPS policy enforcement in Rio. TAPS at POS is banned since 2018, in line with the “E” measure recommended by MPOWER package for tobacco control by World Health Organization (WHO). However, in Rio, there is a lack of compliance and of knowledge of policies.

Through the Partnership for Healthy Cities, funded by Bloomberg Philanthropies in collaboration with the WHO and Vital Strategies, Rio developed a project to promote sanitary inspectors’ and retailers’ incorporation of the TAPS rules.

Intervention or response: Consistent work has been done on the development of trainings for inspectors from the local sanitary agency and representatives of retail locations. In addition, a booklet with rules for tobacco control and communication strategies were developed and implemented. As a strategy to exemplify non-compliance, POS were visited to collect data.

Results/Impact: A total of 272 sanitary inspectors were trained. A booklet was published online and delivered to inspectors and the regulated sector. A communication campaign targeting general public about the TAPS policy and tobacco use harm was disseminated on social media networks. Inspectors fined illegal advertising at POS at the entrance to Rock’n Rio’s facilities.

A city ordinance updated the guide for inspectors related to TAPS. While there was no data collected on compliance in the first years after the policy was passed, 31 sanctions were issued and registered in 2021.

Conclusions: The points of sale are numerous and spread throughout Rio. While the adoption of TAPS policies is an achievement in Brazil, cities’ role is key to overcome this challenge. Updating of current policies, developing mechanisms for data collection, implementing strategies for dissemination, reducing the density of POS in Rio have a great potential to advance in the E-measure of MPOWER. Rio’s experience on compliance with TAPS can be enforced at the subnational level.

EP-37-467 To explore the situation of the ban on tobacco advertisement, promotion, and sponsorship ban in Khulna Division of Bangladesh, 2021

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Background: Bangladesh was the first developing country to sign the WHO Framework Convention on Tobacco Control (FCTC) in 2003. Bangladesh Government enacted the Smoking and Tobacco Product Usage (Control) Act in 2005 and amended it in 2013. The Law bans all direct and indirect Tobacco Advertisements, Promotions, and Sponsorships (TAPS). In 2020 The Local Government Division of Bangladesh has published a tobacco control guideline to control and monitor tobacco vendors by issuing licenses from Local Government Institutions (LGI's).

In recognition of this reality, the tobacco industries are promoted to advertisement and tactics within the point of sale (POS).

Design/Methods: To know the present situation of TAPS ban and tobacco sales licensing for the introduction of an LGI's guideline in Khulna Division of Bangladesh. A digital survey with a simple questionnaire was distributed and data was saved digitally on a server. Data was collected by volunteers with the support of the BATA member organization in the respective area.

A total number of 4,520 samples were collected among the targeted communities such as tea stalls, small grocery shops, kiosks, and wholesalers of tobacco products.

Results: The tobacco vendors have received different types of promotional advertisement and multiple ads are displayed in the same store where: flyers 57%, empty packets arranged to show 43%, advertising on windows 39%, sticker 37%, and banner 32%. In some shops (61) cigarette branding shelves are also found.

Most of the tea stalls are selling tobacco products. During the monitoring survey, it came that the Khulna City Corporation has the maximum number of tobacco pos respectively other districts. However, direct advertisement is still banned by the existing Tobacco Control Law 2005.

Conclusions: Need some special efforts like better enforcement of the law, effective mobile court, and tobacco vendor licensing required controlling violation of TAPS.

EP-37-468 Implementer experiences of the tobacco cessation intervention package at non-communicable disease clinics in Punjab, India: a qualitative study

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Background and challenges to implementation: 38 million of the world's 56 million deaths are accounted to Non-Communicable Diseases (NCDs) with tobacco use being a major preventable and modifiable risk factor for NCDs. The National Programme for Prevention and Control of Cancers, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS), facilitates the screening of risk factors for NCDs besides providing them treatment and behavioral advice for NCDs. However, NCD clinics are not being used optimally utilized for providing cessation services to tobacco users.

Intervention or response: We used in-depth interviews (IDI) as qualitative method to ascertain implementer experiences from the pilot implementation of the tobacco cessation intervention package at NCD clinics. 5-6 IDI's were conducted with each category of stakeholders (program managers of NCD control and tobacco control program, doctors, counselors, nurses working at NCD clinics) using a semi-structured IDI guide and carried out until no new responses emerged. Thereafter, the verbatim collected were transcribed, translated and data extraction was done. Codes were extracted, followed by categories by using a standard thematic content analysis framework.

Results/Impact: The implementer experiences were ascertained under three domains i.e, adaptability, practicality, and integration. Under adaptability individual level and structural level factors such as provision of regular training, performance-based incentives emerged. Under practicality, favorable factors (empathetic attitude of HCPs, availability of all services under one roof, mutual benefit to both programs with increased outreach) stemmed. Barriers included lack of adequate IEC material, non-availability of separate counseling room at the level of HCPs while lack of health literacy, lack of willingness to quit among tobacco users surfaced on existing health care landscape. Conditioned integration was highlighted with respect to integration of health promotion perspective, and provision of additional resources.

Conclusions: The stakeholders suggested strengthening the individual and structural level factors to keep the HCPs motivated and incorporation of integrated policy development for common factors from programmatic lens.

EP-37-469 Corporate social responsibility activities of the tobacco industry during the Covid-19 pandemic in Jammu and Kashmir, India

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Background: Tobacco companies in India used the COVID-19 pandemic to build their corporate image by doing Corporate social responsibility activities. Article 13 of WHO FCTC considers CSR activities to be a form of tobacco advertising and recommends its prohibition by all parties to the treaty. This study documents the CSR activities by the tobacco industry in the Union Territory of Jammu and Kashmir (J&K).

Design/Methods: An online search of twenty national and regional newspapers and news outlets was done in the Union Territory of Jammu and Kashmir by State Tobacco Control Cell, Directorate of Health Services, Kashmir on daily basis. The research was carried from March 2020 to July 2020.

Results: Out of the twenty newspapers, three newspapers reported CSR activities by Godfrey Philips India and ITC Limited as under:

1. One lakh masks were distributed to District Administration, Srinagar by Godfrey Philips, India.
2. Distribution of PPE kits to inspector General of Police, Office by Godfrey Philips.
3. Distribution of juices and soaps to the police department of Jammu and Kashmir by ITC.

Such contributions were appreciated during the Covid-19 crisis by the media and people in the administration.

Conclusions: CSR activities help tobacco companies to exert influence on the government in the implementation of tobacco control policies in the state. Such instances of CSR activities by the tobacco industry should be banned under the proposed Cigarettes and Other Tobacco Products Amendment Bill 2020.

ABSTRACT PRESENTATIONS WEDNESDAY 20 OCTOBER 2021

ORAL ABSTRACT SESSION (OA)

OA-12 Adverse events during treatment of drug-resistant TB

OA12-673-20 Optimised loading period strategies for bedaquiline at the restart of drug-resistant TB treatment

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Background: Interruption of therapy is common among patients with drug-resistant tuberculosis (DR-TB) due to the long treatment duration and adverse events. Bedaquiline is an important component of DR-TB treatment and has a long terminal half-life which leads to accumulation. Recommended bedaquiline dosing consists of a two-week loading period (400mg daily) and a continuation phase (200mg three times weekly). Restarting bedaquiline after an interruption without a loading period could lead to low drug exposures, development of resistance, and poor treatment outcomes.

We aimed to identify the most suitable reloading strategies for bedaquiline in different interruption scenarios.

Design/Methods: A model-based *in silico* study was performed. Pharmacokinetic profiles of bedaquiline and its metabolite M2 (associated with QT-prolongation) were simulated for 5000 virtual patients for treatment interruptions with different durations and starting points.

For each interruption scenario, we compared the weekly bedaquiline area under the concentration-time curve (AUC) and M2 maximum concentration (C_{max}) before treatment interruption and after reloading to assess the efficacy and safety of the evaluated reloading regimens (figure).

The reloading strategy resulting in the smallest bedaquiline weekly AUC deviation while not increasing M2 C_{max} was selected.

Results: Bedaquiline weekly AUC and M2 C_{max} deviation were mainly driven by the duration of interruption and only marginally by the starting point of interruption. For interruptions shorter than two weeks, restarting with continuation phase dosing is recommended. For interruptions between two weeks and one month, one month and one year, and longer than one year, reloading periods of three days, one week, and two weeks, respectively, are recommended.

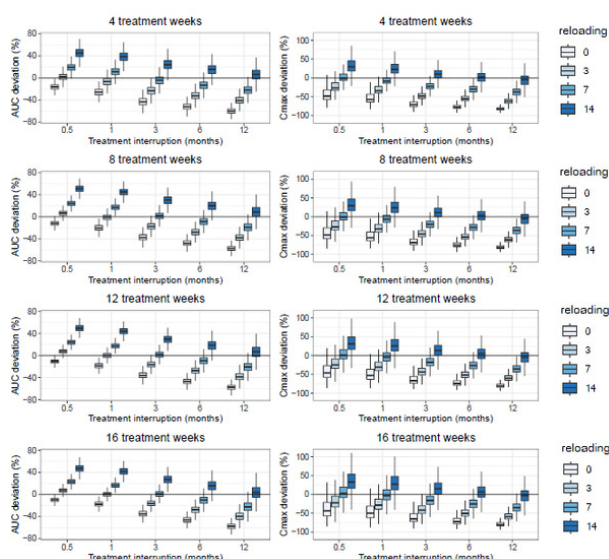


Figure. Boxplots of the weekly bedaquiline AUC deviation (left) and M2 C_{max} deviation (right) under different interruption scenarios with reloading strategies.

Conclusions: This study presents easy-to-implement reloading strategies for clinicians faced with the challenge of restarting a patient on bedaquiline therapy after a treatment interruption.

OA12-674-20 A modelling-based clinical guide for safe reintroduction of bedaquiline after dose interruption: a population pharmacokinetics study

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Background: Usage of bedaquiline in treatment of multi-drug resistant tuberculosis (MDR-TB) is increasing worldwide. Given its complex pharmacokinetics, with a terminal half-life of approximately 5 months, and safety concerns such as QT prolongation, associated

with concentrations of its metabolite M2, reintroducing bedaquiline after dose interruption is not intuitive. In this simulation-based study, we investigated a strategy to reintroduce bedaquiline after dose interruption, taking safety and efficacy into account.

Design/Methods: Multiple scenarios including no loading dose, 1- and 2-week loading dose (400 mg daily) were simulated from a previously developed population pharmacokinetic model describing bedaquiline and M2 for a virtual MDR-TB typical patient, excluding between-patient-variability (Figure 1). Change in average bedaquiline and M2 concentrations over time was evaluated following different scenarios of dose interruption and reintroduction. The efficacy target was defined as 95% return to average bedaquiline concentration without dose interruption within two weeks after treatment reintroduction. The safety target was to not exceed the maximal M2 concentration in a scenario without dose interruption by more than 5 ng/mL.

Results: Predictions of bedaquiline and M2 exposures suggested that dose interruptions between treatment week 1 and 52 (interruption length: 1 to 8 weeks) requires a 1-week loading dose in the typical patient (Figure 1), except for interruptions at week 1 for 4 or 8 weeks. There, a 2-week loading dose is required for efficacy, but the risk for QT prolongation is increased as the safety target is exceeded.

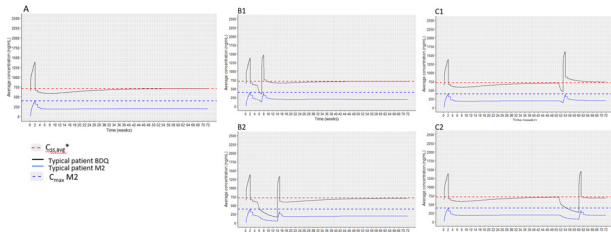


Figure 1. Predictions of average bedaquiline (black solid line) and M2 (blue solid line) concentrations in the typical patient following different dose interruption scenarios. The red dashed line represents the efficacy target (average bedaquiline concentration at steady state) and the blue dashed line is the safety target (maximal M2 concentration in a scenario without dose interruption). A. Scenario without any dose interruption. B1. Dose interruption after 6 weeks, 1 week loading dose 400 mg daily and thereafter continuing treatment at 200 mg 3 times weekly. B2. Dose interruption after 6 weeks, 8 weeks break, 1 week loading dose 400 mg daily and thereafter continuing treatment at 200 mg 3 times weekly. C1. Dose interruption after 52 weeks, 1 week loading dose 400 mg daily and thereafter continuing treatment at 200 mg 3 times weekly. C2. Dose interruption after 52 weeks, 8 weeks break, 1 week loading dose 400 mg daily and thereafter continuing treatment at 200 mg 3 times weekly. *Calculated from the AUC in the last week of treatment period and a weekly dose of 600 mg

Conclusions: Reintroducing bedaquiline after dose interruption optimally is crucial to ensure safety and efficacy. This study shows that dose interruptions occurring between treatment weeks 1 and 52 (interruption length: 1 to 8 weeks) require 1-week loading dose (400 mg daily) in the typical patient, except for dose interruption during week 1 (length: 4 to 8 weeks), where the initial 2-week loading dose of 400 mg should be restarted.

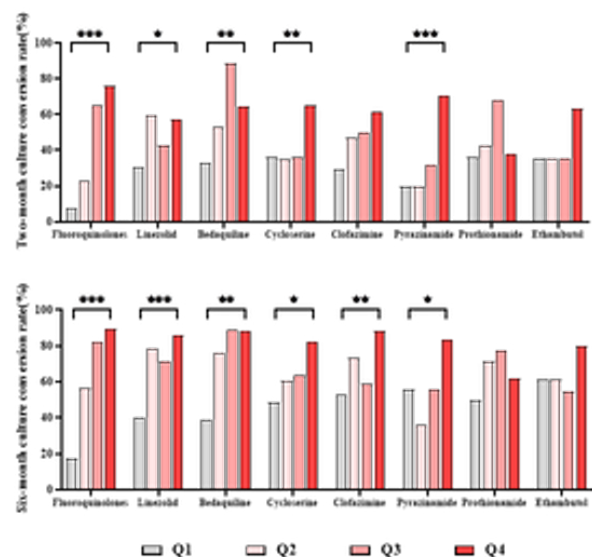
OA12-675-20 Drug exposure and susceptibility to second-line drugs correlate with treatment response in patients with multidrug-resistant TB

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Background: Understanding the impact of low drug concentration and drug susceptibility on treatment response of multidrug-resistant tuberculosis (MDR-TB) may help to optimize treatment. This study aimed to investigate the association between area under drug concentration-time curve/minimum inhibitory concentration (AUC₀₋₂₄/MIC) and response to MDR-TB treatment.

Design/Methods: This was a multicenter cohort study in Guizhou, Henan and Jiangsu Province in China. The study was approved by the ethics committee of the School of Public Health, Fudan University (IRB#2015-09-0565) and written informed consent was obtained from all subjects. In pulmonary MDR-TB patients, second-line drug concentrations were measured after intensive blood sampling and drug susceptibility testing of *Mycobacterium tuberculosis* isolates was performed.

Univariate and multivariate analysis were performed to identify factors associated with sputum culture conversion. Classification and regression tree (CART) analysis was used to identify critical drugs and their targets.



Results: In total, 197 MDR-TB patients with an average age of 42.0 (±9.9) years had fully evaluable pharmacokinetic profiles, thus included for analysis.

Using quartiles of drug AUC_{0-24}/MIC for grouping, fluoroquinolones and pyrazinamide were found to be strongly associated with two-month sputum culture conversion ($P<0.001$) while fluoroquinolones and linezolid were most predictive of six-month sputum culture conversion ($P<0.001$).

Multivariate analysis results showed that patients with fluoroquinolones AUC_{0-24}/MIC above previously reported targets (56 for moxifloxacin and 160 for levofloxacin) had higher probability of two-month culture conversion (aOR 2.91, 95% CI 1.42-5.94). CART analysis selected moxifloxacin AUC_{0-24}/MIC of 231 and linezolid AUC_{0-24}/MIC of 287 as predictors for six-month culture conversion in “moxifloxacin+linezolid+/-bedaquiline” and “levofloxacin+linezolid+/-bedaquiline” based regimens, respectively.

Conclusions: Our findings indicated that fluoroquinolones and pyrazinamide were associated with early sputum culture conversion. The CART-derived thresholds can serve as targets in a randomized controlled study evaluating the impact of therapeutic drug monitoring to improve the treatment outcome of MDR-TB.

Funding: NSFC (No. 81874273)

†: Equally contributed.

OA12-676-20 Analysis of gender-based, WHO-defined outcomes in STREAM Stage 1 trial participants

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Background: Some studies indicate that tuberculosis outcomes are worse in men, attributed to gender-based differences in exposure to TB, health-seeking behavior, extent of disease at presentation, and completion of treatment. We report the gender-specific outcomes of STREAM Stage 1 participants, using WHO-outcome definitions.

Design/Methods: Associations between gender and baseline characteristics were assessed for all participants in the mITT population. Treatment allocation and factors associated with gender were included in multinomial logistic regression models for WHO-defined outcomes, and logistic regression models for WHO favourable outcome. Separate models were fitted for gender-specific outcomes.

Results: At baseline, compared to women, men were older (mean 35.05 vs. 29.49 years; $p<0.001$), more likely to have ever smoked (55% vs. 5% ; $p=0.001$), had lower BMI (13.7% vs. 10% BMI<16 kg/m^2 ; $p=0.047$) but

had higher haemoglobin (mean 11.63 vs. 13.13 $mmHg$; $p<0.001$). After adjustment for treatment allocation and baseline characteristics, no statistically significant difference in odds of any WHO-defined unfavourable outcome were seen by gender: treatment failure (aOR (men/women): 1.56 (95%CI 0.47, 5.24)), death (aOR: 1.06 (0.30, 3.77)) and loss to follow up (aOR: 0.56 (0.17, 1.9)).

There was also no evidence of difference between the genders in risk of death (HR: 1.42 (0.53, 3.85)). In the male model, after adjustment for treatment allocation and covariates, HIV status ($p=0.01$) and BMI ($p=0.02$) were associated with WHO-defined favourable outcome. In the female model, HIV status ($p=0.09$), smoking ($p=0.005$), and previous FQ treatment ($p=0.04$) were associated with WHO-defined favourable outcome.

	Men N=234	Women N=149	OR	P-value	AOR	P-value
Treatment success (WHO definition)	196 (84)	125 (84)	1	-	1	
Treatment failed (WHO definition)	18 (8)	7 (5)	1.64 (0.67, 4.04)	0.282	1.56 (0.47, 5.24)	0.468
Death	13 (6)	6 (4)	1.38 (0.51, 3.73)	0.523	1.06 (0.3, 3.77)	0.924
Lost to follow up (WHO definition)	7 (3)	11 (7)	0.41 (0.15, 1.07)	0.070	0.56 (0.17, 1.9)	0.353
			HR			
Median time to death (weeks)	-	-	0.98 (0.46, 2.1)	0.953	1.42 (0.53, 3.85)	0.486

Conclusions: Men and women in STREAM achieved similar outcomes (WHO-defined), despite men having less favorable baseline characteristics. The reasons for this are unclear, although the more intensive follow up received in a clinical trial setting may have contributed. Further assessment of interventions to improve male treatment outcomes in programmatic settings is warranted.

OA12-677-20 Predictors of adverse treatment outcomes among people with multidrug-resistant TB in Sierra Leone: a national retrospective cohort study

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Background: Multi-drug-resistant Tuberculosis (MDR-TB) is a global public health emergency. In Sierra Leone, a high-burden country, we analysed the sociodemographic and clinic factors associated with adverse MDR-TB treatment outcomes in order to improve person-centred MDR-TB care.

Design/Methods: This retrospective cohort study recruited all people notified with MDR-TB to the Sierra Leone National TB Program between April 2017 and September 2019. Follow-up data were collected to May 2021. Data collected routinely at diagnosis were used to construct a multivariable logistic regression model of sociodemographic and clinical characteristics associated with WHO-defined treatment success (cure or treatment completion) vs adverse treatment outcomes.

Results: There were 365 people notified with MDR-TB. Of these, 341/365 (93%) started treatment, 317/341 (93%) with the WHO-recommended short 9-11 month regimen and 24/341 (7%) with the WHO-recommended long 18-24 month regimen. Median age was 35 years (interquartile range 26-45), 263/365 (72%) were male, 51/365 (14%) HIV-positive, and 127/365 (35%) severely underweight. Overall, 267/365 (73%) people had treatment success, 95/365 (26%) had an adverse outcome, and 3/365 (1%) were still on treatment.

Treatment success was 81% (95% CI=77-85) in those receiving the short treatment regimen vs 54% (95% CI=33-76) in those receiving the long treatment regimen.

Factors associated with adverse outcome vs treatment success were age 45 to 64 years (adjusted odds ratio [aOR]=2.5, 95% CI=1.1-5.4), severe underweight (aOR=4.7, 95% CI=2.0-11), chronic renal failure (aOR=5.8, 95% CI=1.3-25) and chronic lung disease (aOR=2.5, 95% CI=1.2-5.3).

Conclusions: MDR-TB treatment success rates in Sierra Leone were higher than global rates. The increased treatment success rates seen in people receiving a short treatment regimen are likely to reflect better tolerability,

effectiveness, and, to a lesser extent, selection bias. The association of age, underweight, and chronic disease with adverse MDR-TB outcomes, suggests a potential role for nutritional support, integrated non-communicable disease management, and targeted active case-finding for people with MDR-TB in Sierra Leone.

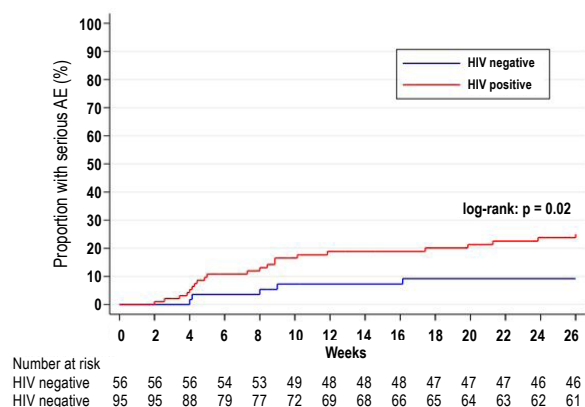
OA12-678-20 Incidence and predictors of clinical linezolid toxicity in drug-resistant TB in a high HIV burden setting: a prospective cohort study

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Background: The frequency and severity of linezolid toxicity in drug-resistant TB has not been characterised in high HIV burden settings.

Design/Methods: We did a prospective observational cohort study to explore predictors of linezolid toxicity and exposure-toxicity relationships. Adults with rifampicin-resistant TB were enrolled at three sites in South Africa between April 2016 and March 2018. Participants were assessed monthly for peripheral neuropathy and cytopenias and underwent pharmacokinetic sampling at three timepoints. Serious toxicity was defined as treatment-emergent Grade 3/4 anaemia, any new thrombocytopenia or leucopenia, or \geq Grade 2 peripheral neuropathy. Linezolid exposures were derived from a population pharmacokinetic model. Time to adverse events was analysed with competing risks Cox regression. ROC analysis was done for drug exposure cut-points, and linear mixed effects models for continuous outcomes.

Results: 151 patients were included; 95 (63%) were HIV-positive (CD4 cell count 212 cells/mm³). 47 (31%) participants had linezolid interruption or dose reduction and 32 (21%) had permanent discontinuation after a median of 60 days (IQR 20 – 99). There were 36 (9%) Grade 3 or 4 events. Cumulative probability of grade 3/4 anaemia was 8% (95% CI, 5 – 14) and \geq Grade 2 neuropathy 2% (95% CI, 1 – 6) at 6 months; median time to any serious toxicity was 6.3 weeks (IQR 13 – 25). HIV was an independent predictor of serious toxicity (aHR 3.6; 95% CI, 1.1 - 11.9). Trough concentration of 2.1 mg/L had a sensitivity of 65% for severe anaemia. Average haemoglobin increased over time ($p < 0.001$) and was negatively correlated with increasing linezolid trough concentrations (coefficient -0.2; 95% CI, -0.3 to -0.1). Platelet counts decreased over time ($p < 0.001$).



Conclusions: Severe linezolid toxicity was uncommon, but those with HIV were at higher risk. Changes in haemoglobin and platelets over time suggest a positive treatment effect. Linezolid trough concentration is a potential biomarker for toxicity.

OA12-679-20 Estimating the benefits of full implementation of bedaquiline-containing regimens in India, South-East Asia, Commonwealth of Independent States and sub-Saharan Africa

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Background: To estimate the clinical and cost benefits of replacing projected use of injectable-containing MDR-TB treatment regimens with all-oral bedaquiline-containing regimens in Southeast Asia (SEA), Commonwealth of Independent States (CIS), India and Sub-Saharan Africa (SSA) in 2021 and 2022.

Design/Methods: A model was built to analyze and compare outcomes and costs associated with two scenarios:

1. Anticipated use of injectable-containing regimens as first-line treatment for MDR-TB,
2. Immediate adoption of bedaquiline-containing regimens to completely replace injectable-containing regimens.

Following costs were accounted for – drugs, hospitalizations, serious adverse events, and other medical and out-of-pocket costs. The number of patients initiating treatment in 2021-2022 was estimated by extrapolating historical WHO data. All inputs (SCR vs LCR, treatment success rates, costs) were derived from secondary

literature for representative country in each high burden region (Indonesia for SEA, Ukraine for CIS and South Africa for SSA), and then extrapolated to the region.

Results: The model estimates that using bedaquiline-containing MDR-TB regimens could successfully treat additional 11.3K patients in India (17% more patients than in injectables scenario), 2.6K in SEA (31%), 2.6K in CIS (28%) and 1.7K in SSA (15%) over 2021-2022. During this period, cost per successfully treated patient is lower with bedaquiline-containing regimens: in India, it is \$3,215 (lower by 24%), in SEA, \$3,207 (-37%), in CIS, \$7,310 (-47%), and in SSA, \$6,114 (-28%).

Conclusions: Treating all MDR-TB patients with bedaquiline-containing regimens is expected to increase successfully treated patients by 15%-30% compared to the scenario of treatment with injectables, potentially helping arrest further transmission of the disease in the high-burden MDR-TB regions. This measure is also estimated to reduce the cost to treat a patient successfully by 25%-50%. Adopting bedaquiline-containing regimens would achieve better outcomes in a more cost-effective manner as the world strives to attain UN's TB Key Targets for 2022.

OA-13 Local barriers to TB care and community-led solutions

OA13-680-20 Driving accountability and community ownership toward health services by involving and empowering elected community leaders

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Background and challenges to implementation: Since 2017, India has proactively attempted to accelerate the pace of its National TB Program. However, community participation, as well as feedback and accountability mechanisms at the community level needed more focus, particularly in the wake of the COVID-19 pandemic and resulting disruptions that occurred.

Intervention or response: Based on previous experience and success, in 2019, GHS adapted its community engagement and leadership development model to a) build awareness on TB and available services (and then COVID-19 as well) b) monitor the quality and availability of TB services at the village level. The program, between March and July 2020, built the capacity of village leaders (*Gram Pradhans*) and frontline health workers (*ASHAs*) to raise awareness on TB and COVID-19, dispel misin-

formation about the diseases, support presumptive TB and COVID-19 patients in accessing care, and integrate TB in COVID-19 screening drives.

Results/Impact: During the lockdown, 272 *Gram Pradhans*, representing a population of 1.74 million people shared over 700 messages on various aspects of COVID-19 and TB across social media platforms (Facebook and WhatsApp) and through outdoor communications (e.g., wall paintings, posters). 16 *Gram Pradhans* worked with local frontline health workers to include TB in their 45-day door-to-door screening program – over 702 people in 16 villages were screened for both COVID-19 and TB, with 2 cases of TB being referred to relevant authorities.

Conclusions: The pilot initiative showed that grass-root 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.

OA13-681-20 Impact of the engagement of community-owned resource persons on TB treatment completion in four districts in the Karamoja sub-region, Uganda

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Background and challenges to implementation: The Karamoja sub-region has one of the highest TB case notifications and lowest treatment completion rates in Uganda. To improve treatment completion rates, the USAID PACT Karamoja project in partnership with CUAMM implemented a patient-centered TB service delivery model involving the use of trained Community-Owned Resource Persons (CORPs) to provide community-based treatment adherence support to patients on TB treatment. We aimed to describe the contribution of the CORPs to patient retention in the Karamoja sub-region.

Intervention or response: In August 2020, 264 CORPs from 66 TB high burden parishes were selected and trained in TB screening, provision of treatment refills, treatment adherence monitoring and contact tracing. Every CORP was assigned a geographical area of operation close to their home and attached to the health facility that serves that area. CORPs were responsible for home-based TB medicine refills, linkage for sputum

monitoring, and follow-up of patients who missed clinic appointments. Supervised by the health facility TB focal persons, CORPs harmonized their weekly reports with the HCWs at the facility of attachment. Monthly allowances to CORPs were performance-based.

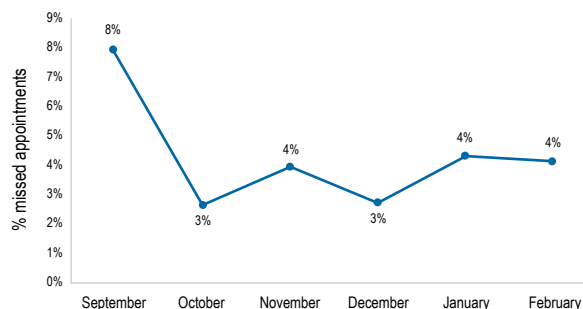


Figure 1. Trend of proportion of patients with missed clinic visits.

Results/Impact: Between September 2020 to March 2021, CORPs carried out 341 home-based TB medicine refills, successfully traced 434 patients who had missed at least one clinic visit and 18 patients who had missed two or more consecutive clinic visits (lost to follow-up), and carried out adherence counseling sessions at community TB treatment points. At the 52 health facilities where these CORPs were attached, the proportion of patients with missed clinic refill appointments decreased from 8% (122/1528) in September 2020 to 4% (59/1417) in February 2021.

Conclusions: Engaging of CORPs in the community-based provision of TB treatment improves retention in care and will in turn improve TB treatment completion in Karamoja.

OA13-682-20 Stigmatisation among TB patients living in Kilimanjaro Region, Tanzania

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Background: Tuberculosis (TB) patients experience stigmatization. The most common cause of TB stigma is the perceived risk of transmission from TB-infected individuals to susceptible community members. We aimed to assess the level of stigma among the TB patients living in Kilimanjaro Region in Tanzania

Design/Methods: A cross-sectional study was conducted among participants who were enrolled in cluster randomized trial done in Kilimanjaro, Tanzania which aimed at investigating the effectiveness of evriMED with reminder cues and tailored feedback on adherence to TB treatment. At baseline, participants were interviewed using van Rie 2008 stigma scale.

Questions could be answered on a Likert scale with four options, strongly disagree (1), disagree (2), agree (3) and strongly agree (4). Two domain scores could be calculated which were Community perspectives (10 Questions) and Patient perspectives (12 questions). Item scores from the questionnaire were summed and scores of 12-40 on community perspectives meant experienced stigma and scores of 12-48 on Patient perspectives meant experience stigma. Cronbach's alpha was considered good for both parts Community perspectives on TB (0.87) and Patient perspectives on TB (0.88). Descriptive analysis was done to investigate scores and differences between sex

Results: Two-hundred and twenty two (53.4%) among 507 participants perceived high levels of stigma from the community and 359 (70.5%) had high levels of personalized stigma. Among men, 154 (69.4%) experienced high levels of community stigma, while 68 (30.6%) women reported high levels (P -value=0.73). For personalized stigma, 256 (71.3%) men and 103 (28.7%) women reported high levels (P -value=0.65)

Conclusions: As in other settings, we have shown that the level of stigma among TB patients in Kilimanjaro is high. Interventions are needed to decrease stigma in these groups. More research is needed to investigate the effect of such interventions.

OA13-683-20 A community of practice for engaging the private sector in TB care

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Background and challenges to implementation: More than 60% of people with TB who were not notified in 2019 were from seven countries ("Big Seven"): Bangladesh, India, Indonesia, Myanmar, Nigeria, Pakistan and Philippines. The private health sector dominates service-delivery in these countries. Since the initiation of the public private mix (PPM), the notification rate in private sector has tripled.[1]

Despite this increase in notification, evidence suggests that the quality of care in private sector falls short of international standards.[2]

1. Global TB report. 2020. World Health Organization. Geneva.

2. Stallworthy G, Dias HM, Pai M. Quality of tuberculosis care in the private health sector. *J Clin Tuberc Other Mycobact Dis.* 2020;20:100171. Published 2020 Jun 13. doi:10.1016/j.jctube.2020.100171

Intervention or response: To enhance cross learning and information exchange, a vibrant online community was launched in October 2019. The TBPPM Learning Network (TBPPM LN) facilitates interaction amongst key stakeholders. At the end of first year, in November 2020, with a rapid growth to over 1300 members, a voluntary online survey was conducted to assess the benefits and identify the gaps in the learning network.

Results/Impact: Respondents indicated they learnt about practical steps to engage private sector and about the impact of COVID19 on TB. Most respondents interacted on a weekly basis with the platform (62%). They indicated that TBPPM lessons and information are forwarded to colleagues and used in daily work (57 and 61 on scale of 100). Overall, 78% respondents concluded that the TBPPM LN is worth their time.

Conclusions: In times of COVID-19 with rapidly increased online interaction, the TBPPM learning network has proven to be an effective platform for knowledge exchange toward the End TB goals.

OA13-684-20 A quantitative study of motivations for entering into, remaining in or exiting from community-based TB care among volunteers in Yangon, Myanmar

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Background: Community-based TB care (CBTBC), involving community health volunteers (CHVs) to improve case finding and treatment adherence, assisted by Japan Anti-Tuberculosis Association (JATA), has been started in Yangon since 2018. Evaluation studies have shown that CBTBC can play an important role in the country's TB program, yet sustainability of volunteer-based activities remains a challenge. This study aimed to examine the motivational factors of the CHVs that could influence volunteers entering, and remaining or exiting volunteer work, and understand what could make CBTBC a sustainable activity in Myanmar.

Design/Methods: A self-administered survey, involving close- and open-ended questions, was conducted among the CHVs working for JATA-CBTBC during July 2020 to April 2021. The questions collected basic demographic characteristics of the volunteers, as well as their motivations related to volunteer work.

Results: 69 among a total of 100 CHVs participated in the survey. Majority of CHVs were recommended to JATA by local health workers, and 66 had been working for JATA for more than 6 months. 90% were females, and 60% were aged between 40 and 59 years old. The motivational factors that were relevant to the volunteer process are summarized in table 1. The majority (91%) expressed their willingness to continue working as CHV, while those who were unwilling or unsure about continuing their volunteer work gave reasons such as "housework", "ill-health" and "being busy with other paid work".

Motivations to enter volunteer work	Motivations to remain in volunteer work	Factors that could push them to leave volunteer work
1. Want to improve the wellbeing of TB patients (68)	1. Feel glad to have become CHV (68)	1. Become busy with housework (29)
2. Want to learn new skills/knowledge (67)	2. Have a good relationship with other volunteers (67)	2. Become sick (27)
3. Want to learn more about TB (67)	3. Like doing the things I do as CHV (66)	3. Become busy with other paid work (14)
4. Want to improve community health (66)	4. Feel that trainings are encouraged and rewarded (66)	4. Difficult means of travelling (12)
5. Feel obliged to help people in need (64)	5. Feel satisfied with my working as CHV (66)	5. Have to pay expenses out of pocket (8)

Conclusions: Our findings indicated that the main motivations to enter and remain in volunteer work were based on pro-social values and the wish for self-empowerment, and less so on materialistic/financial expectations. On the other hand, support is needed to ensure that volunteers do not bear any financial burden for their work. Further qualitative research is planned to identify potential factors which might contribute to sustaining CHV participation, with a specific focus on empowerment.

OA13-686-20 Results from Active Media Engagement in TB Coverage During the COVID-19 Pandemic in Uzbekistan

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Background and challenges to implementation: The COVID-19 pandemic has diverted attention and resources from other public health priorities including tuberculosis worldwide. This was the case of Uzbekistan where the focus of full media and public attention on the COVID-19 pandemic was rapidly overshadowing all other issues of public health importance, including the ongoing TB pandemic. USAID Eliminating Tuberculosis in Central Asia project and the National Tuberculosis Program (NTP) of Uzbekistan joined efforts to regain lost media coverage of TB which had led to a rapid decline of precious momentum in the fight against TB built up over decades of hard work.

Intervention or response: The Project and the NTP conducted a media campaign including training and a media contest. Two online trainings of journalists highlighted the challenges to accessing TB services during the COVID-19 pandemic, provided community-level messaging, and put the spotlight on the destructive effect of stigma against people with TB and COVID-19. The trainings were followed by a contest for the best media coverage of TB issues. The USAID-NTP initiative resonated well

with the community of journalists drawing their attention back to TB and generating significant coverage of TB issues.

Results/Impact: The online trainings and subsequent engagement of journalists successfully shifted significant amount of media attention back to TB. Only between January and April of 2021, 116 publications on TB appeared on TV and radio (13), print (9), electronic media (64), and social networks (30). This was a multi-fold increase over only 7 media publications on TB during the same period in 2020.

Conclusions: Trainings and contests for journalists allowed NTP to reorient significant media attention toward TB-related issues and generate increased interest in and coverage of TB. The mechanism of online interactive engagement of journalists was tested and proven effective in achieving greater media coverage that should help regain lost public attention in the fight against TB.

OA13-687-20 Biopolitical management of migration: example of a population of migrants affected by TB and HIV in Russia

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Background: Russia, the largest receiving country in Eastern Europe. It imposes a residence ban on international migrants with HIV or TB to obtain a residence permit in the country.

Design/Methods: Drawing on qualitative methodology, I conducted semi-structured interviews with 15 international migrants who have experienced a life with HIV and/or TB in Russia as well as 10 interviews with health-care providers.

Results: The study finds that diagnosed TB or HIV in a host country becomes a biographical event that severely affects migrants' life trajectories and excludes them from access to legal employment, free medical care, as well as TB and HIV care. Migrants are having a hard time to leave Russia as requested by the law due to debts, stigma. Migrants are left behind with no TB treatment.

Conclusions: The results support the claim that residence bans restricting migrants' access to a legal status and health services severely affects their life trajectories, self esteem and access to HIV and TB services.

Therefore, such legislations need to be amended in Russia to allow international migrants access adequate health no matter of their HIV status or a possible dis-

nosed TB. This would allow to effectively eradicate the HIV and TB epidemic in Russia as well as in Eastern Europe and Central Asia.

OA-14 Complexity of the TB and COVID-19 epidemics

OA14-688-20 Characteristics and outcomes of confirmed and probable Covid-19 patients hospitalised in Lesotho: a retrospective observational study

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Background: The sub-Saharan African country of Lesotho designated two hospitals as national treatment centers for COVID-19, the disease caused by SARS-CoV-2. We report outcomes of patients with confirmed or probable COVID-19 at treatment centers.

Design/Methods: We conducted a retrospective study of medical charts from treatment center patients between April 1, 2020 and March 31, 2021. Confirmed cases were SARS-CoV-2 polymerase chain reaction or antigen test positive; probable cases lacked diagnostic results. Hypoxemia was a peripheral oxyhemoglobin saturation (SpO₂) <94%. Heated high flow nasal cannula (HHFNC) treatment by eight Airvo™ 2 devices began December 2020. Healthcare workers prospectively documented patient care onto paper-based case forms; data clerks electronically entered data. The Lesotho National Health and Johns Hopkins Institutional Review Boards provided ethical approval. We used standard statistics to describe patient characteristics and fit random effects multivariable logistic regression models to examine associations between outcomes and exposures of interest. Analyses were done with Stata v16.1.

Results: A total of 593 patients were hospitalized; 308 (52%) were confirmed cases. The median age was 50 years and hypoxemia was common (n=398; 67%). Among hypoxemic patients, 86% (344/398) received oxygen and 4% (n=26) also HHFNC. Hypertension (n=182, 31%) and HIV (n=141, 24%) were frequent comorbidities. Among 565 patients with outcomes, 180 (32%) died. The adjusted odds ratio (aOR) for death increased by 5% for every year increase in age (aOR 1.05, 95% confidence interval (95%CI) 1.04, 1.07; p<0.001), and decreased by 8% for every 1% SpO₂ increase (aOR, 0.92, 95%CI, 0.90, 0.94); p<0.001). Patients receiving

HHFNC treatment, compared to no HHFNC, had an 89% lower aOR for death (0.11 aOR, 95%CI, 0.02, 0.51; p=0.005).

Conclusions: Patients with confirmed or probable COVID-19 were severely ill at presentation to national treatment centers and mortality was high. Earlier identification of COVID-19 patients and broader implementation of oxygen and HHFNC should be prioritized.

OA14-689-20 Development and evaluation of a multiplex assay for the detection of SARS-CoV-2 IgM and IgG antibodies: a serological tool for Covid-19 surveillance in Madagascar

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Background: Facing the ongoing COVID-19 pandemic, highly performant multiplex anti-SARS-CoV-2 serology tests are needed to precisely describe and date infection.

Design/Methods: We developed a multiplex assay based on the Xmap technology of Luminex, addressing specific IgM and IgG antibodies against the Spike 1 (S1), Spike 2 (S2), Receptor Binding Domain (RBD) and the Nucleocapsid Protein (NP) of SARS-CoV-2. Blood samples collected periodically for 12 months from 43 COVID-19 diagnosed cases from Madagascar and enrolled starting in March 2020 were tested. Receiver operating characteristics (ROC) curves were generated to determine the cut-off limits and the sensitivity and specificity of the multiplex assay.

Results: Our test showed a good performance for the detection of anti-IgG and anti-IgM antibodies at day 14 after enrolment. The sensitivity and the specificity were equal to 100% (89,85-100) for S1, RBD and NP (S2 had a lower spe = 95%) for IgGs. The area under the ROC (AUC) curve reached 1. We compared this multiplex assay with two commercialized ELISA tests (IDVet IgG-NP and Wantai Ig-RBD). The results showed a higher sensitivity for the in-house multiplex assay. Principal Component Analysis was performed using these eight parameters (IgGs and IgMs against 4 targets) and discriminated well the patients depending on both the time of sample collection and clinical presentations.

Conclusions: We developed a multiplex assay that quantifies the IgG - IgM response to SARS-CoV2 that is highly performant and enables approximate dating of the infection event. This tool may be useful for global surveillance and dating of both SARS-CoV-2 recent

and past infections. This assay, developed within the APRECIT project which aim to evaluate strategies to improve the management of tuberculosis (TB) infection in Madagascar, will be used to monitor the COVID-19 status of TB patients and their household contacts.

OA14-690-20 Impact of Covid-19 on TB services in the Kyrgyz Republic

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Background: The COVID-19 epidemic emerged in Kyrgyzstan in March 2020, triggering government lockdowns and restrictions on movement, partial re-purposing of health facilities, and reallocation of resources to COVID-19, with the potential to undermine TB services, access to care, and infection control. A national health facility survey using Quality of TB Services Assessment methodology was conducted from November 2020 to March 2021, with a new module designed to assess the impact of COVID-19 on TB services.

Design/Methods: Almost 1,000 interviews were conducted in 258 facilities randomly selected using cluster sampling to gather both provider and patient perspectives on COVID-19 impacts. Statistical analysis was conducted by facility type/level and location (region, rural/urban), and examined the impact of COVID-19 on resource allocation, case detection (testing/diagnosis and contact investigation), patient health-seeking behavior, treatment and case management, and infection control.

Results: Overall, 61% of facilities indicated that COVID-19 affected delivery of TB services, with almost half of all facilities indicating a decrease in TB diagnosis or treatment. One-third of facilities indicated health system resources were reallocated to COVID-19; half of all inpatient facilities reallocated TB beds for COVID-19. Results show a 21% and 36% decrease, respectively, in the average daily number of people with presumptive or diagnosed TB presenting to health facilities for testing or treatment monitoring. Increased contact investigations for COVID-19 resulted in decreased contact investigations for TB. Changes to treatment practices show increased uptake of remote treatment support, take-home drug supplies, and virtual clinical services. Infection control practices were amended in 62% of facilities.

Conclusions: Decreased TB case detection due to COVID-19 may lead to a future surge of TB cases. However, expanded remote patient support strategies implement-

ed in response to COVID-19 have improved patient-centered care and mitigated the impacts on treatment adherence. Lessons learned will help guide TB decision-makers to address gaps while retaining positive outcomes.

OA14-691-20 Efficacy of a university-led testing and contact tracing programme in response to a surge in Covid-19 cases, Georgia, February–March 2021

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Background and challenges to implementation: Many universities have created testing and contact tracing programs to minimize transmission and respond to COVID-19 outbreaks. Here we describe the response of a university-led Contact Tracing Program (CTP) to a surge in cases during the Spring 2021 semester.

Intervention or response: In June 2020, a surveillance and CTP was created at Emory University. All students, faculty and staff diagnosed with COVID-19 are interviewed to collect demographics, symptoms, locations visited, and close contacts two days preceding and since illness onset.

During a surge in cases in February 2021, we analyzed quality metrics to determine the proportion of cases and contacts interviewed and time to completion of each step from case diagnosis to testing of contacts. Construction of transmission networks was performed to assess clustering and identify groups for targeted testing

Results/Impact: Between February 10–March 4, the university identified 266 COVID-19 cases confirmed by either saliva PCR or nasopharyngeal RT-PCR testing. Most cases (n=244; 92%) were undergraduates and 41% (n=108) lived on-campus. Median time to reporting cases to the CTP was one day (interquartile range [IQR]=0-2). Nearly all (96%) cases were interviewed the same day as their positive test. Of close contacts, 99% (304/339) were traced and 88% (267/304) were tested by the university. Median time to first test was two days (IQR=0-6); 43% tested positive during the quarantine period. Over 70% of cases (n=187) were affiliated with student organizations.

Network analysis identified one large cluster of 198 individuals (104 cases and 94 close contacts). The surge was considered “under control” within 17 days, after which new cases were no longer epidemiologically linked.

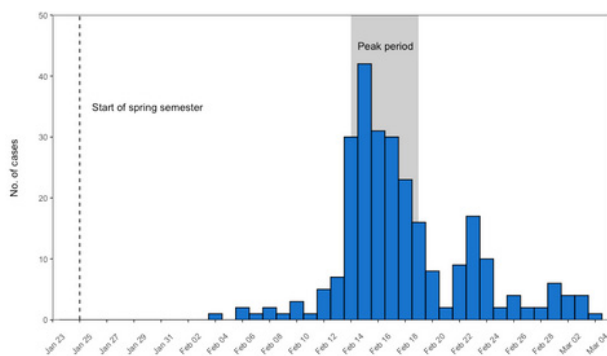


Figure. Earliest date of illness identification

Conclusions: Early detection through systematic testing protocols, rapid and near-complete contact tracing paired with isolation and quarantine measures, and subsequent widespread testing effectively contained the surge.

This report highlights that efficient university contact tracing programs can effectively contain COVID-19 outbreaks on campuses.

OA14-692-20 Patient delays in accessing TB care in four African countries: a cross-sectional study

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Background: Delayed tuberculosis (TB) treatment initiation can lead to increased morbidity and mortality. We describe time-to-treatment initiation (TTI) among symptomatic TB patients in four African countries and identify patient-related factors associated with delays in treatment initiation.

Design/Methods: Pulmonary TB patients (≥ 18 years) initiating treatment at health facilities in South Africa (SA), Tanzania (Tz), Mozambique (Moz) and The Gambia (Gam) were enrolled between September 2017 and December 2019 (TB Sequel). Structured questionnaires were used to collect data on demographics and the presence and duration of TB symptoms since onset. TTI was calculated as time (weeks) between the onset of the first TB symptom and the initiation of treatment at the health facility. We developed a logistic regression model

to test causal models associated with patient delay (TTI ≥ 6 weeks) - directed acyclic graphs were created for each potential casual factor.

Results: We enrolled 1,419 patients (SA:359, Tz:273, Moz:417, Gam:370) (median age 34 years [IQR 27-43], 35% female, 52% completed high school). Overall HIV prevalence was 42% but varied by country [SA:247(69%), Tz:133(52%), Moz:188(46%), Gam:27(7%)]. The majority of patients (89%) reported experiencing ≥ 2 TB symptoms (cough, night sweats, weight loss, fever and haemoptysis) at the onset of their TB disease. The proportion of patients with delayed TTI (50%) varied across countries [SA:153(44%), Tz:202(74%), Moz:163(40%), Gam:188(51%)]. HIV status, anti-retroviral therapy (ART), experiencing more TB symptoms and country (Tanzania) were factors associated with delayed TTI (Table 1).

Variable	Unadjusted OR	p-value	Adjusted OR	p-value	Adjusted covariates
Age (A)	1.00 (1.0 – 1.0)	0.516	1.00 (1.0 – 1.0)	0.612	C, U, S
Female (S) (vs Male)	0.93 (0.7 – 1.2)	0.533	0.92 (0.7 – 1.2)	0.476	C, U
Unemployed (U) (vs Employed)	0.85 (0.7 – 1.1)	0.164	0.86 (0.7 – 1.1)	0.219	C, Education, S
Previous TB (vs no Previous TB)	0.69 (0.5 – 1.0)	0.028	0.71 (0.5 – 1.0)	0.060	A, HIV, S
HIV+ (vs HIV-)	0.72 (0.6 – 0.9)	0.003	0.64 (0.5 – 0.8)	0.001	A, C, Education, S
HIV+ ART (vs HIV+ no ART)	1.64 (1.1 – 2.4)	0.007	1.63 (1.1 – 2.4)	0.016	C
Number of symptoms	1.35 (1.2 – 1.5)	0.000	1.33 (1.2 – 1.5)	0.000	A
Country (C)					
Tanzania (vs Gambia)	2.75 (2.0 – 3.9)	0.000	3.21 (2.1 – 4.9)	0.000	U, HIV, Education, S
Mozambique (vs Gambia)	0.64 (0.5 – 0.8)	0.002	0.75 (0.5 – 1.1)	0.097	
South Africa (vs Gambia)	0.75 (0.6 – 1.0)	0.057	0.93 (0.6 – 1.3)	0.691	

Table 1: Factors associated with patient delays (≥ 6 weeks) in accessing TB care among TB patients in four African countries

Conclusions: Across all countries, there were significant delays in TTI. HIV findings highlight the need for better programmatic integration to ensure TB treatment is started as soon as possible after ART is initiated. High number of symptoms highlight why passive case finding is not sufficient and a greater focus on implementing active case finding interventions may help overcome delays in TTI. Country specific interventions are required to address contextual factors.

OA14-693-20 Laboratory diagnostic monitoring of South Africa's HIV, TB and Covid-19 syndemic

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Background: South Africa has a mature national HIV and tuberculosis (TB) molecular diagnostic laboratory program, that supports >5.5 million HIV viral load (VL), >0.5 million early infant diagnoses and >2.5 million Xpert MTB/RIF Ultra TB tests per annum in the public sector. In April 2020, this molecular platform was leveraged for SARS-CoV-2 testing and the test results interfaced with the National Health Laboratory Services laboratory information system (LIS). Ongoing centralised evaluation and monitoring of all laboratory operations, during the COVID-19 pandemic, highlighted a decrease in attention for non-COVID-19 programs.

Design/Methods: Aggregated test results reported per day were monitored by the lockdown levels and by months since January 2020. Data comprised the number of HIV VL, Xpert MTB/RIF Ultra and SARS-CoV-2 tests performed; number of HIV VL>1000copies/ml; number of positive Xpert MTB/RIF Ultra; and number of positive SARS-CoV-2 tests. The percentage rate of change for testing is reported by lockdown levels.

Results: The cyclical nature of SARS-CoV-2, showed daily testing rates increased from 3000tests/day in April 2020, to over five-fold in the first wave (July 2020) and nine-fold in the second wave (January 2021) with >4.6million tests (of 10.8million total country testing) captured by April 2021.

During lockdown level 5 (03/27/20 – 05/01/2020), HIV VL daily testing rates reduced by 12.7%, which temporarily recovered from pre-lockdown levels by Q2/2020. Virological failure remained stable at ~13%. Xpert-MTB/RIF Ultra daily testing rates reduced by 50% between pre-lockdown to level 4 (05/01/2021) and only started recovering by September 2020 (Figure). TB test positivity increased from 8.5% pre-lockdown to 10.5% by level 2 (August 2020), returning to ~8.7% since October 2020.

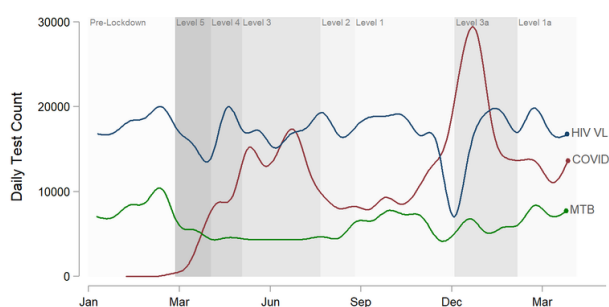


Figure.

Conclusions: COVID-19 in South Africa negatively affected other communicable diseases, especially during high-level lockdown, restricting patient's access to care. New era of centralised data alerts across syndemics is required to ensure ongoing support.

OA14-694-20 Programmatic adaptations to address challenges to the TB programme during Covid-19 in rural India

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Background and challenges to implementation: As the world grapples with the COVID-19 pandemic, TB remains a silent killer. With nationwide lockdowns, health systems directed towards pandemic response, and disruption of essential services for people with TB, the pandemic threatens to reverse the progress made towards achieving global TB targets in recent years.

Intervention or response: We run an active case finding TB program in 10 rural blocks (covering 54%) of Samastipur, Bihar. Case findings in our catchment continued despite lockdown, through planning and coordination with the public health system (PHS). Presumptive patients were identified through telephonic contact with community health workers and screened over the phone. TB diagnosis in the PHS was affected as laboratory personnel was assigned for COVID-19 duty. To meet demands, we re-allocated the program budget to purchase an additional GeneXpert machine that increased our testing capacity. Sputum samples of presumptive patients were collected from home and tested upfront using GeneXpert and chest radiography was facilitated at private facilities. Co-morbidity tests were also ensured from private laboratories. The program team collaborated with district officials for an uninterrupted supply of medicines and where necessary additional drugs were procured. Telephonic follow-ups were ensured 2-3 times every week to monitor treatment adherence and provide counseling.

Results/Impact: Between April and December 2020, 10,917 presumptive cases were identified from the community and 90% (n=9,844) of them were screened over phone. 1906 cases of TB were diagnosed in our intervention area, representing 78% of all cases in the district. The overall rate of treatment initiation was > 95%. Total 89% of diagnosed TB cases were offered UDST and 73% offered co-morbidity test (HIV test).

Conclusions: Prompt planning and action, collaboration with the public health system, and a people-centric approach are the key ways to address the various challenges posed by the pandemic on TB programs in high burden countries like India.

OA-15 Strategies to find the missing millions

OA15-695-20 The double-X strategy: increasing TB detection in community and facility settings in Vietnam

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Background and challenges to implementation: The Vietnam National Tuberculosis (TB) Program (NTP) aims to increase detection and treatment of TB disease and latent TB infection (LTBI) to end TB by 2030. The NTP's Double X (2X) strategy prioritizes chest X-ray (CXR) and GeneXpert to increase TB screening sensitivity, while integrating LTBI detection.

Intervention or response: From March—December 2020, the NTP implemented 2X in 18 districts of seven provinces in Vietnam with USAID support. TB risk groups in health facilities and communities were screened with CXR, and if abnormal, sputum GeneXpert. 2X intensified case finding (ICF) in health facilities screened outpatients with any respiratory symptoms, inpatients with lung diseases, and outpatient diabetics with TB symptoms. 2X active case finding (ACF) community campaigns screened household contacts of adult pulmonary TB patients diagnosed within two years and high-risk groups (elderly, diabetics, smokers, those with

pulmonary or chronic diseases, and those previously treated for TB). Tuberculin skin testing (TST) was conducted in ACF participants to detect LTBI.

Results/Impact: We screened 171,718 people with CXR of which 13,540 (7.9%) were abnormal, leading to 12,992 people with sputum GeneXpert examination. A total of 1,652 people with GeneXpert-confirmed pulmonary TB were detected from ICF (n=962) and ACF (n=690). Respiratory outpatients comprised the largest proportion of 2X ICF (571/962, 59.4%), while yield was highest for diabetics (n=117, 1,810/100,000 CXR). 2X ACF yield was high: 690 people were diagnosed with TB, who were predominantly high-risk groups (n=605, 87.7%), male (n=570, 82.6%), and a mean age of 58.8 ± 14.6 years. TST (≥10 mm) in 24,449 ACF participants detected LTBI in 3063 (12.5%) people.

Conclusions: The Vietnam NTP's 2X strategy was high yield for detecting TB disease in community and health facility settings, while efficiently integrating LTBI detection. Risk group selection, symptom screening algorithms, and quality of CXR interpretation likely impact 2X yield for TB disease detection.

2X setting	Risk group or facility setting	Symptom screening	No. evaluated with CXR	No. (%) abnormal CXR	No. tested with GeneXpert	No. (%) GeneXpert-confirmed pulmonary TB	Yield for GeneXpert-confirmed TB patients per 100,000 CXR
Intensified case finding (ICF) in health facilities	General outpatient clinics	Any respiratory symptoms	90260	2569 (2.8%)	2353	571 (24.3%)	633
	Inpatients with lung diseases	Not required	22127	1614 (7.3%)	1566	274 (17.5%)	1238
	Diabetes outpatient clinics	TB symptoms per NTP guideline	6463	1402 (21.7%)	1327	117 (8.8%)	1810
	TOTAL 2X ICF		118850	5585 (4.7%)	5246	962 (18.3%)	809
Active case finding (ACF) in community campaigns	Household Contacts	Not required	12932	1298 (10.0%)	1266	85 (6.7%)	657
	High Risk Groups	Not required	39936	6657 (16.7%)	6480	605 (9.3%)	1515
	TOTAL 2X ACF		52868	7955 (15.0%)	7746	690 (8.9%)	1305
TOTAL 2X ICF AND ACF			171718	13540 (7.9%)	12992	1652 (12.7%)	962

OA15-695-20 Table.

OA15-696-20 Integrating paediatric TB case detection at paediatric entry points in sub-Saharan Africa: results of the INPUT stepped-wedge cluster-randomised study

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Background: Underdiagnosis of TB in children is a critical gap to address. The INPUT study aims to assess the effect of integrating TB services into child health care services on TB diagnosis capacities in under-five children.

Design/Methods: We implemented a stepped-wedge cluster-randomized study to assess the effect of the Catalyzing Pediatric TB Innovations (CaP TB) interventions package (including integration of TB screening into child health care services, improved clinical, radiological, and bacteriological diagnosis capacity) on the proportion of pediatric TB cases diagnosed among under-five children attending health care, compared to standard of care (SOC). Twelve clusters in Cameroon and Kenya started the study under the SOC and transitioned to the intervention at randomly assigned times. Weekly aggregate numbers of under-five child attendees were collected. With parental consent, children identified as presumptive TB were monitored through diagnosis and treatment.

Comparisons were made using generalized linear mixed Poisson models and presented as rate ratio and associated 95% confidence interval (CI).

Results: From May 2019 to March 31, 2021 (close of enrolments), 220,715 under-five children were seen in pediatric entry points, 788 were enrolled as TB presumptive and 156 (20%) were diagnosed with TB. The mean age was 1.5 years (SD 1.3), and 88/156 (56%) were male. Overall, 96/156 (62%) had an X-ray and 74/156 (47%) had an Xpert performed, with 140/156 (90%) diagnosed clinically/radiologically and 16/156 (10%) bacteriologically-confirmed. In Cameroon 2/40,668 were diagnosed in SOC (0.05/1000, 95%CI [0.01-0.18]) and 33/38,838 (0.85/1000 [0.58-1.19]) in intervention. In Kenya, 77/84,691 (0.91/1000 [0.72-1.14]) were diagnosed in SOC and 40/56,518 (0.71/1000 [0.51-0.96]) during the intervention phase, impacted by healthcare workers strikes (Figure 1).

Conclusions: Preliminary results show an effect of CaP TB intervention on TB case detection in Cameroon. Final results will be available in August 2021 and will inform innovative approaches on the organization of TB care in children.

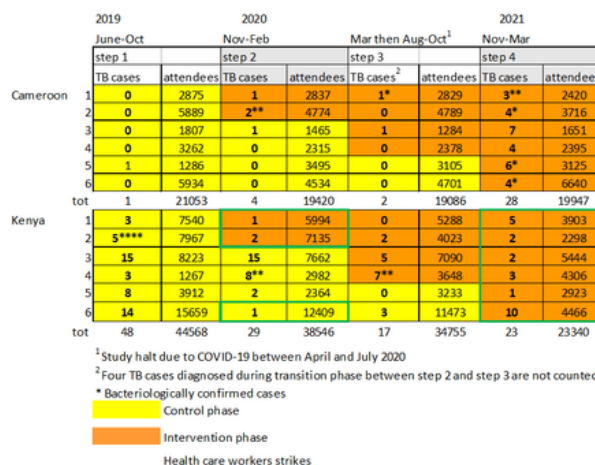


Figure 1. Number of TB cases and attendees per cluster and step in the study.

OA15-697-20 Strategic approach to the optimisation of TB contact investigation: the KNCV Nigeria experience

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Background and challenges to implementation: To meet the UNHLM targets, the NTP in Nigeria adopts systematic contact investigation (CI) as an effective method for the timely diagnosis of TB patients and provision of TB preventive treatment (TPT) to eligible contacts. However, this process has been largely passive and not client centered. The USAID funded TB LON project implemented by KNCV introduced an inclusive approach to CI

Intervention or response: Active CI intervention implemented across 14 states in Nigeria. Contact investigators were identified from adhoc TB screening and DOTS officers with cultural sensitivity as a key criterion. They were trained on contact investigation, Index TB patients were mapped, a convenient time was set with the index patient to visit their households, house-to-house case search within 2 km radius was done to eliminate stigma, specimen was collected and transported to diagnostic facilities, diagnosed patients were linked to treatment, weekly cascade monitoring and monthly quality improvement meetings were held

Results/Impact: CI was received as a continuum of care for TB patients among care providers. After 3 quarters of implementation, 13,447 (83%) index cases were visited and 96% (62,399) of their contacts were screened for TB with 19,761 (32%) presumptive for TB, out of which 19,068 (96%) were tested for TB with 2,225

(12%) diagnosed with TB of which 2,154 (97%) were started on treatment. Overall, 2,652 clients were enrolled on TPT. This represents a 488%, 214%, 232%, 216% and 619% average quarterly increase in index patients visited, contacts screened, presumptive TB cases tested, TB patients enrolled on treatment and clients enrolled on TPT respectively compared to 3 months prior to intervention.

Conclusions: Systematic contact investigation is a targeted high yielding case finding intervention that not only facilitates TB case detection but also TPT. To optimize the gains of CI, it must be active, patient-centered and implemented as a continuum of TB care.

OA15-698-20 Evaluation of the MATCH Framework for targeting populations and maximising yields during active TB case-finding

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Background: The MATCH framework uses geospatial and TB program data to identify and visualize potential disease hotspots and gaps in health services. We conducted a retrospective evaluation of the MATCH framework to understand whether prioritizing active TB case finding (ACF) implementation using this approach could result in higher yields of TB.

Design/Methods: Between October 2018 and October 2019, 82 days of community-based, mobile chest X-ray (CXR) screening events were organized across three districts of Ho Chi Minh City, Viet Nam. We collected data from participants aged ≥ 15 years residing in the ward where each screening event occurred. Ward-level case notification rates (CNRs) for 2018 were calculated and split into quintiles for each district. A mixed-effect log-binomial model, using ward as a random effect and controlling for individual- and event-related factors, was fitted to compare TB detection rates across the CNR quintiles using adjusted prevalence ratios (aPR). A sensitivity analysis was conducted using imputed data for missing Xpert MTB/RIF test results.

Results: The final data set included 19,719 participants screened by CXR, of whom 124 were Xpert-positive (TB detection rate = 629 / 100,000). The final model controlled for age, sex, history of TB, contact status, cough

duration and distance from the CXR screening event to the District TB Unit. Screening events conducted in wards with the lowest CNRs had significantly higher TB detection rates compared with events from the middle CNR quintile (aPR = 1.84 [1.04-3.27], $p=0.036$). The TB detection rate was also significantly higher when imputing missing Xpert results. Screening events organized in the highest CNR quintile, i.e., presumptive hotspots, also tended to have higher yields, but this was not significant.

CNR Quintiles	Without Data Imputation		With Data Imputation	
	aPR (95%CI)	p-value	aPR (95%CI)	p-value
1 (High)	1.59 (0.84- 2.99)	0.155	1.57 (0.84 - 2.94)	0.158
2	1.35 (0.70- 2.61)	0.374	1.29 (0.67 - 2.47)	0.447
3	<i>Ref</i>		<i>Ref</i>	
4	1.27 (0.66-2.43)	0.480	1.25 (0.66 - 2.37)	0.486
5 (Low)	1.84 (1.04- 3.27)	0.036	1.77 (1.01 - 3.12)	0.046

Conclusions: Prioritizing ACF in wards with the lowest CNRs with presumptive health service gaps can result in higher yields of TB and more cost-effective ACF implementation.

OA15-699-20 Implementation of systematic screening for TB disease and administration of TB preventing therapy among PLHIV attending ART clinics in Ghana

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Background: Among people living with HIV (PLHIV), tuberculosis (TB) is a leading cause of death. To detect TB among PLHIV, Ghana's TB screening algorithm utilizes Xpert MTB/RIF and digital chest x-ray (CXR). To date, administration of TB preventive treatment (TPT) to PLHIV without evidence of TB disease has not been widely implemented. We aimed to assess the yield and cost of implementing systematic screening of TB disease among PLHIV and initiation of TPT among those without disease.

Design/Methods: We did a prospective study from August 2019 to December 2020 at 10 antiretroviral treatment (ART) clinics across Ghana. Staff at each site were trained prior to study implementation. All persons at

tending ART clinics were screened for TB symptoms and offered digital CXR. For PLHIV with abnormal CXR and/or symptoms who could produce sputum, Xpert MTB/RIF was done. For PLHIV without evidence of TB disease, TPT (six-months isoniazid) was offered. We did micro-costing to estimate health system costs of the program from staff training to TPT or TB disease treatment completion in 2020 \$USD.

Results: Overall 2639 PLHIV consented to participate in the study and received TB symptom screening; 95.5% had a digital CXR and 8.5% were further screened with Xpert MTB/RIF. In total, 53 (2.0%) were diagnosed with TB, including 26 (1.0%) who were asymptomatic. Of the 53 diagnoses, 14 (0.5%) were bacteriologically confirmed and 39 (1.5%) were clinically diagnosed.

Of the 2586 PLHIV eligible for TPT, 2581 (99.8%) initiated. Overall, the cost per person was \$76.24 USD—45% was attributed to TPT, 37% to TB disease screening and treatment, and 18% to training.

Conclusions: In Ghana, systematic TB screening and offering of TPT among PLHIV was acceptable, high yield, and of modest cost. A significant proportion of TB would be missed by symptom screening alone. These findings warrant further evaluation and wider implementation.

OA15-700-20 An innovative public-private mix model for finding missing TB cases in Nigeria

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Background and challenges to implementation: Nigeria is among the 30 high burden Tuberculosis (TB) countries globally with over 323,000 TB cases undetected in 2019. Public-Private Mix (PPM) is an approach that could help in finding missing TB cases. Active engagement of the private sector in TB control in Nigeria has not been prominent.

Intervention or response: The active engagement of private providers in TB control with support from the Global Fund in 21 States commenced in January 2019. Innovative approaches implemented include:

- i. Systematic facility-based screening of persons attending OPD by trained providers.
- ii. Engagement of trained and incentivized Patent Medicine Vendors, Community Pharmacist, Traditional Birth Attendants, Standalone Laboratories and religious houses to provide referral services.

iii. Activation of hub-and-spoke model to facilitate referrals.

iv. Engagement of Linkage Coordinators to ensure completion of referrals.

v. Intensified follow-up care by facility officers and Linkage Coordinators.

vi. Deployment of a mobile application to enhance TB screening.

vii. Access to TB diagnosis using Xpert MTB/RIF assay, smear microscopy or chest X-ray.

viii. Establishment of sputum sample transportation mechanism in facilities without on-site diagnostic facilities.

ix. Appropriate capacity building and intensive mentoring.

We conducted a cohort study using project and surveillance data reported to the National TB Programme (NTP) from 2017 - 2020.

Results/Impact: TB case notification from private providers increased from 9,276 in 2017 to 27,922 in 2020 in the twenty one States with contribution to total notification increasing from 16% in 2017 to 36% in 2020.

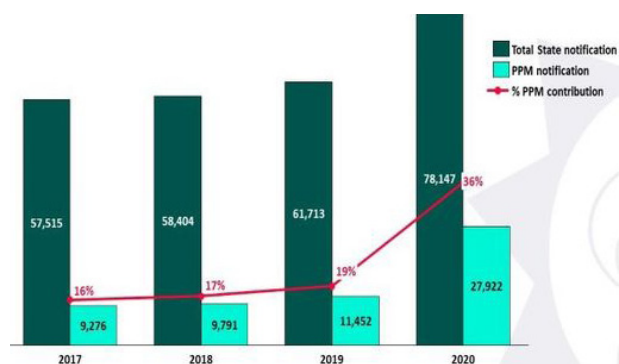


Figure 1: PPM contribution to TB notification in twenty-one States in Nigeria from 2017 to 2020

Conclusions: The active engagement of all types of private health providers in TB control has shown to help in finding missing TB cases in Nigeria. This engagement should be scaled up nationwide by the NTP. A detailed cost effectiveness analysis should be conducted to inform this decision.

OA15-701-20 Pilot implementation of active TB case-finding in Nigerian prisons: the USAID-funded LON Region 3 Project

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Background: The World Health Organization recommends systematic TB screening among inmates and other individuals in closed settings and penitentiary institutions. Prisons remain the reservoirs of TB transmission as a result of overcrowding, poor ventilation and limited access to healthcare. Unlike passive case finding, active case-finding (ACF) of TB in prisons enhances early diagnosis and treatment of inmates and disrupts the chain of transmission. We aimed to present the pilot results of active TB case search in selected Nigerian prisons within the USAID-funded LON 3 project implemented by the Institute of Human Virology of Nigeria.

Design/Methods: Between April and May 2021, we conducted advocacy and sensitization/awareness creation visits to prison authorities across two Federal and State prisons in Ogun and Lagos State, in collaboration with the State TB Program and Civil Society Organizations. Following approval by the authority, five rounds of active case search visits were implemented in phased approach. Inmates were clinically screened for symptoms of TB and responses were documented in screening register and other recording and reporting tools. Sputum were collected from symptomatic inmates and transported for genexpert analysis. Data were entered into Microsoft Excel for analysis.

Results: Across the two states, a total of 740 inmates eligible were screened for TB of which 15% (111) were presumptive. Of the 111 presumptives, 11% (12) were diagnosed with TB using Genexpert and 67% (8) of them were enrolled on treatment, 8% (1) died before treatment started while the remaining 3 were yet to be commenced on treatment. This gives a point prevalence rate of 1,622 TB cases per 100,000 prison inmates.

State	Inmates eligible for screening	Screened	Presumptive	Evaluated	Diagnosed	TB Yield	Started on Tx	DRTB	NNS	NNT
Lagos	240	240	74	74	9	12%	6	0	27	8
Ogun	500	500	37	37	3	8%	2	1	167	12
Total	740	740	111	111	12	11%	8	1	62	9

Conclusions: The prevalence of TB among inmates was several folds higher than that of general population as demonstrated by the results of the ACF. There is an urgent need to scale up this strategy nationally across prisons combined with contact investigation as an effective TB control measure.

OA15-702-20 A clinical prediction tool to improve treatment decision-making for children with TB

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Background: Tuberculosis (TB) diagnosis in children is complicated by the presentation of non-specific symptoms, difficulty producing sputum, and low sensitivity of conventional diagnostic in children. The WHO recommends that, in the absence of diagnostic tests, children should be treated for TB if there is sufficient clinical evidence of disease. However, it is unclear what clinical evidence is sufficient to make the decision to initiate treatment. We derive a clinical prediction tool to improve the clinical diagnosis of TB in children for timely TB treatment initiation.

Design/Methods: We conducted a prospective intensified TB patient-finding intervention at four facilities in Pakistan (2014-2016). A case of TB disease was determined through either bacteriologic confirmation or a clinical diagnosis. Using Classification and Regression Tree (CART) analysis we developed decision trees to identify algorithms that more accurately classify children with TB. Identified predictors were used in logistic regression to estimate their association with TB disease. Trees were developed for children 0-14, 0-4, 5-9, and 10-14 years old. Final trees will be validated locally and regionally.

Results: 105,338 children <15 were screened for TB; 5,880 (5.6%) were presumed to have TB. Upon further evaluation, 1,417 (24.1%) were diagnosed with TB. CART identified chest x-ray results and having a family history of TB disease as the most important predictors of TB in all children 0-14 years old. Area under the receiver operating characteristic curve was 0.95. In regression, having a chest x-ray suggestive of TB disease increased risk of TB diagnosis (RR: 17.4; 95% CI: 15.3-19.8; p<0.01). Of those with a normal chest x-ray, having a family history of TB increased risk of TB diagnosis (RR:13.3; 95% CI: 10.4-16.9; p<0.01).

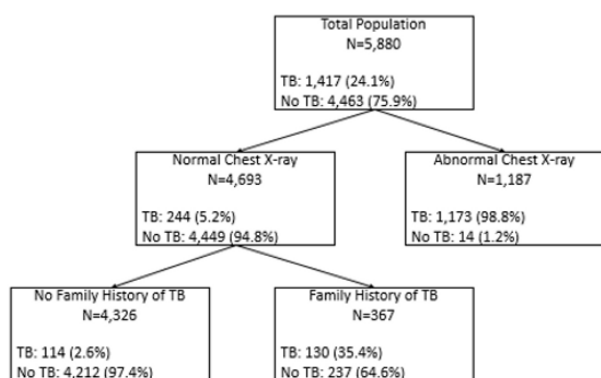


Figure 1. Decision tree of predictors of TB disease in children 0-14 years old.

Conclusions: Use of clinical evidence was sufficient to accurately predict TB disease in children. This tool may be useful to inform rapid treatment initiation in children, however external validation needs to be completed.

OA-17 Stakeholder interaction in TB care

OA17-710-20 Mobile application for TB screening (MATS): a mobile technology revolutionising TB case-finding in Nigeria

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Background and challenges to implementation: Reaching the over 300,000 undetected Tuberculosis (TB) cases in Nigeria with TB services is a huge challenge especially in the private sector. Inadequate human resources, high staff turnover, the burden of documentation on paper based-tools, etc. poses a threat to TB case notification in the private sector. The use of mobile technology in TB notification has not gained prominence in Nigeria.

Intervention or response: The Mobile Application for Tuberculosis Screening (MATS) was upgraded to a screening and notification app by the Institute of Human Virology, Nigeria in partnership with the National Tuberculosis Programme and PharmAccess Foundation with funding from the Global Fund. The app is used by

private healthcare providers including; private-for-profit and faith-based organization facilities, patent medicine vendors, community pharmacists, traditional birth attendants/healers, and standalone laboratories in 21 states of Nigeria. Providers only need to download the app on their mobile devices and register to use it. Based on responses to certain questions prompted by the app, MATS can identify a presumptive TB case and request further evaluation.

Results of the evaluation are notified on the app while confirmed TB cases are linked to appropriate treatment. Before deployment in June 2020, users were trained and mobile phones and Tablets were procured for users without android-enabled devices. The app is user-friendly and tutorial videos on how to use the app have also been developed.

Results/Impact: After 11 months, over 3,500 private healthcare providers have used the app to screen 397,467 persons, resulting in the identification of 30,078 presumptive TB cases with 732 confirmed TB cases linked to treatment.

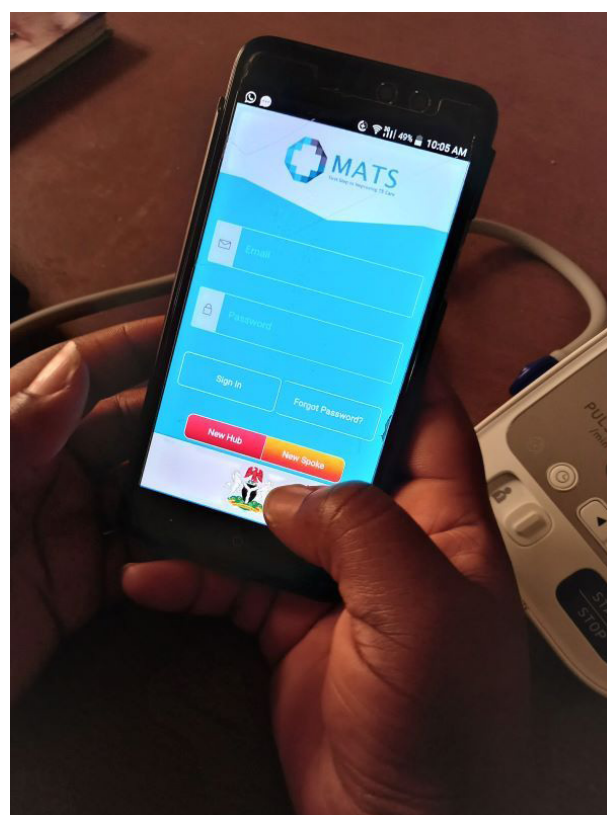


Figure 1: A provider using MATS for TB screening and notification

Conclusions: The MATS app is a novel technology with the potentials to improve access to TB diagnosis and treatment. The NTP should consider scaling it up nationwide and possibly extending its use to the public sector.

OA17-711-20 Changing the narrative in low TB reporting local government areas in South-South Nigeria: is PPM the game changer?

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Background and challenges to implementation: Public-Private-Mix (PPM) is recommended by the World Health Organization as a key strategy to close the gap in missing TB cases in high burden TB countries. Nigeria is one of such countries with a low case notification.

This study reviews the impact of the PPM intervention on TB case finding in Local Government Areas (LGAs) with historically Low TB case notification.

Intervention or response: The PPM intervention under the USAID-funded KNCV TB LON Regions 1 & 2 project started from July 2020 in Nigeria. It involved the engagement of Private-for-profit (Pfp) facilities, Patent Medicine Vendors (PMVs) and Community Pharmacists (CPs) in the provision of TB services ranging from identification and referral of presumptive TB, to treatment of TB cases. Coordination was done by a Linkage coordinator under a Hub and Spoke system and implementation was facilitated by an incentive-based negotiated business model.

In Akwa Ibom and Cross River State, 4 LGAs with historically low TB notification rates were among sites selected for implementation. Data from these LGAs was reviewed to assess the impact of the intervention within 6 months of implementation.

Results/Impact: Across the 4 LGAs, a total of 4,030 presumptive TB were identified and evaluated between July and December 2020. This resulted in the diagnosis of 195 TB cases of which 37 (19%) were clinically diagnosed. The KNCV-PPM Intervention contributed 48% to the presumptive TB identified and evaluated, 54% to TB cases diagnosed, 41% to clinically diagnosed TB and 49% for enrolled on treatment in the 4 LGAs.

In the intervention period, the LGAs cumulatively reported an increase in TB case-finding of 181% and 267% compared to the preceding semester and year-on-year respectively (Table 1).

Indicators	Jan-Jun 2019	Jul-Dec 2019	Jan-Jun 2020	Jul-Dec 2020 (Intervention period)
Presumptive TB identified and evaluated	864	632	2254	4030
TB Cases diagnosed	71	73	108	195
Clinically diagnosed	3	8	11	37
Enrolled on treatment	58	71	97	208*

Table 1.

Conclusions: The PPM strategy is a promising intervention for accelerated TB case-finding. It is critical that this collaborative partnership with private healthcare providers is sustained and scaled up.

OA17-712-20 Factors associated with delayed care-seeking among TB patients in the private sector in Indonesia

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Background: This study aims to investigate the associated factors with delayed care-seeking among TB patients treated in private health facilities.

Design/Methods: From September 2020 - January 2021, a total of 751 TB patients were recruited using proportional sampling in 27 private clinics and hospitals within six districts. Multivariate regression was used to assess factors affecting patients' delay in TB care-seeking. We transformed the number of days delay to a logarithmic scale with 95% confidence intervals (CI).

Results: Demographics of TB patients surveyed include: 57.8% male, 76.7% without college/university degree, and 53.4% non-working/unemployed. On average, TB patients delayed seeking care for 24 days (CI:16-32). The majority of patients initially sought care at private hospitals (38.5%; CI:31.9-45.2) or public primary health centers (PHC) (20.7%; CI:15.9-25.5). Average score on perceived TB-related stigma was 32.1% (CI:30.0-33.6), and not associated with delays in care-seeking. Female TB patients had a shorter delay in seeking care by 39.1% ($\beta=-.330$, $SE=0.048$, $p<0.01$) compared to male after experiencing TB-related symptoms. Patients with college/university education level also had a 50.4% shorter delay in care-seeking ($\beta=-.408$, $SE=0.147$, $p<0.01$) compared to those with lower education level. Patients with access to national health insurance or private insurance had shorter delays in care-seeking by 80.4% ($\beta=-.590$, $SE=0.120$, $p<0.01$) and 46.2% ($\beta=-.380$, $SE=0.080$, $p<0.01$) respectively, as compared to those without health insurance. Patients who initially sought care at private hospitals had 2.2 times ($\beta=.771$, $SE=0.062$, $p<0.01$) more delays as compared to those visiting public PHC.

Conclusions: Factors found to increase TB patient's delay in care-seeking included being male, lower than college/university education level, lacking access to health insurance (either national health insurance or private-owned) and preference to first visited private hospitals for TB services. Expanding health insurance coverage among TB patients, and optimizing private health facilities empanelment in national health insurance scheme could significantly reduce TB care-seeking delays.

OA17-713-20 Do drug sales data help in estimating TB notification gaps?

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Background and challenges to implementation: India contributes, most world's "missing TB cases." These missed cases are either undiagnosed, untreated, or unreported, thus representing significant hurdle to TB elimination. Several measures, including mandatory notification, private providers engagement, have been taken in the past yet many cases continue to go unreported. Pharmacies are also required to notify TB patients via Schedule-H1 reports (as per amendment in 'Drug and Cosmetic Act-1940' in 2013). Here, we used pharmacy-based surveillance to gain insight on missing TB cases and their causes in Hamirpur, Uttar Pradesh.

Intervention or response: Two urban/semi-urban blocks (DTC and Maudaha) in Hamirpur were selected in the study. All pharmacies in the selected blocks were mapped and approached for Schedule H1 report for the period January-March, 2021. Patients who were notified via Schedule-H1 reports, were contacted to know whether they had been notified by any medical practitioners. Data gathered from pharmacies and patients was analyzed.

Results/Impact: As per Schedule-H1 report from 10 active-pharmacies, 91 patients were receiving anti-tuberculosis treatment. However, no medical practitioner (public or private) notified any of them. In DTC block, the ratio of private notified patients to missed TB cases was 1:3.7. Private patient notification in Muadaha was nil, but information on anti-TB drug sale was received for 20 patients. The key reasons of under-reporting were i) despite the ban, government doctors practicing in private, contributing 48% (95% CI 46.3-59.3) missed cases in DTC Hamirpur block ii) Allopathy practice by informal practitioners, contributing 60% (95% CI 38.6-78.2) missed cases in Maudaha block and iii) Cumbersome process of recording, reporting and verification of schedule H1 report.

Conclusions: The information on drug sales (Schedule H1-report) is an important tool that should be used strategically to reduce the number of missing TB cases. Furthermore, all health providers (public and private) must be sensitized periodically for TB notification.

OA17-714-20 Surveillance of drug sales at pharmacies helped in improving TB care standards in India

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Background and challenges to implementation: The Schedule H1 notification of the Government of India, as an amendment to the Drugs and Cosmetics Rules of 1945, has come into force from Mar 1, 2014. Eleven anti TB drugs were included in Schedule H1. The law mandates that Schedule H1 drugs can be sold by chemists only on production of a valid prescription by a modern medicine practitioner. The chemist also needs to maintain a separate register (Schedule H1 Register) in which identity of the patient, contact details of the prescribing doctor, the name and dispensed quantity of the drug will be recorded with date.

Intervention or response: Kerala the southern Indian state has implemented schedule H1 surveillance and used the information from schedule H1 register to:

1. Identify the missing TB cases and strengthening TB notification,
2. Identify providers for engagement and extending support to them for ensuring standards of TB care and,
3. Provide feedback to doctors regarding prescription practices.

Results/Impact: TB notifications from private sector in the state has improved (2018-3981, 2019-4927, 2020 -5795). Estimated number of unnotified TB per 100,000 population based on total sales of rifampicin containing products in the state also shows an annual decline of 22% in last three years closing the gap in surveillance system. Proportion of microbiologically confirmed cases among TB notified from the private sector has increased from 25% in 2018 to 34% in 2019 and 38% in 2020. Uptake of NTEP drugs from private sector improved to 50%. Qualitative studies revealed a drop in the use of 'empirical ATT' by clinicians and a 'self-standardisation' in the practice of diagnosing and treating TB.

Conclusions: Pharmacy based surveillance in Kerala India has helped to

- i. improve TB patient notifications from private sector,
- ii. build better public private partnership and;
- iii. improve the quality of TB diagnosis.

OA17-715-20 Organisational readiness for the implementation of a 3-month short-course TB preventive therapy regimen (3HP) in four healthcare facilities in Zimbabwe

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Background: Zimbabwe rolled out 3HP, a three-month short-course tuberculosis preventive therapy (TPT) regimen to address the poor uptake of the standard 6-9 month regimens. We measured the level of organizational readiness and identified barriers and facilitators to implementing 3HP in four health facilities.

Design/Methods: A convergent, parallel mixed-methods approach was used to collect data from four primary healthcare clinics in Bulawayo and Harare Metropolitan provinces, Zimbabwe. Twenty healthcare providers completed a 35-item, self-administered questionnaire designed on a 5-point Likert scale and developed from the Weiner organizational readiness model. Nine of the providers and five TB program managers took part in 20-30 minute individual semi-structured key-informant interviews. Median scores with interquartile ranges were calculated wherein a score of 3.3 or greater indicated readiness. Differences between facilities were assessed using a Kruskal-Wallis rank test. Qualitative data on barriers and facilitators were transcribed and analyzed using a framework approach.

Results: Readiness to implement 3HP across the four facilities was positive with a score of 3.8 (IQR 3.3-4.1). The difference between the best 4.0 (IQR 3.8-4.2) and worst performing facility 3.2 (IQR 2.7-3.3) was 0.8 and statistically significant ($p=0.039$). The low facility score was due to poor contextual factors 2.5 (IQR 2.0-3.3), task demands 2.6 (IQR 2.3-2.9) and resource availability 2.1 (IQR 1.5-2.5) scores. Key facilitators included provider and management buy-in; collective capability through task-shifting, willingness to generate demand, alignment with existing programmes, perceived need and benefits. Barriers were negative past TPT experiences, suboptimal programmatic monitoring, inconsistent provider remuneration, inadequate staffing, erratic supply chain and an organizational communication gap creating slow program implementation.

Conclusions: The varied scores between facilities suggest distinct underlying conditions for readiness. Healthcare provider motivation is temporary based on the inconsistent resource supply, absence of TPT-specific monitoring and evaluation, and daily contextual challenges in facilities which must be addressed. Similar research is necessary for countries yet to implement 3HP to optimize the design or revision of delivery strategies and increase uptake of TPT.

OA17-716-20 Mentoring a TB laboratory for ISO-15189 accreditation during the Covid-19 pandemic using a customised TB SLMTA facility-based approach: an experience from India

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Background and challenges to implementation: FIND in collaboration with India's NTP under CDC supported project is providing technical assistance to TB laboratories for improving quality management systems (QMS) and achieve ISO-15189 accreditation through National Accreditation Board for Testing and Calibration Laboratories (NABL) in India.

In February 2020, TB laboratory at KIMS Hubli, catering to one-third of districts in Karnataka for DR-TB diagnosis, was included in the project. However, towards end of March 2020, India went into complete lockdown to contain the COVID-19 pandemic.

Intervention or response: Despite COVID-19 related challenges, site was keen to continue preparations for accreditation. FIND adopted a customised facility-based TB SLMTA (Strengthening TB Laboratory Management Towards Accreditation) mentoring approach. Findings of baseline assessment in February 2020 using FIND's TB QMS Harmonized Checklist, were used to develop mentoring plan.

Mentoring was done remotely through weekly online sessions, monthly virtual site visits and offsite support. Staff underwent online training on QMS. Various levels of QMS documentation were developed. Staff was trained to perform in-house calibration of equipment. Risk management and contingency plans were documented. Gaps identified in assessment were converted into simple/complex improvement projects.

Progress was monitored for various quality parameters. Site conducted Internal Audit, Management Review Meeting and resolved Non-Conformities (NCs) under guidance. Online exit assessment helped confirm site readiness before applying to NABL. Mentoring continued as site underwent NABL pre and final assessments.

Results/Impact: QMS improved significantly in six months from baseline score of 48% to 88% in end line assessment in August 2020 (Chart 1). Site overcame challenges related to personnel, monitoring, corrective

action, quality, safety, etc. Site had minimal NCs during NABL pre and final assessments, closed them and achieved ISO-15189 accreditation in May 2021.



Chart 1. Baseline (Feb '20) and end line (Aug '20) assessment scores KIMS Hubli-Karnataka, India.

Conclusions: With a committed team, appropriate use of online-tools, focussed QMS implementation and customized facility-based TB SLMTA mentoring approach, site achieved ISO-15189 accreditation overcoming COVID-19 pandemic challenges.

OA-18 Practical steps to promote affordable TB care

OA18-717-20 Time required for directly observed and self-administered TB preventive therapy among people living with HIV in Uganda: a time and motion study

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Background: Short-course tuberculosis preventive therapy with three months of weekly isoniazid and rifampine (3HP) is being scaled-up for people living with HIV (PLHIV). There are few data on patient time requirements to complete 3HP under different delivery strategies.

Design/Methods: We conducted a time and motion study from October 2020 to March 2021 at the Mulago AIDS Clinic (Kampala, Uganda). The study population consisted of PLHIV enrolled in an implementation trial

comparing self-administered therapy (SAT) versus directly observed therapy (DOT) for 3HP. Following the initial dose, DOT consisted of 11 additional weekly clinic visits with fast-track pharmacy encounters and SAT consisted of 2 clinic visits at weeks 6 and 12 (for refills and evaluation of adverse events). On one randomly selected day per trial week, we observed all clinic encounters to document time required for all clinic-based activities. We surveyed participants to estimate transport and other time required to attend the clinic.

Results: A total of 126 visits were observed: 105 (83%) DOT and 21 (17%) SAT. The median time spent at the clinic per visit was 9 minutes (interquartile range [IQR]= 5-19) for DOT and 24 minutes (IQR= 14-39) for SAT. The median one-way travel time to the clinic was 54 minutes (IQR= 30-76.5) for DOT and 60 minutes (IQR= 30-90) for SAT. Accounting for the total number of visits required (including round-trip transit), the median time spent by patients to attend clinic for 3HP is estimated to be 1,287 minutes for DOT and 288 minutes for SAT.

	Directly observed therapy (N=105, median (interquartile range))	Self-administered therapy (N=21, median (interquartile range))
Patient-provider interaction time	4 (3, 5)	11 (7, 15)
Waiting time	4 (0, 12)	7 (3, 18)
Total* time spent at the clinic	9 (5, 19)	24 (14, 39)
One-way travel time	54 (30, 76.5)	60 (30, 90)

* Total time may be longer than sum of interaction and waiting time, if a patient performed non-study-related activities (e.g. other clinic division visit, etc.) in the middle of the observation

Table. Median time (minutes) spent at a clinic visit day for TB preventive therapy among people living with HIV

Conclusions: For PLHIV receiving 3HP, SAT required one-fifth the time of DOT mainly due to the total travel time. However, DOT visits can be streamlined, and DOT may be a preferred option for some patients for whom transport to clinic is not burdensome.

OA18-718-20 Social health insurance to lower direct pre-treatment medical costs incurred by TB patients in urban Vietnam

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Background: Tuberculosis (TB)-affected households often experience catastrophic financial hardships due to the costs of TB diagnosis and treatment. This study aimed to estimate social health insurance (SHI) coverage and compare direct medical costs prior to TB treatment between TB patients with and without SHI in urban Viet Nam.

Design/Methods: 168 patient costing surveys were conducted in Ho City Minh City, Hai Phong and Ha Noi with confirmed TB patients between Oct 2020 and Feb 2021. Three participant groups were recruited: multi-drug-resistant (MDR-) TB patients, drug-susceptible (DS-) TB patients detected through active case finding (ACF), and DS-TB patients passively detected through routine program activities. The number of pre-treatment health system visits and direct medical costs, including out-of-pocket (OOP) non-reimbursable spending and SHI contributions, were calculated and compared across the participant groups.

Results: 79% of survey participants had SHI at treatment initiation, which is lower than the 91% national average. SHI was associated with lower direct medical expenditure incurred by TB patients (43.2% lower in patients with SHI compared to those without SHI: USD 46 vs. USD 81).

	MDR-TB n=45	ACF DS-TB n=64	Passive DS-TB n=59	Total n=168
Patients with SHI (n, %)	36 (80%)	51 (80%)	45 (76%)	132 (79%)
Median health system visits (IQR)	8 (6-20)	3 (2-5)	5 (4-9)	5 (3-9)
Median direct medical costs (USD, IQR)	136 (43-286)	12 (0-66)	138 (63-350)	80 (12-228)
OOP non-reimbursable costs (USD, IQR)	86 (22-215)	11 (0-25)	92 (43-198)	46 (7-122)
Participants with SHI	59 (19-126)	11 (0-28)	81 (48-201)	46 (5-116)
Participants without SHI	220 (118-262)	11 (0-20)	106 (28-185)	81 (11-197)

Table. SHI coverage, number of health system visits, direct medical costs and source of payment (OOP or SHI) prior to TB treatment in urban Vietnam.

The difference was greatest for MDR-TB patient group (-73.2% lower with SHI than without). Participants detected through ACF had the lowest number of health system visits and pre-treatment costs (USD 11); OOP costs were the same for ACF participants whether they did or did not have SHI.

Conclusions: SHI is an impactful social protection tool for TB patients in Viet Nam, covering nearly half of the medical costs associated with TB diagnosis. ACF should also be considered as a form of social protection, given its ability to reduce pre-treatment medical costs. Further evaluations examining the impact of SHI and ACF on catastrophic cost incurrence throughout the full duration of TB treatment are essential.

OA18-719-20 A simplified TB cascade efficiency scoring system to guide resource allocation for TB screening programmes in high-burden countries: the USAID TB LON 3 Project, Nigeria

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Background: The 2021 guideline on systematic TB screening by World Health Organization noted that the most efficient screening strategy is the one that combines multi-indicator performance of high total yield of true-positive cases of TB, few false positives, low NNS, low cost, a rapid and simple algorithm and high client acceptability. However, there are no standardized tools to benchmark and compare cascade efficiency of many screening programs and interventions.

We aimed to present a simplified TB cascade efficacy measurement tool that could guide evaluation of screening programs and resource allocation in High Burden Countries.

Design/Methods: We developed a graded scoring system for each component of the cascade and across interventions based on regional epidemiology data, prevalence surveys and review of relevant literatures on cascade efficiency and number needed to screen (NNS) across four screening programs (community, private facilities, public facilities and contact investigation). Based on the performance of each screening program between Oct-Dec 2020, efficiency scores were assigned.

Results: The scoring instrument was highly reliable with Cronbach's alpha score of 0.9 and was able to predict performance of each screening program in subsequent quarters. The most efficient screening program was the community with a total efficiency score of 16 followed by public providers (13) and contact investigation (12) while the least efficient was screening by private provider (11).

Indicator	Community screening	Screening by Private providers	Screening by Public providers	Screening contacts of Bacteriologically +ve
Screening Coverage	≥95%=3; 80-94%=2; <80%=1	≥95%=3; 80-94%=2; <80%=1	≥95%=3; 80-94%=2; <80%=1	≥95%=3; 80-4%=2; <80%=1
Presumptive Yield	≥6%=3; 4-<6%=2; <4%=1	≥6%=3; 4-<6%=2; <4%=1	≥6%=3; 4-<6%=2; <4%=1	≥6%=3; 4-<6%=2; <4%=1
Evaluation Rate	≥95%=3; 80-94%=2; <80%=1	≥95%=3; 80-94%=2; <80%=1	≥95%=3; 80-94%=2; <80%=1	≥95%=3; 80-94%=2; <80%=1
TB Yield	≥10%=3; 6-<10%=2; <6%=1	≥10%=3; 6-<10%=2; <6%=1	≥10%=3; 6-<10%=2; <6%=1	≥10%=3; 6-<10%=2; <6%=1
Treatment enrolment Rate	≥99%=3; 90-<99%=2; <90%=1	≥99%=3; 90-<99%=2; <90%=1	≥99%=3; 90-<99%=2; <90%=1	≥99%=3; 90-<99%=2; <90%=1
NNS	<489=1; ≥489=2	<284=1; ≥284=2	<208=1; ≥208=2	<34=1; ≥34=2

Conclusions: The simplified efficiency scoring tool is highly reliable in measuring performance of TB screening programs and serves as a useful tool for program realignment, resource planning and allocation. There is a need for revalidation of this tool in other settings with consideration for local TB epidemiology. Integration of cost elements is a major area for future improvement.

OA18-720-20 Cost and cost-effectiveness of decentralised Xpert testing in Uganda

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Background: Loss to follow-up after receiving a positive test result for tuberculosis (TB) is a major challenge to achieving global targets for TB control. Decentralized molecular testing for TB using GeneXpert Edge could improve linkage to care, but little is known about the cost of decentralized testing in resource-limited settings.

Design/Methods: We conducted a costing and cost-effectiveness study nested in an ultra-pragmatic cluster randomized trial evaluating the effectiveness and implementation of on-site (decentralized) versus centralized (hub-and-spoke) Xpert testing across 20 community health centers (XPEL-TB). Empiric cost data related to the implementation and operation of decentralized Xpert testing were collected at four sites.

Costs of centralized Xpert testing were estimated empirically before study initiation (with specimen transport costs added), inflated to 2019 US dollars and adjusted based on service volume from XPEL-TB. Time-and-motion studies were performed to estimate activity-based service provision costs.

Cost-effectiveness was assessed as the incremental cost per patient initiating treatment within 14 days of diagnostic testing, and per additional TB diagnosis. Deterministic (one-way and multi-way) and probabilistic sensitivity analyses were performed to assess robustness of results.

Results: The average per-test cost was slightly lower for centralized testing (\$18.47) than for decentralized testing (\$20.48), primarily reflecting higher costs of Xpert modules (\$6.79 decentralized vs \$3.06 centralized) and implementation of decentralized testing (\$2.26).

Decentralized testing was estimated to cost \$427 (95% uncertainty range: \$221 – \$633) per additional TB diagnosis but only \$134 (\$119 – \$148) per additional treatment initiation within 14 days of diagnostic testing,

reflecting more efficient linkage to care. In both arms, the primary driver of cost-effectiveness was the number of patients receiving Xpert testing annually, with higher testing volumes leading to better cost-effectiveness.

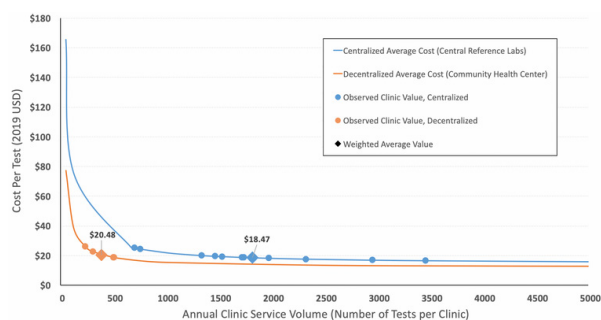


Figure. Cost per test vs. service volume by study arm.

Conclusions: Decentralizing Xpert testing to community health centers increases the cost of testing by roughly 10% and is likely to be cost-effective compared to centralized hub-and-spoke testing in Uganda.

OA18-721-20 Social determinants of the decline in TB prevalence in Vietnam

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Background: Historically, relationships between economic development and reductions in tuberculosis (TB) prevalence have been observed. Between 2007 and 2017, Viet Nam experienced rapid economic development (GDP per capita increased from US\$906 to US\$2192) with an equitable distribution of resources (Gini coefficient remained at 36) and a 37% reduction in TB prevalence. Analysing consecutive Viet Nam TB prevalence surveys, we examined how the observed reduction in TB and subclinical TB prevalence was concentrated between socio-economic groups.

Design/Methods: We combined data from nationally representative 2007 and 2017 Viet Nam TB prevalence surveys to district-level measures of poverty. We constructed asset indices using principal component analysis of asset ownership data collected for the prevalence surveys. Illness concentration indices were estimated to measure cross-sectional socio-economic position (SEP) inequality in TB. We fitted multi-level log binomial models, taking into account clustering to investigate relationships between household SEP, neighbourhood poverty and change in TB prevalence observed during a period of economic growth in Viet Nam.

Results: Data from 94156 (2007) and 61763 (2017) individuals were included. Of people with microbiologically confirmed TB, ~30% (64/218 in 2007 and 46/124 in 2017) had subclinical disease. The illness concentration index changed from -0.104 (95% CI: -0.079 to -0.157, p-value=0.003) in 2007 to 0.066 (95% CI: 0.060-0.180, p-value=0.158) in 2017, indicating that while TB was concentrated among the poorest households in 2007, there was a shift towards more equal distribution between rich and poor in 2017.

In multilevel models, after controlling for neighbourhood poverty levels we found that remote compared to urban neighbourhoods, and households with greater absolute wealth were associated with reduction in TB prevalence (b=-0.478 (-0.881; 0.076) p-value=0.020 and b=-0.006(-0.013; 0.000) p-value=0.065 respectively). Findings were similar for subclinical TB.

Conclusions: We found that with equitable economic growth and a reduction in TB burden, TB became less concentrated among the poor in Viet Nam.

OA18-722-20 Impact of free chest X-ray vouchers intervention on the uptake of X-ray services for TB diagnosis: experience from Southwest Nigeria

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Background and challenges to implementation: Despite the high sensitivity of chest X-rays for TB clinical diagnosis, there are barriers limiting the accessibility of this service by patients in Nigeria. Key among these factors is the affordability of this service by patients and the proximity of the X-ray center to health facilities.

The USAID-funded Tuberculosis Local Organization Network, Region 3 (TB-LON 3) project being implemented by the Institute of Human Virology Nigeria (IHVN), sought to bridge this gap by providing X-ray vouchers to eligible presumptive TB clients by signing agreements with nearby X-ray centers to accept these vouchers in lieu of cash.

Intervention or response: A comparative analysis assessing the impact of free Chest X-ray vouchers on TB radiological assessment for clinical diagnosis. Data were collected for two quarters from TB-LON 3 supported health facilities across 4 States, 3 months before this intervention (July-September 2020) and 3 months after this intervention (October-December 2020). Data from

105 health facilities were analyzed from Lagos 26 (25%), Ogun 40 (38%), Osun 23 (22%), and Oyo 16 (15%), using SPSS.

Results/Impact: From July-September 2020, 154 hospital attendees accessed X-ray services for TB diagnosis before TB-LON 3 X-ray voucher intervention, while from October-December 2020, 581 hospital attendees accessed X-ray services showing 277% increase in X-ray uptake. Likewise, a total of 71 and 265 patients were clinically diagnosed before and after the introduction of the X-ray voucher intervention respectively, showing 379% increase in clinical diagnosis. These show a significant increase ($p < 0.000$) in uptake at 95% C.I

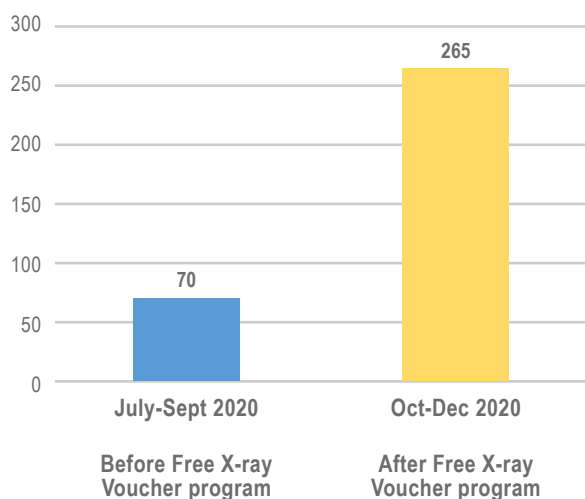


Figure. Impact of free voucher program on clinical diagnosis for Tuberculosis, SW Nigeria.

Conclusions: The provision of free X-ray vouchers increased the uptake of X-ray services by eligible presumptive TB clients. This intervention is a promising strategy for increasing the uptake of X-ray services towards improving clinical TB diagnosis amongst hospital clients that would have been included in the pool of missing TB cases due to the unaffordability of X-ray services.

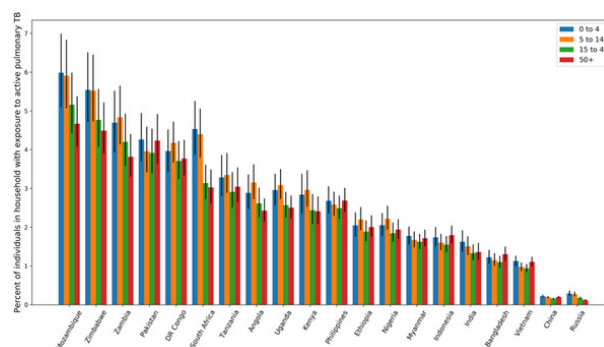
OA18-723-20 How many people are at increased risk for TB because of household exposure? Estimates derived from GBD 2019

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Background: Household contacts of people with pulmonary TB are at increased risk of developing TB. The World Health Organization expanded recommendations in 2018 to offer TB preventive therapy to household contacts ages ≥ 5 years living in high-incidence countries, in addition to the existing recommendation for children < 5 . We estimated the population with household exposure to active pulmonary TB by age group for 20 TB high burden countries in 2019.

Design/Methods: We used a household-based model to combine the estimates of active pulmonary TB prevalence from the Global Burden of Diseases Study 2019 and household age and sex structure from public-use microdata samples of survey or census data. We propagated a 95% Bayesian uncertainty interval (UI) to the estimates of household TB exposure using draws from the posterior distribution GBD estimates and bootstrap resampling of households in the household microdata.

Results: The number of individuals in with household exposure to active pulmonary TB across all ages and 20 countries was 62 million (95% UI of 55 to 71). Children under five accounted for 12% of the population with household exposure to active pulmonary TB, while adults ages 15 and older accounted for 64%. The largest population exposed was in India, with 20 million people (95%UI 17-23) with household exposure to active pulmonary TB. The countries with the highest prevalence of pulmonary TB exposure were Mozambique, Zimbabwe, Zambia, and Pakistan.



Conclusions: The population of household contacts who are ages 5 and older is more than 7-fold larger than children under 5, indicating a large population that may be newly eligible for TB preventive therapy in high-burden countries in order to avert future TB disease. Our estimates of the population size may be informative for program planning, as effectively reaching this population with contact tracing and TB preventive therapy will require a massive expansion in global effort.

E-POSTER SESSION (EP)

COVID-19: opportunities for improving TB care?

EP-02-110 Systematic screening for TB in suspected or recovered Covid-19 patients with persistent respiratory signs: experiences from Niger and Guinea

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Background and challenges to implementation: Evidence suggests that the COVID-19 pandemic impacted negatively on tuberculosis (TB) control, reducing TB screening. As TB and COVID-19 have similar symptoms, integrated COVID-19 and TB screening was implemented to overcome these challenges. We assessed the effectiveness of this strategy in patients with presumptive COVID-19 and/or those recovering from COVID-19 but with persistent respiratory signs.

Intervention or response: Guinea and Niger used different screening approaches from May 2020 to March 2021. In Guinea, TB screening concerned symptomatic patients after a negative COVID-19 PCR test or after recovery from COVID-19. In Niger, all presumptive COVID-19 patients with respiratory symptoms were tested simultaneously for COVID-19 (PCR test) and TB (sputum smear microscopy and/or Xpert MTB/RIF). The health workers or community workers were responsible for sample transport, retrieving results, entering data using Open Data Kit application. Data were sent to a secured server.

Results/Impact: A total of 863 persons (Guinea: 758, Niger: 105) with presumptive COVID-19 and/or persistent respiratory symptoms after COVID-19 treatment were screened for TB (table). 60.3% of them were male with a median age of 34 years (IQR: 26-45) and 4.7% were previously treated for TB. Symptoms were cough ≥ 2 weeks (49.4%), fever (44.7%), and weight loss (30.3%). Only 16.3% reported contact with a coughing person. In

Guinea TB screening occurred in patients with a known COVID-19 status. In Niger 45.7% (48/105) tested COVID-19 positive. Overall, 43 (4.9%) were diagnosed with active TB. The proportion with active TB was 4.6% (35/758) and 7.6% (8/105) in Guinea and Niger, respectively ($p=0.2$). Five patients were COVID-19 co-infected. All 5 belonged to the Niger cohort. Cough ≥ 2 weeks, fever, and weight loss were symptoms associated with TB in people with presumed COVID-19 or recovering from COVID-19 ($p<0.05$).

	Guinea (N=758) N %	Niger (N=105) N %	p-values [§]
Indication for screening			
Presumptive COVID-19	0 (0)	105 (100)	<0.001
With negative COVID-19 test	745 (98.3)	0 (0)	
Recovering from COVID	13 (1.7)	0 (0)	
COVID-19 #			
Positive	13 (1.7)	48 (45.7)	<0.001
Negative	745 (98.3)	57 (54.3)	
Tuberculosis			
Positive	35 (4.6)	8 (7.6)	0.2
Negative	723 (95.4)	97 (92.4)	
COVID-19/TB co-infection among those with tuberculosis			
Yes	0 (0)	5 (62.5)	<0.001
No	35 (100)	3 (37.5)	
TB diagnoses among patients			
With presumptive COVID	0 (0)	8 (100)	<0.001
With a negative COVID test	35 (100)	0 (0)	
Recovering from COVID	0 (0)	0 (0)	

In Guinea screening occurred in patients with a known COVID-19 test result, while in Niger patients were tested for both conditions.

§ Chi-squared when all cells had at least 5 observations, otherwise Fisher's exact test

Table: Active TB in presumptive COVID-19, negative or recovering from COVID-19 patients stratified by country

Conclusions: Scaling up integrated COVID-19/TB screening will improve tuberculosis detection during the ongoing COVID-19 pandemic.

EP-02-111 Interventions to mitigate impact of Covid-19 on TB services in the Kyrgyz Republic

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Background and challenges to implementation: In March 2020, Kyrgyzstan enacted a national state of emergency in response to COVID-19, including lockdowns and restrictions on movement compromising access to health facilities. The National Tuberculosis Center (NTC), National Reference Laboratory (NRL) and other health facilities were partially re-purposed for COVID-19 treatment and testing, and health system resources were reallocated to COVID-19 with the potential to undermine TB services and infection control. Already at increased risk for negative COVID-19 outcomes, TB patients risked interruption of their treatment.

Intervention or response: The USAID Cure Tuberculosis Project helped mitigate the impacts of COVID-19 on TB services by:

1. enabling remote treatment support for TB patients: 14-day TB drug supply, community-based and video-observed treatment, and online patient support groups;
2. launching virtual clinical services for Concilia;
3. supporting COVID-19 infection control measures at the NTC and NRL, including adapting protocols and conducting trainings;
4. adapting the existing TB Laboratory Data Management Information System (LDMIS) to capture COVID-19 testing;
5. developing an integrated TB/COVID-19 diagnostic algorithm;
6. Piloting a COVID-19 module in the Quality of TB Services Assessment (QTSA) national health facility survey.

Results/Impact: Nationwide rollout of these initiatives helped maintain TB testing and diagnosis, and allowed TB patients to continue treatment uninterrupted. Thanks to infection control efforts, NTC health workers have the lowest COVID-19 incidence among all re-purposed health facilities. The adapted TB LDMIS system became the country's primary source of COVID-19 information.

The TB/COVID-19 diagnostic algorithm detected new TB cases. The QTSA provided comprehensive information about the impact of COVID-19 on health system resources and TB case detection, treatment, and infection control.

Conclusions: USAID Cure Tuberculosis Project interventions helped monitor and mitigate the impact of COVID-19 on TB services. Despite COVID-19 effects on the health system, implemented activities will have lasting benefits for TB services in Kyrgyzstan, potentially replicable in other countries.

EP-02-112 TB case-finding during the peak of the Covid 19 pandemic: implementing clinician-led outpatient TB screening

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Background and challenges to implementation: Nigeria is among the 14 most TB burden Countries in the world. One major issue affecting TB case finding in Nigeria is 'Missing Cases'. Screening of all OPD attendees is one of the active case search strategies that has yielded results.

However, during the peak of COVID pandemic presumptive TB cases identification by the screening officers reduced drastically as patients refused to disclose their Cough history hence a clinician led OPD TB screening was implemented in 10 high volume faith-based facilities in Anambra state Nigeria.

The aim of this abstract is to review the impact of the clinician led OPD on TB case finding and also compare the result with the screening officers led OPD screening

Intervention or response: Advocacy to the Hospital management on the need to institutionalize TB screening, a one-day Orientation was conducted for all the clinician on TB signs and symptoms. TB screening SOPs were placed in all the consulting rooms, weekly phone call reminder to all OPD clinicians. The Screening Officers at the end of the day, go to the laboratory to collate results of all the presumptive sent by the clinicians, then send reports weekly.

Results/Impact: Four months pre and post intervention data was reviewed, a 25% increase in presumptive identified and 68% increase in TB case diagnosed was observed post intervention.

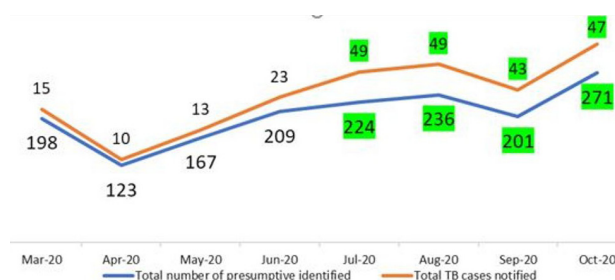


Figure. Pre -intervention post-intervention.

Conclusions: The institutionalization of TB intervention services in healthcare providing settings through Clinicians led OPD TB screening is very effective in identifying TB suspect especially during the peak of COVID 19 Pandemic. The screening officers are also important in this process as they ensure proper documentation and reporting of the OPD activities

EP-02-113 Improved TB preventive therapy for contacts during Covid-19 in Ethiopia

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Background and challenges to implementation: Scale up of tuberculosis (TB) preventive therapy (TPT) for high-risk populations including contacts has been one of the key interventions to meet milestones of End TB strategy. TPT is recommended for eligible children and adolescents <15 years of age who are contacts of bacteriologically confirmed pulmonary TB (PTB) cases nationally. COVID-19 was first diagnosed in Ethiopia on March 13, 2020. It has negatively affected health care services in many situations including TB diagnosis and treatment. We assessed the progress of TPT service delivery for household contacts during COVID-19 in Ethiopia.

Intervention or response: Data were collected using DHIS-2 from July 2019 to December 2020. We analyzed and described the quarterly performance of TPT coverage among household contacts <15 years before and after the emergence of COVID-19 in Ethiopia.

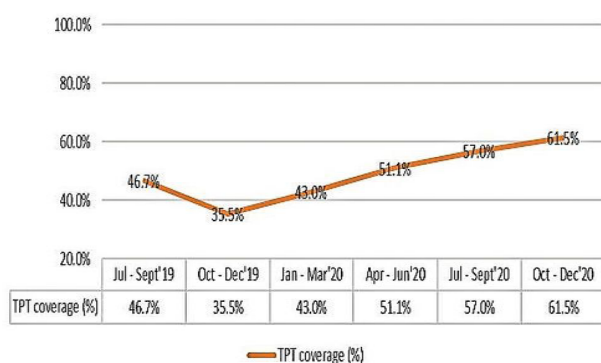


Figure. Trend in TPT uptake among <15 contacts.

Results/Impact: A total of 17858 contacts <15 years were screened for TB before emergence of COVID-19, and 41.2% (6280/15257) of eligible household contacts

<15 years were started on TPT. After the occurrence of COVID-19, 19592 contacts <15 year were screened for TB and 57.3% (10321/18020) eligible contacts < 15 years were initiated on TPT, P<0.001.

Conclusions: Our finding indicated that TPT initiation among household contacts has significantly improved even during COVID-19. COVID-19 mitigation efforts, strengthening community TB support and frequent TPT focused performance monitoring should continue for scale up of TPT service delivery among household contacts.

EP-02-114 SWOT analysis of the impact of the Covid-19 pandemic on the healthcare system in Russia

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Background: The COVID-19 pandemic has had a varied and widespread impact on all aspects of our lives in a relatively short period of time. This influence has affected the health care system to a greater extent.

A correct SWOT analysis of the results of such an impact will make it possible to identify strong and weak areas and use rational measures to correct them. The existing health care information systems in countries, including Russia, already made it possible to quickly undertake conscious executive actions against the pandemic in real time.

Design/Methods: Scientific literature scoping review from open information sources such as various PubMed databases, eLibrary.ru, websites of government departments and organizations, Mass media publications on the Internet. Standard database search engines were used. More than 210 scientific articles and publications were analyzed.

SWOT analysis is an effective tool for assessing the current state and the basis for adopting a new strategy for the organization. The SWOT analysis is intended as a starting point for discussion and by itself cannot show managers how to achieve improvement, especially in a rapidly changing environment.

Results: At least 6 weaknesses and 10 threats from the effect of the COVID-19 pandemic on the health care system have been identified and confirmed in the scientific literature. At the same time, 9 opportunities were identified that arose due to the pandemic as well as 7 effects that strengthened the capabilities of the health care system.

Conclusions: The revealed multidirectional impacts of the COVID-19 pandemic will help the healthcare system, including TB care, to more rational use of available resources and targeted actions against other diseases.

EP-02-115 The impact of Covid-19 on latent TB infection testing at a reference laboratory in the United Kingdom

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Background and challenges to implementation: The heavy focus on the Covid-19 pandemic has had an impact on tuberculosis (TB) services with delays in diagnosis. TB services prioritise the care they deliver, focusing on active TB rather than prevention of latent TB infection (LTBI). There is a need for efficient LTBI diagnosis and treatment, which can decrease TB burden and community transmission. Migrant screening has been shown to succeed in decreasing transmission and TB levels in the UK [1, 2].

Intervention or response: This study examines retrospectively the number of samples that were processed from January 2017 to March 2021 in a national reference laboratory named Oxford Diagnostics Laboratory (ODL). ODL processes thousands of samples yearly for LTBI testing, providing the highest quality results.

Results/Impact: We observed a significant reduction in the number of blood samples received for LTBI testing at ODL during the pandemic. There was a 60% drop during the first lockdown in the UK, with numbers of samples starting to increase in 2021 (Figure 1). A decrease has been observed in the number of TB routine tests, contact tracing and migrant screening. Looking at specific groups, there was a 95% drop in samples received from migrants and 50% reduction in paediatrics testing.

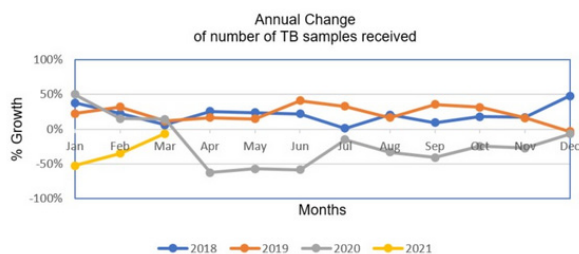


Figure 1. Decrease in the number of TB samples received at ODL during the pandemic.

Conclusions: One year on into the pandemic, the results of this study highlight the urgent need to get back on track with LTBI testing and aim to reduce the accumulated pool of undetected people with TB. Ending the global TB epidemic requires a focus on treating LTBI individuals to prevent future cases and transmission. Such measures could be rigorous community engagement and contact tracing to maintain awareness of TB symptoms. Dealing with COVID-19 is important, but let's not forget TB, which is meeting us on the other side of this crisis.

References:

1. Aldridge et al. *Lancet*. 2016;19;388(10059):2510-2518
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EP-02-116 Local solutions that helped mitigate the impact of Covid-19 on TB case detection in remote rural zones in southern Ethiopia

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Background and challenges to implementation: Following the detection of the first COVID-19 case in March 2020, Ethiopia took aggressive measures to contain the spread of the pandemic. For Kaffa and Bench-Sheko zones which are located about 500 km south of Addis Ababa where TB programs operate at an extremely constrained conditions, ensuring smooth functioning of the TB program was equally important.

Our objectives were to make health facilities safer for patients and providers, to facilitate specimen transport with digital applications and to support integrated screening for COVID-19 and TB.

Intervention or response: We started our support by assisting the national TB program in updating the national TB screening algorithm in which bidirectional screening for COVID-19 and TB was included. Then, we provided personal protective materials, oriented health workers in their use, and organized trainings either remotely or in small groups with appropriate social distancing. We prepared a standard package of slides for use during every training or meeting opportunity. We also used every contact with the media as an opportunity to raise awareness about COVID-19 and availability of TB services under safe conditions.

Results/Impact: TB service use peaked to near pre-COVID-19 levels within 3-4 months of initiating the mitigation measures. Between September and December 2020, 1629 patients with presumptive TB were screened for TB in the two project zones. Of those screened, 326 (20%) had TB and were directed to treatment. Of 1629 patients with presumptive TB enrolled in the two zones, 1027 (63%) were also screened for COVID-19 symptoms or contacts but none was diagnosed. Similarly, 161 patients with suspected COVID-19 were screened for TB.

Conclusions: Having appropriate guidelines in place, ensuring adequate supply of protective materials, training, and regular communication helped ensure continuity of TB services during the peak COVID-19 period in remote rural districts in Ethiopia. The approach can be applicable to similar settings.

EP-02-117 Household contact screening of TB: a public-private joint effort to mitigate the impact of Covid-19 in Jharkhand, India

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Background: Household contact screening of tuberculosis (TB) is a priority activity to identify the missed cases and the recently infected individuals with TB symptoms. The recent global COVID-19 pandemic has strongly impacted the TB elimination programme and a large number has been missed which are further fueling the transmission in household contacts.

To mitigate the impact of COVID-19 and to improve the household contact screening and treatment adherence counselling, TB elimination programme of Jharkhand collaborated with Health and Wellness Centres (HWCs) and engaged the Community Health Officers (CHOs).

Design/Methods: A collaborative framework was discussed with State HWC team and the district NTEP team and CHOs were sensitized on the activity planning and trained in TB symptom screening, TB testing, family counselling and the state advisory on Covid appropriate behaviour.

A two-weeks household contact TB symptom screening was undertaken among the line listed TB cases notified in last two years (2019 and 2020) 'Nikshay' national digital TB notification platform and the TB patients and their families were counselled on TB, COVID-19 and personal protective measures

Results: During the study period, 75,571 (73%) of TB cases notified in 2019 and 2020 were approached, and their household contact TB screening was conducted. A total of 1,96,998 (88%) household contacts of TB were screened of which 8,390 (4.3%) were found TB symptomatic. Out of TB symptomatic 7,875 (94%) were put on TB diagnostic modalities using smear microscopy, NAAT testing and X-ray chest and diagnosed 3,032 TB cases.

Conclusions: Screening TB among the household contacts of index TB cases during the COVID-19 pandemic is one of the measures to mitigate the impact of pandemic when the normal TB activities are compromised. A joint collaborative effort provides not only the accessibility and human resource support, but also the quality counselling for other diseases apart from TB.

EP-02-118 Bilateral screening and integrated testing of TB and Covid-19: experiences from Kerala, India

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Background and challenges to implementation: COVID-19 has restricted essential health service delivery. Nine of the countries with the most TB cases saw a decline in diagnosis of TB in 2020, ranging from 16%-41%. Kerala, the southern Indian state had cumulative 22314 confirmed COVID-19 cases per million population by Dec 31, 2020. There were an estimated 2000 missing TB cases in September 2020 in Kerala. An unusual delay in diagnosis of TB and an increase in case fatality were also observed in individuals with COVID-19 and TB together

Intervention or response: State had developed a COVID-19 surveillance system – universe being all individuals at risk for developing COVID-19. All such individuals at risk are being followed up by the primary health care team daily for symptom surveillance. Policy was made to screen all individuals with Influenza like Illness/ Severe Acute Respiratory Illness for TB also. Systems were established to offer both TB and COVID-19 testing in an integrated manner to all those found eligible

Results/Impact: During November 2020, there were 1701 TB cases notified and 168227 COVID-19 new cases diagnosed in the state. 34 individuals were diagnosed with both TB and COVID together. During November 2020, 34417 individuals with ILI were screened for TB, 2437 presumptive TB cases were identified among them and 69 were diagnosed as TB (Yield per 100000 screened is 200). Out of 6716 SARI cases, 852 were identified as presumptive TB and 61 were diagnosed as TB (Yield per 100000 cases screened is 988). Together it constituted 8% of all TB notified in November 2020

Conclusions: The experiences shows that bilateral screening and integrated testing for TB and COVID-19 is feasible in routine program setting. TB case finding could be improved and delay in diagnosis could be averted by integrating TB case finding into the screening and testing systems established for COVID-19.

EP-02-119 Ensuring continuity of TB care services by private healthcare providers during Covid-19 in Pakistan

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Background and challenges to implementation: In Pakistan, the COVID-19 affected the continuity of the TB care services, resulting in decline in TB case notification. The main challenges that impacted the program continuity and TB case notification included movement restrictions in the field, non-availability of the public transport, closure of private healthcare facilities and labs, fear of contracting COVID-19, stigma attached to both TB and COVID-19, COVID-19 affecting healthcare providers (HCPs) health, low community referrals, and lack of availability of personal protective and hygiene items

Intervention or response: With the increase in number of cases and local transmission of COVID-19 in the program areas, the safety and security of Mercy Corps staff and project participants has been held at the highest importance. Program continuity guidelines were developed and disseminated among the implementing partners, covering modifications in program activities, where required, and the infection prevention guidelines for the team and participants to effectively implement program activities. Field teams and private HPCs were equipped with basic personal protective equipment (PPE). In order to ensure that all registered TB patients continue their treatment without interruption, medicines were delivered at their doorstep. Regular patient follow-up and contact screening was completed by the field teams through telephone. The infection prevention and triage guidelines were distributed among private HCPs

Results/Impact: During March 24, 2020 and July 17, 2020, 98% of the registered TB patients were able to continue their treatment without interruption. 16,664 patients received follow-up calls, 3,121 household members were screened using online tools, 1,078 presumptive were identified

Conclusions: Timely program adaptation, provision of PPEs and use of online tools can help in the continuity of TB care services even during emergency situations like COVID-19 without putting lives of millions of people at risk.

TB in vulnerable populations

EP-03-120 Migration between districts by TB patients in India and the odds of their receiving TB programmatic services and their overall treatment outcomes

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Background: Migration leads to incomplete and irregular tuberculosis (TB) treatment. India witnessed migrant laborers chose to return to their home districts during the Covid-19 restrictions from 24 March 2020. We studied the characteristics of TB patients who migrated to other district with their odds of receiving programmatic services and treatment outcomes.

Design/Methods: Retrospective analysis of 0.361 million TB (DS-TB) patients data extracted in MS-Excel from 'Nikshay' (national electronic TB database) between 1st April to 30th June 2020. Migrant TB patients were identified from Nikshay whose diagnosing and current health facility are in different districts. Demographic, clinical, programmatic services and treatment outcome variables for migrant and non-migrant TB patients were compared in proportion and odds of receiving programmatic services and treatment outcomes was analyzed at statistical significance level of <0.05 using Chi square test.

Results: During the study period, 707 (93%) districts witnessed some migration of TB patients. Of the 327204 TB patients registered, 34769 (10%) migrated to other districts. Migrant TB patients had significantly lower odds of pulmonary site involvement (OR 0.42, $p < 0.05$) and higher odds of initial loss-to-follow-up (OR 3.27, $p < 0.05$). Although percentage of females and microbiologically confirmed were higher in migrants, variables on services viz. bank account seeding for DBT, contact tracing, screening for co-morbidities, follow-up smears during treatment and universal DST were proportionately lower in migrants but not significant statistically ($p > 0.05$). Favorable treatment outcome was proportionately lower in migrant and statistically significant ($p < 0.05$).

Conclusions: Our study reveals that TB services to the migrant TB patients need to be strengthened to meet their specific needs through targeted interventions, more pro-active features like push notifications from Nikshay to providers in other districts to prompt patient tracking, service continuity and patient support.

EP-03-121 How useful is it to systematically screen pregnant women for TB in rural India?

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Background and challenges to implementation: Tuberculosis is a significant contributor to maternal mortality and is one of the three leading causes of death in women of reproductive age in high TB burden countries. Despite this, maternal TB remains unrecognised and underestimated. There is a need to identify the actual burden of TB in pregnant women.

Intervention or response: Between February 2020 and February 2021, 8229 pregnant women were actively screened for TB at home by community health workers (CHWs) in 8 rural blocks of Samastipur district (pop. 2.8M), Bihar using an online symptom-based screening tool. Screening was undermined by women's reluctance to present symptoms due to stigma and the association of certain symptoms, like fatigue and night sweats, with pregnancy.

Where presumptive pulmonary tuberculosis was found, sputum samples were collected and taken for GeneXpert testing.

Where swollen lymph nodes indicated possible extrapulmonary tuberculosis, women were supported to visit a private health facility for a Fine Needle Aspiration Cytology test.

Results/Impact: Despite screening challenges, 1.03% (85/8299) of the women were found to have presumptive TB. 43% (37/85) of the presumptive patients underwent diagnosis resulting in 18 cases of confirmed TB. Of these, 83% (15/18) were pulmonary and 17% (3/18) were extra-pulmonary TB; 78% (14/18) were bacteriologically positive and 22% (4/18) were clinically diagnosed. The screening yield for active TB was 0.21% (18/8229) equating to a number needed to screen of 457. The reasons for pre-diagnostic loss-to follow-up included inability to produce sputum sample, hesitation in getting tested, preference towards undergoing diagnosis post-delivery and loss to follow up by CHW.

Conclusions: Prompt identification of TB in pregnant women can be supported by routine systematic screening for active TB as part of antenatal care accompanied by counselling around stigma and adequate diagnosis support.

EP-03-122 TB infection and disease among pregnant, postpartum and non-pregnant women exposed at home to TB

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Background: Few studies describe tuberculosis (TB) risk in pregnant and postpartum women (PPW). We sought to compare the rates of TB infection and disease progression among PPW and non-pregnant women (NPW) of childbearing age exposed at home to TB.

Design/Methods: We analyzed data from a prospective cohort of TB household contacts identified between 2009 and 2012 in Lima, Peru. Screening for TB infection (tuberculin skin tests) and TB disease was conducted at baseline, six-, and 12-months. We calculated the incidence rates (IR) and incidence rate ratios (IRR) for TB infection and disease in women who were pregnant and not pregnant at baseline.

Results: Among 3541 females between age 15 and 44 years with pregnancy status available at baseline, 40% (44/111) of PPW and 47% (1542/3302) of NPW had TB infection at baseline (Figure).

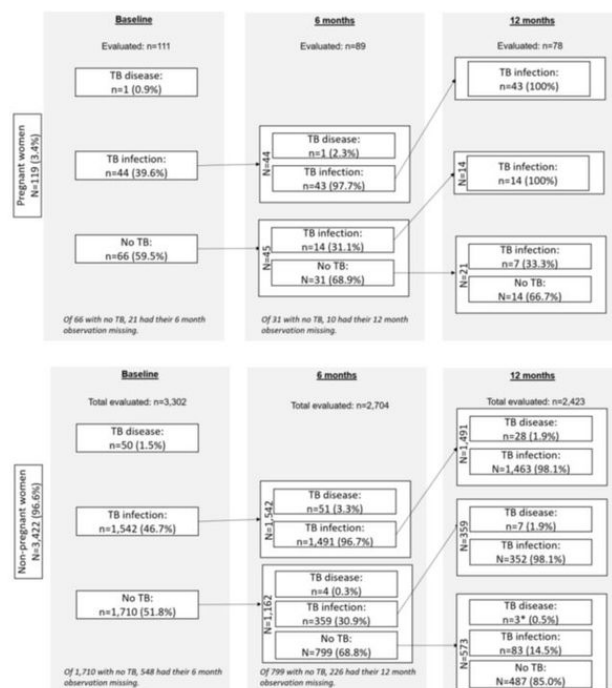


Figure. Risk of TB infection and disease for women at baseline, six, and twelve months.

One percent (1/111) of PPW and 2% (50/3302) of NPW had co-prevalent TB disease. At six months, 31% (14/45) of PPW as well as 31% (359/1162) of NPW progressed to TB infection, while two percent (1/44) of PPW and 2% (55/2704) of NPW progressed to TB disease. At 12

months, 33% (7/21) PPW and 15% (83/573) NPW progressed to TB infection. No PPW and 2% (38/2423) of NPW developed TB disease at 12 months. Comparing PPW to NPW, the IRR at six months was 1.0 for TB infection and 0.6 for TB disease; at 12 months the IRR was 2.2 for TB infection and 0 for TB disease.

Conclusions: At one-year follow-up, the women who had been pregnant at baseline had more than twice the rate of TB infection compared to the women who were not, while the rates of TB disease were similar. Screening women for TB as part of routine prenatal care in high burden settings could be beneficial for prompt TB detection and treatment.

EP-03-123 Assessing stool-based Xpert test results for paediatric TB diagnosis in Nigeria

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Background: In Nigeria, most children with tuberculosis present at the primary health care clinics where skilled personnel and necessary equipment for diagnosis are lacking. Since children find it difficult to expectorate quality sputum, a large proportion of cases are missed. To address this challenge, through the support of the USAID funded TB LON 1&2 project, KNCV Nigeria implemented a stool-based Xpert method for childhood TB diagnosis.

Design/Methods: Implementation commenced with a stakeholder's meeting to highlight childhood TB diagnostic gap and way forward. Subsequently, the national laboratory SOP on the use of stool for TB diagnosis was reviewed and disseminated to laboratories. This was followed by training of 203 laboratory staff across 187 GeneXpert laboratories in 14 states on stool test procedure.

The training ran concurrently with sensitization of health care workers for demand creation. A webinar was organized to sensitize a larger audience including NTP, pediatricians, implementing partners etc. on the benefits of the stool-based Xpert test. A video demonstration of the stool test procedure was also developed and uploaded on You tube for country wide use (<https://youtu.be/CSVWBsj0ZCY>). This was to guide lab staff that may not have the opportunity of a formal training.

Results: Implementation was from July 2020 to March 2021. All children visiting health facilities who were presumed to have TB but unable to produce sputum provided a stool sample instead. Out of 2974 children

referred for stool examination, 2929 had their stool samples examined with 150(5%) positive cases and 98% enrollment rate.

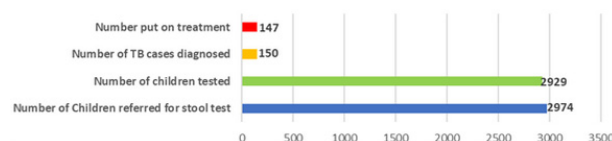


Figure. Cascade of stool-based Xpert test.

Conclusions: A 5% TB yield makes stool-based Xpert a promising option for TB diagnosis in children. Synergizing efforts to increase awareness and demand for the test as well as build capacity of more lab staff would expand diagnostic access and ultimately improve childhood TB notification in Nigeria.

EP-03-124 Screening people with TB at high risk of severe illness at notification in Karnataka, India

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Background: In any potentially fatal illness, an assessment of severity is essential. This is not systematically done for people with drug-susceptible tuberculosis, mostly due to lack of policy and/or limited availability of diagnostics and capacity. In this operational research from India, we assessed the i) feasibility of using a severe illness screening tool (using simple and easy to measure indicators) by para-medical programme staff and ii) burden of high risk of severe illness

Design/Methods: In this cross-sectional study, screening was done at diagnosis among adult (≥ 15 y) tuberculosis patients notified from public facilities (15 October to 30 November 2020) of 16 districts in Karnataka (state in south India). We defined 'high risk of severe illness' using indicators of severe under nutrition, abnormal vital signs and poor performance status (any one) i) body mass index (BMI) ≤ 14.0 kg/m² ii) BMI ≤ 16.0 kg/m² with bilateral leg

swelling iii) respiratory rate >24/minute iv) oxygen saturation <94% v) inability to stand without support. The para-medical programme staff collected screening data in a paper-based form, checked for errors and then entered the data in a mobile-based application 'EpiCollect5' (installed in the mobile tablet used to notify patients).

Results: Of 3020 adults, 1531(51%) were screened (district-wise range: 13%-90%). Low screening coverage in some districts was due to the prevailing COVID19 pandemic. Of 1531, a total of 538(35%) were classified as 'high risk of severe illness' (indicates high burden). Contribution of each indicator is depicted in the Figure.

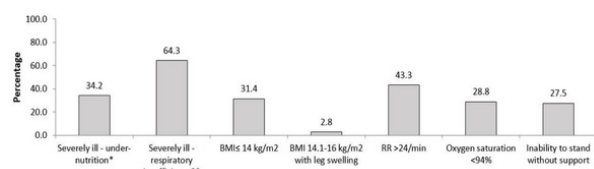


Figure. Contribution^s of individual indicators to 'high risk of severe illness' at notification among adults (≥15 years) with TB (without known drug-resistant disease at diagnosis) from public health facilities of 16 districts in Karnataka, India, 15 October to 30 November 2020 [N=538=100%][‡]

TB - tuberculosis, BMI - body mass index. ^sPercentages will add up to more than 100%, more than one indicator may be present in an individual; [‡]Of 3020 people with TB, a total of 1531 were screened; of 1531, a total of 538 had 'high risk of severe illness'; *Presence of any one indicator = BMI≤14.1-16 kg/m² with leg swelling; **Presence of any one indicator - respiratory rate >24/minute, oxygen saturation <94%

Short time interval between screening and notification (median five days, inter quartile range 1-12) and all five indicators being collected for 88% of patients suggested feasibility in programme settings.

Conclusions: To end tuberculosis deaths, screening should be incorporated in routine and severely ill patients should be referred for appropriate inpatient care. Future studies should assess the validity of this screening tool (especially sensitivity).

EP-03-125 Gaps in the early diagnosis of TB among rural populations in Ukraine

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Background and challenges to implementation: Ensuring equal access to tuberculosis (TB) treatment and prevention is critical to the success of a TB control strategy. This study was conducted to assess the time spent on the diagnosis and treatment of TB in rural areas and to identify individual factors that influence the detection of TB cases in rural areas.

Intervention or response: A retrospective cross-sectional study was conducted based on data from 946 rural patients diagnosed with TB and registered in the national

TB registry from 01.01.2017 to 01.01.2019 from selected 3 sites (districts) with the highest incidence of tuberculosis in four regions of Ukraine. We assessed the delay of the pathway to a TB diagnosis, from the onset of symptoms to the initiation of TB treatment. Cox binary regression analysis, which provides a hazard ratio and their 95% confidence intervals (CI), was used to estimate prognostic delay factors

Results/Impact: In total 946 patients were included in the analysis. The median patient delay was 7 days, median diagnosis delay after the patient's visit to the family doctor was 7 days (IQR: 2.4-14), in case patient's self-referral to TB facility - 21 days (IQR: 11-36), treatment initiation median delay - 9 days (IQR 5-18). Overall 73% of patients had an unacceptable treatment delay beyond the WHO recommendation of 7 days. The female gender was associated with having an unacceptable treatment delay (RR = 0.80, 95% CI: 0.67-0.95).

Conclusions: The key gaps in providing access to early TB diagnosis are delayed sputum collection along a patient-initiated pathway. Travelling long distances to access a health facility for TB testing outside one's location can be a limiting factor for most suspected TB patients.

Improving TB testing services targeting rural primary health care clinics, improving patient's diagnostic pathways and sputum logistics should be a priority intervention to overcome the identified gaps.

EP-03-126 Factors associated with treatment interruption among people with TB in Equatorial Guinea

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Background and challenges to implementation: Lost-to-follow-up (LTFU) to antituberculosis treatment has been over 20% in Equatorial Guinea in 2018 with 1482 new tuberculosis (TB) patients enrolled for treatment. The National Tuberculosis Programme (NTP) decided to explore factors associated with LTFU in new TB patients, by assessing access to care, availability of services and socio-economic factors.

Intervention or response: In 2020, the NTP designed a strategy that includes two phases: 1) A mixed-methods assessment of factors associated with LTFU through the conduct of a cohort study and 2) The implementation of tailored response to cope with LTFU based on study results.

We report here the results of the first phase that enrolled new cases of all forms of TB. All new TB patients who started treatment in 2020 were eligible for the study.

Data collection forms that included clinical, socio-demographical data were entered in Epi-Info software and cross-checked with TB cards and registers.

Results/Impact: A total of 324 patients were enrolled, their median age was 30 years [IQR 23-40] and 166 (52%) were women. After 6 months of treatment, 49 (15%) patients were LTFU. Drugs and health staff availability among LTFU compared to non-LTFU ranged between 84 to 98% (p-values > 0.6). The proportion of unemployed in LTFU versus non-LTFU was 84% and 62% respectively (p-value >0.6).

The factors associated with stopping earlier the treatment were: age ≥ 45 , belonging to a minority ethnic group, diabetes mellitus and alcohol use with an adjusted relative risk (aRR) and 95% confidence interval (CI) of 1.6 (95% CI 1.16-2.31), 9.8 (95% 2.4-40.3), 6.2 (95% 3.4-11.4) and 1.7 (95% 1.21-2.41) respectively.

Conclusions: To improve treatment adherence NTP should implement specific interventions in adults older than 45, TB/diabetes coinfection, minority populations and those with consumption of alcohol. Community and multidisciplinary teams could help in designing a person-centred approach for improving adherence.

EP-03-127 Best practices and lessons learnt during TB stigma assessment in urban slums in Lagos State, Nigeria

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Background and challenges to implementation: Lagos State has 8.4% of Nigeria's TB burden. As the TB incidence drops, TB will be concentrated on the key and vulnerable groups. Recent CRG assessment revealed that Stigma exists in different settings and therefore impacts accessibility to TB services and adherence to treatment. Furthermore, The current COVID-19 situation has been perceived to worsen the TB stigma. Currently, with significant inroads made towards ending TB, Lagos State does not yet have systematic and targeted actions for awareness and providing psychosocial support to those experiencing TB related stigma. The Lagos State TB Program fund activities including actions to combat stigma in Lagos, however, levels of stigma in different settings are not known making it impossible to track stigma performance indicator targets and for measuring change over time.

Intervention or response: We commenced our interventions through advocacy for high-level commitment from relevant stakeholders. Thereafter, using proportionate sampling methods, we proceeded with the adaptation and implementation of the STOP TB Stigma Assessment tool.

Further, we went ahead to implement TB stigma assessment advocacy and communication activities - these activities engaged top-notch celebrities in the country. Finally, we commenced the engagement of legislators to advocate for policy reforms related to TB stigma and discrimination based on the assessment result.

Results/Impact: The engagement of Celebrities to draw attention to issues of CRG and stigma during the assessment has brought a lot of recognition to relevant stakeholders at all levels to the problems of stigma. Also, our community engagements efforts have drawn a reasonable amount of attention from COVID-19 to tuberculosis.

Conclusions: Our methodology and approach have helped to bring attention to TB management in Lagos State and our results will support the effort of the TB program and partners towards achieving human rights and gender-related commitments of the United Nations High-level Meeting (UNHLM) on TB Targets.

EP-03-128 Feasibility of a cash transfer intervention to improve TB diagnostic evaluation in Uganda

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Background: Cash transfers may be a promising intervention for improving tuberculosis (TB) outcomes among socioeconomically at-risk patients. We assessed the feasibility of providing cash transfers (CT) to people undergoing TB evaluation in a high-burden, programmatic setting.

Design/Methods: We conducted a pilot interventional trial of a one-time CT intervention at 10 community health centers in Uganda from October 2019-March 2020. We collected mobile phone numbers from all eligible adult patients initiating TB diagnostic evaluation at health centers and used a mobile money transfer platform to send patients 20,000 Uganda Shillings (US\$; ~\$5.34USD). We collected process metric data to assess fidelity of implementation and conducted surveys with a subset of patients to evaluate the use and perceived impact of the CT on completion of TB diagnostic evaluation and household financial security.

Results: 3,145 people were eligible and 2,541 (81%) were enrolled in the CT intervention. Of those who enrolled, CTs were sent to 2,212 (87%) and 100% of those attempts were successful (Figure 1).

The median time to CT receipt was 1 day (IQR: 0-1). The most commonly reported use of the cash among 193 surveyed recipients was for food (n=60; 31%) or additional healthcare (n=45; 23%). Most respondents “strongly agreed/agreed” that receiving the cash made it easier to obtain transportation and food (n=173; 90%; n=128; 66%), respectively.

A majority (n=156; 81%) “strongly agreed/agreed” that knowing about the transfer affected their decision to return to the health center and 169 (88%) “strongly agreed/agreed” that receiving the CT made it easier to complete diagnostic evaluation.

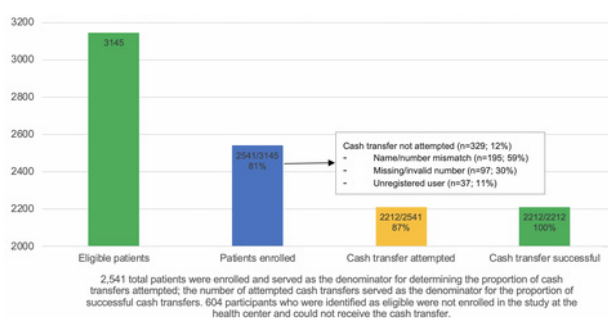


Figure 1. Fidelity of patient cash transfer intervention process, October 2019 - March 2020.

Conclusions: CT interventions can be implemented with high fidelity within routine TB care in a high-burden setting using a mobile money platform. Such interventions may enhance the ability for patients to complete TB diagnostic evaluation by mitigating financial barriers to accessing TB care.

EP-03-129 Outcomes of chest radiographic screening, treatment and nursing management of TB in a prison in Thailand

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Background: Tradition screening criterion using any chest X-ray (CXR) abnormality to be eligible for sputum examinations creates laboratory workloads causing diagnosis delay. Also, the nursing management from screening the entire prison to treatment completion is challenging.

The study aimed to:

1. Assess crude prevalence of pulmonary tuberculosis,
2. Evaluate sensitivity of CXR reading categories,
3. Analyze factors associated with TB and
4. Evaluate treatment outcomes.

Design/Methods: This study used secondary data of CXR screening and its treatment outcome from July 2017 to June 2018. The retrospective analytic study enrolled a total of 2,382 male and female prisoners in a prison, Thailand. CXR readings were classified in 6 categories:

1. normal;
2. abnormality detected-not significant;
3. abnormality detected, significant-no active disease;
4. abnormality detected, significant-not tuberculosis;
5. abnormality detected, significant-tuberculosis; and,
6. abnormality detected, significant-unclassified.

Those with categories 3-6 submitted 2 sputum samples tested on microscopy and Xpert for MTB/RIF assay. Screening schedule, sputum collection and patient care were managed by prison nurses. Data were analyzed to calculate descriptive statistics and multiple logistic regression.

Results: Of 2,382 prisoners screened, 6.3% had abnormal chest radiographs as categories 3-6. Crude prevalence of bacteriologically confirmed TB cases was 953/100,000 (27/2,832). The sensitivity of category 5 was highest (96.3%). Prisoners with BMI <20 kg/m² were 3.21 times more likely to have pulmonary TB than those with BMI ≥20 kg/m² (aOR=3.21; 95% CI=1.2-8.5). Of 21 susceptible TB patients, 16 (76.2%) completed the treatment, and of 6 Rifampicin-resistant TB patients, only 2 (33.3%) completed the treatment.

Conclusions: TB remained prevalent in prisons, and high transferred out rate continued to challenge the program. Six CXR reading categories showed different percentages of sensitivity which helped nurses to prioritize a sputum submission queue. BMI <20.0 kg/m² should be used to screen TB when needed.

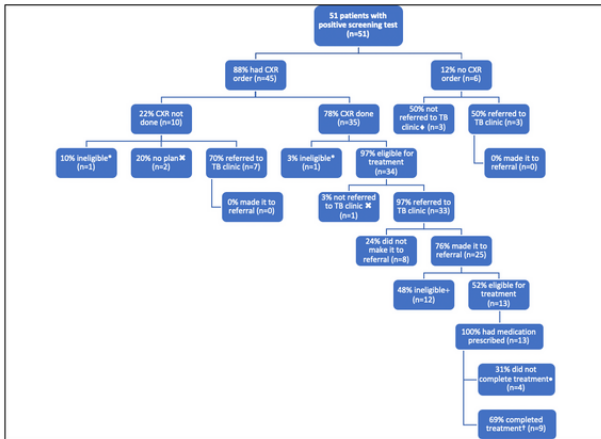
EP-03-143 Latent TB infection treatment outcomes in an at-risk underserved population in Rhode Island, USA

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Background: Within the United States (US), there are significant racial and ethnic disparities in the incidence of tuberculosis (TB) disease, with a disproportionate number of TB cases seen within individuals born outside the US. The purpose of this study was to evaluate the latent tuberculosis infection (LTBI) treatment outcomes within a Federally Qualified Health Center in Rhode Island, US, which serves a large, underserved and diverse population that is at-risk for LTBI.

Design/Methods: A quantitative retrospective chart review of clinic patients > 18 years was conducted to assess LTBI treatment outcomes including referrals, initiation, and completion within the LTBI care cascade.

Results: Charts of 51 patients who had positive LTBI tests between April 2019 to April 2020 were reviewed. 73.9% of individuals were born outside of the US; 80.4% of individuals identified as Hispanic or Black and 74.5% spoke a preferred language other than English. 43/51 (84%) were referred to the local TB clinic and only 58% of those were successfully seen at the TB clinic. 17.6% of those deemed eligible and/or uncertain eligibility initiated treatment for LTBI.



CXR= chest x-ray
 * Ineligible due to previous LTBI treatment
 * No plan for treatment was documented
 * One patient was ineligible due to previous treatment and two patients had no plan documented for treatment
 + Five patients were deferred due to pregnancy; five patients were previously treated for LTBI; one patient was ineligible due to the treatment risks outweighed the benefit, and one patient was deferred due to travel
 † Five patients completed Rifampin treatment, three patients completed INH treatment, and one patient completed 3HP treatment
 • One patient was still in treatment during chart review timeframe

Figure 1. Flow chart of LTBI screening and treatment initiation.

Conclusions: This study identified various losses across the LTBI care cascade particularly related to referral success and treatment. Expanding LTBI treatment access into primary care settings could be a potential solution to decrease health inequities among marginalized communities at high risk for developing TB disease.

TB elimination in the increasingly digital era

EP-07-157 Gauging the severity of Covid-19 using computer-aided tools in hospital settings, India

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Background: We propose a prognostic tool for predicting the risk of mortality for COVID-19 patients at the time of admission using Artificial Intelligence (AI). The model takes as input the patient’s chest X-ray scan and other clinical parameters and predicts the risk of mortality.

We propose that this will ensure better prioritization of treatment for high-risk patients.

Design/Methods: This retrospective study was conducted for 400 COVID-19 patients from a private Indian hospital. The data used for AI modeling consisted of 67 features including the chest X-ray, patient information, clinical observations, symptoms, comorbidities, etc. A deep learning model was trained to read the X-ray and make two predictions:

1. Probability of patient being infected by COVID-19 and,
2. Area of infection as seen on the X-ray.

These two predictions were added as input features for predicting mortality. The end-to-end process involved the following steps: preprocessing the data, removing aberrant or missing values and discarding geospatial and contact tracing information, finding the appropriate hyperparameters using grid search, and training a Random Forest model on the processed datasheet.

Results: The model obtained a sensitivity of 0.83 [95% C. I.: 0.64-1] and a specificity of 0.7 [95% CI: 0.64-0.77] for predicting mortality. The features that contributed most significantly towards making the decision included the patient’s age, the probability and predicted area of infection by our X-ray AI model, and co-morbidities.

Metric	Value [95% CI]
Sensitivity (High-risk)	0.83 [0.64, 1]
Precision (High-risk)	0.22 [0.12, 0.32]
Specificity (Low-risk-Recall)	0.7 [0.64, 0.77]
F1-score (High-risk)	0.34 [0.21, 0.47]
Kappa Score	0.24 [0.12, 0.35]

Table. Performance of the AI Algorithm

Conclusions: Using AI to take into account the digital radiographic findings and clinical parameters to predict accurately patient outcome during admission. We think it can be a good prognostic tool for prioritizing treatment for patients at high risk of mortality.

EP-07-158 Implementation and evaluation of the WHO PREVENT-TB mobile application for TB contact investigation in Beira, Mozambique

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Background: New strategies are imperative to overcome under-diagnosis of TB disease and infection. The PREVENT-TB mobile application, developed by WHO, was piloted for TB household contact investigation in Beira, Mozambique.

Design/Methods: Procedures for TB contact investigation in Beira were reviewed, the PREVENT-TB app was adapted, translated into Portuguese, and loaded onto tablets. Community Health Workers (CHWs) at 6 health facilities (2 CHW/facility) were trained to use PREVENT-TB and on COVID-19 mitigation.

Three control facilities used paper-based forms for data collection; 3 intervention facilities piloted PREVENT-TB. In July-December 2020, new TB cases were enrolled and referred for contact investigation.

Contacts <5 years were referred for TB preventive treatment (TPT) assessment. Contact investigation indicators were compared between intervention and control facilities. Post-intervention qualitative survey on acceptability/feasibility of PREVENT-TB was administered. Yields were compared using paired-t-tests.

Results: Yield of screened contacts diagnosed with TB disease and started on treatment was similar using PREVENT-TB versus paper forms [13/1939 (0.67%) versus 14/2047 (0.68%) respectively (p=0.94)]. The proportion of contacts tested for TB disease was lower in the PREVENT-TB group 71.4% (n=25/35) compared to paper group 96.6% (n=28/29) (p=0.01).

All TB patients in both groups received treatment. The proportion of child contacts starting TPT was 100/214 (46.7%) in PREVENT-TB group versus 115/228 (50.4%) in paper group (p=0.44). TB case finding during the COVID-19 pandemic were lower than prior years.

Interviews with CHWs using PREVENT-TB suggested factors such as CHW age, experience with technology,

fear of tablet theft may have impacted optimal functioning of the app.

Conclusions: The PREVENT-TB mobile app largely performed as well as paper tracking systems, but provided added agility in data management that paper lacks. Access to devices that are less vulnerable to theft is important.

Training in contact investigation and digital literacy will be critical for TB service scale-up and could synergize with COVID-19 mitigation efforts.

EP-07-159 Use of digital hotspots to conduct targeted community outreaches in Cross River State, Nigeria

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Background and challenges to implementation: Nigeria is a high burden country for tuberculosis (TB), HIV-associated TB, and multidrug-resistant TB with a case detection rate of 27%. Exploring targeted approaches to finding the missing TB cases is necessary. This review aims to demonstrate the advantage of using e-health platforms to identify TB hotspots for targeted TB screening and case finding.

Intervention or response: The TB surge intervention carried out in the TB LON 1&2 project states across Nigeria is captured real-time on the Commcare mobile app (electronic reporting platform). Data is triangulated through this medium to identify TB hotspots. An alert system is shared weekly with the implementing states. In Cross River State, this informed targeted community screening to find TB cases. The community screening had 2 approaches, mobilization of community members for mass screening and house-to-house case search.

Results/Impact: During the 8 weeks of the intervention between January to March 2021, 3346 (48.2% male, 51.8% female) persons were screened. Three hundred & thirty-five 335 (10%) presumptive were identified. Three hundred & twenty-five (97%) of identified presumptive completed diagnostic evaluation, 38 (11.6%) TB cases were diagnosed. 52.6% of the TB cases were diagnosed clinically and 44.7% pediatric TB cases.

Conclusions: The use of digital solutions can and will add value to targeted TB case finding. Although there are hitches in the specificity of the business intelligence (BI) portal used in the project, this can be upgraded to meet the current project requirements. There is a need to expand the use of the BI portal nationwide and harness the potentially huge database for users, government, and other stakeholders to access analytics for positive decision making.

EP-07-160 Mobile applications for TB that include mental health support for patients

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Background: Tuberculosis (TB) patients face a higher risk of mental health problems, including almost four times higher odds of depression. Integrating TB and mental health treatment services, particularly in low- and middle-income countries, can improve treatment outcomes, quality of life and save lives.

The purpose of this review was to systematically review mobile applications (apps) for patients with TB and evaluate them for the type of mental health support features.

Design/Methods: We systematically searched 3 app stores in May 2021 for apps that were intended for use by patients to manage and support TB treatment completion. Apps were identified by searching “Tuberculosis” and “TB” in app stores that included: GooglePlay, Samsung and Apple. Apps were included if they focused on TB information and targeted patients. Apps were excluded if they were unrelated to TB, targeted healthcare professionals, only accessible if part of a study, and in a language other than English or Spanish.

We used the 16 recommended mental health features for smartphone apps to evaluate the presence of mental health features. Examples of mental health features include cognitive behavioral therapy based; reporting of thoughts, feelings, or behaviors; mental health information; reminders to engage (with app/intervention); and links to crisis support services.

Results: To date, of the 52 apps included thus far, 4 included a mental health related feature. The most common mental health related feature was supportive messaging and reminders to engage with app or treatment. The majority of recommended mental health features were not identified in the TB apps.

Conclusions: Given the increased risk of mental health problems among those with TB and the tremendous potential to improve outcomes, we recommend that more mental health support features are integrated into TB apps for patients.

EP-07-161 Active case-finding using artificial intelligence in prison facilities in Karachi, Quetta and Peshawar, Pakistan

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Background and challenges to implementation: Prison facilities are considered TB reservoirs, with a higher prevalence of pulmonary tuberculosis (PTB) than the general population. Prison settings pose an inherent challenge in screening and Tuberculosis control. Systematic screening for TB using automated chest radiography (ACR) with Computer-Aided Detection software (CAD4TB) amongst prison facilities in 3 cities was conducted as part of a larger TB case finding program in Pakistan.

Intervention or response: Screening for Tuberculosis was conducted at prison facilities in the cities of Karachi, Peshawar and Quetta between 2018 and 2020. Screening was conducted using portable x-ray units temporarily fitted at the facilities. Trained healthcare workers and x-ray technicians offered chest x-rays to all prison inmates ≥ 18 years that were accessible.

Of those screened prisoners with a CAD4TB score ≥ 70 and/or symptomatic (cough > 2 weeks, fever, night sweats, weight loss) were identified as presumptive TB, and requested to submit a sputum sample for GeneXpert testing. Identified TB presumptive were also evaluated by a physician for signs of clinical TB.

Results/Impact: 20,557 inmates (mean age = 32) were screened, of which 313 (1.5%) were females. 1,964 (10%) were identified as presumptive TB; of those 1,804 (92%) submitted sputum samples. A total of 104 (0.5%) TB cases were diagnosed (mean age = 35), of which 71 (68%), were bacteriologically confirmed (MTB +ve), 3 (4%) tested positive for Rifampicin Resistance (RR), and 33 were diagnosed based on clinical evidence.

The findings indicate a TB prevalence of 506 per 100,000 at these facilities, approximately 1.8x higher than the estimated national prevalence (268 per 100,000) of the country.

Process Indicators	Karachi		Peshawar		Quetta		Total	
	N	%	N	%	N	%	N	%
(A) X-ray screening	14,876	-	3,662	-	2,019	-	20,557	-
(B) Presumptives (B/A)	1,695	11	146	4	123	6	1,964	10
(C) Samples collected (C/B)	1,590	94	111	76	103	84	1,804	92
(D) Diagnosed Cases (C/A)	84	0.6	9	0.2	11	0.5	104	0.5
(D1) MTB+ve (RIF+ included) (D1/D)	55	65	5	56	11	100	71	68
(D2) RIF+ (D2/D1)	3	5	0	-	0	-	3	4
(D3) Clinically diagnosed (D3/D)	29	35	4	44	0	-	33	34
(E) Prevalence of TB (D/A)* 100,000	565		246		545		506	

Conclusions: The findings validate the need for integrating TB screening as part of routine practice. Use of technology enables mass screening and higher yields of MTB+ cases (especially RR+) reducing transmission. National case finding programs must collaborate with prison authorities to implement efficient screening/testing algorithms at these facilities.

EP-07-162 Using CAD4TB scores to streamline clinical diagnosis

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Background: The Wellness on Wheels (WoW) was launched in Nigeria in 2017 to bridge the gap of missing TB cases through active case finding in communities with high risk of TB transmission. The thrust of cases diagnosed over the past 4 years have been bacteriological with an increasing number of clinical diagnosis seen recently, this was due to engagement of a consultant radiologist to further evaluate CXR'S of the bacteriologically negative clients.

Design/Methods: The WoW truck is equipped with a digital X-ray and CAD4TB (Computer Aided Detection for Tuberculosis) which is an AI software in addition to 2 units of a 4-modular GeneXpert machine, the CAD4TB score ranges from 0-100. Presumptive TB were identified through symptom screening and or a CAD4TB cut off score of 56 and then evaluated using Xpert MTB/Rif on the WoW truck.

Clients with a CAD4TB score of ≥ 80 but negative on Xpert MTB/Rif evaluation had their CXRs further evaluated by a Consultant radiologist alongside other clinical examination findings.

Results: From August 2020-March 2021, 485 symptomatics that tested negative on Xpert MTB/Rif with CAD4TB score of 80 and above were further evaluated by radiologist and clinician, of which 307 were eventually clinically diagnosed with TB. These 307 cases contributed to 60% of TB cases diagnosed by the WoW truck during the period under review and 100% of them showed improvement in symptoms within weeks of anti-TB drugs treatment start.

Conclusions: Artificial intelligence such as CAD4TB is a useful add-on to the already existing screening methods for the diagnosis of TB, its use should be encouraged to reduce false negatives from bacteriologic tests such as the Xpert MTB/Rif.

Results from this pilot study can be replicated for further studies to ascertain possible causes of the negative Xpert results for those cases that returned suggestive of TB from the radiologist review.

EP-07-163 Video treatment support in the era of Covid-19: a useful tool to monitor adherence and well-being of endTB participants in Kazakhstan

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Background and challenges to implementation: The COVID-19 pandemic has posed difficult challenges in MDR-TB clinical trial implementation. Government mandated lockdowns, public transportation restrictions, and conversion of TB hospital wards to COVID-19 isolation units inspired the endTB clinical trial team in Kazakhstan to expand innovative solutions to provide treatment support to participants. We describe the implementation of video treatment support (VTS) to maintain contact with trial participants and ensure their safety during the pandemic.

Intervention or response: The endTB team previously established options to supervise treatment administration for trial participants. These included: treatment administration locations for participants living far from the clinical trial site, home visits by nurses, and the incorporation of VTS. When the first wave of the pandemic affected Kazakhstan in March 2020, treatment administration locations were inaccessible to participants. The endTB team responded by expanding VTS to all trial participants who consented to ensure continuity of care and follow up visits.

Results/Impact: The team conducted 8359 VTS visits for 51 participants from March 2020 to March 2021. VTS enabled study staff to monitor adherence and focus on the participants' wellbeing despite lockdowns and transportation restrictions. VTS utilization and success was dependent on reliable internet and smartphone availability from participants. Although VTS provided convenience and mitigated participant and staff risk of infection, it cannot entirely replace in-person visits. In situations where it was necessary to physically assess participants, study staff traveled to participant homes or other outdoor locations.

Conclusions: VTS can be a valuable tool for clinical trial teams in order to maintain close contact with participants during the pandemic. MDR-TB trials, in particular, stand to benefit from such an intervention considering the long length of treatment, propensity for loss to follow up cases, and vulnerability of the patient population. Although VTS was born out of necessity during this trial, it could have benefits in routine TB care.

EP-07-164 Active case-finding through artificial intelligence-assisted mass radiography in Chennai, India

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Background and challenges to implementation: Delayed or no care-seeking and misdiagnosis of TB symptoms contribute significantly to increased TB incidence and transmission in India. In Chennai, passive case finding (PCF) and door-to-door (D2D) were the dominant service modalities prior to 2019. From January 2019 to March 2020, we deployed mobile diagnostic units (MDU) followed by overnight AI-supported interpretation of digital chest x-rays (dCXR) across Chennai slums where ~30% of the population lives.

Intervention or response: We compare the yields of MDU modality with AI-supported diagnostics to the previous modality. Seven MDUs with mobile digital x-ray machines were deployed, each with a driver, radiographer, and field supervisors. MDU camps were held at convenient times in slums across Chennai. Respondents over 18 years old and guardians of children over 5 years old were sensitized about upcoming camps. Camp visitors were verbally screened and a dCXR was taken. If they had chest symptoms, sputum samples were collected and analyzed by SSM. AI was used to classify dCXR for TB and other abnormalities with human radiologists checking the results and reporting within 24 hours. Confirmatory CBNAAT testing was then conducted prior to treatment initiation.

Results/Impact: 104,576 individuals were screened during the period of analysis. 80,697 chest x-rays were taken, and sputum samples were collected from 72% (29,720) of 41,289 symptomatic individuals. 548 TB patients were diagnosed and initiated on treatment, of which 239 were microbiologically confirmed and 309 were clinically diagnosed. The yield was 524 per 100,000 screened vs. 17 per 100,000 screened for D2D.

Conclusions: Early case-finding and higher yield may be achieved for individuals with low access to quality diagnostics through an ongoing community-level MDU intervention with dedicated staff and high-sensitivity screening tools like dCXR. Delays in diagnosis may be further reduced through AI and molecular diagnostics after a single high-sensitivity moderate-specificity screening step.

EP-07-165 Experiences and learnings of integration of India NTP MIS - Nikshay with other platforms

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Background and challenges to implementation: Integration between health systems and NTEP has been achieved in provision of services, including administration, financial management and monitoring and supervision. Expanding this integration to include all digital interventions in the health and allied domains would be crucial in the fight towards Ending TB. Integrations of digital interventions would enable strengthening surveillance (IHIP portal), aid in beneficiary authentication (Aadhar), support in creation of longitudinal health records of an individual (Health ID - National Digital Health Mission), reduce duplicate data entry at the field level.

Intervention or response: Nikshay has been developed as a microservice architecture with Application Programme Interface (APIs) available for integrating and exchanging data with other health systems.

Results/Impact: The Nikshay platform is integrated with 9 different digital systems as on date, which include diagnostic machines and services, various adherence modalities including 99DOTS, Medication Event Reminder Monitoring (MERM), Virtually Observed Treatment (VOT), payment modalities for Direct Benefit Transfer through Public Financial Management System (PFMS), dashboards for visualization of programme performance.

Conclusions: In order to further strengthen and ease the process of integration, plans are underway for adoption of various standards including SNOMED-CT, ICD-10, MDDS and HL7/FHIR) as well as enabling a sandbox environment to enable different third-party organizations to access various APIs available under Nikshay.

EP-07-166 Optimising community TB active case finding using the Delft Light Backpack: preliminary results from a 6-month pilot study in Nigeria

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Background and challenges to implementation: Nigeria is ranked first in TB burden in Africa with a 73% gap in TB case notification. In order to continue to bridge the gap in TB case notification in Nigeria, the National TB Program (NTP) adopted innovative active TB case (ACF) finding strategies. The NTP and KNCV TB Foundation Nigeria piloted community TB ACF using the DLB, a portable x-ray with CAD4TB artificial intelligence (AI) to assess its effectiveness in TB case finding within hard-to-reach rural communities in Niger Delta Region, Nigeria.

Intervention or response: The DLB was deployed to 7 LGAs in Akwa Ibom and Cross River states of Nigeria between Dec 2020 and March 2021. Children above 4 years and adults with TB symptoms were enrolled for screening. All enrolled clients were screened for TB using DLB and CAD4TB score of 60 and above were regarded as presumptive TB. All presumptive identified had sputum collected for GeneXpert and negative results were subjected to further review by a Radiologist. Identified TB cases were referred for treatment and notified to the TB program.

Results/Impact: Within 4 months of implementation of TB ACF with DLB, 6,232 clients were enrolled, 6,218 screened with DLB, 778 presumptive TB identified, and 757 evaluated with GeneXpert MTB/RIF with a total of 70 TB cases diagnosed and 68 started on treatment and notified to NTP. The number needed to screen (NNS) for the DLB ACF compare favorably with that for WoW mobile diagnostic unit and targeted community ACF implemented by the project within the same period and same project locations, see Table 1.

Indicator	DLB	WoW truck mobile diagnostic unit	Targeted community ACF
Attendees	6,232	14,751	5,245
Screened	6,218	14,674	5,245
Presumptive	778	863	1,046
Evaluated	757	847	921
Diagnosed	70	184	98
Treatment	68	159	86
NNS	88	80	54
NNT	11	5	9

Table 1: TB cascade for three community based active TB case finding interventions

Conclusions: The deployment of DLB for community TB ACF has shown to be effective in finding missing TB cases especially among the underserved hard to reach population.

The result from the pilot supports the need for scale up of this intervention to more hard-to-reach communities in Nigeria.

Economics of TB prevention and care

EP-09-177 Cost-effectiveness of 3 months of weekly rifapentine and isoniazid in an urban Canadian setting

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Background: To achieve the global End TB targets of 30 million people treated for latent TB infection (LTBI), novel, shortened preventive treatment regimens are needed. In Canada, the current standard of care is 9 months of daily self-administered isoniazid (9H SAT). Shortened treatment regimens, such as 3 months of weekly rifapentine and isoniazid (3HP), have shown improved completion rates.

Patients may prefer these novel regimens due to shortened treatment duration. However, 3HP requires directly observed therapy (DOT) in Canada which may increase costs.

Our study aimed to assess the cost-effectiveness of 3HP in an urban Canadian setting.

Design/Methods: A Markov model was developed to assess the cost-effectiveness of 3HP compared to the standard of care (9H SAT). Parameters were derived from programmatic data, a local implementation study of 3HP and the published literature. Costs were obtained from local, empirically collected data from a health systems perspective and reported in 2019 Canadian dollars. Results were projected over a 30-year time horizon.

Results: A shortened, preventive treatment regimen of 3HP was shown to be cost-effective compared to the standard of care (9H SAT), with an incremental cost effectiveness ratio of CAD\$651 per quality-adjusted life year (QALY) saved.

The 3HP regimen costs were higher than the 9H regimen (CAD\$1209 vs. CAD\$1045/person) and health outcomes were slightly improved (19.95 vs. 19.70 QALY/person). The 3HP regimen also resulted in fewer TB cases (15 vs. 31/1000 persons initiating treatment) and TB deaths (1 vs. 3/1000 persons).

Conclusions: In an urban Canadian setting, a shortened preventive treatment regimen (3HP) was shown to be cost-effective when compared to the standard of care (9H) despite the requirement of DOT. Consideration of patient costs would likely improve the cost-effectiveness value of shortened regimens and bolster the evidence for changing the standard of care in the Canadian setting.

EP-09-178 Adapting the WHO TB Patient Cost Survey for use in the United Kingdom

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Background and challenges to implementation: Eliminating catastrophic costs is a target of WHO's End TB Strategy. Despite anecdotal reports, there is scarce evidence of the economic impact on TB-affected households in high-income, low-burden countries. We did formative research to adapt WHO's generic Tuberculosis Patient Cost Survey tool (TB-PCS) for future use in the UK.

Intervention or response: In March 2019, a national workshop brought together 24 purposively-selected, multisectoral stakeholders with experience of TB and/or social protection, including clinicians, researchers, policy-makers, and TB-survivors. Thematic analysis synthesised workshop recommendations, which were then used to draft a UK-adapted TB-PCS. In February 2021, the draft TB-PCS was circulated among UK TB networks alongside a concise survey to explore the perceived economic impact of TB in the UK and garner feedback on the adapted TB-PCS's suitability to capture UK-specific costs.

Results/Impact: The workshop recommended UK-specific direct costs, lost income, coping, and socioeconomic position indicators, and data-linkage (Table).

The concise survey was completed by 32 respondents: 25/32 (78%) TB healthcare professionals, 5/32 (16%) researchers, and 2/32 (6%) TB survivors. The severity of economic impact on TB-affected households in the UK was reported as "a lot"/"great deal" by 20/32 (63%). Among healthcare professionals, 12/25 (48%) reported having given their own money to support people with TB. Most respondents "agreed"/"strongly agreed" that the adapted UK TB-PCS tool would adequately capture direct costs (87%, 27/31), lost income (78%, 25/32), and coping strategies (72%, 23/32). Suggested improvements included: reducing tool length; prefilling responses with national Enhanced TB Surveillance (ETS) data; capturing the costs of children with TB, their carers, and people treated for TB infection; and ensuring multilanguage translation.

Theme	Recommendation
Design, timing, and location	<ul style="list-style-type: none"> Longitudinal study Data collection at commencement, end of intensive phase, and towards treatment completion Health facility based initial survey interviews with telephone follow up at subsequent interviews
Defining and calculating costs and catastrophic costs	<ul style="list-style-type: none"> Adapt travel costs to UK systems (e.g. travel cards & car parking) Include direct costs and lost income incurred by carers and consider costs of TB screening and latent TB infection treatment Use locally validated expenditure modules (e.g. Office for National Statistics Living Costs and Food Survey) Integrate coping strategies into the survey including use of food banks, pay-day loans, sub-letting, second jobs, and selling sex Consider measures of economic wellbeing
Estimating income and socioeconomic position	<ul style="list-style-type: none"> Establish proxy for permanent or pre-TB income Account for employment conditions including people who have variable income due to zero hours contracts Use validated measures tailored to UK setting to measure socioeconomic position (e.g. UK Household Assets Survey) Use national categorisations to describe e.g. occupation and level of education
Linking with existing data sources	<ul style="list-style-type: none"> Aim to link data collected during the survey with existing electronic databases, including: <ul style="list-style-type: none"> Indices of Multiple Deprivation Hospital Episode Statistics Department of Work and Pensions database Enhanced TB Surveillance

Table. Workshop recommendations for a UK-adapted TB patient cost survey.

Conclusions: WHO's generic TB-PCS required adaptation to adequately capture TB-related costs and indicators distinct to a high-income, low burden setting. Our UK-adapted TB-PCS tool received favourable feedback and is ready to be piloted.

EP-09-179 Initiating strategic health purchasing for TB programme in Indonesia: a budget impact analysis

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Background: We assessed the financial impact and value for money of the TB program's strategic health purchasing (SHP) pilot intervention in Medan city, Indonesia. The SHP intervention is expected to create an efficient and effective payment scheme for TB services, as it provides incentives to primary care physicians to offer on-site TB services and reduces unnecessary referrals to secondary care, to improve the TB notification and treatment completion.

Design/Methods: Our budget impact analysis, developed based on the Ministry of Health's guidelines on TB services for drug-sensitive TB, employs the payer's perspective and primarily includes direct medical costs. We projected the cost per person with TB symptoms, cost per person with TB (PWTB) treated, and cost per treatment completed. Model inputs—defined from multiple national datasets—included TB incidence, insurance coverage, number of person with TB symptoms who do not access health facilities, diagnostics utilization, TB notification, treatment initiation, and treatment completion rates.

Results: Our model estimates that the SHP pilot intervention can improve TB notification and treatment completion rates by 64% (4,140 PWTB without SHP intervention vs. 6,802 PWTB with intervention) and 241% (1,617 vs. 5,509 PWTB), respectively, although the intervention will increase expenses by 59% (\$1 million vs. \$1.65 million).

As the TB program is supported through a multi-payer scheme, the model demonstrates that the SHP intervention will reduce the Health Social Security Organizing Body's expenses by 24% and increase the Ministry of Health and Global Fund's expenses by 3.7 times and 17 times, respectively.

The cost per person with TB symptoms will increase by 82% (\$15.3 vs. \$27.8), while cost per PWTB treated and cost per completed treatment will decrease by 23% (\$102.4 vs. \$79) and 53% (\$642.3 vs. \$300.2), respectively.

Conclusions: The SHP intervention is expected to improve TB notification and treatment completion rates, although total investment needed for providing TB services will increase under SHP scheme.

EP-09-180 Cost and cost-effectiveness of digital adherence technology for TB in Uganda

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Background: Treatment adherence for drug-susceptible tuberculosis (TB) is suboptimal in high burden settings. 99DOTS is a Digital Adherence Technology (DAT) that has potential to facilitate patient treatment management, but little is known about the 'real-world' costs and cost-effectiveness of DAT implementation in high TB burden settings.

Design/Methods: We assessed the costs of implementing 99DOTS as part of a stepped-wedge randomized trial analyzing the impact of 99DOTS on treatment outcomes in Uganda. We performed costing exercises at five of 18 study facilities. Costs were assessed from the health system perspective and reported as 2019 US dollars. Time-and-motion data were used to assess activity-based service costs. 99DOTS-based treatment support costs were estimated under three scenarios: (a) considering duration of the study period alone ("trial-specific"); (b) assuming a 5-year time horizon for implementation and operations ("extended activities"); and (c) assuming 99DOTS system infrastructure was in place, and only additional clinics needed to be added, under a five-year horizon ("marginal clinic scenario"). Cost-effectiveness was assessed as cost per patient successfully completing treatment.

Results: The total cost of implementing 99DOTS in the trial period was \$100,532 across 18 clinics (range: \$3,771 - \$6,283 per clinic). The estimated cost per treatment success in the trial alone was \$355 (range: \$229-\$394), falling to \$54 (range: \$38-\$95) assuming extended activities, and \$44 (range: \$33-\$74) in the marginal clinic scenario. If the incremental number of patients completing treatment, relative to no DAT, was 16 per 100 patients (estimated in the per-protocol trial analysis), then incremental cost-effectiveness of 99DOTS in the extended-activity scenario was \$304 per incremental treatment success.

Scenario	Trial-Specific	Extended Activities	Marginal Clinic
Overhead	\$0.10	\$0.08	\$0.08
Building	\$0.01	\$0.01	\$0.01
Equipment	\$91.96	\$3.91	\$3.91
Staff	\$2.62	\$1.99	\$1.99
Supplies	\$11.59	\$10.96	\$10.96
Technology Support/ Hosting	\$44.25	\$25.21	\$25.21
Implementation	\$204.81	\$12.18	\$2.24
Total	\$355.34	\$54.34	\$44.40

Table 1. Cost per treatment success by scenario

Conclusions: Costs and cost-effectiveness of 99DOTS were influenced by the degree to which infrastructure is scaled over time. If sustained and scaled-up, 99DOTS can be a cost-effective approach to TB treatment adherence support in high-TB-burden settings like Uganda.

EP-09-181 Economic evaluation of community TB active case-finding approaches in Cambodia: a quasi-experimental study

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Background: We conducted an economic evaluation of two community tuberculosis (TB) active case finding (ACF) strategies in Cambodia that targeted key populations for TB by assessing the cost per disability-adjusted life years (DALY) averted among people with TB.

Design/Methods: We analyzed program and national TB notification data from a quasi-experimental study of a cohort of people with TB in 12 intervention operational districts (ODs) and 12 control ODs between November 2018 and December 2019. The intervention sites that were purposively selected comprised two ACF interventions that were implemented concurrently—1) ACF seed-and-recruit (ACF SAR) model and 2) one-off roving (one-off) ACF—and passive case finding (PCF) was also present by default. The matched control sites included PCF only. We estimated costs using the program and published cost data in Cambodia. The primary outcome was the incremental cost per DALY averted

between the intervention and the control sites over 14 months. We considered the gross domestic product per capita of Cambodia in 2018 as the cost-effectiveness threshold.

Results: In total, 12074 were screened and tested via the seed-and-recruit model and 51636 via the one-off roving ACF model. The former needed to test 7.7 presumptive TB to identify 1577 all-forms TB, while the latter needed to test 22.4 to identify 2303 all-forms TB. The cost per DALY averted was US\$ 238 for ACF using a seed-and-recruit model and US\$ 164 for one-off roving ACF.

Conclusions: Community-based ACF interventions that targeted engagements with key populations for TB in Cambodia were highly cost-effective.

EP-09-182 Expenditure incurred by households for TB diagnostic services during hospitalisation in India

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Background: The National Tuberculosis Elimination Program (NTEP), has over the years provided free Tuberculosis (TB) diagnostic and treatment services. Though the services are free of charges, there is evidence to show that households spend out-of-pocket for TB services. However, the household expenditure for TB diagnostic services is yet to be studied.

Design/Methods: The National Sample Survey (NSS), published by the government of India collects information on self-reported ailments including TB. The 75th round of NSS data (2017-2018) was analyzed for arriving at expenditure incurred by household for TB diagnostic services. The current analysis included expenditure reported for inpatient/hospitalization in last 365 days at the time of survey. The expenditure pertaining to TB services is collected for both medical care [including doctor consultation, medicines, diagnostic tests (X-rays/ECG/EEG, & other diagnostic tests), and other medical expenses] and non-medical care (transport, food, expenditure on escort, lodging charges etc.).

Results: The results showed 610 households reported hospitalization due to TB (67.5% in public sector and 32.5% in private sector). The median total expenditure for TB services was US\$ 110 (IQR:34-279) (Private sector: US\$ 261(IQR:163-484); Public sector: US\$ 56 (IQR:18-140)). The overall medical expenditure contributed to more than 70% of the total expenditure of which 18% was for diagnostic services. The diagnostic expenditure reported from the private sector (US\$ 28

(IQR:12-61)) was 4 times higher than the public sector (US\$ 7 (IQR:0-23)). The expenditure data is presented in table across household income quintiles (1st Poorest-5th Richest). Poor households reported spending more in the private sector for diagnostic services than higher income quintile.

Income quintile	Total Expenditure (in US\$) Median (IQR)			Medical expenditure (in US\$) Median (IQR)			Expenditure for Diagnosis (in US\$) Median (IQR)		
	Total (N=610)	Public (N=412)	Private (N=198)	Total (N=610)	Public (N=412)	Private (N=198)	Total (N=610)	Public (N=412)	Private (N=198)
First quintile (N=121)	76(34-346)	65(15-172)	281(110-748)	63(10-279)	38(5-107)	264(98-668)	12 (3-61)	10(2-38)	31(8-123)
Second quintile (N=123)	88(27-249)	34(4-146)	249(161-825)	60(5-220)	23(2-73)	220(111-726)	8 (0-31)	2(0-19)	23(8-100)
Third quintile (N=125)	169(48-304)	65(28-120)	261(261-396)	138(30-226)	31(4-92)	226(226-362)	27 (4-37)	4(1-21)	28(28-56)
Fourth quintile (N=125)	100(33-217)	58(28-150)	260(130-439)	61(23-184)	38(13-74)	240(92-384)	12 (2-31)	5(0-18)	28(15-43)
Fifth quintile (N=116)	110(43-338)	49(18-134)	244(110-619)	82(23-232)	23(9-86)	230(107-537)	12 (3-61)	13(5-25)	23(10-32)
Overall (N=610)	110(34-279)	56(18-140)	261(163-484)	81 (22-230)	31(5-92)	226(123-461)	15 (3-34)	7(0-23)	28(12-61)

Note: The annual average of US\$ exchange rate for 2017 was rupees 65.12. IQR: inter quartile range.

Table 1. Household expenditure for hospitalization due to tuberculosis across wealth quintiles in India (2017-2018).

Conclusions: The diagnostic expenditure for TB in private sector is 4 times higher compared to public and this burden is also higher among the poor. There is a need to develop strategies to engage private sector diagnostic services to reduce the household medical expenditure.

EP-09-183 The household economic burden of drug-susceptible TB diagnosis and treatment in The Gambia: the TB Sequel Project

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Background: Information regarding patient and catastrophic costs incurred through tuberculosis (TB) care is critical to inform health and social protection programs. However, there is a lack of information on such costs in The Gambia. Therefore, this study aimed to determine the costs and catastrophic costs incurred by drug-sensitive TB (DS-TB) patients with pulmonary TB in The Gambia as part of the TB Sequel Project.

Design/Methods: This observational study collected cost and socioeconomic data using a micro-costing approach from the patient perspective from 244 adult DS-TB patients with pulmonary TB receiving treatment through the national treatment program in The Gambia. Data was collected between 2017 to 2020 using an adapted version of the WHO generic patient cost survey instrument to estimate costs and the proportion of patients experiencing catastrophic costs (Greater than 20% of household income). Sensitivity analyses were conducted to explore the impact of assumptions around wages, household ability to pay for TB, and catastrophic cost thresholds.

Results: The mean total cost of the TB episode was \$103 (2018 USD). Direct medical costs were highest before treatment (\$23), driven by medication fees (\$13). Before treatment, the mean cost was greatest at traditional practitioners (\$31). Indirect costs accounted for over 50% of the entire episode costs. 70% of patients used coping strategies like selling assets or using savings. Using different income estimation approaches, 0.4-75% of participants encountered catastrophic costs, showing the variability of results given different assumptions.

Conclusions: We show that despite the benefits of free TB care and treatment in The Gambia, DS-TB patients incur substantial direct and indirect costs. Cases of impoverishing expenditure varied widely based on the approaches and assumptions used. Reducing the costs faced before treatment by potential TB patients is critical to engaging and retaining patients in care and reducing the joint health and economic burden of TB disease.

EP-09-184 Assessing the impact of dissaving on TB treatment outcomes in Uganda

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Background: Tuberculosis (TB)-affected households often face catastrophic costs associated with treatment, leading to both negative financial and TB outcomes. However, enumerating patients' costs is challenging in routine clinical settings. Dissaving, an economic indicator defined as taking out a loan, selling an asset, or withdrawing from savings is simpler to identify. We sought to assess whether dissaving is associated with risk of negative socioeconomic and health outcomes for TB patients.

Design/Methods: Trained study staff surveyed TB patients on treatment at 17 health centers in Uganda between December 2018-July 2019. Surveys included three questions to assess if participants undertook dissaving to facilitate TB treatment. We constructed a multidimensional poverty index (MPI) using patient personal/household characteristics. We used modified Poisson regression to assess the association between the dissaving and treatment success, adjusting for age, sex, HIV status, and MPI category.

Results: Of the 230 patients surveyed, the median age was 39 years (interquartile range (IQR): 30-51). Eighty-nine (39%) were female and 38% were HIV+. Fifteen percent (15%) of patients (n=34) were categorized as in severe poverty, 31% (n=72) were in poverty, 43% (n=99) were vulnerable to poverty, and 11% (n=25) were neither poor nor vulnerable to poverty based on MPI. Almost all (n=222; 97%) indicated that they used savings, while 43% (n=98) took out a loan, and 41% (n=95) sold an asset to cover costs associated with TB treatment. Engaging in dissaving was significantly associated with poor TB treatment outcomes (adjusted Rate Ratio=0.88; 95% CI: (0.82-0.95); p<0.001, Table). Those classified as severely impoverished were 1.47 times more likely to engage in dissaving compared to those not in poverty.

	Unadjusted Rate Ratio (uRR)	uRR 95% Confidence Interval (CI)	p-value	Adjusted Rate Ratio (aRR)	aRR 95% CI	p-value
Dissavings composite (took loan or sold asset)*	0.90	(0.84-0.97)	0.004	0.88	(0.82-0.95)	<0.001
Age (continuous)	1.00	(0.99-1.00)	0.44	1.00	(0.99-1.01)	0.15
Female sex	1.01	(0.90-1.13)	0.90	1.00	(0.89-1.13)	0.99
HIV positive	0.98	(0.91-1.05)	0.57	0.97	(0.91-1.04)	0.43
Multidimensional Poverty Index (MPI): Not poor and not vulnerable to poverty	Reference			Reference		
MPI: Not poor but vulnerable to poverty	1.01	(0.87-1.17)	0.89	0.99	(0.86-1.13)	0.87
MPI: Multidimensionally poor	0.93	(0.84-1.04)	0.23	0.93	(0.82-1.05)	0.26
MPI: Severely multidimensionally poor	1.02	(0.88-1.19)	0.77	1.04	(0.88-1.23)	0.62

Table. Unadjusted and adjusted modified Poisson analyses assessing for the association between engaging in dissaving (selling an asset or taking out a loan to cover the costs of tuberculosis (TB) treatment) and treatment success, defined as being cured or having completed treatment. Standard errors adjusted for clustering at the health center (n=230).

*The composite variable includes only taking out a loan and selling an asset as withdrawal from savings was widely prevalent.

Conclusions: Engaging in dissaving may lead to poor TB treatment outcomes and is more likely among those most vulnerable. Simple strategies to identify TB patients in need of socioeconomic support may improve treatment outcomes.

EP-09-185 The first National Patient Cost Survey among TB patients in Burkina Faso, 2020

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Background: In Burkina Faso, the economic burden of TB-affected households, its consequences and drivers were only documented once, for six districts and a decade ago.

Filling such knowledge gap, this first national patient cost survey aims to support decision-making towards improved financial protection for health, social protection and other policies supporting increased access to quality TB care.

Design/Methods: From February 24 to March 12, 2020, a national cross-sectional survey was conducted in 20 clusters (treatment and diagnosis centers) selected proportional to the cluster size and 465 patients.

Following global WHO survey guidance, a structured questionnaire was administered to patients to report on the direct (medical and non-medical), indirect costs measured as a valuation of time loss, annual household income/expenditure and the coping strategies developed by the TB-affected families.

Multiple logistic regression was performed to identify factors associated with catastrophic costs due to TB.

Results: A majority (54.4%) of households incurred TB-related costs greater than 20% of their annual income. On average, households incurred in USD 962.64 per episode of care. Indirect costs accounted for 77% of the total burden (mean=USD 741.7), direct medical costs for 13% (USD 122.3) and non-medical costs for 10% (USD 98.6). Risk of experiencing catastrophic costs increased with poverty condition and hospitalizations. 25.8% of

TB-affected households resorted to coping strategies such as loans. Besides, patients faced job loss (28.4%) or food insecurity (20%).

Conclusions: Reducing the economic burden of TB is essential to reach the sustainable development Goal 3 and the WHO End TB strategy. New evidence in Burkina Faso provides a key baseline to inform national decision-making and support effective policy implementation. A stakeholders' workshop will be held end 2021 to disseminate the results and support the design of health and non-health measures towards reducing the newly evidenced economic burden supported by the TB-affected households.

Supporting TB screening, care and adherence

EP-18-268 Experience of mainstreaming various Digital Adherence Technologies under National Tuberculosis Program in India

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Background and challenges to implementation: Digital adherence technologies (DATs) have previously been implemented individually in different geographies of India. Health system related key challenges included supply chain management of various DATs, technology access, defining target population, lack of dashboard / analytics for visibility and supervision, price point of some of the DATs.

Intervention or response: In May 2019, Integrated digital adherence technology initiative (IDAT) was launched, enabling patient and provider choice in technology selection. DATs are now part of central procurement system. Toll Free lines and SMS services has been transitioned within NTP along with standardised envelopes. Significant price reduction in MERM costing has made it easier to procure them. Real time data availability, interactive UI and integrations with Communication Module also provide relevant staff with important updates around high-risk patients for follow ups. Very recently a patient facing application TB Aarogya Saathi was deployed that allows patients to monitor their own adherence and reach out to staff in case of issues.

Results/Impact: More than 10 states across India have either procured or are in the process of procuring various DATs. 500 MERMs and more than 70 lacs 99DOTS envelopes for roughly 4 lakh patients procured so far. In the year 2020, there were 1.99 lakh patients enrolled on 99DOTS and 56 patients enrolled on MERM. Over 19,412,947 SMS have been sent via governments SMS gateway and more than 3000 patients have accessed their adherence summary through the TB Arogya Saathi Application.

Conclusions: To continue to have high acceptability of tools, ensure DATs seen as person-centered treatment support tools and passive patient management tools. Streamlining the procurement and supply chain processes helps in smoother implementation and uptake. This coupled with seamless connectivity, real time data availability, stable technology platform plays an essential role in DAT uptake, uninterrupted treatment, and early cure for TB patients.

EP-18-269 The role of treatment community-based support to improve TB outcomes among TB-HIV patients in high HIV burden setting in Gaza Province, South of Mozambique, 2018–2019

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Background and challenges to implementation: Tuberculosis (TB) and HIV co-infection is an important determinant of poor TB treatment outcomes. This study aimed to assess the outcome of TB treatment after the initiation of TB treatment community-based support, and compare against the outcomes in the pre-intervention period, among TB/HIV co-infected patients in Gaza Province, South of Mozambique.

Intervention or response: A retrospective observational study was carried out utilizing registry data from 3416 co-TB/HIV and 2772 TB patients at 6 Districts of Gaza Province. Treatment outcomes for the patients' cohort enrolled in the pre-intervention period (July 2018 to December 2018) and in the first semester of intervention (July 2019 to December 2019) were compared using a chi-square test with a significance of $p < 0.005$. The approach included community-based direct observed treatment and psychological support.

Results/Impact: Among co-TB/HIV patients, TB successful treatment outcome increased from 89% pre-intervention to 93% after the onset of intervention ($p < 0.001$), death and lost to follow up (LTFU) reduced from 9% to 6% ($p = 0.002$) and from 2% to 1% ($p = 0.003$) respectively. There was an increase of failure from 0% to 1% without significance ($p = 0.37$). There was no significant variation observed on TB outcomes ($p = 0.21$) among HIV-negative TB patients.

Conclusions: Community engagement is a key strategy to improve treatment outcomes and reach WHO targets among co-TB/HIV patients within HIV high burden settings.

EP-18-270 Increasing private provider engagement in TB screening and diagnosis in urban Uganda

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Background and challenges to implementation: In Uganda, 40% of presumptive TB patients first present to the private care providers. However, private provider engagement in TB screening and testing has been low. In 2019, only 455 (0.7%) of all TB cases countrywide were notified by private health providers. We set out to increase engagement of the private sector in TB case notification in two large urban districts in Uganda (Kampala and Wakiso).

Intervention or response: We focused on community pharmacies and drug shops serving large urban slum populations. We trained and equipped 62 healthcare workers and 190 pharmacies/drug shops for TB screening and sputum collection. We transported sputum to public health facilities for GeneXpert testing through the national specimen transportation system. Patients diagnosed with TB were linked to treatment at public health facilities. Additionally, we trained 62 community healthcare workers to provide community sensitization, conduct contact tracing and provide adherence support to patients diagnosed with TB. Data was collected using standardized Ministry of Health tools. Patients and health workers received sputum results via SMS messages/calls from project team.

Results/Impact: From Jan 2020 to Feb 2021, we screened 132,942 people of whom 12,257 (9.2%) had presumptive TB. We performed 10,112 GeneXpert tests and diagnosed 368 patients with TB. 344 patients (93%) of all bacteriologically confirmed TB patients were started on treatment. In addition, chest X-rays were performed on 149 GeneXpert negative patients and of these 30 (20%) were diagnosed with TB and started on treatment. Furthermore, 21 presumptive patients were diagnosed clinically and started on treatment bringing the total number of TB cases notified to 419. This represented 3% (419/11,093) of all TB cases notified by in the two districts in that time period.

Conclusions: We demonstrate that a strong public-private partnership along with robust community engagement can increase participation of the private sector in TB case notification.

EP-18-271 Partnering with industries for TB elimination through corporate TB pledge

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Background and challenges to implementation: National Strategic Plan envisages continued engagement of industries to improve access to TB services. The corporate TB Pledge under the Employer Led Model is envisioned as means to reaching TB elimination by 2025. The focus is to implement a comprehensive programme on TB care and prevention in industries by integrating awareness, health education, and service delivery within existing systems, structures, and resources of the industries or mining establishments.

Intervention or response: Through a series of sensitization meetings and consistent follow ups, 25 industries signed the letter of intent with respective district health societies in 2019 to show their commitment to support TB services. Taking the intervention to the next level, industries were sensitized on signing of TB corporate pledge. A state level virtual sensitization meeting under the chairpersonship of senior state health officials, district NTP officials and industry representatives was conducted. This was complemented with one to one follow-up meetings with district level officials of NTP and industry representatives.

Results/Impact: Nine industries signed the corporate TB pledge under gold category and ensured their commitment to raise awareness on issues surrounding TB in workplace and community. Several industries also undertook various awareness generation activities in their catchment area during the World TB Day.

Conclusions: The TB pledge is a MoHFW initiative supported by USAID. The signing of corporate TB pledge will pave a way for creating sustainable systems by establishing linkages with NTEP and industries. It is crucial for industries to implement TB focused activities and work towards implementing a robust work place policy in their establishments.

EP-18-272 A non-randomised assessment of the impact of providing monetary incentives to patent medicine vendors for TB case-finding

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Background and challenges to implementation: Nigeria accounts for about 9% of the 3.6 million global missing Tuberculosis (TB) cases. The Patent Medicine Vendors (PMV) are becoming key stakeholders in health care service provision in Oyo State. This study was designed to assess the impact of providing monetary incentives to the PMVs for TB case finding in a high burden Local Government Area (LGA) in Oyo State.

Intervention or response: A group of PMVs at the LGA were trained on TB case identification and referral at the beginning of the 12 months' study period. Financial incentive for cases notified was introduced to this same group of PMVs six months of commencement of study. Case notifications in the first 6 months were compared with the last 6 months. Non-parametric method was used to test the null hypothesis of no difference between two dependent samples. Wilcoxon Signed Rank Sum test was used in comparing the differences of presumptive and confirmed cases, pre and post the introduction of incentives.

Results/Impact: Data in the first 6 months (November 2018 to April 2019) showed 116 confirmed TB cases notified from a total of 495 TB presumptive cases. The subsequent 6-month period (May 2019 to October 2019), 212 confirmed TB cases were diagnosed from a pool of 730 presumptive cases. This signifies a 47 and 82 percent increase in presumptive and confirmed cases respectively. A Wilcoxon signed-rank test showed that the provision of financial incentive elicited a statistically significant increase in presumptive and confirmed TB case finding within the 6-month period with ($Z=-2.201$, $p = 0.028$) and ($Z=-2.207$, $p = 0.027$) respectively.

	Cases notified between Nov 2018 to April 2019	Cases notified between May 2019 to Oct 2019	Difference	Rate of Increase (%)
Presumptive cases	495	730	235	47
Confirmed cases	116	212	96	82

Conclusions: The study concludes that provision of monetary incentives to PMVs increases TB case finding. There are however grave concerns about the sustainabil-

ity of incentivized interventions in resource limited settings. Further studies to address strengthening the existing health system might be necessary.

EP-18-273 Putting primary health facilities at the centre of TB case-finding: lessons from the TB Surge intervention in selected primary health centres in Akwa Ibom State, Nigeria

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Background and challenges to implementation: The Primary Health Centre (PHC) is the 1st point of contact with formal health services in most communities. Nigeria has about 30,000 PHCs but still struggles with low TB case detection (27%). Akwa Ibom State has 538 DOTS sites (mostly PHCs). The PHCs hold a strong potential for early diagnosis and treatment of Tuberculosis if appropriately exploited.

Intervention or response: In July 2020, the TB Surge intervention implemented by USAID-funded KNCV TB LON project in Akwa Ibom was expanded to include PHCs. They were linked to secondary health facilities with Gene Xpert machines through a sample transport mechanism using a Hub and spoke model. Two (2) dedicated PHC staff were trained for 100% OPD screening for TB using the TB-symptom screening tool and algorithms for further evaluation using CXR. They reported TB screening data weekly, were supported with a communication stipend and received regular mentorship from technical staff. The result of 5 selected PHCs from 5 LGAs is presented as a model of impact amidst the COVID19 pandemic.

Results/Impact: In the intervention period - 2nd half (H2) of 2020, the 5 PHCs cumulatively reported 546 presumptive identified and evaluated and 123 TB cases. The TB Surge contribution was 86% (469) for presumptive evaluated and 74% (91) for TB cases diagnosed. The intervention period reported a 38% and 64% increase in presumptive evaluated and TB cases diagnosed respectively compared to the preceding period (H1 2020). There was also a 51% and 186% increase in presumptive evaluated and TB cases diagnosed year-on-year (H2 2020 vs H2 2019). Program quality indicators also showed significant improvements.

Conclusions: Findings show that with the presence of dedicated staff and adequate program support, the PHC has the potential of leading Active case-finding for TB in their communities. The implementation approach adds to health systems strengthening and sustainability and is recommended for scale-up.

EP-18-274 Systemic health of the patient at start of TB treatment influences adherence

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Background: Tuberculosis is a chronic disease predominantly caused by *Mycobacterium tuberculosis*, for which standard treatment for non-resistant strains typically involves four different antibiotics taken for six months. Patient engagement with therapy is therefore required to ensure adherence, maximising chances of favourable outcomes for patients, reducing the risk of further spread and bacterial resistance to antibiotics. This study aimed to assess how health status of patients at the start of treatment influenced adherence over the treatment course.

Design/Methods: Data from the REMoxTB randomised controlled trial was analysed¹. This study recruited patients from across the world to compare a four-month regimen to a six-month regimen. Adherence data was obtained as a percentage of total doses taken, with adherence defined as >90%². Systemic health status at baseline was assessed using marker variables – body mass index (BMI) and blood albumin concentrations. Univariable and multivariable logistic regression models were generated adjusting for age (grouped in 10 year increments), sex, smoking status, HIV status, smear status (proxy for tuberculosis severity) and course length.

Results: 1611 patients had a complete dataset, with 91.8% being considered adherent. There was no apparent relationship between BMI and albumin concentration at baseline (Chi-square $p=0.10$), so they were assessed independently in the models. Regression modelling suggests that patients with low albumin are less likely to be adherent (OR 1.75 (1.15-2.66)).

	UNIVARIABLE MODEL	MULTIVARIABLE MODEL
<i>BMI (Weight in kg/Height in m squared)</i>		
Underweight (<18.5)	Baseline	Baseline
Healthy (18.5<25)	0.91 (0.63-1.32)	0.92 (0.63-1.33)
Overweight (>=25)	0.82 (0.36-1.87)	0.96 (0.40-2.30)
<i>BLOOD ALBUMIN CONCENTRATION</i>		
Below reference range	Baseline	Baseline
Within reference range	1.62 (1.12-2.34)	1.75 (1.15-2.66)

Table 1: Univariable and multivariable regression models of the effect on adherence.

Relative risk of achieving 90% adherence based on systemic health status at baseline. In univariable analysis there is a strong suggestion that low albumin concentrations lead to a greater likelihood of poor adherence ($p=0.01$), whereas in the multivariable model there is less statistical certainty ($p=0.32$). In both univariable ($p=0.83$) and multivariable ($p=0.38$) models BMI appears to be less likely to influence adherence.

Conclusions: Patients with low albumin concentrations at baseline may be nearly twice as likely to be non-adherent as patients with healthy concentrations. Low albumin suggests more compromised patients, or patients less able to compensate for the effects of tuberculosis. If patients with more severely compromised general health are also less likely to be adherent, then this potentially further reduces chances of a favourable outcome.

EP-18-275 Using digital adherence technologies in TB outpatient treatment in local settings in Ukraine: a mixed-methods study

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Background: DATs, such as the EvriMED pillbox, may facilitate more effective allocation of limited healthcare personnel resources where populations are hard to reach. Ukrainian health NGOs are experienced implementers of social incentives to improve adherence in patients from vulnerable groups. To explore practical aspects of using DATs to monitor adherence, W6 TB REACH project piloted the use of EvriMED in two Ukraine oblasts with high TB burden. The study addresses feasibility and applicability of using DATs in TB out-patient treatment models.

Design/Methods: The study, designed within the implementation research framework, aimed to understand the factors promoting or hindering implementation and performance of DATs in supporting treatment adherence. Data collection took place over 5 months at 20 project sites. Participants were purposively selected to represent patients at different stages of treatment (Table 1). Two semistructured surveys were administered for 200 patients and for 23 HCWs. Quantitative data were analyzed based on the scores on the preference scale to assess satisfaction and acceptability. Qualitative data was analysed to identify and examine thematic content.

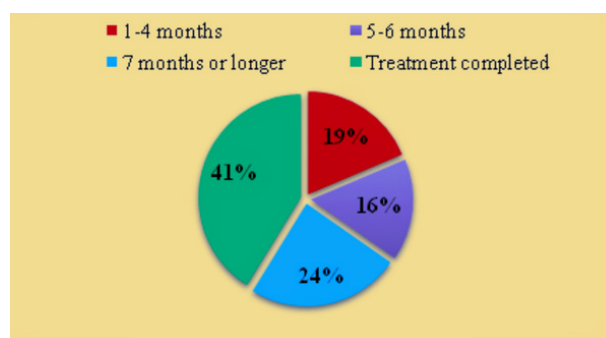


Table 1. Respondents distribution according to month of treatment, in %.

Results: This study was the first in Ukraine to assess the acceptability and perceptions of evriMED and 99DOTS platform. From a total of 1712 TB patients on treatment at project sites, 902 (53%) were enrolled on evriMED devices. Over 11 months of project implementation, EvriMED was fully integrated with the 99DOTS platform allowing clinicians to check daily adherence records for the patients they monitor and differentiate patients capable of self-administration and those requiring a different approach.

Conclusions: EvriMED smartbox can be effective to monitor treatment adherence. However, in Ukraine health context, its use would require significant spending, and selective patient inclusion meaning high discretion of an individual doctor. Surveyed HCWs outline DATs feasibility to identify 'reliable' patients so that resources can be focused on 'less reliable' ones who will most benefit from selective DOT.

EP-18-276 TUWAFIKIE Project: reaching out to the unreached to end TB through accredited drug dispensing outlets (ADDOs) in Tanzania

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Background and challenges to implementation: Sustainable full coverage of Tuberculosis (TB) services provision remains a major challenge especially in rural and under-served populations. This project "Reaching out to the unreached to end TB-TUWAFIKIE Project" aimed to reach out more individuals in rural and remote communities in Tanzania through Accredited drug dispensing outlets (ADDOs) for TB case detection.

Intervention or response: The project was conducted in 7 districts of Iringa and Kagera regions between 2019 and 2010. The primary intervention was engagement of ADDOs to screen clients for TB symptoms and to collect sputum samples from those identified as person to be evaluated for TB. Sputum samples were picked up from the ADDOs by sputum transporters already working for the National TB Program (NTP) to the GeneXpert diagnostic sites. All samples were diagnosed using GeneXpert. Laboratory results were communicated back to the ADDOs by SMS and for the positive results, both ADDOs and Community Health Workers (CHWs) were contacted with the test result and client's contact information. Confirmed TB positive clients were accompanied by the CHW to the nearest DOTS center to start treatment. Community and religious leaders were trained in stigma reduction methods and supporting TB clients on treatment to improve treatment adherence.

Results/Impact: A total of 592,147 people were screened for TB by ADDOs; 52.9% (279,092) were males. Of the screened clients, 1.1% (6,527) were persons to be evalu-

ated for TB and out of those, 296 (4.5%) were diagnosed with TB; 98% (290) were bacteriologically confirmed. All 296 patients were enrolled on treatment with 95% treatment success rate. TB case notification quarterly trend was increasing in both regions during the implementation phase.

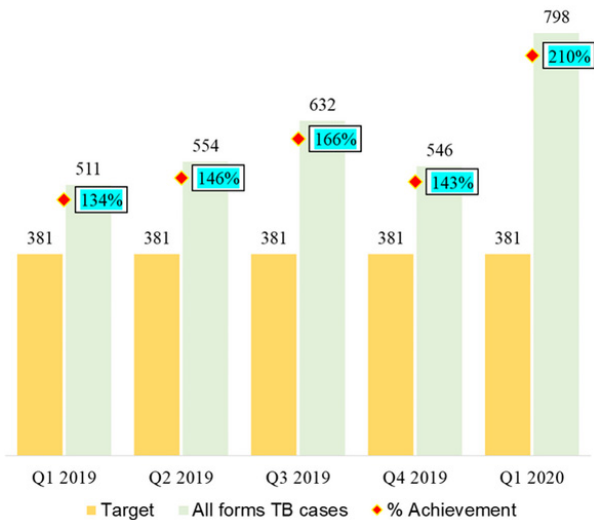


Figure. All forms of TB cases notification trend.

Conclusions: Our community intervention was able to reach out more people in the community and increased TB case notification and this has led to scale-up of this initiative to NTP under Global fund initiative.

EP-18-277 Barriers to retention on treatment for TB in northern Uganda

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Background and challenges to implementation: The treatment success rate (TSR) for all forms of TB in Lango sub-region, northern Uganda improved from 75% (October - December 2019) to 85% (July - September 2020), against a national target of 90%. Despite this improvement, several districts in the region had TSR below acceptable levels. An analysis of project data in 13 high-volume facilities showed an average lost to follow-up (LTFU) rate of 16%, with LTFU and deaths as major factors contributing to sub-optimal TSR. A root cause analysis (RCA) among 279 clients on TB treatment who had missed their appointments was conducted to establish the barriers to retention in care at 20 high-volume facilities

Intervention or response: Project data for July - September 2020 was reviewed to identify and prioritize sites with high LTFU rates for TB clients. A RCA tool was developed and pre-tested for validity and reliability. District TB and Leprosy supervisors and health facility TB focal persons were oriented on the use of the tool. Patients who had missed TB medicine refills during this time were interviewed to identify reasons for missing refills.

Results/Impact: A total of 279 patients (mean age 37 years) who had missed a TB medicine refill were interviewed (65% male); 91% were newly diagnosed TB patients; 7% returned after LTFU, while 3% were relapse patients. Lack of transport (32%), relocation to another area (9%), forgotten appointment (8%), sickness (8%) and resolved symptoms (6%) ranked highest among reasons for missed appointments. Solutions proposed by patients included representation at the clinic by a treatment supporter, use of community volunteers to refill medicines, transfer to treatment facilities closer to their home, appointment reminders, and delivering medicines in the community.

Conclusions: High transport costs to a treatment unit is the most common barrier to retention on treatment for TB in northern Uganda. Strengthen community support systems for TB patients.

Impact of COVID-19 on TB case rates

EP-22-308 Changes in TB notifications in Vietnam associated with the Covid-19 pandemic

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Background: Vietnam, a low-middle income country in Southeast Asia, is a high-prevalence setting for tuberculosis. The country was successful in curtailing the case load and mortality due to COVID-19 during the first year of the pandemic. Nationwide lockdown, strict border controls and social distancing policies were implemented to curb disease transmission. However, the impact the pandemic upon notification of TB remains uncertain.

Design/Methods: This study compared the monthly cases of TB and multi-drug resistant TB (MDR-TB) notified to the Vietnam National TB Program in 2019 and 2020. Data for sex, gender, previous treatment history, treatment outcome were obtained. Sputum smear and culture status at diagnoses was obtained for MDR-TB. Monthly TB and MDR-TB notifications and change in notifications between 2019 and 2020 were summarized.

Results: In 2019 a total of 105,680 individuals were registered for treatment for TB, and 2,889 individuals with MDR-TB were registered. In 2020, 96,998 individuals were registered for TB and 2,851 individuals with MDR-

TB. Differences in monthly notifications for both TB and MDR-TB are summarized in Table 1.

The largest drop in TB notifications occurred in April 2020 (29% for TB and 25% for MDR-TB), which coincided with the implementation of a nationwide lockdown in Vietnam.

There was a subsequent increase in notifications in June and July, following the lockdown. The overall TB notifications were 8% lower for TB and only 1% lower for MDR-TB between the two years. There was no statistical difference between smear or culture status between 2019 and 2020.

Month	2019 (TB) n	2020 (TB) n	Difference	2019 (MDR-TB) n	2020 (MDR-TB) n	Difference
Mar	9,259	8,252	-11%	204	253	24%
Apr	8,698	6,217	-29%	215	161	-25%
May	9,802	8,185	-16%	247	216	-13%
Jun	8,497	8,887	5%	253	267	6%
Jul	9,609	9,824	2%	308	256	-17%
Aug	9,722	7,880	-19%	313	293	-6%
Sep	8,311	8,328	0%	277	251	-9%
Oct	9,663	8,618	-11%	272	267	-2%
Total	105,680	96,998	-8%	2,889	2,851	-1%

Table 1 Change in monthly notifications for TB and MDR-TB in Vietnam (abridged)

Conclusions: The COVID-19 pandemic was associated with a modest decline in case notification for TB and MDR-TB in Vietnam. This study provides evidence that an effective public health policy targeted at protecting the population from a pandemic may also minimise adverse effects on other health services.

EP-22-309 Impact of the Covid-19 pandemic on TB notification rates in high-burden states in India

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Background: India had made significant progress towards the goal of ending TB which have been negatively impacted by the COVID-19 pandemic. Frequent lockdowns, diversion of healthcare workers, and utilization of diagnostic facilities - CBNAAT and Truenat for COVID-19 testing have significantly impacted the program services.

Given this, there is a need to understand the COVID-19 impact on TB case notification rate in high-burden states in India.

Design/Methods: The TB notification rate from year 2010 to 2020 was retrieved from the annual TB reports published by the Central TB Division, Ministry of Health and Family Welfare, Government of India. The data analysis was done for the top ten high TB burden states reported in the annual TB report 2020. The rate of change in the notification was calculated over ten years considering 2010 as the base year.

Results: The notification rate showed a declining trend from 2010 to 2015 and it has increased since 2016. However, in comparison to the base year, 2019 recorded the highest rate of change of 37.2%. As a result of COVID-19 pandemic, the TB services were impacted, and the rate of change reduced to 1.6% in 2020. Therefore, the decadal notification rate increased marginally from 129/100,000 in 2010 to 131/100,000 in 2020 (Figure 1).

In 2019, the change in notification rate was reported more than 70% in Delhi (104.6%), Madhya Pradesh (82.3%), and Gujarat (73.1%) whereas in 2020, the same states showed 40-50% decline.

Among the high TB burden states- West Bengal (-31.3%), Tamil Nadu (-30.1%), Andhra Pradesh (-10.3%), and Bihar (-2.5%) were adversely impacted due to COVID-19.

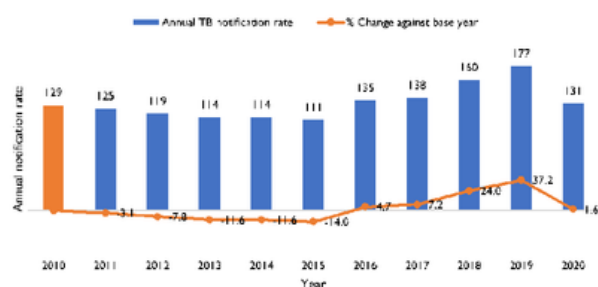


Figure 1. Rate of change in the annual TB case notification rate. *Base year 2010

Background and challenges to implementation: India had made significant progress towards the goal of ending TB which have been negatively impacted by the COVID-19 pandemic. Frequent lockdowns, diversion of healthcare workers, and utilization of diagnostic facilities - CBNAAT and Truenat for COVID-19 testing have significantly impacted the program services. Given this, there is a need to understand the COVID-19 impact on TB case notification rate in high-burden states in India.

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Conclusions: The COVID-19 pandemic has adversely impacted TB services as a result the notification rate has declined. There is need to focus on remedial measures and intensify the efforts towards the End TB goal by 2025.

EP-22-310 The impact of Covid-19 responses on TB care cascade in Bandung, Indonesia

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Background: COVID-19 pandemic has impacted the tuberculosis (TB) prevention and care program. This study aimed to identify its impact on TB cascade of care in Bandung, Indonesia.

Design/Methods: We constructed a cohort from people with TB identified in 6 community health centers (CHC) and 1 lung hospital in Bandung, Indonesia, from December 2020 to March 2021. Subsequently, we interviewed a total of 21 people, of whom 6 were people with TB, 6 TB program managers, 1 head of CHC, 4 laboratory analysts, 2 TB program managers in a lung hospital, and 2 staff from the local health office. Most of the interviews were held online and lasted for 30 until 60 minutes. The interviews were analyzed using standard thematic analysis.

Results: The number of notified TB cases decreased by about 30% in 6 selected CHC and 1 lung hospital in the period after the pandemic started compared to the same time period before the pandemic started. After the pandemic, sputum examination was conducted less frequently due to lack of personal protective equipment, reallocation of healthcare workers to fight COVID-19, and fear of contracting COVID-19 from performing sputum test. Stigma against COVID-19 worsened the existing TB stigma and led to the decreasing number of patient visits to healthcare facilities. Active TB case finding at the community level were also reported to be reduced during the pandemic.

Conclusions: COVID-19 affected the TB care cascade by decreasing the number of people who sought care to healthcare facilities and by a reduction in diagnosis workup. Allocating more resources, updating knowledge about COVID-19 among healthcare workers, and improving TB screening were needed at the early phase of the pandemic.

EP-22-311 Spatial analysis of TB and Covid-19 in Brazil, 2019–2020

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Background: Tuberculosis became the leading cause of death from infectious disease worldwide in 2015, when it surpassed HIV infection. However, on April 1, 2020, COVID-19 surpassed tuberculosis in terms of the number of deaths per day. The combination has great potential for morbidity and mortality.

In addition, the COVID-19 pandemic has had a significant impact on the diagnosis and treatment of tuberculosis. Therefore, the objective was to analyze the spatial distribution of cases due to tuberculosis and COVID-19 in Brazil.

Design/Methods: An ecological study carried out in Brazil with a population composed of all cases of tuberculosis and COVID-19 in the DATA-SUS from 2019 to 2020. From the geocoding of the cases, the Getis-Ord Gi and Gi*.

Results: In all, 2806 cases of tuberculosis were identified, of which 211.707.713 were caused by COVID-19. It was possible to identify hotspots for cases due to COVID-19 in the North, West and Southeast region. For Tuberculosis hotspots occurred in Southeast region. In both diseases the coldspot areas noticed in Northeast.

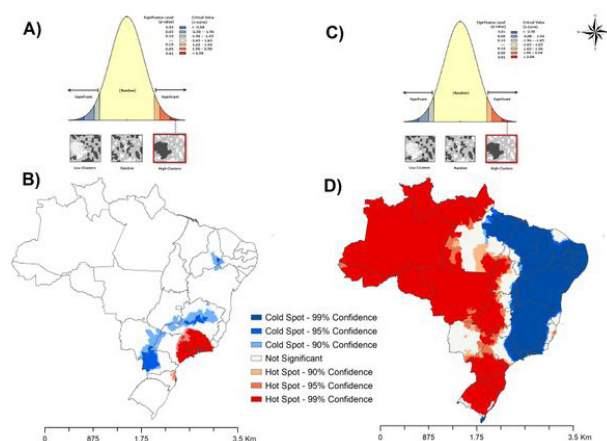


Figure 1- Hotspots and coldspots for Tuberculosis and COVID-19, Brazil, 2019-2020.

(A) Level of statistical significance of Getis-Ord G for cases due to Tuberculosis.

(B) Clusters of Tuberculosis according to the level of confidence.

(C) Level of statistical significance of Getis-Ord G for cases from COVID-19.

(D) Clusters of cases due to COVID-19 according to the level of confidence.

Conclusions: It was possible to identify risk areas for cases due to Tuberculosis and COVID-19 in Brazil. The reduction in demand for the diagnosis and treatment of tuberculosis may be reflected in future incidence and mortality rates.

Actions aimed at the elimination of tuberculosis also implies knowing the epidemiological reality of COVID-19 rates. The findings lead to the hypothesis that among COVID-19, there may be many under-notifications of tuberculosis, which requires future studies to confirm this hypothesis.

EP-22-312 Impact of the Covid-19 pandemic on TB case detection using GeneXpert, Dhaka, Bangladesh

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Background: The COVID-19 pandemic response particularly lockdown measures, reassignment of health care personnel and equipment are affecting TB detection and management. Due to the pandemic, countries with fewer resources have experienced the shared use of GeneXpert for COVID-19 and TB. The diversion of attention and resources away from TB compounded by the lockdown has had a devastating effect on TB diagnosis. The objective of this study was to compare the case detection data between the year 2019 and 2020 to understand the impact of the pandemics.

Design/Methods: Data of GeneXpert test for the year 2019 and 2020 was collected from the National Tuberculosis Reference Laboratory (NTRL), Dhaka and compared to determine the changes in case detection before and after pandemic.



Figure. Covid impact on TB testing.

Results: A total of 20,459 presumptive TB patients were tested in 2019 whereas only 9,167 patients were tested in 2020 which means the test decreased by 55% because of the pandemic situation. Detection of TB testing through GeneXpert was decreased approximately 37%, 91%, 58%, 23% respectively from first to fourth quar-

ter in 2020. The highest decrease rate was observed in the second quarter (91%) when the country declared the lockdown to restrict movement. The drop in testing also reduced drug susceptible TB case detection from 2725 to 1810, and Rifampicin Resistant TB detection from 174 to only 78 case in year 2020 compared to year 2019.

Conclusions: The pandemic has badly affected the TB case detection which is alarming for the National TB Control Program (NTP). The undiagnosed TB cases which may remain as unreported, can cause a greater number of deaths, and spread infections in the community silently. Bangladesh NTP needs to prepare itself to bridge the gap through utilizing the existing resources properly and introducing bidirectional COVID-19 and TB screening program.

EP-22-313 Bridging the gap in TB case notification during the Covid-19 pandemic in 2020 through private facilities engagement in TB service provision in Nigeria

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Background: The advent of COVID19 pandemic with the lockdown measure introduced in Nigeria from March 2020 greatly impacted on the health service delivery including TB service provision, this present a major threat to the already low TB treatment coverage of 27% as at 2019.

The programme as a major strategic shift prioritized expansion of TB services into the private sector to cover the huge clientele in the sector and address service interruption in public services. This retrospective study was conducted to evaluate the contribution from the private sector in bridging the gap in case notification during the COVID19 pandemic in 2020.

Design/Methods: The TB programme data from the 36 states and FCT were analyzed by type of providers (private or public), programme reports reviewed to evaluate contributions from private sector during the pandemic in 2020.

Results: The number of TB cases notified from the private sector increased by 108% from 17,250 in 2019 to 35,865 in 2020 while that of public sector decreased by 0.2% during the same period. The country recorded a 15% increase in TB notification in 2020 due contribution from the private sector that effectively bridge the gap during the lockdown. There was huge patronage of the private sector especially the patient medicine vendors (PMVs) during the pandemic with resultant increase in

the number of presumptive TB cases in 21 states by over 500% from 38,040 presumptive TB in 2019 to 237,560 presumptive TB in 2020.

Conclusions: The uninterrupted services and huge patronage in the Private sector enhanced programme TB case finding efforts during the pandemic resulting in 15% increase in National TB notification. TB programme must expand to all private health facilities to find the missing TB cases.

EP-22-314 Pre- and post-Covid-19 lung function among patients successfully treated for drug-susceptible TB: a case series from the country of Georgia

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Background: As the COVID-19 pandemic continues, little is known regarding the impact of COVID-19 on lung health of TB survivors. We aimed to describe lung function before and after COVID-19 diagnosis among successfully treated TB patients in the country of Georgia.

Design/Methods: We used data from an ongoing prospective cohort that evaluates pulmonary impairment after TB treatment. For this case series, we included patients successfully treated for drug-susceptible pulmonary TB who tested positive for COVID-19 within 12-months of completing TB treatment. Participants were screened for COVID-19 during follow-up and had a positive result from a 1) COVID-19 antibody, 2) SARS-CoV-2 rapid antigen, or 3) nucleic acid amplification test. Pulmonary function (chest radiograph, spirometry, body plethysmography) was measured at the end of TB treatment and within 30-days after COVID-19 diagnosis.

Results: Of 68 post-TB patients enrolled and followed for >6 months, n=5 had a positive COVID-19 test during 40.4 person-years (incidence rate 1.24 per 10 person-years). All 5 study participants had mild COVID-19

symptoms (three had fever, two experienced loss of either smell or taste). Mean ratio of forced expiratory volume in 1 second and forced vital capacity (FEV1/FVC%) at the end of TB treatment was 77.0% (standard deviation [SD]=9.6) vs. 76.4% (SD=10.0) post-COVID-19 (mean difference=-0.58).

Body plethysmography was performed among 4 participants. Among these, one had reduced total lung capacity (TLC) (% predicted difference=-3%), and two had reduced diffusing lung capacity (DLCO) post-COVID-19 (% predicted difference was -1% and -10%, respectively).

We did not observe meaningful pathological changes when comparing chest radiographs from end of TB treatment vs. post-COVID-19.

Patients	Spirometry				Body Plethysmography					
	End of TB treatment	Post-treatment COVID-19	End of TB treatment	Post-treatment COVID-19	TLC % Predicted End of TB treatment	Post-treatment COVID-19	RV % Predicted End of TB treatment	Post-treatment COVID-19	DLCO % Predicted End of TB treatment	Post-treatment COVID-19
1*	5.86	6.19	4.30	4.40	96	96	80	80	65	65
2	3.17	3.41	2.92	3.15	77	81	61	58	61	60
3	4.97	5.19	3.77	3.94	100	122	75	133	63	71
4	3.30	3.22	2.54	2.49	100	124	87	153	67	67
5	3.62	3.64	2.40	2.39	88	85	105	94	55	45

*Patients with missing data were excluded from the mean calculation.

†Indicates reduced lung function measures after COVID-19 diagnosis.

*Patient only had spirometry test done.

Abbreviations:

DLCO: Diffusing capacity of the lungs for carbon monoxide

FEV1: Forced expiratory volume in 1 second

FVC: Forced vital capacity

RV: Residual Volume

TLC: Total Lung Capacity

Table 1. Lung function measures of formerly treated drug-sensitive TB patients who were later diagnosed with COVID-19 in Tbilisi, Georgia (2019 - 2021).

Conclusions: In our cohort of patients formerly treated for TB disease, we reported a 7% cumulative incidence of COVID-19. We did not observe meaningful changes in lung function or pathophysiology when comparing results from the end of TB treatment and post-COVID-19 diagnosis.

EP-22-315 Impact of Covid-19 on TB detection and case notification in Benin in 2020

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Background: Due to respiratory symptoms COVID-19 shares with tuberculosis (TB), restrictions measures and stigmatization, there is a risk that the current pandemic has a huge impact on TB control. The objective of this study was to assess the effect of COVID-19 on TB detection and cases notification in 2020 in Benin.

Design/Methods: Laboratory and clinical data reported quarterly by TB centres for 2020 across the country were reviewed and compared against 2019 data. Variations in the number of presumptive cases and TB cases notified were assessed for the year and by quarter, region, type of TB, sex, age group and HIV status.

Results: Overall, 28944 presumptive cases were tested for TB in 2020 versus 37148 in 2019 corresponding to a drop of 22.1%. The diminution only happened during Q2 and Q3 (40.4% and 45.9% respectively). This decrease was observed in all the regions with a maximum drop of 67% (Q2) and 72% (Q3) in Cotonou, the largest city in the country.

The number of TB cases notified dropped by 9% nationwide. This drop occurred during the last 3 quarters (17%, 16% and 6% respectively) and was similar for all TB types. It was higher in women than men (12.0% vs 6.5%) and differed slightly across age groups: 6 to 7% for those <24 years and above 45 years and 11.0% for 25-44 years. The number of coinfecting TB/HIV patients notified dropped by 17.3%.

Conclusions: The decrease of 22.1% of presumptive TB cases reflects barriers to access to TB diagnosis during the pandemic. In this context, a decreased by only 9% of TB cases notification might suggest that the more severe cases sought care despite the pandemic.

Nevertheless, the gap in patients notified might result in an increase of the morbi-mortality related to TB in the coming months.

EP-22-316 Adapting TB services during the Covid-19 pandemic in Papua New Guinea

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Background and challenges to implementation: Tuberculosis (TB) is one of the major public health issues in Papua New Guinea (PNG), with a high rate of morbidity and mortality. Médecins Sans Frontières (MSF) supports the National TB program in Gerehu, Port Moresby. The COVID-19 pandemic led the PNG government to declare two lockdowns in March-April and July-August 2020. We describe measures taken to minimize the impact on TB patients.

Intervention or response: Actions taken to minimize the impact of COVID-19 on TB patients included:

COVID-19 screening after triage for COVID symptoms for symptomatic patients attending TB clinic;
Spacing of drug-refill appointments;
Decentralization of drug dispensing;
Treatment support through phone calls including counselling sessions, reminders of refill appointments, monthly telephonic consultations for drug-resistant TB patients (DR TB) and as-needed for drug-susceptible TB patients (DS TB);
Reorganization of clinic activities including temporary reduction of health care staff; training of health staff on COVID-19 screening and infection control measures.

Results/Impact: We followed 414 DS TB and 68 DR TB in March-April and 429 DS TB and 69 DR TB patients in July-August. Refill appointments were respected and only 3 patients were lost to follow-up during the lockdown periods. For DR TB patients, adherence ranged between 92 and 95%.

A reduction in TB diagnosis was observed, compared to the same periods of 2019: 68% reduction in March-April (226 TB cases in 2020 vs 332 in 2019) and 79% reduction in July-August (256 TB cases in 2020 vs 322 in 2019).

Conclusions: The actions taken were effective in ensuring the continuity of care for TB patients affected by COVID-19 lockdown measures in Port Moresby. The results encourage expanding this patient-centered approach to providing care for TB patients. More work is needed to minimize the impact of COVID-19 on TB case finding.

EP-22-317 Impact of the Covid-19 epidemic on TB diagnosis and transmission in Taiwan

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Background: Pandemic COVID-19 could negatively impact tuberculosis (TB) control, but some suggested that physical distancing and facial masking interventions might limit *Mycobacterium tuberculosis* (*Mtb*) transmission and partially compensate for the adverse effects of COVID-19. We aimed to investigate the impact of COVID-19 on TB notification, diagnostic services and disease transmission in Taiwan where the incidence and mortality rate was among the lowest globally.

Design/Methods: TB Notification and contact tracing data were extracted from National Tuberculosis Management Information System. Interrupted time-series modelling method was used to estimate COVID-19-attributed deficit in TB notification. National health insurance outpatient visit and laboratory *Mtb* culture reports data were analysed to quantify change in health service utilization. Contact tracing data of TB patients were analysed as surrogate markers to determine impact of COVID-19 control measures on reducing TB transmission.

Results: After adjusting for the declining trend of TB notification, the COVID-19 epidemic was associated with 6.4% (95% CI 3.5-9.3%) additional decline of newly confirmed TB cases in 2020. There was a decrease in the number of general health care visits (9.1%) and *Mtb* cultures (14.0%) compared with the previous year. Among the close contacts of culture-positive TB patients, the prevalence of latent TB infection as measured by the interferon gamma release assay decreased from

15.3% in 2019 to 13.1% in 2020, causing a relative reduction of 14.4%, which was more prominent in non-household contacts (15.9%) and in those 5-24 years old (20.9%).

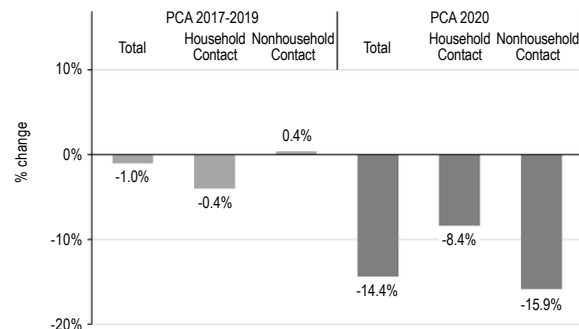


Figure 1. Proportion of positive IGRA tests among TB contacts, January - October 2017-2020. Percent change annualized (PCA).

Conclusions: While the COVID-19 epidemic was successfully contained in Taiwan, a deficit of TB notification was observed during the same period, along with reduced healthcare utilization and TB diagnosis. Despite these negative impacts of COVID-19, there was evidence of reduced TB transmission among close contacts of TB patients during the COVID-19 epidemic. Further analyses are needed to evaluate the overall impact of COVID-19 on TB control in this setting.

Stool testing and TB diagnostics in children

EP-25-339 TB-Molecular Bacteria Load Assay detects and quantifies viable *M. tuberculosis* in stool samples of presumptive pulmonary TB patients

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Background: Not all patients provide adequate sputum, yet available TB tests have low yields for alternative samples. We investigated utility of the tuberculosis-Molecular Bacteria Load Assay (TB-MBLA) to detect *Mycobacterium tuberculosis* (*Mtb*) in stool as a potential additional diagnostic test for pulmonary TB (PTB).

Design/Methods: Stools from one hundred presumptive PTB patients were treated with Mtb preservative (OM-Nigene.SPUTUM) and tested using Xpert MTB/RIF Ultra (Xpert Ultra), auramine-O smear microscopy, Mycobacteria Growth Indicator Tube (MGIT) culture and Lowenstein Jensen (LJ) culture. The remaining portions were stored at -20°C and tested by TB-MBLA. MGIT sputum culture was used as the confirmatory for TB diagnosis and a reference for other diagnostic tests.

Results: 61/100 participants were confirmed positive for TB by MGIT sputum culture, 20 (33%) of whom were HIV co-infected with median CD4 cells count 70.5 cells/ μ l. TB-MBLA detected Mtb in 57/100 of stool samples. In reference to sputum MGIT culture, sensitivity and specificity (95% CI) of stool assays were: 80% (68-89) and 80% (63-90); 90% (79-98) and 91% (76-98); 64% (32-58) and 62% (45-77); 44% (32-58) and 80% (64-91) for TB-MBLA, Xpert Ultra, MGIT and LJ culture respectively. 26% of the MGIT stool culture, and 21% of the LJ stool culture results were indeterminate due to contamination. 57% of the indeterminate culture results were determined TB positive by TB-MBLA. Mean bacterial load quantified by TB-MBLA was $5.1 \pm 1.59 \text{Log}_{10} \text{eCFU/mL}$ indicating high bacillary burden in stool.

Conclusions: TB-MBLA demonstrated high potential to accurately detect and quantify viable Mtb in stool. This raises the utility of stool as a non-sputum alternative for TB diagnosis.

EP-25-340 Stool Xpert MTB/RIF test for the diagnosis of childhood pulmonary TB in South West Nigeria

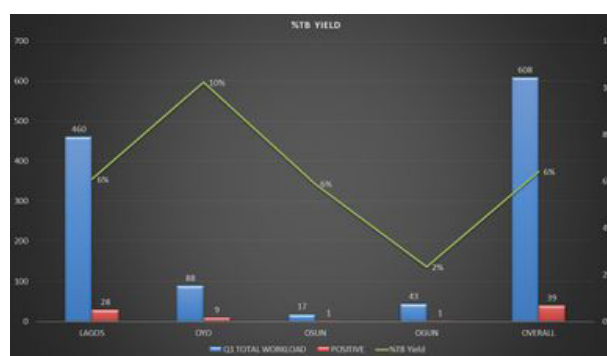
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Background: Despite being treatable, curable & preventable, TB is still associated with high morbidity and mortality in children. TB diagnosis in children is quite difficult due to challenges associated with sample collection procedure. As such, there is an urgent need for innovative solutions to find the “missing TB cases” among this vulnerable population. WHO has endorsed & recommended the use of Xpert MTB/RIF and Xpert Ultra to detect MTB DNA and Rif resistance using stool samples from children.

This initiative took off in the four USAID TB-LON 3 supported States in Q4 of 2020 and we hereby present the outcomes and lessons learnt in the implementation of this diagnostic method.

Design/Methods: This is a retrospective analysis of 608 stool samples collected from children less than 15 years old with presumptive TB and processed using standard microbiological procedures that involved the use of Xpert Ultra to detect MTB DNA and Rifampicin resistance in these samples.

Results: 608 stool samples were tested with Xpert Ultra between November 2020 to March 2021 out of which 39 (6.41%) were positive for MTB, 569 (93.58%) tested negative and 7 (1.15%) showed results has Rif resistant indeterminate. The TB yield ranged between 2.33% in Ogun State and 10.23% in Oyo State. These results are consistent with the TB yields of the States using sputum samples over the same time frame (11.08% in Ogun, 14.04% in Oyo, 10.83% in Osun, 9.54% in Lagos).



Conclusions: With 6.4% TB yield, stool Xpert test holds great promise as an alternative to sputum Xpert testing, since stool collection is easier and relatively safer compared to sputum collection in children. Also, sputum from children is often paucibacillary while sputum induction and gastric aspirate collection requires skillful Clinicians to obtain quality samples and is accompanied with discomfort, stress, pain in addition to high cost of the needed consumables.

EP-25-341 Reduced stool culture contamination with high *Mycobacterium tuberculosis* recovery: performance of the OMNIgene sputum-based stool processing method among presumptive TB patients in Uganda

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Background: We investigated performance of stool processed with a sample transport reagent OMNIgene SPUTUM (OM-S) to diagnose Pulmonary *Mycobacterium Tuberculosis* disease (PTB)

Design/Methods: Stool (2gms) and sputum (5mls) were collected from Ugandan TB presumptive adults. Stool was split into 2 equal fractions. One portion was homogenized in OM-S and the other in phosphate buffered saline (PBS) as the control. Sputum and stool were examined using concentrated smear microscopy (CFM), Xpert, Lowenstein Jensen (L-J) and mycobacteria growth indicator tube (MGIT) cultures. Sensitivity, specificity and predictive values of each test were calculated using sputum LJ and MGIT cultures as the reference. STATA 12 was used for Data analysis .

Results: We enrolled a total of 204 participants and of these 122 (60%) were Male, 75 (36.7%) HIV infected and 137 (67.2%) had sputum MGIT confirmed PTB. Compared to PBS, OM-S processed stool samples had lower culture contamination rates on MGIT (61.3% vs 25.3%, $P < 0.001$) and on L-J (49.7% vs 23.4% $P < 0.001$). Average time to positivity on MGIT culture was [12-days for stool vs 6-days sputum]. Using sputum L-J as reference sensitivity-specificity of OM-S processed stool were 92% (95% Confidence Interval (95%CI): 85–97) - 91% (95% CI: 81–97) for Xpert, 49% (95%CI: 39.5–58.70) - 97.4% (95%CI: 90.8–99.7) for CFM and 66% (95%CI: 55–76) - 98.4 (95%CI: 91.2–100) for L-J . Using sputum MGIT as reference, sensitivity-specificity of OM-S processed stool were 88.8% (95%CI: 81.2–94.1)-94.8% (95%CI: 85.6–98.9) for Xpert, 45% (95%CI: 36.1–54.3)-97.1% (95%CI: 89.8–99.6) for CFM and 76% (95%CI: 66.3–84.2) - 93.6% (95%CI: 82.5–98.7) for MGIT.

Conclusions: Stool treated with OMNIgene SPUTUM was associated low stool culture contamination and high MTB diagnostic yield on Xpert and culture tests. This protocol has potential to enhance PTB diagnosis using stool among populations with difficulty to produce sputum.

EP-25-342 Acceptability of nasopharyngeal aspirate and stool for TB diagnosis in children with severe pneumonia: parents' and healthcare workers' perspective

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Background: Innovative and simplified microbiological sample collection methods may contribute to improved TB diagnosis among young children with severe pneumonia. We assessed the acceptability of nasopharyngeal aspirate (NPA) and stool sample collection among parents and health care workers.

Design/Methods: In TB-Speed Pneumonia study, we conducted a cross-sectional qualitative study in 15 tertiary hospitals in Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Uganda and Zambia. Social sciences research assistants conducted semi-structured individual interviews with selected parents of children enrolled and all study nurses. Audio records were transcribed and translated in English when needed. Data was coded and analyzed based on the Theoretical Framework of Acceptability.

Results: Nineteen parents (median age 31 years, 16 female) and 12 nurses (median age 34 years, 7 female) were interviewed. Although NPA was perceived and experienced as a painful procedure, often requiring repeated aspiration, all participants reported positive attitudes as it aims to improve child health. Nurses reported that NPA and stool collection were quicker and less invasive than gastric aspirates. Parents trusted nurses' skills and novelty of NPA as a technique but did not always understand the diagnostic aim of NPA (often described as facilitating child breathing) and of stool samples. Parents and nurses easily engaged in stool collection, but were frustrated to depend on children passing stool. Nurses believed information and counselling increased parent cooperation during NPA – notably to restrain the child which nurses could not perform alone, and improved timely and adequate stool collection. Nurses suggested continuous training and mentoring to sustain their confidence and efficacy in obtaining adequate samples.

Conclusions: Parents and nurses having experienced NPA and stool sample collection reported positive attitudes, despite perceived pain with NPA and delays in stool collection. Main factors contributing to acceptability were valuing child health benefits, being informed and supported, and obtaining quicker results.

EP-25-343 Robustness of the Simple One-Step (SOS) stool processing method for Xpert MTB/RIF testing: preliminary results from Ethiopia

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Background: The Simple One-Step Stool (SOS) processing method was developed to process stool samples for Xpert testing using a protocol that is as simple as the standard sputum protocol. We assessed the SOS method's robustness as, for global roll-out, it should be applicable under diverse transportation, storage, and processing conditions.

Design/Methods: We enrolled children (≤ 10 years) and adults (≥ 15 years) diagnosed with tuberculosis by Xpert (Ultra) in 10 health facilities in Addis Ababa, Ethiopia. MTB was detected in the nasogastric aspirate or stool of children and in sputum and stool of adults. Three stool specimens were collected within 5 days of starting TB treatment from each participant. The following experiments were conducted: 1) sampling - assessing if MTB is universally mixed in the stool; 2) storage conditions; 3) optimum processing and incubation time; 4) maximum contact time between stool and sample reagent (SR); 5) amount of stool processed.

Results: Until March 2021, 5 children and 5 adults were enrolled. There was variation in MTB load within and between stool specimens from the same person. For patients with a maximum bacterial load of MTB detected, very low, Xpert failed to detect MTB at least one-third of the samples. The proportion of unsuccessful tests increased with sample storage temperature (up to 37°C), but not with sample storage time (up to 10 days). It also was higher when the stool/SR mixture was kept at room temperature (27%) vs in the fridge (8%). The proportion of unsuccessful tests increased from 0% at 0.3g of stool to above 30% at 1g and above.

Conclusions: The SOS stool processing method is robust at varying storage and processing conditions. Adding the right amount of stool is important, this should be 0.8g or less to minimize the risk of unsuccessful Xpert test results.

EP-25-344 Comprehensive molecular drug resistance profiles derived from stool-based targeted sequencing of *Mycobacterium tuberculosis*

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Background: Stool has emerged as an important diagnostic specimen for tuberculosis disease (TB). In populations in whom sputum collection is difficult, such as children or people living with HIV, testing for *Mycobacterium tuberculosis complex* (MTBC) in stool is particularly relevant. However, as culture of MTBC strains performs poorly, phenotypic drug resistance testing is currently limited from stool specimens.

Design/Methods: We evaluated the performance of a targeted next generation sequencing assay to detect mutations associated with resistance of MTBC strains to 15 drugs (Deeplex® Myc-TB). The assay was performed from stool specimens provided by participants with TB disease enrolled in a prospective cohort in Eswatini; this included specimens from 56 unique participants with, and 10 participants without MTBC DNA detected in stool by Real Time PCR.

Results: The Deeplex Myc-TB assay successfully detected MTBC DNA in 32 out of 56 (57%) of specimens that were positive by MTB PCR. Resistance prediction for up to 15 drugs was possible in 27 (84%) specimens. There was a concentration dependent relationship between the performance of Deeplex Myc-TB for resistance prediction, it was possible in 8/8 (100%), 17/28 (61%) and 2/18 (11%) of specimens with stool PCR cycle thresholds of under 20, 20 to 30 and greater than 30, respectively ($p < 0.0001$).

Conclusions: The Deeplex Myc-TB assay can detect MTBC and identify drug resistance via analysis of MTBC DNA isolated from stool provided by TB patients. This novel strategy affords the opportunity to obtain critical diagnostic information for TB patients who struggle to provide a respiratory specimen.

EP-25-345 Clinical usefulness of loop-mediated isothermal amplification of bronchoalveolar lavage fluid in children with active TB

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Background: At least one million children become ill with tuberculosis and around 200,000 children die each year. Rapid tests for children active tuberculosis are urgently needed because it is often associated with delayed health-care seeking, leading to serious consequences. Of which, loop-mediated isothermal amplification (LAMP) is a unique temperature-independent way of DNA amplification.

Because of its limited infrastructure requirements and relative ease of use, TB-LAMP is being explored as a rapid, point-of-care diagnostic test for resource-limited settings. This study evaluated the performance of the TB-LAMP in the rapid diagnosis of children active tuberculosis with bronchoalveolar lavage fluid (BALF) specimens.

Design/Methods: In all, 228 suspected patients aged 0–18 years were included from the Shenyang Tenth People's Hospital and Shenyang Chest Hospital, China, between 2019 and 2020. They were tested with TB-LAMP, smear, and MGIT 960 culture. The performance of the assays was evaluated against MGIT 960 culture and a composite reference standard (CRS).

Results: Among all participants, 119 (52.2%) had CRS-positive tuberculosis, of whom 32 (26.9%) were culture-confirmed. Against culture, TB-LAMP and smear achieved a sensitivity of 71.9% (95% CI: 53.0–85.6%) and 34.4% (95% CI: 19.2–53.2%), respectively. Against CRS, the sensitivity of TB-LAMP, smear and culture was 51.3% (95% CI: 42.0–60.5%), 13.4% (95% CI: 8.1–21.2%), and 26.9% (95% CI: 19.4–35.9%). The PPV and NPV of TB-LAMP the CRS data were 98.4% and 65.1%, respectively.

Conclusions: TB-LAMP had better performance than smear and culture in detecting children active tuberculosis from BALF samples and could be considered for the diagnosis of children active tuberculosis. It is a good rule-in test but has limited value as a rule-out test for the diagnosis of children active tuberculosis.

EP-25-346 Assessment of loop-mediated isothermal amplification for the diagnosis of childhood pulmonary TB

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Background: Most difficult task in childhood tuberculosis (TB) is the diagnosis, especially in the early and latent stages. Loop-Mediated Isothermal Amplification (LAMP) is a cheap, simple and rapid diagnostic modality that can be used for a highly sensitive and specific diagnosis of TB in respiratory samples.

Design/Methods: A cross-sectional study was conducted in a tertiary care centre from July 2014– June 2015 involving 60 children presenting with the symptoms suggestive of TB.

The study is a continuation of a previously published paper. In this study, we used latent class analysis (LCA) for determining the sensitivity and specificity of BACTECTTM MGIT 960 culture, PCR, and LAMP assay. The population was stratified based on age (≤ 5 years and > 5 years) and BACTECTTM MGIT 960 culture (positive and negative). The LCA analysis was performed within each of these stratifications, to give a clearer idea of the utility of the diagnostic test.

Results: In the whole population comparing the diagnostic test with each other, the sensitivity of LAMP was higher (83%) as compared to PCR (62%) and BACTECTTM MGIT 960 culture (49%). BACTECTTM MGIT 960 culture had the highest specificity (100%).

In using age as a stratifying factor, LAMP showed highest sensitivity in both the age groups of ≤ 5 years and > 5 years (81% and 100%), respectively. Specificity of BACTECTTM MGIT 960 culture and PCR was 100% in age group less than 5 years and greater than 5 years, respectively.

When BACTECTTM MGIT 960 culture was used as a stratifying factor, LAMP had 100% sensitivity 100% specificity. In our previously published paper also, LAMP had the highest sensitivity when compared to BACTECTTM MGIT 960 culture and PCR.

Conclusions: Our finding showed that LAMP had the highest sensitivity compared to BACTECTTM MGIT 960 culture and PCR and can be successfully employed in the diagnosis of paucibacillary pediatric PTB.

EP-25-347 Childhood TB case detection by culturing samples submitted for Xpert testing at the National TB Reference Laboratory Zimbabwe, January 2018–December 2020

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Background: The END-TB strategy has fallen short of its intended targets with significant attrition arguably in the pediatric population of developing countries. Approximately, 15–20% of all TB cases in sub-Saharan Africa are reported among children. The inability to expectorate sputum and lack of children friendly approaches for TB diagnostic results in only <10% of cases being diagnosed in the laboratory.

Despite the adoption of World Health Organization recommended rapid diagnostic technologies (WRD), Xpert® MTB/RIF Ultra assay by Zimbabwe for primary TB diagnosis from presumptive patients, reports show poor case detection rates among pediatrics. In this study, we set out to evaluate the utility of culture as a supplementary test in an attempt to increase pediatric tuberculosis case detection.

Design/Methods: A cross-sectional study was conducted on secondary data of samples collected from pediatrics and referred for routine analysis to the NTBRL between 01 January 2018 and 31 December 2020. Xpert® MTB/RIF /Ultra assay and liquid/solid culture were utilized with rapid kits being used for identification of Mycobacterium tuberculosis. Xpert® MTB/RIF Ultra assay and culture results were recorded, and imported into a Microsoft Excel spreadsheet. Data was analyzed using STATA v.12 and presented in the form of descriptive statistics.

Results: Out of the 1853 samples that were received at the laboratory, only 1773 were included in data analysis. Xpert® MTB/RIF Ultra assay and Culture were in agreement in 12 (0.68%) MTB positives and 1702 (96%) negatives. However, culture detected 15 (0.85%) MTB and 24 (1.35%) Mycobacterium other than Tuberculosis (MOTT) which had been missed by Xpert® MTB/RIF Ultra assay.

Conclusions: Culture increases detection of TB in children and also detects MOTT which is not detected by Xpert.

Consider culture for pediatric presumptive samples missed by Xpert.

Further studies to assess the clinical significance of MOTT in children presumed to have TB.

EP-25-348 Development and implementation of training on simplified chest X-ray interpretation for childhood TB diagnosis

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Background and challenges to implementation: Chest X-ray (CXR) plays an important role in the process of TB diagnosis in children. However, its beneficence is limited by the lack of clinician's skills to interpret CXRs in children in many resource-constrained settings where radiologists are scarce.

Intervention or response: As part of the implementation of the TB-Speed Decentralization study, we developed a simplified 1.5-day training course on CXR interpretation for health staff at peripheral level.

The course approved by a working group of international experts focuses on the detection of 6 key radiologic lesions suggestive of TB: *enlarged lymphadenopathy, alveolar opacity, airway compression, cavitation, pleural or pericardial effusion, miliary*. The trainings included national experts further involved in the CXR External Quality Assessment (EQA) at country level.

We performed pre and post training tests with scores based on accurate readings of 20 CXR and considered 15/20 as a cut off to be considered a reliable reader.

A randomized sample of normal CXR, all not readable and all TB suggestive CXR are re-read by national re-reader and reviewed by international experts.

Results/Impact: International trainers and national facilitators conducted 12 training sessions in 2020, in 6 countries (Cambodia, Cameroun, Cote d'Ivoire, Mozambique, Sierra Leone, Uganda) attended by 219 healthcare workers from district hospitals and primary health centers (34% doctors, 39% nurses, 13% X-ray technicians and 14% others).

Overall, 30% of participants, 45% of those with previous CXR reading experience and 45% of X-ray technicians reached more than 15/20 post-test score.

Staff with and without experience before the training reached about same score after training. CXR EQA reached 94% concordance in Cambodia and 100% concordance in Sierra Leone.

CXR course participants	N	Pre test score	Post test score	Proportion with pre to-post test increase	Proportion with scoring $\geq 15/20$
All 6 countries	219	7.5	12.6	68%	30% (55/186)
Experience in CXR reading in 3 countries Cambodia Cote Ivoire, Sierra Leone					
Previous experience	20	7.3	13.4	85%	45% (9/20)
None	60	7.9	12.8	62%	27% (16/60)
Health staff categories in 3 countries Cambodia, Cote Ivoire, Sierra Leone					
Medical doctors	28	7.82	12.3	69%	32% (9/28)
Nurses	32	7.97	13.2	66%	35% (11/32)
X-ray technicians	11	6.91	13.2	100%	45% (5/11)
Other	13	7.75	11.0	57%	17% (2/13)

Conclusions: A simplified 1.5 days training course on CXR interpretation based on 6 radiologic lesions suggestive of TB was successfully deployed to screen and diagnose childhood TB. EQA CXR is essential to monitor CXR interpretation skills.

TB drug resistance and the mycobacterium cell

EP-26-349 Determining viability of sputum for *Mycobacterium tuberculosis* culture after long-term storage at -80°C

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Background: Currently there are limited published data on long-term storage (>6 months) of sputum samples and subsequent recovery of *Mtb* by culture. Long term sample storage for later *Mtb* culture may be useful where samples need to be collected, batched, and shipped and where there is a need to compare strains collected before TB treatment to strains collected from TB recurrence episodes to differentiate between relapse and reinfection, for example TB vaccination prevention of recurrence studies.

Design/Methods: Sputum samples were obtained from 76 adult participants with confirmed pulmonary TB disease prior to onset of treatment and again after at least 1 dose (and before the fifth dose) of anti-TB treatment. All samples were cultured using MGIT. Untreated and

un-decontaminated sputum samples were frozen and stored at -80°C for 10 and 20 months and then thawed, decontaminated and cultured.

Results: Recovery of *Mtb* from sputum obtained prior to onset of treatment and after long-term storage (10 and 20 months) were statistically non-inferior to the yield of *Mtb* from fresh, never-frozen sputum samples. Culture results of frozen samples obtained after treatment initiation did not achieve statistical non-inferiority when compared to results obtained from fresh, never-frozen sputum, however we recovered *Mtb* by culture in $\geq 85\%$ of samples following 10 and 20 months of storage. There was evidence that time to culture positivity was prolonged in samples collected after treatment initiation.

	Fresh Pre-Tx	Fresh Post-Tx	10-mo storage (Pre-Tx)	10-mo storage (Post-Tx)	20-mo storage (Pre-Tx)	20-mo storage (Post-Tx)
N*	66	67	65	68	65	68
Positive culture, n (%)	64 (97)	65 (97)	60 (92)	58 (85)	61 (94)	59 (87)

* Number of evaluable samples

Conclusions: This study supports freezing pre- and post-treatment (within 5 days of treatment onset) sputum samples for culture for up to 20 months after collection.

EP-26-350 In vitro antimycobacterial activity of new synthetic (+) camphor derivatives

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Background: Drug resistant *Mycobacterium tuberculosis* strains continue to emerge and present a global threat. A search for new anti-TB compounds is required. Here, we performed synthesis of new compounds and tested their efficiency on *Mycobacterium tuberculosis* reference strain.

Design/Methods: Two series of new (+)-camphor derivatives were synthesized (Figure). These were compounds with aryl substituent at position 3 of the camphane skeleton (1) and with aryl-substituted 2-aminopyrimidine moiety, fused to the camphane scaffold (2). The EUCAST recommended broth microdilution reference method was used for minimal inhibitory concentration (MIC) determination of the compounds on the reference strain H₃₇Rv.

Results: The first stage of our synthetic strategy was based on transformation of easily accessible commercial (+)-camphor to series of corresponding conjugated ketones 1, by using of different aromatic aldehydes. In a second stage, most of the ketones 1 were converted to the corresponding new 2-aminopyrimidines 2 by condensation with excess of guanidine hydrochloride in basic conditions. All compounds were obtained in good to excellent yields and pure form after column chromatography. They were characterized by using of 1D/2D NMR, MS, melting points and elemental analysis. A total of 23 compounds were synthesized and were evaluated *in vitro* toward reference laboratory strain *Mycobacterium tuberculosis* H₃₇Rv. While their MIC values ranged from 0.39 to 50 μM, two the most active compounds showed MIC values of 0.39 μM.

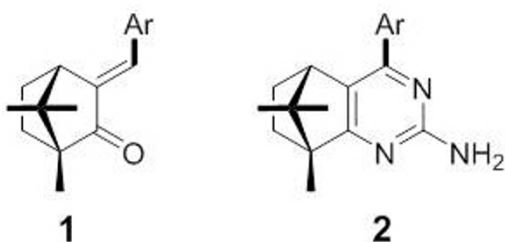


Figure. New synthetic (+)-camphor derivatives.

Conclusions: The synthetic (+)-camphor derivatives appear to be a promising approach for design of new chemical compounds with anti-tuberculosis activity. Acknowledgements: Russian Science Foundation (grant 19-15-00028) and National Science Fund of Bulgaria (grant KP-06-H39/7).

EP-26-351 Heat or guanidine thiocyanate inactivates *M. tuberculosis* while preserving adequate RNA for downstream molecular testing

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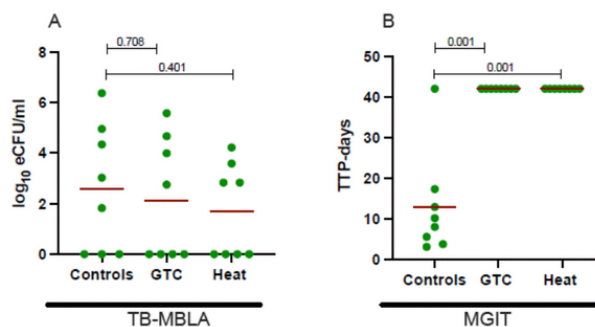
Background: *Mycobacterium tuberculosis* (Mtb) is classified by United nations as category B infectious pathogen which requires category 3 containment laboratories to handle.

Objective: To assess the efficacy of heat- and Guanidine thiocyanate- (GTC) to inactivate Mtb and render TB positive samples safe for tuberculosis Molecular Bacterial Load Assay (TB-MBLA) in a non-containment laboratory.

Design/Methods: We performed *in vitro* experiments using 0.5 McFarland equivalent to 1.50x10⁸ CFU/mL concentration of *M. tuberculosis* (H37Rv) strain and

serially diluted in Middlebrook 7H9 media to 10¹ CFU/mL. Three replicates containing 1 mL of each dilution were inactivated by boiling at 80°C for 20 minutes and/or treatment with equal volume of GTC for 15 minutes at room temperature. A fraction of inactivated cultures for each dilution was propagated in Mycobacterium Growth Indicator Tube (MGIT) to test for any growth and bacterial load (BL) quantification using TB-MBLA. Non-treated (live) cultures were used as controls for both MGIT and TB-MBLA.

Results: No growth was observed in MGIT culture for both heat and GTC treated samples. In contrast, controls grew Mtb with an average (±SD) time to positivity (TTP) of 3.01±0.61 days for neat culture which increased to 17±2.14 days in subsequent dilutions. A corresponding TB-MBLA-measured BL was 6.36±0.33log₁₀ eCFU/mL in neat controls. This reduced to 4.25±0.05 log₁₀ eCFU/mL and 5.5±0.03log₁₀ eCFU/mL in heat and GTC inactivated cultures, respectively. The overall bacillary load reduction of 1.5log₁₀ and 0.4log₁₀ by heat and GTC treatment respectively was not significant (p=0.401) and (p=0.708). Using Bowness TTP to CFU conversion formula, the neat culture TTP translated to 6.67log₁₀ CFU/mL which was consistent to TB-MBLA-measured neat BL of 6.36log₁₀ eCFU/mL.



Conclusions: Heat or GTC efficaciously inactivate Mtb and could obviate the need category 3 containment laboratories, increasing the potential of performing TB-MBLA at microscopy laboratory level in routine health-care settings.

EP-26-352 Intercellular mosaic methylation: the 24-hour path to new phenotypes in *M. tuberculosis*

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Background: Epigenetics, in particular DNA methylation has been observed to cause phenotypic change in many species including bacteria. This study investigated whether changes in DNA methylation patterns in *M. tuberculosis* can engender phenotypic consequences undetected by current molecular diagnostics. Furthermore, this study identified the sites and frequency of clinically relevant methylomic changes in *M. tuberculosis* genome. **Design/Methods:** This study combined fully-annotated, finished, *de novo* assembled genomes, DNA adenine methylomes, and RNA expression of 93 *Mycobacterium tuberculosis* complex (MTBC) isolates from seven lineages to identify methylomic changes associated with changes in gene expression and phenotype.

Results: Integrative analysis yielded four key results. First, methyltransferase allele-methylome mapping corrected methyltransferase variant effects previously obscured by reference-based variant calling. Second, heterogeneity analysis of partially active methyltransferase alleles revealed that intracellular stochastic methylation generates a mosaic of methylomes within isogenic cultures, which we formalize as 'Intercellular Mosaic Methylation' (IMM). Mutation-driven IMM was nearly ubiquitous in the globally prominent Beijing sublineage. Third, promoter methylation is widespread and associated with differential expression in the *hdsM* transcriptome, suggesting promoter HsdM-methylation directly influences transcription. Finally, comparative and functional analyses identified 351 sites hypervariable across isolates and numerous putative regulatory interactions.

Conclusions: This multi-omic integration revealed features of methylomic variability in clinical isolates. Importantly, this study uncovered a novel mechanism coined *Intercellular Mosaic Methylation* (IMM). IMM presents *M. tuberculosis* with the mechanism for rapid diversification and creation of clinically-relevant subpopulations within an isogenic population. Finally, this study provides a rational basis for hypothesizing the functions of DNA adenine methylation in MTBC physiology and adaptive evolution.

EP-26-354 In vitro synergism of combinations of anti-TB agents against drug-resistant *M. tuberculosis* isolates

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Background: Retreatment tuberculosis (TB) has become a major source of drug-resistant TB. In our previous study, pasiniazid (PAS), rifabutin (RFB) or rifapentine (RFP) and moxifloxacin (MXF) showed better activity *in vitro* against drug-resistant *Mycobacterium tuberculosis* (MTB) than isoniazid (INH) and rifampin (RFP). However, potential synergistic effects of different combinations of PAS, RFB or RFP and MXF has not been investigated.

Design/Methods: In the current study, we used the checkerboard method to evaluate the *in vitro* synergy of these anti-tuberculous agents against 90 drug-resistant strains isolated from retreatment TB patients, including 54 extensively drug resistant strains (XDR-TB), 29 multidrug resistant strains (MDR-TB), and 7 INH mono-resistant strains, through calculating the fractional inhibitory concentration index (FICI) of joint action *in vitro* to judge the combined effect. with fractional inhibitory concentration index (FICI) ≤ 0.5 and FICI ≤ 0.75 as the basis of 2 drugs and 3 drugs showing synergy.

Results:

1. The synergetic activity of PAS+RFB and PAS+RFP were higher than that of INH+RIF and MXF+PAS ($P < 0.05$), and the synergetic activity of PAS+RFP was higher than that of PAS+RFB ($P < 0.05$), although MIC₉₀ of RFP was much higher than RFB.
2. After both combinations were mixed with MXF, the MXF+PAS+RFP combination and the MXF+PAS+RFB combination had similar synergistic effects but the MXF+PAS+RFP combination had lower FICI value.
3. Further stratification analysis showed that even in XDR-MTB, the synergistic effect of PAS+RFP was also better than that of INH+RIF, PAS+RFB and MXF+PAS ($P < 0.05$), and MXF+PAS+RFP combination was similar to MXF+PAS+RFB.

Conclusions: This study verified that regimen containing MXF+PAS+RFP can be recommended for the treatment of drug-resistant MTB.

EP-26-355 Efficacy of treatment of extensively drug-resistant pulmonary TB

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Background: An experimental clinical research was performed to improve the treatment of pulmonary extensively drug-resistant tuberculosis (XDR-TB). The treatment regimen was enhanced by a combination - bedaquiline (Bq) and thiouredoiminomethylpyridine perchlorate (Tpp).

Design/Methods: Two series of experiments were performed. Mice (n = 50 and 53) were infected with 2 strains of XDR Beijing MBT with various combinations of gen mutations (C57BL/6). The effectiveness of the treatment was assessed by the index of pulmonary lesion and by colony-forming units count of MBT in lung tissue. It was shown that the four-month course of complex therapy with the use of Bq and Tpp in both series of experiments significantly increased pulmonary MBT clearance, as well as ITPL - 1.4 times (p <0.001) and 1.3 times (p <0.02). Of 69 enrolled patients with pulmonary XDR-TB, 46% (the main group (MG, n=32) received the combination of Tpp and Bq along with a background regimen of anti-TB drugs according to the culture-based drug susceptibility test. The control group (CG) included 37 patients, who received the same therapy without Tpp and Bq. Patients of both groups were comparable in clinical, radiological and laboratory parameters. XDR was identified among all patients and confirmed by the culture-based drug susceptibility test (BACTEC MGIT-960 system).

Results: By the second month of the treatment the therapy proved to be significantly more effective (sputum culture conversion) in the MG than in the CG 25 (78.1%), versus 29.7%, respectively, p<0.05). By the fourth month of chemotherapy - 96.8% and 48.6% (p<0.05) respectively. The same tendency could be observed by the sixth month of therapy.

Conclusions: Overall, the combined use of Tpp and Bq in the therapy of patients with pulmonary XDR-TB significantly increased the effectiveness of the treatment in comparison to the CG in whose therapy no Tpp and Bq were incorporated.

EP-26-356 Pyrazinamide resistance among rifampicin-discordant *Mycobacterium tuberculosis* strains

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Background: Rifampicin resistance is known to be associated with resistance to other rifamycins (rifapentine and rifabutin) as well as isoniazid and pyrazinamide. However, the recently discovered *Mycobacterium tuberculosis* strains with phenotypically susceptible *rpoB* mutations (rifampicin discordant strains) have shown high rates of susceptibility to isoniazid and rifabutin than phenotypically rifampicin resistant strains. On the other hand, pyrazinamide susceptibility testing results have not been reported among these strains.

Therefore, the aim of this study was to determine the prevalence of pyrazinamide resistance among rifampicin discordant *Mycobacterium tuberculosis* strains

Design/Methods: Stored *Mycobacterium tuberculosis* strains that showed *rpoB* mutations on the GenoType MTBDRplus while susceptible on the 1% agar proportion method were tested for pyrazinamide resistance by sequencing of the *pncA* gene.

In addition, 25 known rifampicin and isoniazid susceptible strains were tested using the same method.

Results: Out of 75 discordant strains tested, 9 (12%) harboured mutations in the *pncA* gene. Among these nine strains, seven different mutations were found that were widely distributed along the *pncA* gene. No *pncA* gene mutation was found among the 25 known rifampicin and INH susceptible TB strains.

Conclusions: Pyrazinamide resistance was relatively low among rifampicin discordant MTB strains. Therefore, this anti-TB drug still has a significant role in the treatment of these strains.

EP-26-357 Detecting gene mutations related to bedaquiline, delamanid and linezolid resistance in multidrug-resistant *Mycobacterium tuberculosis* isolates in Myanmar

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Background: In Myanmar, treatment of multidrug resistant tuberculosis (MDR-TB) is in the transition stage from injection based to fully oral regimens but the

primary resistant status of new and repurposed drugs like bedaquiline, delamanid and linezolid are yet to be known. Whole Genome Sequencing (WGS) allows simultaneous identification of all known resistance mutations and provides a rapid information for resistance status of new anti-TB drugs when there is no standard phenotypic drug susceptibility test for those drugs.

Design/Methods: This study was aimed to analyze the whole genome sequences of phenotypically identified MDR, pre-XDR, and XDR-TB isolates from Myanmar collected during 2015 - 2016. Twenty-three genomic DNAs from seven MDR, nine pre-XDR and seven XDR-TB were subjected to WGS on Illumina MiSeq Next Generation Sequencer. PhyResSE analysis software was used for strain classification, anti-TB susceptibility and variant calling. In addition to anti-TB-resistant result listed by PhyResSE, the genes responsible for anti-TB susceptibility were analyzed for mutations in interested new and repurposed anti-TB drugs targets and efflux pump genes.

Results: Reported and non-reported mutations in bedaquiline, delamanid and linezolid target genes and efflux pump genes were detected in four MDR, one pre-XDR and five XDR-TB. Non-target-based mutations in *Rv0678* and *Rv1979c*, genes which are related to bedaquiline resistance, were Arg96Trp, Asn98Asp, Ala99Val, Leu117Pro, Insertion G at nucleotide 138-139 and Val426Ile, Ser18Arg respectively. Among delamanid and linezolid target genes, the mutations in *FbiA* (Thr302Met) and *rplC* (Gly122Arg) were detected. Apart from one Euro-American, the rest were Beijing genotype.

Conclusions: The presence of primary drug resistance mutations for new anti-TB drug(s) is a challenge to the management of MDR and XDR-TB. The in-vivo response of those drugs on the mutated strain, when combined to other drugs, should be investigated.

EP-26-358 Genotypic drug susceptibility profiles of non-tuberculous mycobacteria species circulating among patients diagnosed with pulmonary TB in Tanzania

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Background: While most NTMs are saprophytic, a number of species have been associated with human diseases, from localized infection to disseminated diseases. Pulmonary NTM infectious lead to TB-like disease called NTM pulmonary disease (NTM-PD). Due

to variation in treatment options among NTM species, it is necessary to identify the species and determine drug susceptibility profiles to inform choice of appropriate regimen for the disease.

Design/Methods: A total of 188 culture-positive isolates from patients diagnosed with TB were screened for NTM at the Central Tuberculosis Reference Laboratory. All NTM were further speciated using GenoType® Mycobacterium - Common Mycobacterium and Additional species (GenoType® CM/AS) kit. *Mycobacteria avium* complex (MAC) and *Mycobacteria abscessus* complex (MABC) which could not be identified with the test to species were subjected to GenoType® Mycobacteria NTM-DR for further speciation. Using the same test, identified MAC and MABC were genotyped to determine drug susceptibility profile for each isolate to macrolide and aminoglycosides.

Results: Of all samples that tested positive to mycobacteria, 24 (13%) were positive for NTM. Fifteen isolates could be identified to species level of which prevalent species was *M. avium* sub. *intracellulare* 4 (27%). A total of 10 isolates were MAC (6) and MABC (4), these were subjected to GenoType® Mycobacteria NTM-DR for determination of macrolide and aminoglycoside susceptibility. Three of the four MABC had a mutation at the T28 position of the *erm* (41). All MAC were susceptible to both drugs.

Mycobacterium NTM-DR assay									
MAC/MABC Species	Gene						Macrolides	Aminoglycosides	Frequency
	<i>erm</i> (41)		<i>rrl</i>		<i>rrs</i>				
	C28	T28	WT	MUT	WT	MUT			
Intracellulaire	NA	NA	+	-	+	-	S	S	4
Abscessus	-	+	+	-	+	-	R	S	2
Abscessus	+	-	+	-	+	-	S	S	1
Bollettii	-	+	+	-	+	-	R	S	1
Avium	NA	NA	+	-	+	-	S	S	2

WT – Wild type, MUT – Mutation, S – Susceptible, R – Resistant and NA – Not applicable

Table. Summary of wild type bands and associated mutations in the GenoType®

Conclusions: In this study, MAC species were the most frequent isolated NTM species followed by MABS. While all of MAC and MABC identified, were susceptible to aminoglycosides, three MABC were resistant to the macrolides due to mutation at position 28 of the *erm* (41) gene. For this, it is important for clinicians need to rule out NTM, understand species and their drug susceptibility for optimal case management.

Implementation of tobacco control policies

EP-39-480 Compliance of collaborative tobacco control actions with MPOWER measures in Rajasthan, India

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Background and challenges to implementation: To analyze the impact of collaborative approach of Government and NGO in effective implementation of tobacco control laws and find out the impact of project entitled as “Advancing comprehensive tobacco control to make Rajasthan a MPOWER compliance model State” in 16 districts of a state.

Intervention or response: The study has been conducted in 16 districts (Banswara, Baran, Bundi, Churu, Dausa, Dungarpur, Hanumangarh, Jhalawar, Jhunjhunu, Pratapgarh, Rajasmand, Sawai Madhopur, Sirohi, Sikar, Sri Ganganagar and Tonk) by capturing the compliance status through Field Survey Questionnaire (FSQ) designed with the objective:

-To measure the level of compliance to Section 4, 5, 6 a&b and 7 of COTPA¹

A District-wise Consolidated Summary of the Field Survey Outcomes on the basis of the field survey briefs about the district wise compliance of MPOWER measures through implementation of tobacco control laws.

1. COTPA- Tobacco control law in India called Cigarette and Other Tobacco Products Act.

Results/Impact: High level of awareness on the part of the Society was observed. This was evident from the fact that in 85% instances no cigarette or bidi¹ butts were found near the Vendor points or in public places and the people were also not found to be largely smoking in public places. In 89% instances the smoking aids i.e ash-tray; match-box etc. were also non-visible. Around 90% of the Academic Institutions were found to be compliant to the Display of Signage conditions as stated in 6(b) while minor correctible defect. Further in majority cases no in-campus Sale of Tabaco product was found to be taking place.

Conclusions: The compliance level in respect of the provisions forming scope of this project was found to be well under control with outcomes around 90% in majority areas. Regular compliance reviews are recommended ensuring sustainability of the good efforts made so far in this direction.

EP-39-481 Standard packaging a tool to ensure effective use of graphic health warnings for smokeless tobacco and bidis in Bangladesh

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Background: In Bangladesh *Cigarette & Bidi use as smoking tobacco and Zordha, Gul & sada pata or ala pata* (Raw tobacco leaf) are used as smokeless tobacco. Overall 37.8 million adults currently used tobacco among these 27.3 million smokeless tobacco and *bidi* user (GATS-2017). Graphic Health Warnings (GHW) is one of the proven methods of MPOWER package and the country has been implemented from 19 March 2016 but still now the implementation on *Bidi* and smokeless tobacco are not satisfactory.

Design/Methods: Cross-sectional study design, qualitative and quantitative techniques, purposive sampling methods and all types of tobacco products (as per availability) was analyzed for monitoring the implementation. Graphic Health Warnings Monitoring software has been developed by using Open Data Kit (ODK) tools and a check list was developed on the basis of section 10 of tobacco control law for measuring the compliance.

Results: The team identified 265 big market areas and 583 wholesale shops that covered full distribution channel of SLT. Total 10,641 packets have been collected from all 64 districts and a sub-district from each district. The research identify that he implementation of GHWs on smokeless tobacco and *bidi* has increased but not satisfactory because of un-regulated market structure & different shapes, size and structures of the Packets. Beside this Tobacco Industry using attractive clour, Mosque theme design, Halal, Arabic Letter, Indian packets design with hindi letter, religious brand name, logo and colour (Muslim and Hindu) for draw customer attention.

Conclusions: For overcoming this barrier, the team analyzed 10,641 packets to find out and recommended a suitable and affordable pack size called standard packaging. Later on the team identified the two sizes of packets for *Jordha* and *Gul* and another size for *Bidi* which are already exist in the current market and submitted to the government through health ministry.

EP-39-482 Effectiveness of the nationwide ban on ENDS in India: a study from Eastern India

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Background: Electronic cigarettes (e-cigarettes), both containing nicotine and non-nicotine devices, are banned in India by the Ministry of Health & Family Welfare in September in 2019, under the “The Prohibition of Electronic Cigarettes Act, 2019”.

One year after the ban, we initiated a study to assess the compliance of ban on sale of electronic cigarettes and other nicotine delivery systems (ENDS) in different socio-economic status (SES) zones of Kolkata, West Bengal.

Design/Methods: In this cross-sectional study, a total of 55 e-cigarette retailer points of sale (POS) from Kolkata city were included during July to August 2020, following SES mapping and online search (Google). ENDS selling POS were located at market places as well as at residential areas. A study tool of 8 observational items and 2 interview questions was used for data collection.

Descriptive analysis, i.e., distribution (%) of POS w.r.t general characteristics, availability of type of ENDS products, and compliance status of various sections of the Act was reported.

Results: ENDS and its accessories were widely available across Kolkata, with products being visible to the customers in approximately half of the POSs. Reporting of the ENDS stock to the enforcement agencies was not done by most (76%) of the vendors.

Conclusions: ENDS and its accessories were widely available across all SES zones of Kolkata city, with most of the POS violating the ENDS ban. Stricter and more intensive monitoring and enforcement of the legislation is needed to eliminate ENDS trade.

EP-39-483 How compliant are handmade cigarillo (bidi) brands in terms of pictorial health warnings? A case study from Eastern India

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Background: Bidis are most smoked tobacco product in India, roughly 7 to 10 bidis are smoked for every cigarette. We surveyed locally available bidi brands from seven municipal corporations of West Bengal and assessed the compliance to pictorial health warning (PHW) notified under COTPA Amendment rules 2018 and other.

Design/Methods: This cross-sectional study was conducted in November 2019 to January 2020 covering all seven municipal corporations of West Bengal state, namely Kolkata, Siliguri, Asansol, Durgapur, Bidhanagar, Howrah and Chandannagar. One vendor with maximum tobacco product was approached in all five areas in each municipal corporation, i.e., religious structures (temples, mosques, and churches), educational institutions (primary and secondary schools, universities, colleges, and madrasahs), market areas, areas near Government Offices, and Low SES region. A questionnaire on PHW parameters and brand details was filled by trained researchers after collection of bidi packs. Descriptive statistical analysis was done to compute percentages.

Results: We collected 133 bidi packs from all seven municipal corporations. Of 133 bidi packs, only 64% had registration number mentioned on the pack. More than 75% bidi brands were in kiddie packs (less than 20 sticks in a pack), highest being in Kolkata. None of the bidi packs followed 85% PHW coverage, or coverage of 60+25, or both sides display of PHW. Majority (61%) of the bidi packs had below 40% PHW and only few bidi packs (7%) had quit line number. Promotional tag line was present in majority (61%) of the bidi packs with around two third of bidi packs with picture of an adult (66%) followed by child's picture (22.5%).

Conclusions: Given the high prevalence of bidi smoking, non-compliance to pack warning rules is a big concern in combating tobacco use. Strict enforcement is required for proper implementation of the COTPA rules in the state with complete restriction on bidi kiddie packs.

EP-39-484 Top-down approach resulted in effective implementation of vendor licensing for tobacco products in the state of Madhya Pradesh, India

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Background and challenges to implementation: Tobacco products can be purchased by anyone without any check. Children, youths and females are the main target of the industry. Due to easy availability of tobacco products they are easily accessible by children & youth. Vendor licensing mandates tobacco shopkeepers to obtain licenses to sell tobacco products and follow Indian Tobacco Control Act and other laws.

Intervention or response: Top down approach was followed. The senior officials at policy making level were sensitized. Commissioner Urban Administration was oriented and briefed about the importance of vendor licensing in the state. Continuous media advocacy on the need for vendor licensing was done. Orientation of officials of Municipal Corporation done on Indian

Tobacco Control Act (COTPA) and vendor licensing, COTPA compliance included in the Smart City meeting minutes. Officers have also been nominated as nodal officer for tobacco control in the municipal corporations. Commissioner of Gwalior, Bhopal, Indore, Ujjain and Chambal division briefed.

Results/Impact: Directives from the Ministry of Urban Administration issued to have vendor licensing for tobacco shops, further commissioner Urban Administration issued letters to all Commissioner Municipal Corporation and Chief Municipal Officers of the state for Vendor Licensing. Directives included inclusion of COTPA compliance in all licenses issued to tobacco vendors, tobacco shop owners are allowed to sale only tobacco and sale of other products disallowed. Mayor In Council of capital city Bhopal has took unanimous decision and Vendor Licensing approved. Further conditions were uploaded on licensing website of urban administration department.

Conclusions: To bring changes in the old traditional practices, top level advocacy was required in implementation of Vendor Licensing. Licensing helps government to generate revenue and also regularize COTPA act in urban local bodies. Challenge is to implement it in whole state. Children /youths and females protected. Easy accessibility of tobacco products reduced.

EP-39-485 A “bottom-up approach” in devising national and sub-national policy framework in compliance with WHO FCTC Article 5.3 in India

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Background: India became a Party to WHO Framework Convention on Tobacco Control (WHO-FCTC) in the year 2004. FCTC Article 5.3 calls Parties in setting and implementing tobacco control policy they should protect these policies from commercial and other vested interests of the tobacco industry. This study aimed to assess the implementation of Article 5.3 policy in India.

Design/Methods: A detailed policy analysis of 31 sub-national Article 5.3 policy and related documents (circulars/notifications/orders/letters) from 14 Indian states was carried out.

Results: In the absence of national level policy, a sub-national approach has been carried out in India-wherein 12 states and 18 districts have adopted and implemented Article 5.3 policies. Out of 31 documents, while 9 mention about the constitution of empowered/special com-

mittee, 8 of them have a protocol for the respective committee to implement the policy in the respective state/district and only 2 discuss the process of sending a notice to the visitor. The code of conduct for employees/public servants is mentioned in 8 of the subnational documents, released in and before the year 2019. Additionally, India also has a Code of Conduct (2020) that applies to all the officials of Ministry of Health and Family Welfare, its departments and all the autonomous institutions and offices under its jurisdiction and to any person acting on their behalf.

Conclusions: India has made significant progress in relation to WHO-FCTC Article 5.3 policy. However, there is an urgent need for development and adoption of a whole of government national policy applicable to all departments of the local and national governments. Other states in India and other Parties to the FCTC can use this “bottom-up approach” as learning from India, as they embark upon similar efforts.

EP-39-486 Declaration of a ban on hookah bars amidst the Covid pandemic: a case study from Chandigarh, North India

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Background and challenges to implementation: Hookah smoking is an old social activity. It has emerged as a new craze among teenagers/youth leading to mushrooming of Hookah Bars all over India. These hookah bars serve tobacco molasses laced with Nicotine, which is a highly addictive agent. Carbon Monoxide produced by even so-called flavored hookahs is also detrimental to health. The Cigarettes and Other Tobacco Products Act, 2003 (COTPA) prohibit smoking in public places and ban tobacco advertisement, promotion, and sponsorship, sale of tobacco products to minors and there are other legal provisions being violated, including Poison Act 1919 & Drugs and Cosmetics Act 1940, etc. There were media reports about Hookah bars running in Chandigarh, a city with a population of around 1.2 million.

Intervention or response: Strategic Institute for Public Health Education and Research (SIPHER), an advocacy focussed organization conducted a survey of restaurants serving hookahs. Letters were written and meetings held with Deputy Commissioner, Director Health Services, Secretary Health, and Administrator Chandigarh. Earned Media stories were also published in diverse local newspapers. In addition, a cross-sectional survey was conducted between April 2020 to September 2020 in various sectors in Chandigarh.

Results/Impact: 15 restaurants were found serving hookahs, violating various provisions in the law. The administration was informed about the illegal activity.

The administration banned the Hookah Bars on 12th October 2020. The owners of about 10 hookah bars were booked for a violation under Section-144 of Indian Penal Code (IPC), Disaster Management Act 2005, and Epidemic Diseases Act 1897, and their operations were subsequently closed.

Conclusions: Hookah bars violate COTPA and other Indian laws. To curb the menace of hookah bars strict implementation of the ban is required. Inspection by concerned authorities should be done on regular basis in order to prevent illegal activities by hookah bars. Such efforts will also supplement the check on the COVID pandemic.

EP-39-487 Public opinions on the prohibition of smoking in public places in Odisha, India

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Background: Tobacco-use is the foremost preventable cause of death and disease worldwide. If such trends continue, by 2030 it will kill more than 8 million people worldwide each year. In India, around 926,000 deaths every year are ascribed to smoking and exposure to second-hand smoke. Current prevalence of smoking tobacco in Odisha is 7%.

Design/Methods: **Study objectives:** To ascertain public understanding on smoke-free-legislation and to assess perceptions and behaviour of public regarding smoking and its health effects.

Study questions: How do people opinion on smoke-free-legislation, smoking at public places and its health effects? Do such understanding has impact on their smoking habit?

Methods: A cross-sectional study was conducted to take opinions (N-985) from five districts of Odisha through semi-structured questionnaire. Data collected through Epicollect 5, entered in excel sheet and analyzed.

Results: Current smokers viewed smoking gives pleasure - 332-89.7%, cost economic burden - 185-50%, harmful for health - 268-72.4%, second-hand-smoking is equally dangerous - 182-49.2% and smoking is a part of culture-308.1%.

Current smokers were aware on law (COTPA) on smocking in public places -245-66.2%, smoking in public places should be banned -322-87%, seen anybody charged fine for smoking in public -160-43.2%, agreed-“No Smoking” signage in public helped in creating smoke-free-environment -284-76.8%.

Overall 43.8% people were ever smoked. Out-of-those, 85% were current smokers, and among them 55.7% wished to quit smoking and 45% had prior attempts to quit. Most of them had a history of smoking for more

than 10 years-41% than compared to smoking for last 5-10 years-19% and smoking since past 1-5 years-30% and smoking since past 1 year-7.7%. It shows, no significant level of reduction of new-smokers over the years.

Conclusions: Many people had improved knowledge on tobacco control and its implications, but still people indulged in smoking. Hence, not necessarily, adequate knowledge would results to positive perception; so, change in health seeking behaviour is essential for such public health important issue.

EP-39-488 Efforts to stop a virtual cultural event sponsored by the tobacco industry

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Background and challenges to implementation: During COVID Pandemic period and in the Kerala State local festival time, i.e. Onam Indian Tobacco Company sponsored a cultural event organised by Red FM, a famous FM media. The promotional advertisement was noticed in social media with logo of Tobacco Company. Kerala Voluntary Health Services filed Public Interest Litigation in Kerala High Court with pray that either stop the event or ban of presentation of tobacco industry logo in promotional advertisement as well as in the event.

Intervention or response: The Hon'ble High Court issued a direction to State Tobacco Control Cell to stop the event after hearing the views of event organisers.

Results/Impact: After the high court direction the organisers withdraw its re-transmission.

Conclusions: The case is not concluded. We expect a total ban of logo placement in cultural events.

Community-led, rights-based and gender-responsive health interventions

EP-40-489 TB, Covid-19, and the ethics of disease exceptionalism: opportunities for shared learning

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Background and challenges to implementation: The negative repercussions of diverting public health resources – human and monetary – away from TB programs and toward COVID-19 efforts will likely be severe and hinder global efforts against TB. One aspect of this challenge lies in the concept of disease exceptionalism, i.e., that a particular infectious disease is so different from other infections so as to require new and different legislation and approaches. Succumbing to disease exceptionalism diverts attention away from the myriad of social and political congruencies that infectious diseases share and that are ethically relevant.

Intervention or response: We convened the Union's TB Ethics Working Group to discuss this challenge and explore public health ethics approaches toward responding to the ethical quandary of disease exceptionalism in the case of TB and COVID-19. Using Powers and Faden's health and social justice arguments, based on the philosophical literature on capabilities and functionings, we arrived at two salient considerations for policy makers and healthcare workers.

Results/Impact: The themes were:

- Recognition that the social and political injustices that affect persons with TB and those with COVID-19 are similar and, as such, some advocacy needs to occur across disease areas where common concern is shared; and;
- Opportunities for bi- or multidirectional learning on ethical issues between disease areas, e.g., regarding surveillance, COVID-19 has foregrounded the ability to monitor transmission dynamics in a very public way. How can TB use that experience to advance our ethical frameworks for whole genome sequencing in public health?

Conclusions: Risk of distraction from new and emerging issues is inevitable but can be mitigated. Advocates, health care workers, and civil society need to work together and across disease areas to target social determinants of health that are unjust and underpin many – if not most – infectious diseases. TB programs can contextualise these findings to ensure TB systems are robust and person-centred.

EP-40-490 Activating a human rights-based TB response: a multi-country approach

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Background and challenges to implementation: Despite commitments in UN SDGs to “transform the TB response to be...rights-based and people-centred”, it is not a reality in most countries for lack of knowledge about health as human right.

GCTA is a coalition of TB affected individuals bringing the lived experience of TB to the global platform. GCTA endeavours to bridge the gap between civil society organizations and stakeholders, while ensuring that community is involved in all TB processes. Cognisant of lack of rights-based response in TB policies, GCTA initiated work on inculcating such a response.

Intervention or response: GCTA developed resource material laying out interventions for developing human-rights based response to TB. It also conducted the first ever workshop bringing TB community and legal community from across the globe together, on the side-lines of the 50th Union World Conference on Lung Health. This workshop supported by North-western University and the Stop TB partnership saw community members and lawyers from Nepal, India, Cambodia, Kenya, Philippines, Indonesia and Botswana. Through further community engagement, GCTA realised that national and local community organisations need to be supported in training and advocacy on human-rights based response to TB. GCTA therefore, with support from STOP TB worked on training networks to activate human-rights based response to TB in Cameroon, India, Indonesia and Peru.

Results/Impact: The intervention saw communities better understanding health as a legally enforceable right. The community-based organisations were empowered to identify lawyers and also build support networks. This empowered the community to reach out for remedies in case of treatment and service denial.

Conclusions: While the WHO End TB strategy is developed on the foundation of rights-based interventions, the real transition will only occur by empowering the different levels of the health systems, starting with the TB affected community. Such intervention has to be done periodically to ensure sustenance of networks.

EP-40-491 Closing the deadly divide between TB commitments and TB realities through community empowerment and accountability

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Background and challenges to implementation: The United Nations High Level Meeting on TB (UNHLM) resulted in countries establishing ambitious targets and commitments to end TB.

A summary of those targets and commitments is available at: http://www.stoptb.org/assets/documents/global_advocacy/unhlm/UNHLM_Targets&Commitments.pdf

Intervention or response: Two years on from the UNHLM on TB the UN Secretary General released a progress report. Complementing this report, and providing enhanced nuance on the experience of TB affected communities, civil society, human rights and gender, the first ever global accountability report was developed by TB affected communities and civil society, marking a significant moment in the development of global TB accountability. The accountability report, entitled *A Deadly Divide: TB Commitments vs TB Realities* was, informed by inputs of over 150 community partners was launched in five languages on International Human Rights Day, 2020.

Results/Impact: There were 5 key results:

1. A community led global TB accountability report that was the product of unprecedented community consultation and leadership;
2. Clear priorities and operational guidance on advancing a rights based and gender sensitive TB response,
3. engagement of Members of parliament, journalists and celebrities in advancing the 6 calls to action from the report;
4. World TB Day campaigns championing the Calls to Action from the report;
5. Donors supporting the operationalizing of the Calls to Action, through significant scale up of investment in the \$7.5 million USD Challenge Facility for Civil Society (CFCS).

Conclusions: 1. Empowering affected communities and civil society to impact TB accountability efforts will strengthen TB response at all levels;
2. The model of engagement is the new gold standard for the TB response and demonstrates the leadership communities can and will continue to play in global TB multi-sectoral accountability;and
3. TB affected communities and civil society capacity and coordination has significantly grown with support of CFCS and this will continue with the \$7.5m USD 2021 Round 10.

EP-40-492 Building awareness and capacity of people with TB and TB survivors about human rights in the Asia-Pacific

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Background and challenges to implementation: In early 2020, with support from the Stop TB Partnership, we developed the Right to Breathe Human Rights Training Tool for People with and affected by TB to respond to the growing need to increase the awareness of human rights and to build the capacity to employ these principles in the TB response. This is also in line with the 2018 Political Declaration on TB commitments of shifting towards a more rights-based TB response.

Intervention or response: To measure its direct outcomes to civil society, we conducted two 3-day Regional Training of Trainers (TOTs) in partnership with the Activists Coalition on TB – Asia Pacific (ACT! AP) and with support from the Stop TB Partnership. The TOTs, spread through September 24 to October 30, 2020, were participated by 21 representatives from 15 civil society organizations and TB-affected communities in 9 countries in Asia-Pacific. Adjustments were made to transform the activities to fit its virtual delivery. A 15-point pre- and post-test surveys were administered to the participants to assess their progress after the TOT.

Results/Impact: Results from post-test survey show that 53% of the items had an average correct response increase of 15%. These questions were related to human rights orientation sessions and capacity-building activities. Four items related to addressing stigma and discrimination showed a 6% percentage reduction, which reflects the need to increase awareness-raising activities to address internalised stigma and misconceptions towards people with TB.

Conclusions: Participants highlighted the importance of the Right to Breathe Human Rights Training in providing clarity in implementing the principles of human rights in the TB response. TOT participants have also developed advocacy plans to support their national level rollout, and we are currently conducting these rollouts in three countries in the region, namely Nepal, Papua New Guinea, and Viet Nam, to further assess its national-level impact.

EP-40-493 Availability vs. use of social welfare schemes by TB patients, India

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Background and challenges to implementation: India's Direct Benefit Transfer scheme (DBT) - 'Nikshay Poshan Yojana ensures Rs. 500 (6.78 USD) monthly financial incentive for registered TB patient on anti-TB treatment. In tribal areas, additional Rs. 750 (10.17 USD) is provided to patients for travelling to clinics. Besides this, there are several social welfare schemes by the state governments for senior citizens, farmers, widow's, people with disabilities and health being a state subject, the TB affected are allowed to receive both DBT and any one more social scheme. However, the patients are unaware or ignorant for accessing these schemes, the health staff's not have adequate knowledge on the DBT. In the absence of social welfare staff at the TB unit, patient or care taker needs to visit several offices to complete the physical approval formalities which is time consuming and require out of pocket expenditure.

Intervention or response: 1703 patients (534 DS, 1169 MDR) enrolled between 2018-2020, facilitated for DBT cash assistance for nutritional support to bank accounts. Patients and families were sensitized about the procedure of accessing the scheme. GLRA's counsellors has taken this responsibility, helped the patients to access the schemes in its project locations in four states.

Results/Impact: 93% (n=1590) MDR /TB patients were facilitated to access DBT. 7% did not enrolled due to ID issues. Increased cure rate noticed among MDR TB 75% (875) and DS TB 87% (464). Additionally, 1460 patients supported with essential ration as pandemic relief and 20% (n=348) enrolled in other national social (eg; old age pension) welfare schemes.

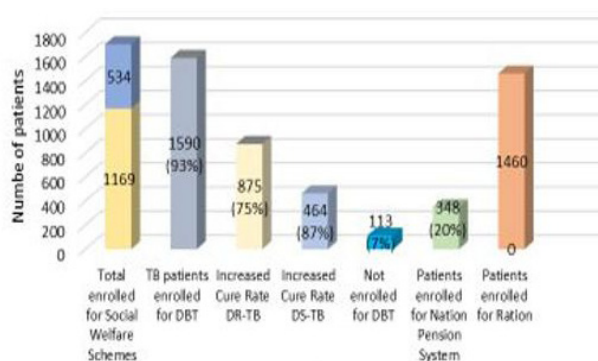


Figure. Patients enrolled for social-support (2018-2020)

Conclusions: TB adversely affects the poor and marginalized as they battle with poverty, malnutrition, poor hygiene, stigma, employment, living and working condi-

tions. There is significant relationship between healthier nutrition and treatment outcomes. Sensitization and process of DBT has to be better streamlined and user friendly for better uptake by patients.

EP-40-494 The civil society as key actor in the successful implementation of bans on tobacco advertising, promotion and sponsorship in Bangladesh

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Background and challenges to implementation: In Bangladesh, use of tobacco is a very alarming situation. 35 percent of adults are currently using tobacco either in smoked in smokeless form (GATS 2017). However, the government of Bangladesh is seriously concerned about this issue and has enacted tobacco control law in 2005 based on FCTC-WHO. Tobacco use is comparatively higher in the coastal region. Due to lack of well communication, tobacco industries are more aggressive in advertising and promoting tobacco products and tobacco users are increasing rapidly.

Intervention or response: In implementing the TAPS ban initiative, Grambangla Unnayan Committee prioritized engagements of civil society as key actor to identify and monitor the point of sales. Grambangla formed 'Civil Society Action Committees' consist of 21 civil society members worked as 'Watchdog' to monitor TAPS ban violations. These committees were actively involved in the enforcement activities conducted by the task force committees, conducted media campaign to sensitize local journalist, creating tobacco free institutions and arranged cultural events highlighting adverse effects of tobacco use.

Results/Impact: Due to efforts of civil society action committee huge number of TAPS violation incidences were identified and documented such as posters, stickers, etc. provided by the tobacco industries. These committees conducted mapping of 6,821 POSs and identified more than 21,000 TAPS violations under 43 types of TAPS violations that include, posters, festoons, leaflets, discount label, empty cigarette packets, etc. Civil society action committees also facilitated in activating 12 local task force committees for initiating mobile courts to enforce incidences of TAPS violations. As an effect, the owners of POSs removed advertisement related materials from their shops.

Conclusions: Active involvement of civil society created positive changes in achieving the vision of SDG. Now the civil society become key actors for monitoring of

incidences of TAPS violation in implementing tobacco control laws of Bangladesh that helps promoting “Tobacco free Bangladesh by 2040”.

EP-40-495 Illicit tobacco trade and the role of the tobacco industry: a case study from Uttar Pradesh, India

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Background and challenges to implementation: Article 15 of WHO’s Framework Convention on Tobacco Control Treaty (FCTC) aims to draw commitment and provide guidelines to Parties to eliminate illicit trade of tobacco products. Previous studies have suggested that illicit tobacco trade in India is large in terms of volume but not in proportion to licit sale.

We attempted to review publicly available reports to assess estimates and government’s knowledge of tobacco industry behaviour.

Intervention or response: A literature survey of publicly available government reports from enforcement agencies (Comptroller and Auditor General of India (CAG), Directorate of Revenue Intelligence, Customs and Excise among others) was carried out and in specific a case study drawn for India’s largest state and tobacco using province, Uttar Pradesh. In addition proceedings from the state’s Legislative Assembly for the past 10 years were also collected.

Results/Impact: The quantum of tax evasions are high and tobacco companies are using different ways for illicit trade, non-payment of taxes, delayed payment of taxes and smuggling of tobacco products for tax evasion. We observe 16 violations from different sources and the quantum of violations is 3196.63 lacs which results a big revenue loss to the government. The violations are mostly observed in major cities like the capital Lucknow, major towns close to state border (Moradabad, Ghaziabad, Gorakhpur, Chandauli) and districts in proximity to international borders.

Conclusions: There is sufficient evidence from within Government of India reports that suggest that tobacco industry and its supply chain stakeholders perpetrate illicit trade of tobacco products. Government reports show massive seizure of illegal trade of tobacco products during transport and transit especially the railway stations of major cities like Lucknow, Kanpur, Gorakhpur.

In order to prevent illicit trade of tobacco products, strong surveillance system needed backed with strict enforcement, which comply and exceed the recommendation of FCTC and India’s excise legislation.

EP-40-496 Interventions to reduce TB-related stigma: a structured literature review

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Background: Tuberculosis (TB) related stigma leads to delayed health-seeking behaviour, reduced treatment adherence, and adverse treatment outcomes. Interventions to reduce TB-related stigma are needed to reach the World Health Organisation’s (WHO) End TB target of eliminating TB. Despite this, process and impact evaluation of stigma-reduction interventions are limited. This structured review examined the quality of studies of interventions to reduce TB-related stigma and evaluated study design, implementation, and intervention impact. **Design/Methods:** Four databases were searched for relevant articles from 1999 to 2017, using pre-defined inclusion and exclusion criteria. Supplementary articles were identified using the snowball method and complementary grey literature searches. Study quality was assessed using the ‘Crowe Critical Appraisal Tool’. Study characteristics, data on stigma measurement tools used, interventions implemented, and mechanism of stigma reduction were extracted and tabulated. A conceptual framework was designed to illustrate the mechanisms of stigma reduction.

Results: 13,443 articles were identified. Following detailed assessment, nine studies were quality appraised of which one study was of high quality. Six studies used questionnaires to assess stigma levels, one of which had been previously validated. Intervention designs broadly consisted of educational or psychosocial support. Seven studies successfully reduced stigma. Three mechanisms of successful stigma reduction were identified: increased knowledge, attitude and behaviour change, and empowerment.

Background and challenges to implementation: Tuberculosis (TB) related stigma leads to delayed health-seeking behaviour, reduced treatment adherence, and adverse treatment outcomes. Interventions to reduce TB-related stigma are needed to reach the World Health Organisation’s (WHO) End TB target of eliminating TB. Despite this, process and impact evaluation of stigma-reduction interventions limited. This systematic review examined the quality of studies of interventions to reduce TB-related stigma and evaluated study design, implementation, and intervention impact.

Conclusions: This review found that studies evaluating TB stigma-reduction interventions were mostly low or moderate quality, with minimal randomised-controlled trial evidence. Cross-study comparison of intervention impact was hampered by the wide variety of tools used to measure stigma. To make meaningful change in this

field, high quality studies, including randomised-controlled trials, of stigma-reduction interventions that use standardised stigma measurement tools, such as that recently developed by the Stop TB Partnership, are required.

EP-40-497 Development of a digital community-led monitoring platform for TB care in Metro Manila, the Philippines, using a human-centred design approach

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Background and challenges to implementation: Some Filipinos with tuberculosis (TB) do not have autonomy over their health due to limited access to information, resources, and social support. It is therefore imperative to provide them with a platform to report and act on these barriers. In this context, this study utilized a human-centered approach in developing a mobile health application for community-led monitoring of TB care in Metro Manila, the Philippines.

Intervention or response: This study used a mixed-methods approach guided by human-centered design or an iterative co-creation approach with end-users. Prior to solution ideation, a needs assessment survey was conducted to empathize with the “pain points” of people with TB. Incorporating feedback from consultations with program managers, patient groups, and civil society organizations, a mobile application prototype was developed, rolled out, and re-designed through iterative cycles of user-feedback workshops.

Results/Impact: Eight user-feedback workshops, involving a total of 43 people living with tuberculosis, were conducted. Outcomes were presented at a high-level meeting attended by representatives from the National Tuberculosis Program, patient advocacy groups, and civil society organizations. The CareTB application, available in three languages (English, Filipino, and Bisaya), is now downloadable on Apple and Android devices. It primarily features a platform for users to report barriers to TB care and their experiences with stigma and discrimination, and to receive prompt responses on these concerns.

Conclusions: Human-centered design methods can be used to effectively engage stakeholders by empathizing, contextualizing, ideating, prototyping, and iterating

public health interventions tailored to target users’ perceived needs and preferences. Extending its application beyond tuberculosis to other solutions, programs, and policies may be worth considering to promote a user-first mindset toward people-centered care.

EP-40-498 Scaling-up access to TB testing through a tailored specimen referral network in four regions of Cameroon

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Background and challenges to implementation: Rapid and high-quality TB testing is vital for effective TB management. In Cameroon, a recent patient pathway analysis showed that most people initially seek care at primary care centers, but only 1% of these provide TB services, and most TB testing sites only provide smear microscopy rather than a WHO-recommended rapid diagnostic.

Intervention or response: We evaluated the impact of an intervention to scale-up access to TB services by intensified case finding at facilities combined with a specimen referral and result reporting system. A total of 224 primary care sites and lower-level laboratories were linked to 71 testing laboratories providing different levels of services across four regions of Cameroon (Littoral, West, Southwest, Northwest). Transportation was tailored to each site and included bikers, commercial agencies, and healthcare workers, who were paid per trip made. Results were sent by automated SMS from an mHealth app. We assessed the number and type of TB tests performed and the number of people confirmed and notified with TB for three years before (2016-2018) and two years during the intervention (2019-2020). We also assessed the cost per TB test result provided. This work was part of CHECK TB, a TB REACH project across six regions of Cameroon.

Results/Impact: A preliminary analysis showed that 57,435 people were tested for TB in 2019 and 54,046 were tested in 2020, which was a +56% and +47% increase, respectively, as compared to the 36,819 people tested pre-intervention in these areas in 2018. The average transportation cost per result was approximately 1,050 CFA (\$1.90).

Conclusions: A specimen referral system tailored to the needs of sites in both rural and urban areas across four diverse regions of Cameroon facilitated cost-effective access for many more people to be tested and diagnosed for TB.

ABSTRACT PRESENTATIONS THURSDAY 21 OCTOBER 2021

ORAL ABSTRACT SESSION (OA)

OA-19 Whole-genome sequencing and imaging for TB disease

OA19-724-21 Exact mapping of Illumina blind spots in the *M. tuberculosis* genome

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Background: Whole-genome sequencing (WGS) is fundamental to *Mycobacterium tuberculosis* basic research and many clinical applications. Many studies also have proposed WGS as a diagnostic platform for drug resistance in tuberculosis (TB). The most popular WGS platforms for TB are short-read Illumina sequencers. Unfortunately, coverage across Illumina-sequenced *M. tuberculosis* genomes is known to vary with sequence context, but this bias is poorly characterized. Here, through a novel application of phylogenomics that distinguishes genuine coverage bias from deletions, for the first time, we systematically discern Illumina ‘blind spots’ in the *M. tuberculosis* reference genome for seven sequencing workflows.

Design/Methods: Illumina sequencing data for 5131 isolates were downloaded from NCBI’s SRA database. Downloaded genomes were assembled and aligned to H37Rv reference genome (NC_000962.3). Regions of low coverage were investigated through a novel phylogenomic approach to determine whether the low coverage was due to natural deletion of the region in the major subpopulation or due to the biases previously documented for Illumina short-read sequencers.

Results: This study finds blind spots to be widespread, affecting 529 genes, and provide their exact coordinates, enabling salvage of unaffected regions. Importantly, 57 *pe/ppe* genes (the primary families assumed to exhibit Illumina bias) lack blind spots entirely, while the remaining *pe/ppe* genes account for 55.1% of blind spots. Surprisingly, we find coverage bias persists in homopolymers as short as 6 bp, shorter tracts than previously reported. While G+C-rich regions challenge all Illumina sequencing workflows, a modified Nextera library prep-

aration that amplifies DNA with a high-fidelity polymerase markedly attenuates coverage bias in G+C-rich and homopolymeric sequences, expanding the ‘Illumina-sequencable’ genome.

Conclusions: This study provides exact locus coordinates to be avoided with seven popular Illumina workflows. Through these findings, and by defining workflow-specific exclusion criteria, we spotlight effective strategies for handling bias in *M. tuberculosis* Illumina WGS.

OA19-725-21 Targeted next-generation sequencing detects uncommon resistance-conferring mutation associated with misdiagnosis of rifampicin resistance: a case study

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Background: Deeplex Myc-TB targeted next generation sequencing (NGS) can predict resistance to 13 anti-tuberculous (TB) drugs/drug classes, directly from sputum. Xpert MTB/RIF assay is routinely used for the rapid detection of rifampicin (RIF) resistance and consequent clinical decision. Phenotypic anti-TB drug susceptibility testing (pDST) is still considered the “gold standard”. Previous reports indicated that low-level RIF resistance associated with uncommon *rpoB* mutations can be missed by nucleic acid amplification tests and pDST.

Design/Methods: This is a part of an interrupted time-series designed observational study conducted in Myanmar during 2019-2021 for biomarker assessment. The study case was a 22-year-old new RIF sensitive pulmonary TB patient diagnosed by Xpert MTB/RIF who enrolled for drug susceptible anti-TB treatment. Bactec-MGIT pDST and Deeplex Myc-TB GenoScreen assay using Illumina Miseq platform were performed on Day 0 sputum. Monitoring of treatment response by clinical history, smear microscopy and/or cultures were carried out at week 2, week 4, week 8, week 20 and week 24.

Results: The study patient was RIF sensitive by Xpert TB/RIF and MGIT pDST but phenotypically resistant to isoniazid, streptomycin, ethambutol and pyrazinamide. Deeplex Myc-TB revealed *rpoB* 1491F minimum-confident RIF resistant mutation and four mutations; *rpsL* K43R, *katG* S315T, *embB* M306I, *pncA* Y103H which were associated with streptomycin, isoniazid, ethambutol and pyrazinamide resistance respectively. Apart from RIF resistance, Deeplex Myc-TB results were concordant with pDST. The

patient undergone treatment failure as he had positive cultures at week 20 and week 24 of anti-TB treatment. Isolated *Mycobacterium tuberculosis* was Beijing SIT 1 spoligotype (Lineage 2).

Conclusions: We described use of targeted NGS can detect uncommon RIF resistance mutation which was missed by commonly used Xpert MTB/RIF and Bactec-MGIT.

Uncommon drug resistance-conferring mutations are likely more common in high-burden countries leading to misdiagnosis and unfavorable treatment outcome, thus, personalized treatment approaches based on genome data should be compromised.

OA19-726-21 Whole-genome sequencing for *Mycobacterium tuberculosis* complex resistance testing: 1 year's experience

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Background: In the Netherlands the secondary routine diagnostic workup for *M. tuberculosis complex* isolates consists of (sub)species identification, drug susceptibility testing (DST) and epidemiological typing. Previously, this was based on several methods, but they were replaced in 2020 by whole genome sequencing (WGS). Phenotypic DST is now only performed on isolates with mutations possibly associated with resistance to first-line drugs.

Design/Methods: All *M. tuberculosis* complex cultures isolated in 2020 (one per patient, except one patient infected with two different strains) were subject to Illumina WGS. Isolates with one or more (potentially) resistance associated mutations were subject to phenotypic DST.

Genes associated with resistance included, but were not limited to, *rpoB*, *katG*, *inhA*, *fabG1*, *ahpC*, *embB*, *embA*, *pncA* and *rpsA*. Multiple mutations associated with resistance to the same antibiotic were counted as one resistance mutation.

Results: 441 isolates were subject to WGS. Based on these results no phenotypic testing was needed for 373 of the isolates (85%). This included 20 *M. bovis* (BCG) isolates and one *M. canettii* for which confirmation of pyrazinamide resistance was not considered necessary. One exception was made for a *M. bovis* BCG isolates belonging to a cluster associated with low level isoniazid resistance. The remaining 68 isolates contained 93 resistance associated mutations. Forty-four mutations (in 36 isolates) contained high confidence mutations, for which resistance was confirmed by phenotypic DST. Five (16%) of the 32 isolates with lower confidence mutations revealed phenotypic resistance.

Conclusions: In a routine WGS based diagnostic algorithm for 93% of the isolates WGS alone was in fact sufficient and only 7% had an ambiguous WGS result requiring phenotypic follow up. No relapse due to a missed resistance was reported. This algorithm reduced phenotypic testing by 85%, with no loss of sensitivity.

OA19-727-21 Combing whole-genome sequencing, geographic and public health information to study transmission dynamics of TB in Taiwan

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Background: We conducted a population-based cohort study of TB, combining whole genome sequencing (WGS), geographic and public health information to understand the transmission dynamics in a metropolitan city in Taiwan.

Design/Methods: All culture-confirmed TB cases in Kaohsiung City since year 2019 were eligible to be included. Isolates were collected through a mycobacterium laboratory collaboration network, and WGS was conducted in all isolates using the Illumina NovaSeq S4 or SP platform. Information of public health information was combined to observe the known epidemiological links between cases.

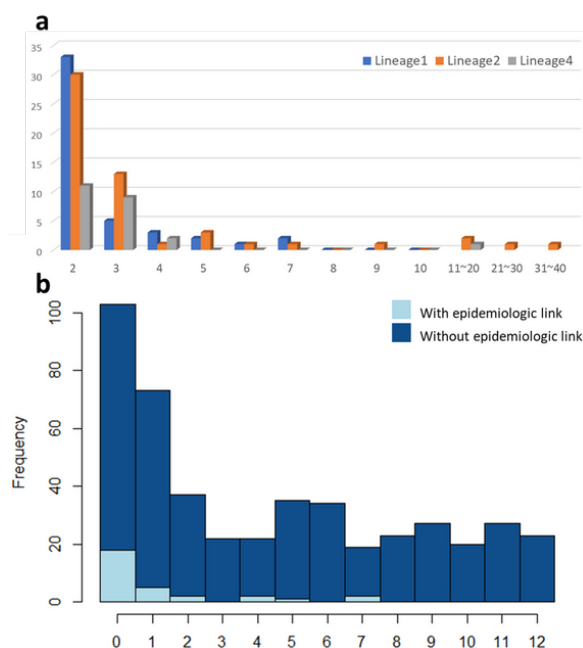
We calculated the shortest distance of any addresses (residential, permanent and occupational/activity address) between cases to represent geographical relatedness.

Results: The included 1677 TB cases represents 80.6% of all cases notified between January 2019 and October 2020. Applying the threshold of 12 single nucleotide polymorphism, 390 cases (23.2%) were classified as genotypically clustered.

The clustered patients were more likely to be <65 years (odds ratio 3.2, 95% CI 2.6-4.1) and to be infected by Lineage 2 strain (odds ratio 2.6, 2.1-3.3). A total of 122 genomic clusters were identified, and 14% of the clusters contained a large number (>=5) of cases (Figure a).

Cases with known epidemiologic link (based on conventional contact investigation) were all associated with genomic clusters, but the majority of cases within genomic clusters had no known epidemiologic link (Figure b). Spatial analyses revealed strong geographic proximity of these genotypically clustered cases (median pairwise

geographic distance among cases within genotypic clusters: 4.0km (Q1-Q3: 2.1-7.4 km), as opposed to that among other cases: 9.7km (5.1-18.3km)).



Conclusions: Our integrated analysis in a metropolitan city of Taiwan revealed potential transmission of TB which was not detected by conventional contact investigation. The knowledge and information obtained from the analysis could be used to direct future efforts to re-investigate the large genomic clusters and to interrupt ongoing transmission.

OA19-728-21 Augmenting case-finding using artificial intelligence-enabled chest X-ray reading in Uttar Pradesh and Assam, India

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Background and challenges to implementation: The COVID-19 pandemic disrupted TB services and its case notification. Computer-aided detection (CAD) is recommended by WHO as an alternative to digital chest X-rays (CXR) for screening and triage for TB. Joint Efforts

for Elimination of TB (JEET) is a project supported by The Global Fund to actively engage with the private sector for managing TB patients. CHRI (a PATH affiliate), the implementer of JEET deployed QXR, the Artificial Intelligence (AI) enabled solution for chest X-ray reading, in collaboration with technology partner Qure.ai, in areas with the unavailability of an interpretation expert.

Intervention or response: The intervention was done across 22 X-ray facilities linked to 29 private providers in 10 districts of Uttar Pradesh (UP) and 14 providers among 2 districts of Assam. It was implemented in two phases, four districts in Phase 1 (December'20 to March'21) and eight districts in Phase 2 (Feb – Mar'21). Private X-ray laboratories were mapped and then selected based on technological preparedness to implement the intervention. Private doctors were provided with vouchers for offering X-rays, the cost of which was reimbursed by JEET.

Results/Impact: As per preliminary results till March 2021,1,490 chest X-rays were screened with 32% being suggestive of TB. The rapid expansion of this intervention faced many challenges namely, the unavailability of digital radiography equipment, computers, and required internet bandwidth in rural UP. This was overcome by persuading providers to procure the required services as well as adapting the technology to function in a low resource environment.

Conclusions: At a private provider level, the acceptance and behavior change towards microbiological confirmation of probable TB cases is yet to be ascertained. In low resource settings and others, with gaps in real-time availability of radiologists, the preliminary results of the intervention emphasize the need for scaling up this model to complement the country's TB elimination goal.

OA19-729-21 Effect of artificial intelligence-based triaging on radiologist workloads during mobile chest X-ray screening for TB

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Background: Ensuring chest X-ray (CXR) interpretation quality and avoiding reader fatigue are real concerns in high-volume CXR screening settings for tuberculosis (TB). Artificial intelligence (AI) software may serve as a decision support tool for radiologists to reduce workloads and save costs by triaging normal CXR images.

Design/Methods: Two CXR image test libraries were constituted using data from a CXR screening initiative in Ho Chi Minh City, Viet Nam. Library 1 was processed using the default settings of Oxipit's ChestEye AI software to identify normal CXR images. After outputs were obtained, the clinical data from Library 1 were used to optimize the software's cut-off threshold. Library 2 was then processed using both the default and optimized cut-off threshold values. We compared the performance characteristics for both threshold values, using field radiologists interpretations as the reference standard. We then calculated the theoretical reduction in radiologist workloads had the optimized threshold been used as a triage tool before human reading.

Results: 9,998 CXR images from Library 2 were processed by the AI software. The default cut-off threshold achieved a 100% sensitivity and negative predictive value (NPV), but triaged just 7.89% of the library's CXR images. The optimized cut-off threshold, selected after training with Library 1 data, achieved a 99.87% sensitivity and a 99.96% NPV. 23.29% of the library's CXR images were triaged, representing a 2.95-fold increase compared to the default cut-off threshold. Only one CXR image was 'inaccurately' classified by the AI software; however, this participant had a negative Xpert MTB/RIF result, so the 'misclassification' would not have resulted in a reduction of TB yields.

Conclusions: With optimized threshold values, Oxipit's ChestEye software accurately triaged normal CXR images, and thereby could have reduced radiologist workloads by almost one quarter. This type of automation can reduce reader fatigue and save X-ray interpretation costs.

OA19-730-21 The diagnostic accuracy of chest radiographic features in paediatric pulmonary TB

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Background: The chest radiograph (CR) is widely and routinely used to diagnose paediatric pulmonary tuberculosis (PTB). We aimed to present the diagnostic accuracy of key CR features for paediatric PTB.

Design/Methods: We analysed CR data from children <13 years enrolled with presumptive PTB in a prospective observational diagnostic cohort study. CRs from

baseline were correlated with clinical and microbiological data. All children had follow-up assessments allowing for classification as "confirmed", "unconfirmed" or "unlikely" PTB according to standard international NIH case definitions. CRs were systematically evaluated for the presence of radiological features by 2 of 3 expert readers blinded to clinical details; each CR generated 2 single, independent reads. Inter-reader agreement was calculated using Cohen's kappa coefficient. Diagnostic accuracy analysis was restricted to children classified as "confirmed" or "unlikely" PTB, using "confirmed PTB" as the diagnostic reference standard; only CR features with kappa ≥ 0.4 (moderate agreement) between ≥ 2 reader pairs were evaluated for their diagnostic accuracy.

	Unlikely PTB n (%) N=512 ³	Confirmed PTB n (%) N=236 ³	Inter-reader agreement Reader 1&2 k (95% CI)	Inter-reader agreement Reader 1&3 k (95% CI)	Inter-reader agreement Reader 2&3 k (95% CI)	Sensitivity %	Specificity %
Any abnormality	379 (74)	225 (95)	0.55 (0.41,0.68)	0.55 (0.40,0.71)	0.46 (0.25,0.67)	95	27
Alveolar opacification	181 (35)	118 (50)	0.47 (0.37,0.56)	0.52 (0.39,0.66)	0.47 (0.31,0.63)	50	65
Enlarged perihilar lymph nodes	25 (5)	100 (42)	0.59 (0.46-0.73)	0.64 (0.48-0.80)	0.81 (0.59-1.0)	28	95
Enlarged paratracheal lymph nodes	10 (2)	54 (23)	0.49 (0.31-0.68)	0.35 (0.10-0.61)	0.79 (0.51-1.0)	45	98
Bronchial deviation/compression	9 (2)	69 (29)	0.54 (0.38-0.70)	0.37 (0.13-0.60)	0.79 (0.51-1.0)	28	98
Cavities	12 (2)	32 (14)	0.42 (0.21,0.62)	0.35 (-0.02,0.71)	0.91 (0.72,1.0)	14	98
Pleural effusion	22 (4)	21 (9)	0.43 (0.19-0.68)	0.75 (0.53-0.96)	0.79 (0.51-1.0)	9	96

k – kappa coefficient; CI – confidence interval

¹Only CR features with kappa ≥ 0.4 (moderate agreement) between ≥ 2 reader pairs were included in this table (interstitial infiltrates, bronchopneumonia, collapse, tracheal deviation/compression, Ghon focus, miliary and perihilar infiltrates had k <0.4 for >1 reader)

²The diagnostic accuracy analysis was restricted to children with "confirmed" and "unlikely" PTB; "confirmed PTB" was the diagnostic reference standard

³Each CR from each participant generated 2 single independent expert CR reads

Table 1. The diagnostic accuracy of chest radiograph (CR) features¹ for confirmed pulmonary tuberculosis (PTB)² in children

Results: CRs from 541 children, generating 1082 single expert CR reads, were included. Median age was 16.9 months (IQR 9.82, 33.48), 13% were HIV-infected. 285/541 (53%) children were classified as TB cases; of these, 118/285 (41%) had confirmed PTB. Table 1 shows the diagnostic accuracy analysis for CR features with moderate inter-reader agreement.

Enlarged perihilar and paratracheal lymph nodes, bronchial deviation/compression, cavities and pleural ef-

fusion all had specificity of $\geq 95\%$ for confirmed PTB. “Any abnormality” on CR was 95% sensitive; all other features had poor sensitivity.

Conclusions: Selected CR features have high specificity for the diagnosis of PTB in young children. Diagnostic algorithms for paediatric PTB may be improved if CRs are scored by the presence of these CR features rather than by an overall assessment of being “suggestive of TB”. Such approaches should be systematically evaluated to improve the diagnosis of PTB in children.

OA-20 Lessons learnt along the care cascade

OA20-731-21 Analyzing interventions designed to reduce tuberculosis-related stigma: a scoping review

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Background: Stigma is a barrier to the delivery of quality tuberculosis (TB) care. Yet little is known about the implementation of TB stigma reduction interventions at different stages of the TB care cascade or that target different stigma domains (enacted, anticipated, or internal).

Design/Methods: We conducted a scoping review to map existing literature on TB stigma reduction interventions. We systematically searched the following databases to identify studies that assessed the impact of interventions to reduce TB-related stigma: PubMed, EMBASE, and Web of Science. Two independent reviewers screened and extracted the data. We applied thematic analysis deductively to code studies based on stigma domains and inductively to identify other recurring themes. Results were coded using NVivo (QSR International).

Results: After screening 1441 articles, we extracted data from nine. More than one stigma domain was targeted in 44% (4/9) of studies. Four studies assessed the impact of an intervention on internal stigma, five on enacted stigma, and four on anticipated stigma (Table 1). Six interventions (five of which focused on drug-resistant TB) were targeted towards patients, households, or communities, and included TB clubs or psychosocial support groups (n=3), household counselling (2), and an

educational video. Three interventions were targeted towards healthcare workers (HCWs) and included a public awareness campaign, an educational workshop, and participatory theatre. Interventions were implemented to improve care-seeking (3) or to provide support either during diagnosis (2) or during treatment (4). All studies used different stigma measurement approaches. Interventions reduced stigma in all but one study, in which increased community stigma was attributed to poor staff training.

Included studies	Intervention aim	Intervention type	Stigma domain(s) targeted?	Instructional quotes from included studies by stigma domain(s)
Alcha, 2007	To support MDR-TB patients undergoing treatment	Psychosocial support groups	Internal Anticipated	Former wage earners strained to overcome feelings of 'uselessness' and being 'a burden' on their already struggling families as a result of their inability to work. "I've had to learn to be a liar: 'When people ask why my aim is so dark... I have to come up with whatever I can besides the truth, anything but the truth, because if they found out the truth, they would discriminate against me." - TB club participant
Boad, 2017	To support MDR-TB patients undergoing treatment	Household counselling	Enacted	The prevalence of being made fun of was lower at follow-up than at baseline in the [intervention] communities and higher in the [non-intervention] communities. Disclosure to anyone outside the household increased in both arms at follow-up.
Salogun, 2014	To reduce stigma at the community level	Educational workshop	Enacted	More respondents (21.4% increased) post-intervention responded that they would feel compassion but would also stay away from people with TB than those interviewed pre-intervention.
Demehle, 2003	To support MDR-TB patients undergoing treatment	Psychosocial support groups	Enacted	[Description of stigma pre-intervention] Within a person get TB, everyone used to isolate the patient, and even the spouse and other family members. Instead of encouraging the patient to seek treatment they would keep him/her at home in order not to be identified as a case of TB. "When I was first told about my disease I was shocked. I didn't tell anyone because I was afraid that my wife would leave me. I was afraid that my neighbours would isolate me." - Participant with MDR-TB
Mans, 2008	To support MDR-TB patients undergoing treatment	Psychosocial support groups	Internal	Between baseline and two months post initiation of the intervention, there was a 32.8% reduction in the proportion of participants who agreed with the statement: "I feel ashamed to have tuberculosis."
Siegel, 2015	To reduce stigma among HCWs and to promote health seeking behaviours	Stigma reduction campaign	Anticipated	[On images aimed to reduce anticipated stigma among HCWs] Respondents appreciated the explicit association of office files being passed behind a tool, commenting that it served as a visual reminder of the importance of confidentiality in the workplace. [Post-intervention] Patients and families understood that TB does not just affect 'poor people' but people of any class and profession.
Wilson, 2016	To support MDR-TB patients undergoing treatment and to educate family members	Educational video	Internal	There was a reduction in stigmatization scores in general, which was statistically significant in women, public health workers, 40-49 year olds and those with an education level <12 years, those who had been a volunteer. [During an exercise to demonstrate internalized stigma to health workers] "I feel sad, stupid and angry at myself to be alone here. I tried to listen attentively and to observe but I couldn't get it right. It affected my self-esteem and confidence." - Participant, HCW
Wu, 2009	To reduce stigma among HCWs and to promote health seeking behaviours	Participatory theatre	Internal	[On the stigmatization of those with TB] "The workshop made me realize many areas that I was a perpetrator." - Participant, HCW

Conclusions: Few published studies report the effect of TB-stigma reduction interventions. The quality of intervention reporting was low, compromising applicability. Further research is needed to optimize the design, implementation, and evaluation of TB-stigma reduction interventions to close TB care cascade gaps.

OA20-732-21 Adapting a scale to measure TB- and HIV-related stigma in Ugandan households

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Background: Although tuberculosis (TB) and HIV stigma are associated with reduced engagement in care among TB patients and their household contacts, measuring household stigma is difficult due to lack of validated, quantitative scales. We sought to adapt a short scale to measure perceived TB-HIV stigma.

Design/Methods: We adapted the 22-item Van Rie et al. TB-HIV stigma scales to measure perceived household stigma in four phases:

1. preliminary field testing of the original scales within households of newly diagnosed TB patients in Kampala, Uganda,
2. psychometric evaluation and cognitive interviews with a purposively selected subgroup of participants,
3. adaptation of the scales with subsequent field testing, and
4. selection of final scale items based on factor loading scores (>0.3 , no cross-loading), inter-item covariance (pairs with covariances >0.65 resolved by dropping one item), and alignment of the TB and HIV sub-scales.

Each item had four possible Likert responses (Strongly Disagree to Strongly Agree).

Results: We tested the original scales with 163 contacts from 55 households. The scales had high internal consistency (Cronbach's alpha 0.87 for TB; 0.86 for HIV scales) but was markedly skewed towards higher stigma scores (Table 1).

Final Adapted Scale Items ^a	Pre-Adaptation Median (IQR) ^b	Post-Adaptation Median (IQR) ^b	Final Adapted Scale Items ^a	Pre-Adaptation Median (IQR) ^b	Post-Adaptation Median (IQR) ^b
TB Stigma Subscale^c	26.5 (19–32)	17.5 (7–30)	HIV Stigma Subscale^d	21 (15–27)	9.5 (3–21)
Some household members think that those with TB are disgusting.	2.5 (1–3)	1 (0–3)	Some household members think that those with HIV are disgusting.	2.5 (1–3)	1 (0–2)
Some household members keep a distance from those with TB.	3 (2–3)	2 (0–3)	Some household members keep distance from those with HIV.	2 (1–3)	0.5 (0–2)
Some household members are afraid of those with TB.	3 (2.5–3)	2 (0–3)	Some household members are afraid of those with HIV.	3 (2–3)	2 (0–3)
Some household members try not to touch those with TB.	2 (0–3)	1 (0–3)	Some household members try not to touch those with HIV.	2 (1–3)	0 (0–2)
Some household members prefer not to have those with TB living in their household.	2 (1–3)	1.5 (0–3)	Some household members prefer not to have those with HIV living in their household.	1 (0–3)	1 (0–2)
If a person has TB, some household members will behave differently towards them for the rest of their life even after recovering from TB.	3 (1–3)	1.5 (0–3)	If a person has HIV, some household members will behave differently towards that person for the rest of his or her life.	3 (2–3)	2 (0–3)
Some household members may not want to eat or drink with relatives who have TB.	3 (1–3)	2 (1–3)	-	-	-

^a Each item score ranged from 0–3

^b Interquartile range

^c Possible range of pre-adaptation scale was 0–33; Possible range of post-adaptation scale was 0–36

^d Possible range of pre-adaptation scale was 0–33; Possible range of post-adaptation scale was 0–30

Table 1.

Cognitive interviews revealed that A) wording of the scales led participants to focus on stigma external to the household, and B) participants felt compelled to *Agree* to several survey questions which were commonly misunderstood. After revisions, we tested the new scale with 60 contacts from 38 households. The revised scales had high internal consistency (Cronbach's alpha 0.94 for TB; 0.92 for HIV) without a severe skew, capturing increased variance in participant responses. After final selection, the adapted scales included seven TB and six HIV items.

Conclusions: Using multiple methods, we adapted and validated a 13-item survey tool to rapidly assess perceptions of TB-HIV stigma in households undergoing TB contact investigation.

OA20-733-21 The yield of different TB case-finding strategies in a prison setting, Ethiopia

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Background and challenges to implementation: Prison settings are one of the targeted centers for the tailored tuberculosis (TB) prevention control in Ethiopia. In addition to the routine outpatient department (OPD) TB screening in prison clinics, the country has already adopted mass screenings and screening of inmates at entry and exit as key strategies for identifying TB cases in prison settings. However, the yield of TB screening was not determined for different TB case finding strategies in prisons.

Intervention or response: Health care workers (HCWs) from prison clinics were trained on symptom screening (> 2 weeks of cough, night sweating, persistent fever, and weight loss), diagnosis, and treatment of TB. Besides the regular OPD TB screening at the prison clinics, the HCWs were also oriented to introduce mass screening, entry, and exit screening of the inmates. Gene X-pert was used for diagnosis. From July to December 2020, data on screening, presumed TB cases, and TB cases notification were captured from prisons in four regions of Ethiopia (Oromia, Amhara, SNNP and Sidama). The case notification rate (CNR) per 100,000 screened inmates was computed for each screening strategies and compared using the 95% confidence interval (CI).

Results/Impact: A total of 69,622 inmates were approached and screened; 7,499 (10.8%) and 299 (0.4%) were presumptive TB cases and confirmed TB cases,

respectively. The overall CNR per 100,000 screened inmates was 429 (95% CI: 429-431). The respective CNR for entry screening, OPD screening, mass screening, and exit screening was 46 (95% CI: 45-47), 420 (95% CI: 419-422), 910 (95% CI: 909-912) and 161 (95% CI: 159-162).

Conclusions: Increasing TB CNR after entry to the prison setting shows a higher TB transmission. In addition to contact tracing, combined screening (symptomatic and chest X-Ray) and molecular rapid diagnostics may be introduced as screening tool to improve TB case finding in the prison settings of Ethiopia.

OA20-734-21 Community screening for TB among the San community in Tsumkwe, Namibia

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Background and challenges to implementation: Namibia has the 8th highest incidence rate of TB per capita in the world, with 36% of TB patients going untreated. Tsumkwe is home to the marginalised and often nomadic San (Bushman) communities, which are also disproportionately affected by drug-resistant TB. Tsumkwe has 10% of the Ojozondjupa regional population but 86% of the drug-resistant TB burden. A pilot community-wide screening exercise was conducted to determine the prevalence of active TB among the residents of the Tsumkwe area.

Intervention or response: In a community-wide screening in settlements around Tsumkwe, residents were approached door to door and asked if they had any cough, fever, night sweats, weight loss or lymph node enlargement and were offered sputum testing with Xpert MTB/RIF if they responded in the affirmative. Participants were also asked about a history of TB treatment and HIV testing.

Results/Impact: 2,693 participants were screened, of which 1319 (49%) were male and 1609 (60%) were 15 years and older. Symptoms were present in 711 (26%), with cough being the most prevalent symptom. 408 (25%) of those ≥15 years of age had been treated for TB before (national average 10%).

Three new TB patients were discovered in addition to the 58 known to be on treatment. The prevalence was 2% (or 2,079/100,000), at least four times higher than the national estimate of 465/100,000.

Only 47% had been tested for HIV before with a 3% prevalence, much lower than the national average (13%) but consistent with TB notification data.

Conclusions: TB prevalence in Tsumkwe was very high and there is a high TB-treatment coverage. However, coverage of HIV services is low. The yield of TB screening can be improved by including chest radiography and testing for latent TB infection.

OA20-735-21 Barriers to TB care among nomadic and semi-nomadic communities in Namibia

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Background and challenges to implementation: Namibia is among the 30 high tuberculosis (TB) burden countries globally and has a significant population of marginalised nomadic and semi-nomadic populations, particularly the OvaHimba and OvaZemba pastoralists in the north-west and the San (bushmen) in the north-east.

The objective of this assessment was to identify the potential barriers to accessing TB care services among the nomadic and semi-nomadic communities in Namibia in order to develop targeted interventions.

Intervention or response: A situational assessment was conducted in Kavango, Kunene and Otjozondjupa regions with household interviews and key informant interviews. A mixed quantitative and qualitative approach was adopted, with participants only included if they were aged over 15 years and were resident in the selected areas.

Results/Impact: The majority of household interviewees (63; 90%) had adequate knowledge of TB disease, but 35 (50%) participants cited a positive reaction to a hypothetical TB diagnosis, such as seeking care and engaging healthcare workers, while 12 (17%) cited fear. Another 12 (17%) cited hopelessness and five (7%) cited surprise while six (9%) would not disclose to a family member.

Despite preferring modern healthcare, services are often not accessible, as exemplified by over half (38, 54%) of the households living more than 20km of health facilities. Public transport is often absent.

Less than half of the participants (29, 41%) had been tested for HIV, much lower than the national average of 88%. IEC materials were generally inadequate. Other significant challenges documented included poverty, high illiteracy, the drought, poor sanitation practices (66% open defecation) and negative attitude of healthcare workers.

Conclusions: Although this assessment was limited in both scope and geographical reach, it unearthed significant gaps in HIV programme implementation, sanitation and accessibility. Knowledge and attitudes towards TB were generally good, but the general poor access to health services including HIV testing could be a significant barrier.

OA20-736-21 Factors affecting the behaviour of target groups in healthcare-seeking and TB treatment in Kyrgyzstan

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Background: The USAID Cure Tuberculosis Project designed a formative assessment among target groups in Kyrgyzstan to understand:

- 1) The perspectives of people with TB and their household members on seeking testing and completing treatment;
- 2) The factors underlying widespread stigma; and,
- 3) Support systems and communication channels for reaching target groups, including labor migrants, people who were formerly incarcerated, people who misuse substances, people living with HIV, and people who are homeless.

Design/Methods: A qualitative research study was conducted among 547 participants in February-March 2020 in Naryn, Chui and Jalal-Abad regions and Bishkek city. The study consisted of: 25 focus group discussions, 277 doer/non-doer interviews, and 23 semi-structured interviews, among target groups as well as the general population, health workers, and staff working with target groups. Data were analyzed using qualitative analysis techniques and doer/non-doer frequency tabulations of barriers and enabling factors to care.

Results: The study identified key barriers and enabling factors to seeking testing and completing treatment for TB, which highlight the unique psychosocial challenges patients and their families face, as well as the critical role of family and health workers in supporting patients to complete treatment. Results also show extensive misconceptions about TB, including about causes, transmission, genetic inheritability, treatment and curability, as well as widespread stigma. A causal analysis reveals the community-level and patient-level factors which fuel stigma. The most significant social consequences of stigma include abandonment by family, loss of marriageability, self-isolation and self-stigma.

Conclusions: The research findings informed both a project-specific and national social and behavior change strategy with tailored messages and channels of communication for each target group and actions to counter stigma and discrimination. The research also highlighted the need to develop better patient-centered forms of care, including community-based treatment support taking into account the multiple barriers to care faced by people with TB.

OA20-737-21 Use of smart pillbox to improve TB treatment outcomes in Ethiopia: preliminary findings from the run-in phase of the ASCENT Project

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Background: Tuberculosis treatment based on Directly Observed Therapy employs the same level of monitoring and support for all patients without focusing care on patients that are at higher risk for non-adherence and poor outcomes. Digital Adherence Technologies (DATs) offer approaches to support patient-centred, differentiated care to improve treatment outcomes. We report enrolment and sociodemographic profile, and two-month adherence data of participants in the run-in phase of an ongoing pragmatic cluster-randomized trial in the Adherence Support Coalition to End TB (ASCENT) project in Ethiopia (PACTR202008776694999).

Design/Methods: 78 health facilities were randomised (1:1:1) to (i) smart pillbox or (ii) medication label, both with daily monitoring and differentiated response to patient adherence, or (iii) standard of care. Adult drug-susceptible pulmonary tuberculosis patients in intervention facilities are offered a DAT linked to the ASCENT adherence platform for daily adherence monitoring and support. Participants at standard of care facilities receive routine care. We report on data from patients using the smart pillbox in the run-in phase.

Results: From 31/12/2020–26/4/2021, 561 patients started treatment in intervention health facilities, 267 (47.6%) were eligible and 261/267 (97.8%) consented. The mean age was 33.2 years and 108/261 (41.4%) were female. In Addis Ababa, 16.1% (14/87) had never attended school, the median number of household assets was 5 (total N=14), median households size was 3, and 94.3% (82/87) had access to mobile phone. Of those who reached 2 months of treatment, 57/59 (96.6%) were using the smart pillbox, 18/59 (30.5%) had ≥ 1 dose status unknown and 9/59 (15.3%) had ≥ 2 consecutive doses with unknown status. During this period, due to COVID-19, patients were expected to attend the clinic monthly for medication refill.

Conclusions: DATs such as smart pillbox could potentially support patient-centred care in Ethiopia, particularly in the light of COVID-19. DATs' effectiveness in improving treatment outcomes will be further evaluated.

OA-21 Comprehensive lung health strategies and learnings

OA21-738-21 Vitamin D supplementation and respiratory health outcomes: results of a randomised controlled trial

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Background: We wanted to determine the effects of vitamin D supplementation on respiratory health outcomes in vitamin D-deficient schoolchildren.

Design/Methods: We conducted a Phase 3 randomized, placebo-controlled, clinical trial of vitamin D3 supplementation in 8,851 schoolchildren of Mongolia to determine whether weekly oral supplementation with 14,000 IU vitamin D3, administered for 3 years influenced risk of incident asthma or allergic rhinitis among children aged 6 to 13 in Ulaanbaatar, Mongolia. Sub-studies evaluated effects of the intervention on spirometric lung volumes (n=1,465) and cardiorespiratory fitness (n=615)

Results: A total of 8,117 (91.7%) children completed the study. Mean age at baseline was 9.4 years and mean serum 25(OH)D level was 11.9 ng/ml. Supplementation with weekly vitamin D elevated mean 25(OH)D levels to 29.8 ng/ml in the active treatment group compared to 9.7ng/ml in the placebo group (p=0.001). Vitamin D supplementation did not influence the risk of incident asthma (P=0.32), incident allergic rhinitis (P=0.45), mean forced expiratory volume in 1 second (FEV1, P=0.35), mean forced vital capacity (FVC, P=0.95), or mean peak oxygen consumption (VO₂peak, P=0.22). Effects of the intervention did not differ according to baseline 25-hydroxyvitamin D levels (<10 ng/mL vs. ≥10 ng/mL) or baseline calcium intake (high vs low) for any respiratory outcome studied

Conclusions: A weekly oral dose of 14,000 IU vitamin D3, administered for 3 years, elevated 25-hydroxyvitamin D levels into the high physiological range in vitamin D-deficient schoolchildren, but it did not impact any respiratory outcome investigated.

OA21-739-21 Association of pre-existing comorbidities with mortality and disease severity among patients diagnosed with Covid-19 in Canada

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Background: The novel coronavirus disease 2019 (COVID-19) has infected 1.9% of the world population by May 02 2021. This calls for population-based cohort studies to reveal granular evidence regarding risk factors to COVID-19 mortality and severity as most previous results were reported upon hospitalized patients.

Design/Methods: We conducted a retrospective cohort study based on all patients diagnosed of COVID-19 in Ontario Canada between January 25 and December 31, 2020. We conducted cox proportional hazards regression models and logistic regression models to adjust patient demographic, socio-economic variables and comorbidities.

Results: A total of 167,500 patients were diagnosed of COVID-19 and included. Multivariate Cox regression models revealed that older age posed the highest risk to mortality. Compared with patients without comorbidity, patients who had comorbidities were 116% likely to experience severe outcomes of death or hospitalization (OR=2.16, 95% CI 2.04, 2.29; p<0.001), while the risk substantially increased from 1.70 (95% CI, 1.60-1.86, p<0.001) to 6.17 (95% CI, 5.60-6.81, p<0.001) as the number of comorbidities increased from 1 to 5 or more.

Profound predictors for mortality included comorbidities such as solid organ transplant (HR=3.06, 95% CI 2.03 - 4.63; p<0.001), dementia (HR=1.46, 95% CI 1.35-1.58; p<0.001), chronic kidney disease (HR=1.45, 95% CI 1.34-1.57; p<0.001), severe mental illness (HR=1.42, 95% CI, 1.12-1.80; p<0.001), CVD (HR=1.22, 95% CI, 1.15-1.30), diabetes (HR=1.19, 95%, 1.12-1.26; p<0.001), COPD (HR=1.19, 95% CI 1.12-1.26; p<0.001), cancer (HR=1.17, 95% CI, 1.09-1.27; p<0.001), hypertension (HR=1.16, 95% CI, 1.07-1.26; p<0.001). The risks of comorbidities increased substantially among patients of younger age groups.

Conclusions: Our study highlights that the number of comorbidities was a strong risk factor for deaths or severe COVID-19 outcomes. We also found that the impact of comorbidities was more profound in patients with younger age.

Findings of our study suggests that in addition of targeting on age, vaccination priority groups should also include younger population with multi-comorbidities.

OA21-740-21 Role of obesity in asthma-related Emergency Department visits and hospital admissions, US national estimates, 2014–2018

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Background: Obesity increases the risk of asthma and worsens asthma outcomes. We examined whether obesity is associated with increased healthcare utilization among children and adults with asthma in the United States.

Design/Methods: Data of the National Hospital Ambulatory Medical Care Survey (NHAMCS) (2014-2018) were combined to generate nationally weighted estimates of asthma and obesity-related ED visits and hospital admissions with corresponding 95% confidence intervals (CI). Adjusted logistic regression models were conducted to demonstrate association between obesity and hospital admissions among patients with underlying asthma diagnosis.

Results: Individuals with underlying asthma diagnosis accounted for 9.8% (95% CI, 9.3 – 10.3) of total ED visits and 10.3% (95% CI, 9.3 – 11.4) of hospital admissions that resulted from the ED visits. Among individuals with obesity presenting to the ED, 20.4% (95% CI, 18.5 – 22.5) had underlying asthma diagnosis compared to 9.4% (95% CI, 8.9 – 9.8) of asthma diagnosis among those without obesity. Asthma diagnosis with co-existing obesity accounted for 0.8% of all ED visits, mostly comprising females (74.9%, 95% CI, 70.5 – 78.8), age-group 25-64 years (66.5%, 95% CI, 57.4 – 76.3), and Medicaid insured (43.6%, 95% CI: 38.5 – 48.9).

The percentage of hospital admissions from ED visits was higher for asthma diagnosis with co-existing obesity than asthma diagnosis alone (22.4%, 95% CI, 18.7 – 26.6 vs 9.0%, 95% CI, 7.9 – 10.3).

Asthma diagnosis with co-existing obesity was twice as likely to have resulted in hospital admission compared to asthma diagnosis alone (Adjusted odds ratio [AOR] = 2.50, 1.90 – 3.18), after adjusting for age, sex, race/ethnicity, insurance type, geographical region, study year, mode of arrival at ED, and total number of ED procedures and diagnostic tests.

Conclusions: ED visits and hospital admissions were significantly higher among children and adults with co-existing asthma and obesity than those with asthma alone. Obesity is associated with increased burden of asthma-related healthcare utilization in the United States.

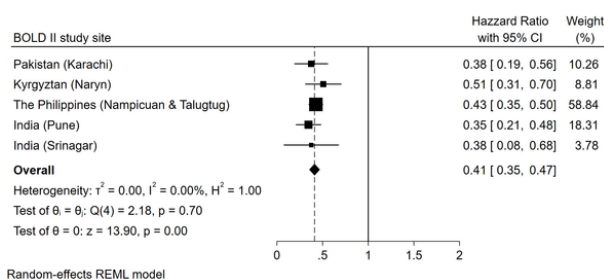
OA21-741-21 Forced vital capacity and mortality in low- and middle-income countries: preliminary findings from the BOLD study

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Background: In high-income countries, better survival has been associated with a higher forced vital capacity (FVC). Whether this is also true in low- and middle-income countries is unknown.

Design/Methods: We used data from 5 sites (Nampicuan-Talugutug in the Philippines, Pune and Srinagar in India, Karachi in Pakistan, and Naryn in Kyrgyzstan) participating in the population-based Burden of Obstructive Lung Disease (BOLD) study that have completed follow-up of study participants. The association between baseline postbronchodilator FVC and mortality within each site was assessed using Cox proportional hazard models adjusted for potential confounders. Effect estimates from all sites were then combined using meta-analysis. Accidental causes of death were excluded from the analysis.

Results: Among the 2,968 followed-up participants, 369 (12.4%) have died (median follow-up=8 years interquartile range (IQR) 6-11). We found an inverse association between FVC and mortality. For each litre higher in FVC at baseline, the mortality decreased by 59% (adjusted Hazard Ratio (aHR)=0.41, 95% CI 0.35-0.47). The association was stronger in Karachi, Pakistan (aHR=0.38, 95% CI 0.19-0.56) and Srinagar, India (aHR=0.38, 95% CI 0.08-0.68), Figure.



Conclusions: Our preliminary findings suggest that in low- and middle-income countries of Central and South Asia, as in high-income countries, people with a higher FVC have a better survival. Incoming data from other BOLD study sites will enable us to further examine this relationship and undertake analyses by cause of death with a special focus on deaths ascribed to respiratory or cardiovascular causes.

OA21-742-21 Post-TB lung disease: health system challenges and research priorities in Kenya and Malawi

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Background: Tuberculosis (TB) remains a major public health challenge across the globe. Despite global efforts to end TB saving 63 million lives since 2000, there is increasing evidence of residual morbidity including post-TB lung damage (PTLD) among TB survivors and no guidelines available for post-TB care.

The aim of this study was to identify stakeholder perspectives on post-TB care, potential models of post-TB care service delivery, barriers to and decision making around its implementation, and existing data gaps in Kenya and Malawi.

Design/Methods: Stakeholder mapping was used to identify individuals with influence or interest in tuberculosis policy, programming, and management in Kenya and Malawi. In-depth interviews were completed with purposively selected key informants. All interviews were audio-recorded, transcribed verbatim, and analyzed thematically.

Results: We interviewed 37 stakeholders; 6 from multi-lateral aid agencies, 8 policymakers, 4 from non-governmental organizations, 11 healthcare providers, and 8 TB survivors/advocates. TB survivors felt that this is an important issue and recommended broadening the agenda beyond clinical care, to include provision of economic, social, and psychological support beyond TB treatment completion. The perceived importance of post-TB care varied widely between other stakeholders and there were mixed opinions about whether this should fall under the remit of National TB Programmes or broader health services. Perceived barriers to implementation included staffing and funding constraints and limited capacity for decentralized diagnosis and clinical care. Lack of data on the local burden of post-TB morbidity, models of service delivery, and evidence-based guidelines for clinical care were highlighted as key evidence gaps.

Conclusions: This work has identified several key data gaps which must be addressed, in order to inform stakeholder decision-making around the need for, and implementation of, post-TB and PTLD care and services.

Further engagement with stakeholders will be needed to explore how and under whose remit these services could be delivered.

OA21-743-21 A south-south inter-country learning approach to design community health systems intervention for chronic lung disease care in sub-Saharan Africa

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Background: As chronic respiratory diseases (CRDs) become increasingly recognized in sub-Saharan Africa, health systems stakeholders and policy makers will need pragmatic approaches to developing context-appropriate interventions. We brought together health system stakeholders from Sudan and Tanzania, two differing health system contexts, to facilitate inter country learning that could inform design of interventions to improve management of CRDs within their routine health systems.

Design/Methods: Using an action research approach that included an intercountry learning visit, investigators, and ministry of health official from Sudan (Sudan team) visited Tanzania to understudy the structure, organization and function of the strong community health systems deployed in the Tuberculosis program. Field trips to health facilities and communities, informal interviews and discussions with policy makers and health workers, and workshops were organised to facilitate learning.

Results: Lessons learnt by Sudan team on recording, referral pathways and linkages of community health workers to routine health system, and approaches to governance and political commitment by policy makers, led to development of a novel community health intervention model for CRD in Sudan. The model was made up of groups identified from the community and assigned to specific tasks in the CRD care cascade: community nurses (case finding, referral, follow up), family medicine doctors (case management, referral, linkage with higher levels), a social services committee (advocacy, health education) and former TB patients (case finding, health education).

Conclusions: Inter-country learning in a south-south collaborative research is an innovative way to exploit the strengths within health systems to address a shared public health challenge across contexts such as chronic respiratory diseases. The applicability of this approach in other disease contexts in sub-Saharan Africa should be explored.

OA21-744-21 Social protection coverage and coping strategies of people with symptoms of chronic lung disease in Meru County, Kenya: a cross-sectional study

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Background: Diagnosis and care of chronic lung diseases (CLD) requires adequate healthcare access and engagement that are associated with significant out-of-pocket payments (OOP). For people affected by CLD and their households, these costs could be catastrophic. Universal health coverage and expansion of social protection schemes, including pre-paid health insurance, can minimize risks of catastrophic costs. We evaluated coverage and use of Kenya's social health insurance "The National Hospital Insurance Fund" (NHIF) amongst people with symptoms of CLD in Kenya.

Design/Methods: This was a quantitative cross-sectional study. We conducted exit interviews of children and adults with symptoms of CLD in five public healthcare settings including primary healthcare facilities (n=2), primary referral hospitals (n=2) and secondary teaching and referral hospital (n=1) in Meru County, Kenya. Data on awareness of eligibility criteria, uptake and coverage, and use of NIHF to access services were collated. Descriptive statistics were performed using R software.

Results: The study involved 338 participants; males (141/338, 41%), mean age 31 years, children 5-17 years (54/338, 16%). NIHF coverage was low (91/338, 27%). Majority (174/247, 71%) of those uninsured were aware of eligibility criteria. Key reported reasons for not having insurance included: lack of information (51/174, 29%) and affordability (99/174, 57%). Only 6/42 (14%) participants made healthcare payments for their CLD care-seeking using NIHF.

Coping strategies adopted to mitigate the financial shock of out-of-pocket hospital bills included: using savings (197/338, 58%); borrowing money (109/338, 32%); taking on additional work (21/338, 5.1%); family support (13/338, 3.7%), sale of property (10/338, 3%).

Conclusions: Kenya's NIHF had limited coverage and use among people attending public healthcare facilities with CLD symptoms in Meru County predominantly due to lack of awareness and issues of affordability. Low

coverage was associated with high OOP that led to multiple coping strategies. NIHF may require adaptation to be more acceptable and affordable.

OA21-745-21 Socio-economic impact of chronic respiratory diseases among patients and their families in sub-Saharan Africa: a qualitative assessment

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Background: Chronic respiratory diseases (CRDs) are major causes of illness and premature mortality in sub-Saharan Africa. However, evidence to inform intervention remains sparse and the socioeconomic impacts are not well understood. We explored the socioeconomic impacts of CRDs on patients and their families as part of the development of context-specific interventions to integrate CRD care into routine health systems.

Design/Methods: We conducted in-depth interviews (IDIs) with purposively selected known or suspected CRD patients and focus group discussions (FGDs) with community members in Gezira state, Sudan and Dodoma region, Tanzania. We explored perceptions, experiences, and priorities of CRDs to gain an in-depth understanding of how participants interpreted and experienced CRDs in their lives.

Results: Sixteen IDIs (9 in Sudan, 7 in Tanzania) and 14 FGDs (6 groups in Sudan, 8 groups in Tanzania) were conducted. In both contexts, CRD was associated with limitations of livelihoods through diminished work capacities and economic impacts of healthcare seeking costs.

Furthermore, patients and their families experienced both enacted and internalized stigma, and social exclusion, due to association of chronic cough with TB and HIV/AIDS in the communities.

Additionally, CRD patients experienced discrimination in the community and at workplace. Among Sudanese young women, CRD could lead to loss of marriage due to stigma or jeopardize marital prospects due to discrimination.

Conclusions: Chronic respiratory diseases are associated with significant social and economic impacts among patients and their families in Sudan and Tanzania. Context-appropriate social safety nets for CRD patients and

measures to address stigma of chronic cough in the communities will help mitigate these impacts and improve care of CRD patients within the health system in these contexts.

OA-23 New treatment regimens for TB

OA23-753-21 Efficacy and safety of 4-month rifapentine–moxifloxacin regimen for TB in adolescent participants

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Background: Persons aged 10-19 with tuberculosis (TB) account for approximately 10% of the global burden. Study S31/A5349, a randomized, open-label, phase III, treatment shortening trial for pulmonary TB, compared two high-dose 4-month rifapentine regimens (with or without moxifloxacin) to the standard 6-month regimen. The study demonstrated non-inferior efficacy of the rifapentine-moxifloxacin regimen compared to the standard regimen. To better understand outcomes among adolescents with TB, we examined efficacy and safety data from this trial in this participant sub-group (Clinicaltrials.gov:NCT02410772).

Design/Methods: The primary efficacy endpoint was TB disease-free survival at 12 months after randomization. We conducted an analysis of efficacy and safety outcomes in adolescents (12-17 years), comparing outcomes across arms.

Results: A total of 2516 participants were enrolled in Study S31/A5349 at 34 sites in 13 countries; 68 (3%) adolescents were enrolled at 10 sites in 7 countries. Mean age was 16.3 years, 59 (87%) of 68 were ≥15 years (range 13-17 years), 85% were born in Africa, 54% were males, none were HIV co-infected, 87% had cavitation on chest x-ray.

Among 63 adolescents in the primary analysis group, the proportion with unfavorable outcomes was 5% (1/19), 8% (2/25), and 11% (2/19), in the control, rifapentine-moxifloxacin, and rifapentine regimens, respec-

tively. Among 67 adolescents who started study treatment, there were no severe adverse events (SAEs) and no deaths among adolescents. 59 (87%) completed at least 75% of the intended regimen, and 43 (63%) completed at least 95%.

Conclusions: Adolescents were successfully enrolled in a large multi-country, phase III TB trial and should be considered for future trials. Adolescent participants in TBTC S31/A5349 had numerically similar safety and efficacy outcomes in the rifapentine-moxifloxacin arm compared to control regimen (although numbers were small). The four-month rifapentine-moxifloxacin regimen can be used in the adolescent population.

OA23-754-21 Efficacy and safety of 4-months rifapentine–moxifloxacin treatment of TB in patients with diabetes

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Background: Diabetes mellitus in patients with tuberculosis may increase risk for poor treatment outcomes. We examined the prevalence of diabetes, its impact on treatment outcomes, and occurrence of adverse events among participants in S31/A5349.

Design/Methods: S31/A5349, a randomized, controlled, phase III study, demonstrated non-inferior efficacy of 4-month rifapentine-moxifloxacin regimen compared to standard 6-month control regimen for drug-susceptible tuberculosis. A rifapentine-only arm included was not non-inferior. The primary efficacy endpoint was tuberculosis disease-free survival at 12 months after randomization. At baseline, participants self-reported any prior diagnosis of diabetes and HgbA1c and/or blood glucose levels were tested.

Results: Among 2516 randomized participants from 34 sites in 13 countries, 83 (3.3%) reported having diabetes and no additional participants were diagnosed at baseline. Diabetes prevalence among individual sites ranged from 0% to 42%. The proportion of participants with diabetes averaged 15.9% (14/88) in South American, 9.5% (27/284) in Asian, 4.0% (13/306) in North American, and 1.5% (29/1838) in African sites, respectively. Among 83 participants with diabetes, one was HIV

positive; the median baseline HgbA1c level reported in 80.7% (67/83) was 10.9% (IQR 9.3-12.5%). Among 77 participants with diabetes in the primary analysis (microbiologically eligible) group, 21 had unfavorable outcomes; 27.0% (8/30), 21.1% (7/33), and 42.9% (6/14) in the control, rifapentine-moxifloxacin, and rifapentine regimens, respectively.

Among 81 participants with diabetes who started study treatment, 34 grade 3-5 adverse events occurred during study treatment in 26 (32.1%) participants; 36.7% [11/30], 28.6% [10/35], and 31.3% [5/16] in the control, rifapentine-moxifloxacin, and rifapentine regimens, respectively. The difference in unfavorable outcomes and grade 3-5 adverse events between each investigational arm to control arm were not statistically significant.

Conclusions: Among S31/A5349 participants with diabetes, there was no significant difference in occurrence of unfavorable outcomes and grade 3-5 adverse events between rifapentine-moxifloxacin and control regimens. Four-months rifapentine-moxifloxacin regimen may be used in people with diabetes.

OA23-755-21 Effectiveness and safety of combining bedaquiline, delamanid and linezolid to treat pulmonary MDR-TB patients with additional drug resistance under programmatic settings

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Background: With availability of newer drugs, there is greater scope to develop patient-friendly treatment regimens, for better treatment outcomes in MDR-TB patients with additional drug resistance to fluoroquinolones or second-line injectables (Pre-XDR).

Design/Methods: A prospective cohort study at five sites in India is evaluating the effectiveness and safety of combining Bedaquiline, Delamanid with Linezolid (LZD) (600mg), and Clofazimine (100/200mg) for 24 weeks in adults with Pre-XDR TB. Primary outcome is favorable

response at end of treatment defined as negative culture with resolution of clinical signs and symptoms. Unfavorable outcomes include bacteriologic or clinical failure or recurrence during 18-month follow-up. Treatment emergent adverse Events are also evaluated.

Results: Total of 167 patients (males 93; median age 27 years) were enrolled, of whom 112 have completed 6-months of treatment, among which 100 (89%) had favorable outcome and 12 unfavorable outcomes including 4 deaths, 2 bacteriological failures, 6 treatment changes due to adverse events.

Twenty-four patients (21%) presented with LZD toxicity - seven peripheral neuropathy (29%) and 15 myelosuppression (63%). In all of them, dose of LZD was reduced to 300mg between 12-24 weeks. Twenty one patients responded well to this dose.

Three patients could not tolerate the reduced dose and LZD was stopped permanently. Twenty-three patients (19%) had QTc(f) >470msec or >60msec from baseline. All drugs were temporarily withheld in three patients, which was later reintroduced.

None of the patients had QTc(f) >500msec during treatment (Fig 1). All patients completed treatment and were declared cured.

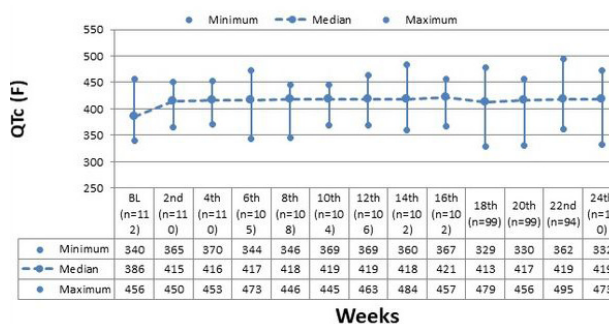


Figure 1. QTc (F) Prolongation at different timepoint.

Conclusions: Fully oral combination of bedaquiline, delamanid, clofazimine, and Linezolid led to high cure rates after 6 months of treatment in Pre-XDR TB patients. Cardiotoxicity was minimal, myelosuppression, though common, was manageable in the field setting. Follow-up will determine recurrence rates. Short-course regimens need to be made standard of care for DR-TB based on emerging evidences.

OA23-756-21 Predicting failure or relapse outcomes in patients receiving the short regimen for MDR-TB in the STREAM Stage 1 trial

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Background: Shorter treatment regimens have been shown to improve treatment outcomes in several observational studies. STREAM Stage 1, a multi-country non-inferiority randomised trial, compared a 9-month regimen with the longer WHO regimen showing comparable success rates. We investigated baseline factors predictive of long-term TB-related outcomes in patients who received the short regimen.

Design/Methods: Baseline demographics, clinical/laboratory, bacteriological and radiological characteristics were collected and all participants in the modified intention to treat population were followed up to 132 weeks post-randomisation. Participants were classified as definitely or probably experiencing a failure or relapse event (FoR) using data up to the time they reached the trial primary endpoint. Baseline variables that were found to be significantly associated ($p < 0.1$) with FoR in univariable analysis were assessed in a multivariable Cox regression model (backwards elimination, exit probability $p = 0.05$) to identify factors that were independently associated with FoR.

Results: On the short regimen, 25 (9.9%) out of 253 participants were classified as FoR; the probability of FoR by week 132 was estimated as 0.11 (95% CI 0.07, 0.15). Sex, smoking status, baseline smear grade, extent of opacities, cavitation, and presence of costophrenic obliteration were significantly associated with an unfavorable outcome (all $p < 0.1$). Male sex, higher smear grade, HIV co-infection, and obliteration of costophrenic angle remained independently associated in multivariable analysis (all $p < 0.05$). These four factors remained independently associated when week 8 culture was included in the multivariable analysis and there was borderline evidence that a positive culture at week 8 was predictive of FoR ($p = 0.052$).

Conclusions: There is evidence to suggest that male gender, HIV status, and high grade smears may be associated with a higher risk of failure or relapse. Novel strategies that target patients with high-risk baseline characteristics are needed. The association of costophrenic obliteration with a worse outcome is most likely an incidental finding.

OA23-757-21 Interim treatment outcomes among patients with rifampicin-resistant TB treated with the modified all-oral treatment regimen in a resource-limited setting

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Background: To evaluate the treatment outcomes of a modified 9- 11 months shorter all oral treatment regimen (mSTR) for Rifampicin resistant tuberculosis (RR-TB) under programmatic conditions in Uganda and document the adverse events.

Design/Methods: We carried out a prospective observational study. Patients aged 6 years and above with RR-TB and without prior exposure (for more than 1 month) to second-line anti-tuberculosis treatments were enrolled for this study. These patients received a 9-11 months RR-TB treatment regimen comprised of Bedaquiline, Linezolid, Levofloxacin, Clofazimine and Cycloserine. All treatment was administered by daily directly observed therapy. Patients attended monthly clinic follow-up visit during treatment and then quarterly after treatment completion for one year.

Results: Between November 2019 and December 2020, we enrolled 235 patients of whom 132 (56%) had primary RR-TB. Out of the patients enrolled, 171(73%) were males, 15(6%) were children aged 6-14 years, 12(5%) were older than 65 years, 95 (40%) were HIV co-infected and on antiretroviral therapy (ART) at initiation of RR-TB treatment. By March 2021, 101 (43%) had completed six months follow-up of which, 88 (87%) had either culture-converted or remained culture-negative, 9 (8.9%) had died, 1(0.01%) was lost to follow up, 1(0.01%) failed treatment and 2(1.98%) not evaluated. The proportion of death was similar among the HIV and non-HIV infected groups (5% vs 6%). The six months interim follow up did not differ by HIV status. 6 (5.9%) patients experienced severe adverse events leading to at least one drug substitution; 1 QTC prolongation, 3 severe anemia and 2 optic neuritis.

Conclusions: Interim outcomes of RR-TB patients treated with the modified all oral treatment regimen showed high rates of patient retention in care and culture conversion. Final outcomes are expected at the end of 2022.

OA23-758-21 The first cohort of TB patients placed on the BPAL regimen in Ukraine: preliminary results

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Background: The BPAL regimen with three oral drugs, bedaquiline, pretomanid, and linezolid, and six to nine months treatment duration, developed by the TBA, is recommended by WHO to treat patients with highly resistant TB under OR conditions.

Design/Methods: Ukraine is the first country in the world to introduce the BPAL regimen. From November 2020 – July 2021, 135 patients with pre-XDR-TB or MDR-TB treatment non-response or intolerance will be enrolled in the BPAL treatment at the National Institute of Phthisiology and Pulmonology (NIPHP). TB patients are selected and treated following the National BPAL OR protocol and monitored by the International Advisory Council of TB experts from NIPHP, NTP, OATH, KNCV, PATH, TBA.

Results: In November 2020 - April 2021, 66 (89.2%) from 74 screened patients were enrolled in the OR. Nine (13.6%) patients were withdrawn from the OR because of baseline resistance to linezolid and bedaquiline (6.1%), hepatotoxicity grade 4 (3.1%), comorbidity, bleeding gastric ulcer (1.5%), and informed consent withdrawal (1.5%). One (1.5%) TB patient died from respiratory failure in the second week of the BPAL treatment. Adverse events (AEs) were reported in 27 (40.9%), more than one AEs were reported in six (9.1%), grade 3 and 4 AEs - in 12 (18.2%), myelosuppression - in 16 (24.2%), and hepatotoxicity - in 9 (13.6%) patients.

Out of 32 patients enrolled in November 2020 - January 2021, 25 (78.1%) patients had culture conversion after one month of the BPAL treatment. The first four patients enrolled in November 2020 were cured.

Conclusions: Preliminary analysis of the first largest cohort of TB patient of the BPAL showed high rates of culture conversion and importance of adequate safety monitoring and management.

OA23-759-21 Metformin as adjunct to anti-TB treatment in adults with pulmonary TB: a randomised clinical trial

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Background: Metformin (MET), by reducing intracellular *M.tb* growth and facilitating phago-lysosomal fusion is suggested as an adjunctive therapy to anti-tuberculosis treatment (ATT). We evaluated whether adding MET to standard ATT reduces time to sputum culture conversion and tissue inflammation in pulmonary tuberculosis (PTB).

Design/Methods: Phase IIB clinical trial, at three sites in India (New Delhi, Pune and Chennai) during 2018-2020, randomized adults with newly diagnosed culture positive PTB to standard regimen alone (HREZ = Control arm) or standard regimen plus daily 1000mg MET (MET-HREZ = MET arm) for 8-weeks of ATT. Primary endpoint was time to sputum culture conversion by liquid culture after 8 weeks of ATT.

Adverse events and plasma cytokine levels in a subset were also recorded. Kaplan Meier estimate and Cox proportional hazard model were used to estimate time and predictors of culture conversion.

Results: Of the 320 patients randomized, 239 (74%) were male, (mean age: 33 and BMI 17), 212 (66%) had bilateral disease on chest radiograph with 54 (18%) showing cavitation. The time to sputum culture conversion was 42 days in MET arm and 41 days in Control arm [HR 0.8, 95% CI (0.624 – 1.019)]. After 8-weeks of ATT, proportion of patients with culture conversion was higher in the Control arm [85% vs 72%, p=0.004]. But, cavitory lesions on chest radiographs [7 (5.3%) vs 18 (12.9%), RR 0.42 (0.18, 0.96), p=0.041] and inflammatory markers like IL-17 α , IL-1 β , IFN- γ and TNF- α were significantly reduced in MET arm (Fig 1).

Higher BMI and lower sputum smear grading were associated with faster sputum culture conversion. Nausea and vomiting were frequent in the MET arm (47 vs 13, p <0.001) and were manageable.

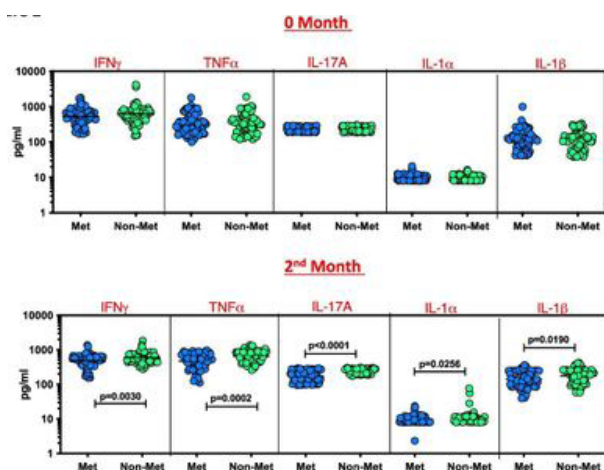


Figure. Plasma levels of pro-inflammatory cytokines in MET arm vs Control arm during 2nd month of anti-TB treatment.

0 Month: MET arm (n=83) and Control arm (n=74)
 2nd Month: MET arm (n=74) and Control arm (n=76)

Conclusions: Addition of MET to standard ATT did not affect sputum culture conversion but diminished excess inflammation thus reducing the lung tissue damage as seen by faster clearance on CXR.

OA-24 Paediatric TB: the way forward

OA24-760-21 Feasibility and yield of systematic TB molecular testing in children with severe pneumonia in countries with high TB incidence

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Background: Tuberculosis (TB) is common in children with pneumonia but is only considered if the child has a history of prolonged symptoms or fails to respond to antibiotherapy, thus leading to missed or delayed TB di-

agnosis. We assessed the feasibility and yield of systematic TB detection using Xpert MTB/RIF Ultra (Ultra) on nasopharyngeal aspirates (NPA) and stools in children with severe pneumonia.

Design/Methods: TB-Speed Pneumonia was a stepped-wedge cluster-randomized trial enrolling children aged <5 years with WHO-defined severe pneumonia in 15 hospitals from 6 high TB incidence countries (Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Uganda, and Zambia). The intervention consisted of systematic Ultra testing on 1 NPA and 1 stool sample at hospital admission. Children were followed-up for 12 weeks.

Results:

Of 1170 children enrolled in the intervention arm – 492 (42.1%) female, median age 11 [6, 20] months, 60 (5.1%) HIV-infected, 289 (24.7%) severely malnourished, median SpO2 at admission 94% [IQR: 88, 97] -, 1141 (97.5%) had NPA collected, 1131 (96.7%) NPA tested with Ultra, 1120 (95.7%) valid Ultra result, and 21 (1.8%) positive Ultra on NPA. 944 (80.7%) children had stools collected, 921 (78.7%) stools tested with Ultra, 905 (77.4%) valid Ultra result, and 16 (1.4%) positive Ultra on stools. Overall, 24 (2.1%) children had a positive Ultra on either NPA or stools. Additionally, 58 (5.0%) children with negative/missing Ultra initiated TB treatment during follow-up (Figure). Microbiological yield was 21/82 (25.6%) for Ultra on NPA alone, 16/82 (19.5%) on stool, and 24/82 (29.3%) on both samples. No severe adverse events related to NPA were reported.

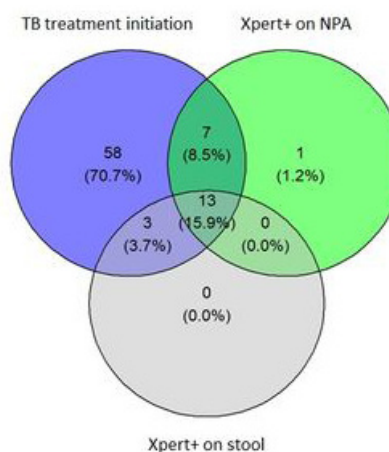


Figure. Microbiological yield of Xpert MTB/RIF Ultra on nasopharyngeal aspirates and stools in children with severe pneumonia - Venn diagram.

Conclusions: In this large multicentric study, 7.0% (82/1170) of children with severe pneumonia were diagnosed with TB in the intervention arm. Combined NPA and stool samples showed high feasibility in this vulnerable population and contributed to microbiological confirmation in 30% of TB diagnoses.

OA24-761-21 Measuring and addressing the childhood TB reporting gaps in Pakistan

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Background: Tuberculosis in children may be difficult to diagnose and is often not reported to routine surveillance systems. Understanding and addressing the tuberculosis (TB) case detection and reporting gaps strengthens national routine TB surveillance systems

Design/Methods: The study design was cross sectional. The study was nationwide in 12 selected districts across Pakistan, each representing a cluster. Health facilities that diagnose and treat childhood TB from all sectors were mapped and invited to participate. Lists of child TB cases were created for the study period (April-June 2016) from all study facilities and compared against the list of child TB cases notified to the national TB surveillance system for the same districts and the same period.

Results: All public and private health facilities were mapped across 12 sampled districts in Pakistan and those providing health services to child TB cases were included in the study. From all private health facilities, 7,125 children were found with presumptive TB during the study period. Of them, 5,258 were diagnosed with tuberculosis: 11% were bacteriologically-confirmed and 89% clinically-diagnosed; only 4% were notified to National TB Control Program. An additional 1,267 children with TB were also registered in the National TB Control Program. Underreporting was measured to be 78%

Conclusions: This is the first nationwide childhood TB inventory study globally and confirmed that childhood TB underreporting is very high in Pakistan. TB surveillance in the country must be strengthened to address this, with particular attention to guiding and supporting general practitioners and pediatricians to notify their TB cases.

OA24-762-21 Characterising drug-drug interactions on QT-interval prolongation in children with rifampicin-resistant TB

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Background: Rifampicin-resistant tuberculosis (RR-TB) involves treatment with drugs that can prolong the QT interval, and the risk may increase with concomitant use of multiple QT-prolonging drugs; however, pediatric data is limited. We assessed QT interval prolongation in children with RR-TB using one or more QT-prolonging drugs.

Design/Methods: Data were from two observational pharmacokinetic studies in South Africa including children <18 years of age routinely treated for RR-TB, with regimens variably including clofazimine (CFZ), moxifloxacin (MFX), bedaquiline (BDQ). Electrocardiograms were performed pre-dose and at various time points between 1- and 10-hours post-dose on pharmacokinetic sampling days. The change in Fridericia-corrected QT (dQTcF) from pre-dose was modeled using non-linear mixed effects. Drug use (yes/no), drug dose (mg), time after dose, body weight, age, and sex were assessed as factors affecting dQTcF.

Results: 76 study children contributed 517 QTcF measures at a total of 113 patient-visits. The median (2.5th-97.5th range) age was 2.8 (0.5-16.0) years; 51 (67%) were <5 years of age. The regimens included CFZ alone (n=40), MFX alone (n=33), CFZ+BDQ (n=12), and CFZ+MFX (n=28). The table below shows the number of QT prolongation events. There were 3 patient-visits with QTcF interval between 450 to 480ms, 4 patient-visits with QTcF interval between 481 to 500ms, and none were >500 ms. In multivariate analysis, CFZ+MFX use was the only significant predictor of dQTcF (p=0.008). The mean dQTcF was 3.6 ms, which increased by 8.9 ms with CFZ+MFX use.

Conclusions: The risk of QTcF interval prolongation in children with RR-TB who received at least one QT-prolonging drug is greater when MFX and CFZ are used together. Future studies understanding exposure-response in children will be helpful for understanding safe and effective doses for multi-drug regimens for RR-TB.

OA24-763-21 High-dose rifampicin with or without levofloxacin for the treatment of paediatric tuberculous meningitis

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Background: Tuberculous meningitis (TBM) is most common among children and associated with high mortality and morbidity, including neurocognitive and neurologic sequelae. In adults, high-dose rifampicin is associated with reduced mortality, and fluoroquinolones can improve treatment outcomes. Data informing pediatric TBM treatment are lacking.

Design/Methods: TBM-KIDS (NCT02958709) is a Phase II open-label randomized trial among children ages 6 months to 12 years in Pune and Chennai, India, and Lilongwe, Malawi with TBM. Participants received isoniazid and pyrazinamide plus:

- High-dose rifampicin (30 mg/kg) and ethambutol (R₃₀HZE, Arm 1);
- High-dose rifampicin and levofloxacin (R₃₀HZL, Arm2); or,
- Standard-dose rifampicin and ethambutol (R₁₅HZE, Arm 3) for 8 weeks, followed by 10 months of standard treatment.

Patients were followed longitudinally to measure functional outcomes (Modified Rankin Scale (MRS)), neurocognitive outcomes (Mullen Scales of Early Learning (MSEL)), and plasma and cerebrospinal (CSF) pharmacokinetics.

Results: Of 1195 children pre-screened, 37 were enrolled. Median age was 72 months, average CSF protein was 109 mg/dl, and 49%, 43%, and 8% had Stage I, II, and III disease, respectively. Median plasma (CSF) rifampicin C_{max} in high-dose arms was 13 ug/mL (0.10 ng/mL) versus 7.2 ug/mL (0.03 ng/mL) in standard-dose arm, with multiple CSF values below the limits of quantification. Adverse events \geq Grade 3 occurred in 58%, 55%, and 36% of children in Arms 1, 2, and 3, respectively, with one death (Arm 1) and six early treatment

discontinuations (4 in Arm 1, 1 in Arm 2, 1 in Arm 3). By Week 8, all children recovered to MRS score of 0 or 1. MSEL scores for most domains improved more quickly and fully in Arms 1 and 2 than Arm 3.

Conclusions: In a pediatric TBM treatment trial, functional outcomes were excellent overall, with a trend towards higher frequency of adverse events but better neurocognitive outcomes in children receiving high-dose rifampicin.

OA24-764-21 Treatment of children and adolescents using bedaquiline and delamanid: results from the endTB study

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Background: Children and adolescents with MDR-TB are under diagnosed and under treated. Few reports exist on the treatment of children and adolescents with newer TB drugs. We assessed the safety and effectiveness of MDR-TB regimens containing bedaquiline and delamanid among children and adolescents.

Design/Methods: The endTB observational study is a prospective, multi-site study. Children and adolescents aged 19 years and below are included in this analysis. We report the frequency and outcomes of clinically relevant adverse events of special interest (AEI) and end of treatment outcomes.

Results: A total of 190 children and adolescents from 14 countries were included (< 5 years: 4, 5-14 years: 20, 15- 19 years: 166), 53% had BMI < 18.5 Kg/m², 6% were HIV positive, 68% previously treated with second-line drugs, 50% had fluoroquinolone resistance, 71% cavity or bilateral disease on chest Xray. Initial treatment contained bedaquiline only (51%), delamanid only (39%) or both (10%) as part of a multidrug regimen. Other frequently used drugs were linezolid (82%), cycloserine (71%), clofazimine (70%) and fluoroquinolones (69%). End of treatment outcomes were 85% success, 5% death, 4% failure, 4% lost to follow and 2% not evaluated. Most common clinically relevant AEIs were peripheral neuropathy, electrolyte depletion and hearing loss with 26 (16%), 24 (15%) and 11 (7%) patients experiencing at least one event respectively.

Two patients (1%) experienced clinically relevant QT interval prolongation which resolved without sequelae. Among patients experiencing hearing loss 4 (36%) resolved, 4 (36%) resolved with sequelae, 1 (9%) did not resolve, and 2 (18%) had unknown outcomes. Among patients experiencing peripheral neuropathy, 14 (54%) resolved, 9 (35%) resolved with sequelae, 3 (11%) did not resolve.

Conclusions: Treatment of MDR-TB with bedaquiline and delamanid is effective and well tolerated amongst children and adolescents. All oral regimens should be scaled up as recommended by WHO for these age groups.

OA24-765-21 Outcomes and safety issues in children with rifampicin-resistant TB treated with shorter all-oral regimens

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Background: Treatment guidelines for rifampicin-resistant tuberculosis (RR-TB) now prioritize shorter regimens without injectables; however, there is limited prospective data on the safety and outcome of such regimens in children.

Design/Methods: This observational cohort study enrolled South African children aged 0-17 years with clinically diagnosed or confirmed RR-TB (2015-2020) routinely treated according to local guidelines. During the study, treatment shifted from the use of 12-18 month injectable-containing to 9-12 months injectable-sparing shorter regimens with routine inclusion of repurposed (linezolid, clofazimine) and novel drugs (bedaquiline). Safety monitoring was conducted throughout. Adverse events were graded for severity, and attribution to RR-TB treatment assessed. Clinical and microbiologic outcomes were documented.

Results: 77 children were included, median age 4.1 years (IQR 1.9-11.4); 6 (7.8%) were HIV-positive. 61 (79.2%) had pulmonary TB (PTB) only, 4 (5.2%) extrapulmonary TB (EPTB) only and 12 (15.6%) both PTB and EPTB. 49 (64%) had bacteriologically confirmed and 28 (34%) clinically diagnosed RR-TB; 14 (18%) were treated for confirmed or probable fluoroquinolone-resistant RR-TB.

The median treatment duration was 12.3 months (IQR 9.2-15.6); 36 (47%) were treated for <12 months and 27 (35%) <10 months. 37 (48%) received all-oral regimens; the median duration of injectables among children receiving them was 93 days (IQR 51-129). Ten (13%) pa-

tients had 11 grade 3 or 4 adverse events attributed to TB medications; linezolid-related anaemia was the most common (5 of 11 [45%]). Of 27 children with confirmed PTB and serial cultures, 16 (59%) were culture-negative by 4 weeks, and 24 (89%) by 8 weeks.

One child transferred out; of the remaining 76, 74 (97%) had a favourable outcome (cure, probable cure or treatment completed) with only 2 (3%) lost-to-follow-up and no deaths or treatment failures.

Conclusions: Children with RR-TB can be successfully treated for shorter durations and with all-oral regimens with excellent treatment outcomes.

OA24-766-21 Improving access to bacteriological confirmation for children under five in nine sub-Saharan countries

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Background: While clinical diagnosis is critical for pediatric TB case detection, bacteriological confirmation is key for early diagnosis and identification of drug resistance. Producing sputum is challenging for children under five years old. Collection of alternative respiratory samples is therefore required but implementation remains limited. We evaluated the feasibility of implementing procedures to collect different samples (expectorated sputum, induced sputum (IS), gastric aspirate (GA), nasopharyngeal aspirate (NPA), and stool) at different levels of the health care system and assessed their contribution to bacteriological confirmation.

Design/Methods: We supported the implementation of sample collection procedures, sample transportation, and Xpert testing in 248 purposively selected health facilities in Cameroon, Côte d'Ivoire, DRC, Kenya, Lesotho, Malawi, Tanzania, Uganda, Zimbabwe. Of the 248 supported sites, 128 were primary health care (PHC) facilities. A pre/post-intervention evaluation on identification of bacteriologically confirmed children under five was performed in 55 of the 128 PHC facilities, for which both pre- (12 months, collected retrospectively) and post-intervention data (prospectively collected between December 2018-December 2020, mean: 18.3 months/site) was available. We compared pre- and post-intervention monthly rates using T-Test for two dependent means. Proportions were calculated using descriptive statistics.

Results: Among children under-five identified with presumptive TB, 57% (10,197/17,755) had a respiratory sample collected, of whom, 66% (6,701/10,197) produced GA. Of the under-five children with presumptive TB, 4% (409/10,197) were bacteriologically confirmed, 71% (292/409) through GA sample testing. Out of 128 PHC facilities, 90.6% (116/128) successfully implemented GA. Among PHC facilities with pre-and post-intervention data available, the site-averaged monthly rate of identification of under-five children with bacteriologically confirmed TB significantly increased by 6.8 folds (p value= 0.00014) in intervention (0.28), as compared to pre-intervention (0.04) period.

Sample Type	Proportion of facilities implementing the collection procedure	Proportion of PHC facilities implementing the collection procedure	Relative proportion of presumptive TB children with a respiratory sample collected per sample type category		Relative proportion of children identified with bacteriologically confirmed TB per sample type category	
			Children 0-4 years	Children 5-14 years	Children 0-4 years	Children 5-14 years
Expectorated sputum	100% (248/248)	100% (128/128)	20.6% (2,099/10,197)	84.0% (10,176/12,116)	20.5% (84/409)	89.9% (902/1,003)
IS	20.2% (50/248)	11.7% (15/128)	2.6% (262/10,197)	1.1% (129/12,116)	2.7% (11/409)	0.6% (6/1,003)
GA	92% (228/248)	90.6% (116/128)	65.7% (6,701/10,197)	13.1% (1,591/12,116)	71.4% (292/409)	8.5% (85/1,003)
NPA	26.6% (66/248)	12.5% (16/128)	5.2% (530/10,197)	1.2% (140/12,116)	3.2% (13/409)	0.6% (6/1,003)
Stool*	10.5% (26/248)	17.2% (22/128)	5.9% (605/10,197)	0.7% (80/12,116)	2.2% (9/409)	0.4% (4/1,003)
Total	N/A	N/A	100% (10,197/10,197)	100% (12,116/12,116)	100% (409/409)	100% (1,003/1,003)

Conclusions: Routine implementation of sample collection procedures is feasible, including GA and stool in PHC facilities, and can improve the identification of under-five children with bacteriologically confirmed TB.

OA24-767-21 Adequacy of the new child-friendly isoniazid, rifampicin and pyrazinamide fixed-dose combination dispersible tablet for TB treatment in children

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Background: The isoniazid/rifampin/pyrazinamide 50/75/150 mg fixed-dose combination (FDC) water-dispersible tablet developed to achieve World Health Organization (WHO) recommended dosages was rollout for tuberculosis (TB) treatment in children.

The aim of this study was to verify that the new tablet achieves pharmacokinetic (PK) reference targets, as well as thresholds for good treatment outcome.

Design/Methods: Children on first-line antituberculosis therapy with the new isoniazid/rifampin/pyrazinamide 50/75/150 mg FDC tablet plus ethambutol for at least 4 weeks had blood samples collected at pre-dose, 1, 2, 4, 8 and 12 hours post-dose. Drug concentrations were measured using validated LCMS/MS and PK parameters calculated by noncompartmental analysis.

The proportion of children with peak concentrations (C_{max}) below minimum adult reference targets (3mg/L for isoniazid, 8 mg/L for rifampin, 20 mg/L for pyrazinamide and 3 mg/L for ethambutol) and threshold of pyrazinamide $C_{max} < 35$ mg/L for poor treatment outcome in adults were examined.

Results: Of 68 children, 41 (60.3%) were male, 14 (20.6%) were younger than 2 years and 34 (50.0%) had HIV coinfection. The median (IQR) plasma C_{max} was 6.6 (4.1-8.5), 7.3 (5.4-9.8), 38.5 (32.1-47.3) and 2.8 (1.8-4.0) mg/L for isoniazid, rifampin, pyrazinamide and ethambutol, respectively. Based on adult reference ranges, low plasma C_{max} was observed in 5/68 (7.4%), 40/68 (58.8%), 2/67 (3.0%) and 23/67 (34.3%) of the children for isoniazid, rifampin, pyrazinamide and ethambutol, respectively. Based on known threshold for treatment outcome in adults, 26/67 (38.8%) children had pyrazinamide $C_{max} < 35$ mg/L. Lower weight-for-age z-score and height-for-age z-score were associated low rifampin C_{max} .

Conclusions: Children treated with the new dispersible FDC tablet achieved target reference ranges of the drugs except for rifampin. The high frequency of low rifampin C_{max} suggests that a higher rifampin dose might be needed.

OA-25 Impact of COVID-19 on TB care

OA25-768-21 Mitigating the impact of the Covid19 pandemic on the delivery of TB services under Project Axshya in India

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Background and challenges to implementation: Project Axshya's TB related project field activities in India came to standstill in 2020 in the wake of COVID19 pandemic and the nationwide lockdown. During the pandemic all medical personnel, project staff and TB centres were roped into the fight against COVID19, placing TB care on the back burner. Project field staff were reluctant to resume duty. Unavailability of public transport minimized the access to health facilities. Presumptive TB patients (PTBPs) hesitated to seek medical care under the apprehension of quarantine. There was a 73% decline in identifying PTBPs, 73% in testing and 64% in treatment initiation in second quarter compared to first quarter of 2020.

Intervention or response: To mitigate the adverse impact, interventions like online training on COVID19 related symptoms and safety measures were initiated. Field staff were provided with masks, sanitizers and PPE kits. Voice clip on differentiating TB & COVID19 symptoms and mode of transmission were shared. Digital platform was used to follow-up with TB patients for treatment completion. Follow-up of PTBPs through stakeholders like village heads for TB testing was initiated. Case finding activities were planned closer to testing centers to get chest X-rays with zero delays. Sputum sample and referrals were sent to testing centres outside containment areas. Focus of field activities was shifted to COVID19 non-containment areas.

Results/Impact: These interventions and collaborative efforts resulted in bringing TB services on the track. PTBPs identification which was 96,870 (Q1 2020) reduced to 25,913 in Q2, was now increased to 68,371 in Q3 and 79,777 in Q4. Similar trend was observed in testing as well as in treatment initiation.

Conclusions: A multi-pronged strategy was adopted to motivate the project staff; digital platform for rigorous follow-up; shifted field activities nearby health facilities for quick accessibility contributed in improving TB related services.

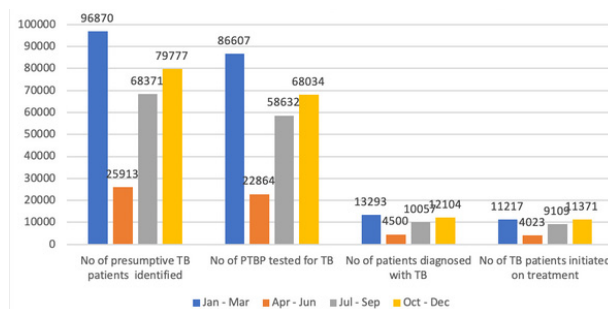


Figure. Project Axshya - TB related services decline due to Covid and project response to mitigate.

OA25-769-21 Barriers and facilitators to accessing and delivering TB services in the Covid-19 pandemic in Nepal

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Background: Tuberculosis (TB) testing fell by 60% globally during the COVID-19 pandemic, including in Nepal. Identifying and addressing barriers and facilitators regarding access to, and delivery of, TB diagnostic and treatment services could enhance care during and beyond the pandemic.

This study explored barriers experienced by people with TB (PTB) and TB care providers (TCPs) and identified strategies to overcome them.

Design/Methods: In March 2021, we conducted in-depth interviews with 43 purposively selected PTB (n=21) and TCPs (n=22) from nine TB-endemic districts in Nepal. Themes and sub-themes were identified and analysed using NVivo-12.

Results: Barriers described by PTB were long journeys on foot to clinics for medicines or testing because of travel restrictions, inadequate psychosocial counselling and job loss. Job loss due to COVID-19 exacerbated financial burden and food insecurity. Fear of contracting COVID-19 caused reluctance of PTB to visit health facilities and a concomitant reported increase in visits to pharmacies to purchase over-the-counter antibiotics to reduce respiratory symptoms. Facilitators of access and medication adherence included nutritional and financial support, provision of counselling, free face-masks and monthly medicines. TCPs reported barriers including households refusing TB screening, limited opening hours of health facilities, inadequate knowledge to dif-

ferentiate and diagnose TB/COVID-19, fear of contracting COVID-19, diversion of TCP including laboratory personnel to COVID-19 response, and delayed test reports. Facilitators included community-based diagnostic and sputum courier services, home delivery of TB medicines, counselling during home visits or by phone, and provision of face-masks and hand sanitizers.

Conclusions: This study provides clear evidence of multiple barriers to accessing and delivering TB services in Nepal during the COVID-19 pandemic. Social protection such as financial and nutritional support to PTB, community-based patient-centred treatment services with counselling support, and prompt training regarding differential diagnosis of respiratory symptoms for TCPs could contribute to overcoming these barriers and improve future resilience of services.

OA25-770-21 Improving access to TB preventative treatment in the era of Covid-19: operational considerations of virtual care initiatives

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Background and challenges to implementation: The implementation of TPT in resource-limited settings is attributable to a plethora of issues encompassing inconsistent commodity supply, socio-economic issues impeding household security, inadequate health care infrastructure and the global COVID-19 pandemic. The deleterious effects of the COVID-19 pandemic have dampened Zimbabwe's National Tuberculosis Program (NTP) aims to reach 90% Treatment Coverage Rate (TCR) from 83% (2019) highlighting the growing importance of TB preventative therapy. The NTP is investigating the operational feasibility of 3HP service delivery and uptake in high burden sites within COVID-19 parameters.

Intervention or response: With 4,100 single dose courses of 3HP, people living with HIV and household contacts of TB patients in six sites were initiated on 3HP. They were given the full three-month course of 3HP at initiation, followed by virtual care models.

Healthcare workers (HCWs) received job aides, updated guidelines, and reporting tools in addition to cellphones and airtime to conduct virtual treatment monitoring in lieu of physical follow-up visits throughout 3HP treatment duration. Despite stringent lockdown measures,

3HP trainings were conducted and implementation commenced in May 2020 in six high-burden TB sites, reaching 220 HCWs.

Results/Impact: Preliminary data over an eight-month period showed a 90% enrolment achievement; with a three-fold increase in PLHIV commencing on TPT. Patients were responsive to virtual care initiatives employed by HCWs, which contributed to high treatment completion rates of 93%, against a baseline of 39% with a 0.08% cessation rate resulting from cutaneous adverse drug reactions.

Challenges associated with TPT initiation were ascribed to fear of adverse drug reactions, lack of integrated monitoring and evaluation systems and perceived high pill burden

Conclusions: The introduction of the 3HP regimen plays an integral role in scaling up TPT uptake among priority populations. Innovative virtual care initiatives are recommended as a sustainable strategy for improved TPT uptake and outcomes during the COVID-19 pandemic.

OA25-771-21 Impact of Covid-19 on private practitioners affecting TB care in India

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Background and challenges to implementation: India's dominant private sector healthcare is the destination for 60-85% of initial TB care-seeking. Joint Effort for Elimination of TB (JEET) is a nationwide program implemented across 406 districts in 23 states, with a key objective to extend quality TB services to patients seeking care in the private sector, building upon successes and learnings from the consortium with PATH, WJ Clinton Foundation and FIND. The COVID-19 pandemic control measures in India, including the 2020 lockdown, drastically affected the notification of TB patients leading to a decline of more than 50%, or about 30,000 monthly cases, in diagnosis in both the public and private sector. We assessed the impact of COVID-19 on private sector healthcare and adaptations made.

Intervention or response: We conducted a rapid survey of 2,750 JEET network providers in Q1 of 2021 across 15 states. Providers were reached in person or telephonically in quarter 2021, and consenting participants interviewed using a 19-questions tool. Questions covered practice before COVID-19, during lockdown periods, and currently, patient turn-out, telemedicine use, testing, and costs of TB service.

Results/Impact: Of the 2,011 providers surveyed (73% response rate), 67% reported reduced daily patient foot-falls, 38% were closed during the lockdown, while 18% offered limited services. In Q1 2021, 11% of practitioners had adjusted working hours, and 1% remained closed. Teleconsultation usage was 16% during the 2020 lockdown, dropping to 6% in 2021. There were no TB testing delays with 92% of providers; and only 9% admitted raising costs to cover costs of PPEs, although 89% have implemented increased infection control. Thirty-two percent of TB providers also offered COVID-19 testing.



Conclusions: COVID-19 restrictions resulted in a significant decline in patient turn-out at private facilities. Most providers were open and costs for TB care remain mostly the same at the end of the first quarter of 2021.

OA25-772-21 Mitigating the Covid-19 impact on TB in Uganda: the role of virtual coordination by Uganda's National TB and Leprosy Programme

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Background and challenges to implementation: The National TB and Leprosy program (NTLP) is mandated to coordinate and monitor TB programming activities nationally. Coordination and review of the performance of donor-funded regional-based Implementing-Partners (IPs) supporting TB programming across Uganda is

conducted through meetings held every quarter. These engagements are facilitated by the USAID Defeat TB, a project providing above-site health-systems strengthening support to NTLP. The COVID-19 national lockdown interrupted physical meetings, posing a challenge to NTLP's oversight role when it needed to respond to a 43% drop in weekly TB case notification nationally. The regional-based IPs were recognized as key in re-invigorating district health teams, nationwide, in addressing the COVID-19 impact on TB programming.

Intervention or response: Defeat TB supported NTLP's stewardship role by providing equipment, internet data, technical back-up and facilitating virtual one-on-one NTLP coordination meetings with the 15 regional-based IPs and district teams. Agreed actions were immediately implemented by the districts with IP support. Weekly TB performance data was generated and submitted to the MOH Emergency Operation Centre (EOC) for analysis. Identified implementation gaps were addressed at virtual bi-weekly meetings.

Results/Impact: Immediate health-system gains included: Identification of programming challenges specific to each of the 13 regions and 136 districts; joint agreements on catch-up strategies with district leaders and IPs from the three lowest-performing regions; performance dashboards generated at the EOC to inform further action. Out of these efforts, there was an average 4.6% increase in weekly TB case notification in the three catch-up regions in the first quarter of 2021. This was achieved at 12% cost of physical engagements.

Conclusions: The virtual platform has become central to Uganda's NTLP's oversight role. IPs can be monitored, supported, and held accountable virtually at greater value for money. Bold adoption of Information Communication and Technology in support of TB program governance will augment efforts towards ending TB.

OA25-773-21 Implementation of integrated TB/Covid-19 screening among presumptive Covid-19 patients referred to an infectious disease hospital laboratory, Lagos, Nigeria

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Background: With the advent of the novel SARS-COV2 virus towards the end of 2019, global reports have shown the negative impact of COVID-19 pandemic on TB case detection in many ways. Since tuberculosis and COVID-19 diseases share overlapping symptoms, integrating COVID-19 and TB screenings in health facilities could be a potential approach to finding missing TB cases. Lagos State was the epicenter of COVID-19 in Nigeria with the first case isolated in February, 2021.

Between January-March 2021, the USAID-funded LON 3 Project implemented by the Institute of Human Virology of Nigeria deployed TB/COVID-19 screening and diagnostic algorithm developed by the National TB program for integrated screening in Nigeria.

The objective of the study was to describe cascade results of joint TB/COVID-19 screening among presumptive COVID-19 patients referred to COVID sample collection Laboratory of the Infectious Disease Hospital, Lagos, Nigeria.

Design/Methods: Between Jan-March 2021, TB/COVID-19 algorithm was deployed to central covid-19 sample collection laboratory of the infectious Disease Hospital and used by trained screening officer to screen patients referred for COVID-19 test based on presumed COVID symptoms. Those with symptoms of TB were tested using genexpert or chest X-ray. Patients' demographic and clinical cascade details were documented in screening register and subsequently entered into Microsoft Excel for descriptive analysis.

Results: Of the documented 115 presumptive COVID-19 patients, all were jointly screened for COVID-19 and TB using NTP algorithm, and 43 (37%) were found to have TB symptoms. Of the 43 presumptive TB patients, all were tested for TB (Genexpert and chest X-ray); 16(37%) were confirmed positive for TB; 33(29%) were confirmed as COVID-19 positive while 12(36%) were TB-COVID-19 co-infected.

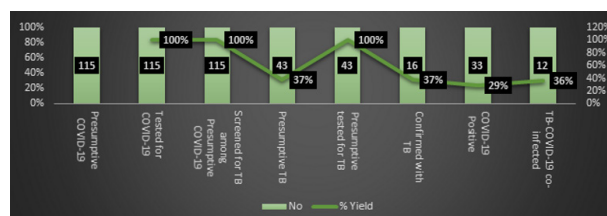


Figure. Cascade of intensified case finding among presumptive COVID-19 patient, Jan-Mar 2021.

Conclusions: Tuberculosis yield among presumptive COVID-19 patients in Nigeria is high and implementation of TB/COVID-19 screening presents a golden opportunity to intensify TB case finding in this population. The algorithm should be deployed for use nationally.

OA25-774-21 Infection control unit in Mumbai, India, strengthens Covid-19 infection control practices in health institutions

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Background and challenges to implementation: As of March 2021, Mumbai, a major metropolis in India, reported >300,000 COVID-19 cases and 11,606 deaths. Mumbai also reported 60,597 tuberculosis (TB) cases in 2019.

SHARE INDIA, the Centers for Disease Control and Prevention (CDC), and Municipal Corporation of Greater Mumbai (MCGM) established a multi-disciplinary airborne infection control unit (AICU) in 2016 to build institutional capacity and strengthen AIC measures in primary and secondary healthcare facilities (HCF) in ten municipal wards of Mumbai. The COVID-19 pandemic highlighted the importance of implementing infection prevention and control (IPC) at HCFs. We report on the pandemic's effect on uptake of IPC practices.

Intervention or response: MCGM's AICU provided on-site AIC training, periodic assessments, intensive follow-up, and mentorship for 313 HCF. Baseline and follow-up assessments were scheduled to understand improvements in IPC practices. A standardized 41-indicator monitoring tool based on national guidelines assessed IPC measures. During the pandemic, the AICU mentored staff by phone to strengthen IPC practices in HCF.

Results/Impact: Baseline assessments were initiated in October 2016 and four follow-up assessments were completed before the COVID-19 pandemic started in March 2020. A fifth follow-up assessment was conducted during January-March 2021 in 313 HCF when lockdown restrictions were lifted. Comparison between the 4th and 5th follow-up showed that AIC compliance was greatest for indicators regarding use of personal protective equipment: N-95 respirator use improved by 22%. Environmental indicators were unchanged as construction/remodelling halted during the lockdown. Some administrative measures improved: crowd management by 16% and use of outside space for social distancing by 17%. Both triage measures, crucial in preventing TB and COVID-19 transmission, were implemented in less than 50% of HCF. (Table 1)

Assessment indicators	AIC compliance pre-COVID-19 pandemic					AIC compliance during COVID-19 pandemic
	Base-line	1 st follow up	2 nd follow up	3 rd follow up	4 th follow up	5 th follow up
Crowd management	48%	52%	55%	58%	63%	79%
Use of outdoor space for social distancing	38%	39%	45%	50%	54%	71%
Triage measures – Screening patients for cough upon entering the facility	14%	43%	46%	48%	48%	50%
Triage measures - Separating coughing patient from others	3%	8%	11%	12%	10%	19%
Triage measures - Fast tracking of coughing patient	9%	29%	35%	51%	49%	47%
Air changes per hour are above 12 in high-risk areas	97%	98%	96%	97%	97%	97%
Use of N-95 respirators correctly	29%	53%	58%	49%	51%	73%

Table 1: Changes in compliance with airborne infection control measures after AIC unit assessments in Mumbai healthcare facilities (n=313)

Conclusions: The AICU built capacity of HCF to implement IPC practices. Use of personal protective equipment improved during the pandemic, but triaging symptomatic individuals at HCF still needs reinforcement.

E-POSTER SESSION (EP)

Chasing SARS-CoV-2

EP-11-197 Seroprevalence of SARS-CoV-2 antibodies and associated risk factors in Zambia: a population based study

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Background: COVID-19 has been the most important public health concern worldwide during 2020-2021. In sub-Saharan Africa, our understanding of transmission patterns, disease severity, and risk factors for infection remains limited. The TREATS-COVID study is nested within the TREATS TB Prevalence survey (TBPS). We aimed to measure the sero-prevalence of SARS-CoV-2 infection, and investigate associated risk factors, in a peri-urban community with high prevalence of TB/HIV co-infection in Zambia.

Design/Methods: A random sample of 3592 individuals aged ≥ 15 years was enrolled in the TBPS and were eligible for antibody testing. Sampling was structured according to geographically-defined blocks of residence of around 150-200 households. Randomly selected blocks were covered one-by-one between October 2020 and March 2021, all households in a block were visited and all those aged ≥ 15 years invited to participate. Antibodies against SARS-CoV-2 nucleocapsid protein were detected using Abbott ARCHITECT SARS-CoV-2 IgG assay. A questionnaire was administered to collect information on potential risk factors for SARS-CoV-2 infection. Multivariable logistic regression was performed to assess risk factors.

Results: To date results for SARS-CoV-2 antibody testing are available for 2,977/3,592 (82.2%) individuals. Overall 400/2,977 (13.4%) individuals tested positive for IgG antibodies. Sero-prevalence was similar in men and women (12.6% vs 14.0%); ranged from 9.7% in individuals aged 15-19 to 16.1% in those aged 40-49, and there was no clear variation by household size. There was strong evidence ($p < 0.001$) of variation by time of enrollment, with prevalence varying from 2.8% (95% CI 0.8 - 4.9) among those recruited early December 2020 to 33.7% (95% CI 27.7 - 39.7) among those recruited mid-February 2021 (figure 1).

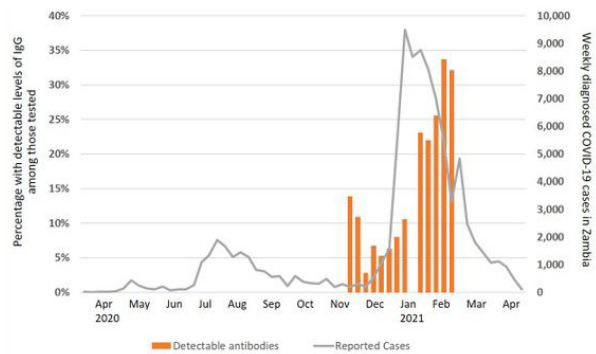


Figure 1. Weekly % of participants between 19/11/2020 and 24/02/2021 with detectable levels of SARS-CoV-2 IgG antibodies in a suburban community in Zambia against the background of nationwide weekly reported COVID-19 cases.

Conclusions: Seroprevalence of SARS-CoV-2 antibodies showed increasing levels during the second wave of infections in our semi-urban community. Using seroprevalence data indicates that community transmission in a typical peri-urban community is greater than is being recorded in national data.

EP-11-198 Do self-taken swabs yield more accurate rapid diagnostic results in SARS-CoV-2 than those taken by healthcare workers?

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Background: Large scale self-testing with rapid diagnostic tests (RDTs) for SARS-CoV-2 has been implemented in the U.K. to enable society to reopen. Pilot studies (including in Liverpool) saw issues with a drop in expected sensitivity when used in the general population. From existing data it is not clear if this is due to poor sampling, poor technique when running the test or incorrect reading of the results. We investigated what is the sensitivity and specificity of self-taken swabs compared to those taken by trained healthcare workers (HCW) when performing a RDT for SARS-CoV-2, and what sensitivity and specificity does this give compared to PCR?

Design/Methods: Adults with symptoms of SARS-CoV-2 were recruited at a drive-through testing centre in Liverpool as part of the Facilitating Accelerated Clinical Evaluation of Novel Diagnostic Tests for COVID -19 (FALCON). Participants self-administered their throat/

nasal swab following written instructions without advice or supervision. A HCW then took a UTM swab for PCR testing and a further throat/nasal swab for RDT testing. RDTs were run in a Cat 3 laboratory by blinded trained staff and read by two trained readers. PCR on UTM swabs was run to compare sensitivity and specificity against.

Results: 250 participants were recruited up to May 2021. Preliminary results showed 90.4% of participants had agreement between the two swabs, 7.2% did not agree and 2.4% had incomplete RDT results. In 3.2% the self-taken swab was positive and the HCW taken swab negative; in 4% the RDT was negative on the self-taken swab and positive on the HCW taken swab.

Conclusions: There is no significant difference in RDT results whether swabs are self-taken or taken by a HCW. The source of poor test performance may therefore be when running or reading RDTs which is an area that needs further research and training.

EP-11-199 Continuous quality monitoring of the Xpert® Xpress SARS-CoV-2 N2 and E gene targets

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Background: The Cepheid Xpert® Xpress SARS-CoV-2 (Xpress) assay is widely used in South Africa for molecular diagnosis of COVID19. Cepheid confirms SARS-CoV-2 polymorphisms in the N2-gene region, may affect the assay, but coverage remains 100% for the E-gene target and >98% for the N2-target (*in silico* analysis). Changes in N2- and E-gene target frequencies and median cycle threshold (Ct) across national data were investigated.

Design/Methods: Xpress test results obtained from the National Health Laboratory Services' (NHLS) laboratory information system were analysed using STATA SEv16. N2- and E-gene target frequencies were monitored over the COVID19 pandemic. Ratio changes for single E-gene targets (i.e. N2-gene drop-out) were reviewed and numbers of single E-gene results with Ct<30 were reported.

Results: Xpress testing contributes ~17% SARS-CoV-2 tests reported by NHLS, with 665,945 Xpress tests conducted over 12 months since April 2020. Of these, 133,986 (20%) detected SARS-CoV-2 (26% first wave [July 2020]; 30% second wave [January 2021]). Figure 1 outlines the number of Xpress tests reporting SARS-CoV-2 positivity, and those tests reporting single E-gene targets only (n=1,402, 1.04%). Over various lockdown levels and during the two infection peaks, the frequen-

cy of single E-gene target detection showed similar trends to the number of positive test results. The ratio of E-gene targets to total positive tests averaged 1.15% (0.69%-1.73%) with overall median Ct=39.94 (Ct range=12.4-45). The ratio has increased to >1.7% since February 2021. Notably, 16/22 single E-gene results were reported from the North West Province (May 2021), of which 2/6 reflected Ct<30 and were received from the same facility <1month apart.

Conclusions: Continuous quality monitoring of commercial SARS-CoV-2 assays in use, their gene target frequencies and Ct values are an important component of laboratory diagnostic surveillance. The potential cluster of Xpress single E-gene specimens described here, warrants further investigation, including specimen retrieval for N2-gene sequencing.

EP-11-200 Strengthening infection control capacity to prevent Covid-19 transmission in a tertiary hospital in North Sumatera, Indonesia

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Background: COVID-19 pandemic is significantly affecting the health personnel in Indonesia with high mortality rate. The strength of infection prevention and control for hospital-related transmission plays important roles in COVID-19 transmission.

However, the hospital's infection control (IC) situation only focuses on nosocomial infection with hand hygiene which led to immediate urges to strengthening its capacity. This study aims to assess the effectiveness of ad-hoc IC-tracing team to prevent the COVID-19 infection in the hospital.

Design/Methods: A descriptive cohort study was carried out in the hospital from June to December 2020. Covid-19 exposed cases were retrieved from tracing and close contacts self-administered questionnaire. IC-tracing team continued to follow-up over the telephone interview to clarify and encourage those who were exposed for swab PCR testing.

Results: Of 3274 total hospital's staffs, 1704 (52%) were exposed to Covid-19. Of those who were exposed, 229 (13.4%) were confirmed positive cases with respiratory tract infection (72.8%). The majority cases were female (70%), aged less than equal to 50 (83%), health personnel (89%), with overweight comorbidity (68.1%).

The transmission source was from hospital (54%) with where 73.2% were transmitted among the health personnel and 28.2% were infected from patients. Among those healthcare personnel infected, 4.7% nurses and 8.4% doctors were work in the COVID-19 wards.

Background and challenges to implementation: COVID-19 pandemic is significantly affecting the health personnel in Indonesia with high mortality rate. The strength of infection prevention and control for hospital-related transmission plays important roles in COVID-19 transmission. However, the hospital's infection control (IC) situation only focuses on nosocomial infection with hand hygiene which led to immediate urges to strengthening its capacity. This study aims to assess the effectiveness of ad-hoc IC-tracing team to prevent the COVID-19 infection in the hospital.

Conclusions: Most of the positive for COVID-19 health personnel were not infected from the COVID-19 patients. Hence, it indicates the need to further improve the hospital tracing program along with the socialization for COVID-19 self-identification among health personnel.

EP-11-201 Findings from Xpert® Xpress and SARS-CoV-quality assurance programme: interventions to limit contamination

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Background: The GeneXpert laboratory footprint decentralised across 165 testing sites, used primarily for tuberculosis disease diagnosis, is being utilised to support the COVID-19 response in South Africa. To support quick scale-up of the Xpert® Xpress SARS-CoV-2 assay, a verification program to ensure the assay was fit-for-purpose and an External Quality Assurance (EQA) program for quality monitoring, were established. Xpert® Xpress SARS CoV-2 assay dried culture spot (DCS) verification and EQA programs were provided by SmartSpot® Quality.

Design/Methods: The verification panel consisted of two DCS cards of non-infectious, inactivated controls (negative and positive-COVID-19 specimens) per module, to meet minimum verification requirements for expected functionality. The EQA DCS panel, consisting of four single DCS-cards per instrument, was provided biannually (Phase 1 and 2) in 2020 and performance reported as a percentage. Both verification and EQA assessment results were uploaded as comma separated files to the TBGxMonitor® (www.tbgxmonitor.com) portal.

Results: 100% submission rate was reported for both Phase 1 and 2 EQA panels. The EQA programme reported an average of 95% correct results for both Phase 1 and 2 in 2020. Of note, Challenges reported included detection of pre-analytical contamination on negative and single gene targets samples. A total of 2/80 (2,5%) negatives reported as positive for phase 1 and 14/188

(7,4%) single targets reported both targets. Analysis of cycle threshold (Ct) values indicated delayed detection which signifies small levels of RNA. Average Ct for contamination reported in phase 1= 41,0 and for phase 2=37,2.

Conclusions: Overall, the verification and EQA programs for Xpert® Xpress SARS-CoV-2 assay were implemented successfully. Identified problems have allowed the programme to introduce Good Laboratory Practice (GLP) training measures to minimise pre-analytical contamination as this may impact COVID-19 public health response.

EP-11-202 Clinical Presentation and Diagnosis of Tuberculosis and COVID-19 among ambulatory adult HIV positive patients in rural KwaZulu-Natal, South Africa

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Background: Real-world data describing Tuberculosis (TB) and COVID-19 diagnosis in high burden HIV-TB settings is important for ongoing understanding of the impact of the COVID-19 pandemic on vulnerable populations. We describe the effect of a TB and COVID-19 diagnostic package among a population of ambulatory HIV positive patients in KwaZulu-Natal, South Africa.

Design/Methods: Prospective study including adult HIV positive patients presenting with at least one TB symptom between 19th October 2020 and 30th April 2021 in Eshowe, South Africa. All patients received clinical examination, AlereLAM, sputum Xpert MTB/RIF, culture (sputum or urine) and chest X-ray. Optional SARS-CoV2 PCR testing (nasopharyngeal or oropharyngeal) was offered. TB diagnosis was defined as initiation on TB treatment. Cough and fever were considered as TB/COVID-19 overlapping symptoms. Night sweats and weight loss were considered as TB symptoms only. Patients presenting with additional COVID-19 related symptoms were those with any of sore throat, rhinorrhoea, otalgia, dysgeusia, anosmia, myalgia, arthralgia, fatigue, headache, abdominal pain, vomiting or diarrhoea.

Results: 95 patients were included. Of them, 71 patients (74.7%) were investigated for both TB and COVID-19 (median CD4 count 405 cells/μL [IQR: 205-613]) with 70 presenting with TB/COVID-19 overlapping symptoms and 1 with TB symptoms only. Overall, 41/71 (57.7%)

presented with additional COVID-19 symptoms. In total, 19 (26.8%) were diagnosed with TB, 3 (4.2%) were diagnosed with COVID-19, and 1 (1.4%) was diagnosed with TB and COVID-19. Three of the four patients diagnosed with COVID-19 presented with at least one additional COVID-19 related symptom. COVID-19 was diagnosed in 3/41 (7.3%) patients presenting with TB and COVID-19 symptoms and in 1/30 (3.3%) patients who did not present with additional COVID-19 symptoms.

Conclusions: Based solely on clinical signs and symptoms, it is difficult to differentiate COVID-19 and TB disease. While this dual pandemic is rampant, additional diagnostic tests are needed to provide best patient care.

EP-11-203 Potential of the interferon-gamma and interleukin-2 signature in monitoring SARS-CoV-2 infection

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Background: Understanding immune protection against SARS-CoV-2 infection needs not only antibody testing but also T-cell response evaluation.

Design/Methods: We performed CoV-iSpot (GenID GmbH, Germany), which detects IFN- γ and IL-2 produced by SARS-CoV-2-specific activated T-cells, in 35 blood samples from patients and healthcare workers (HCW) at the Germans Trias i Pujol University Hospital (Spain) from July 2020 onwards. Samples were grouped depending on their SARS-CoV-2 infection history:

1. Controls consisted of HCW with a negative PCR at sampling and no record of positive PCR and/or IgG;
2. SARS-CoV-2 positive were non-hospitalized HCW and hospitalized patients with positive PCR at sampling;
3. Past COVID-19, were patients with a history of mild or severe COVID-19 that were PCR negative at sampling and with the last positive PCR being more than three months old.

Results: Due to non-valid test results, we excluded five samples from the analysis. Out of the twelve SARS-CoV-2 positives samples, seven (58.3%) came from hospitalized patients with mild/severe COVID-19 and the remaining five (41.7%) from non-hospitalized HCW.

Overall, 50% of the samples tested had a positive CoV-iSpot result, being the majority (86.7%) from individuals with past or present SARS-CoV-2 infection (Table 1). All samples from patients with past COVID-19 and the majority of samples from present COVID-19 (58.3%)

had a positive test with response to both cytokines. Preliminary results show that IFN- γ responses were higher and more frequent than IL-2 (not statistically significant).

	IFN- γ	IL-2	IFN- γ & IL-2	CoV-iSpot test
Overall (n=30)	14 (46.7)	12* (40.0)	11* (36.7)	15 (50.0)
Controls (n=15)	2** (13.3)	1** (6.7)	1** (6.7)	2** (13.3)
SARS-CoV-2 positive (n=12)	9 (75.0)	8* (66.7)	7* (58.3)	10 (83.3)
Past COVID-19 (n=3)	3 (100)	3 (100)	3 (100)	3 (100)

*One sample was borderline for IL-2. **One was a sample from a HCW that had been vaccinated with Pfizer-BioNTech COVID-19 vaccine; the second dose was administered more than 30 days before sampling.

Table 1. Positive test results (%)

Conclusions: T-cell immunity should not be overlooked when evaluating SARS-CoV-2 infection. The high number of double-positive results in the CoV-iSpot, states the importance of detecting cytokines other than IFN- γ , such as IL-2 and potentially IL-17, that could be useful to monitor the immune response against this new viral infection as well as the immunization after vaccination.

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EP-11-204 Prevalence of pulmonary TB in a cohort of patients with a history of Covid-19 in Lima, Peru

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Background: Tuberculosis (TB) prevalence among COVID-19 patients has been described in range 0.5% - 4.5%. Although there are few studies of TB in survivors of COVID-19, it is undeniable that there is an interaction between these two infections. We conducted this study in Lima, Peru to describe the TB prevalence among COVID-19 survivors.

Design/Methods: From January to April 2021, RT-PCR confirmed COVID-19 survivors from were screened using digital X-ray and read by artificial intelligence (CAD4TB

automatic detection system). Those with a CAD4TB score of ≥ 50 or respiratory symptomatic (cough ≥ 7 days) were tested by Xpert MTB / RIF Ultra.

Results: Of 731 COVID-19 screened survivors with median age of 48 years old (range 18 – 88), 405 (58%) were women, 136/731 (48%) were symptomatic respiratory, 2 (0.3%) reported previous TB, 48 (6.6%) reported diabetes and none reported HIV history.

From people screened by chest X-ray, 162 (22%) had an abnormal radiograph of whom 4 (2.5%) were Xpert positive (TB rate notification was 547 cases per 100000) and none were rifampicin resistant. From those four Xpert confirmed TB, 2 (50%) were not symptomatic respiratory and only 2 were culture positive. Two of bacteriological confirmed TB culture negative patients had traces in Xpert result of whom one of them remains under observation and not received treatment.

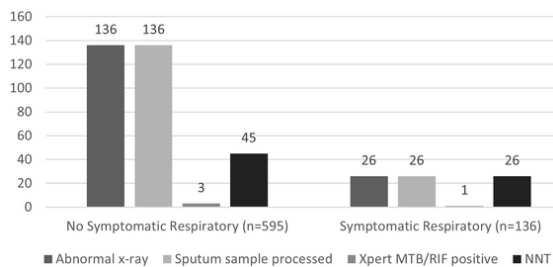


Figure. NNT among symptomatic respiratory vs non-symptomatic respiratory.

Conclusions: A considerable TB prevalence was found among COVID-19 survivors, surprisingly higher than national TB case notification. In the context of a country with a high TB burden, it is necessary to identify high-risk populations such as COVID-19 survivors.

EP-11-205 Face mask and risk of CO₂ retention in COPD during Covid-19

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Background: COPD is a common, preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

In the ongoing pandemic of covid-19 doubts have been raised regarding the use of face-mask as it directly increases the resistance of the respiratory system.

Design/Methods: We included 100 patients of COPD on regular follow-up and treatment. The severity of COPD at the time of inclusion was as per the GOLD criteria: GOLD B & GOLD C. Patients were evaluated and were advised to wear face-mask regularly. After 4-6 weeks the patients were called for follow-up and evaluated for changes of CAT scores. DASI index was calculated in all study subjects. ABG was performed in those with exacerbation requiring hospitalisation.

Results:

- Our study population was male dominated with 70% males and 30% females
- Average age group in our study population was 50±6 years (p value<0.01)
- Average CAT score on initial evaluation was 30±5 (p value<0.01)
- 5 patients had developed an episode of acute exacerbation of COPD during the time of study and required hospitalisation
- Average PCO₂ levels in hospitalised patients was 70±5 mmHg (p value<0.1)
- There was no significant change noted in CAT score post evaluation after 4-6 weeks with average CAT scores being 30±4 (p value<0.01)
- There was no change in physical quality of life as measured by DASI index
- Incidence of covid-19 was approximately 1% with only one study subject developing covid-19 during the study period

Conclusions: It can thus be conclusively said that face-mask does not cause hypercapnia in COPD patients provided proper techniques are followed in regards to wearing the mask and its washing/cleaning. Also the incidence of covid-19 is significantly lower in COPD patients wearing face-mask regularly.

EP-11-206 Mortality among TB-Covid-19 co-infected patients at high-volume health facilities in Uganda

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Background: Uganda is among the 30 high TB/HIV burden countries with an estimated TB incidence of 200/100,000 population (WHO Global TB report, 2020). Uganda's TB Mortality rate stands at 16/100,000 among HIV Negative patients. The influx of COVID19 in March 2020, coupled with Government Lock-down negatively affected access and utilization of TB Services in Uganda hence worsening the situation. During the COVID19 Lockdown period, TB Focal persons at 16 Referral Hospitals in Uganda identified that there was an unusual pattern of TB patient presentation and subsequent death.

This paper describes the mortality among TB-COVID19 co-infected patients at high volume health facilities in Uganda.

Design/Methods: Health Workers on TB Wards identified and documented TB clients on appointment for drug refill, patients admitted on ward and those in ART Clinics. They assigned a person to re-screen TB patients for signs of COVID19.

Patients with symptoms had a sample taken off and analyzed in the laboratory, results were returned to the patients and care givers. Summary data was entered in MS Excel and analyzed for Case fatality. A comparison between general TB mortality as well as TB-COVID Co-Infection Mortality was done

Results: The study revealed that from March 2020 to March 2021, a total of 4,984/6,026 (83%) TB Cases, were screened for COVID19, 57 (1.1%) tested positive for COVID19 and 12 (211/1,000) Died. This is higher than the general TB mortality rate (73/1,000 TB cases) and higher than the country's COVID 19 mortality rate (8.2/1,000 cases).

Conclusions: Two-tiered screening at different points of entry helps to identify the potential clients for COVID Testing, Vigilance of TB Focal persons supplements identification of potential co-infected patients. TB-COVID patients are more likely to die than if they had TB or COVID alone. Bidirectional testing for COVID and TB could save lives with early initiation of TB/ COVID treatment.

The latest Xpert developments

EP-24-328 Evaluation of the Xpert MTB/XDR assay in Uzbekistan: preliminary results

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Background: Drug resistance testing is important for accurate diagnosis and appropriate treatment of tuberculosis patients. We report preliminary results of

the Xpert MTB/XDR assay (Cepheid, USA) evaluation study for detecting resistance to isoniazid (INH), capreomycin (CM), fluoroquinolones (FQs), and second-line injectable drugs (SLID) in sputum specimens which evaluated the concordance between the results of Xpert MTB/XDR and that of first and second-line phenotypic drug susceptibility testing (DST) and line probe assay (LPA) for first and second-line drugs.

Design/Methods: Two sputum samples were submitted to the laboratory per patient. The first sample was tested on Xpert MTB/RIF Ultra, and those with rifampicin resistance were tested using the Xpert MTB/XDR test. For a second specimen from the same patient, a culture followed by MGIT-Bactec DST test was performed, as well as LPA testing using Genotype MTBDR plus, V2 and Genotype MTBDR SL, V2.

Results: We analyzed preliminary data from 45 samples (150 planned sample size) which were tested in NRL Uzbekistan from January – April 2021. Among the RR samples tested by Xpert MTB/RIF ULTRA, MTB was detected among 43 samples by Xpert MTB/XDR test. Two samples were not found to have the MTB complex when tested with Xpert MTB/XDR assay. The results for only those specimens with full results are presented in the table. Sensitivity and specificity for INH, FQL and CM was 100%. Sensitivity for AM was 100% and specificity was 97%.

		Result as per the gold standard		
		Resistant	Not resistant	
Results of Xpert MTB/XDR	Isoniazid	Resistant	34	0
		Not resistant	0	2
	Fluoroquinolones	Resistant	16	0
		Not resistant	0	22
	Amikacin	Resistant	1	1
		Not resistant	0	29
	Capreomycin	Resistant	1	0
		Not resistant	0	30

Conclusions: Preliminary results demonstrated excellent performance of the Xpert MTB/XDR assay for the detection of INH, FQ, and SLID resistance on sputum samples. We expect to complete the study and present the updated results in the Union conference.

EP-24-329 GeneXpert testing and utilisation rates decreased by a quarter after the Covid-19 pandemic in Ethiopia

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Background and challenges to implementation: Ethiopia reported the first case of COVID-19 on March 13, 2020. The restrictions of movement and engagement of tuberculosis (TB) staff in COVID19 response activities are among the major factors potentially affecting TB case finding and delays in diagnosis and TB notification. We evaluated the impact of COVID-19 on GeneXpert (GXP) testing, utilization, and TB case notification in Ethiopia after the emergence of COVID-19.

Intervention or response: From 127 health facilities data were collected on GXP testing and utilization through the GXP connectivity. The expected throughput was calculated based on 10 tests/GXP/day for 22 days/month, over the period of three years, January 2018-December 2020. Performances were summarized in six months interval. The GXP utilization, positivity rate, the rate of decline of testing and the TB case detection were evaluated before and after COVID-19 in Ethiopia.

Results/Impact: During the three years period 914400 tests were expected, 455993 tests were conducted with the overall utilization rate of 49.9% (95% CI: 49.2-50.6%). There was 50397 MTB detected tests with 11.1% (95% CI: 9.6-12.5%) positivity rate. During January 2018-December 2019, the annual declining rate of the GXP testing was 4.6%. After December 2019, the rate of decline increased to 29.4% during January-June 2020, and 20.2% during July-December 2020. The GXP utilization rate was 63% during the January-June 2018 and 2019 but lowered thereafter: 37% (95% CI:36.3-37.9%) in January-June 2020, and 30% during July-December 2020. The TB cases detected using GXP declined by average of 18.2% (95% CI:17.0-19.3%) during January 2018-December 2019, as compared to the declining rate of 22.2% (95% CI: 21.2-23.2%) in the period then after.

Conclusions: After the emergence of COVID-19 in Ethiopia, GXP testing, utilization and TB case detection declined by about one-fourth. Hence, the TB screening, specimen transportation and TB/COVID-19 diagnostic integration needs to be strengthened.

EP-24-330 Comparison of three centrifuge-free stool processing methods for Xpert Ultra testing in children with presumptive TB

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Background: The use of Ultra on stool samples requires laboratory sample processing to remove PCR inhibitors and debris. FIND and the TB Speed consortium are conducting two diagnostic accuracy studies to assess the performance of three centrifuge-free methods for use in resource-limited settings, the Simple One Step Stool (SOS), Stool Processing Kit (SPK) and Optimized Sucrose Flotation (OSF). We present results of pooled data analysis from both studies.

Design/Methods: We enrolled presumptive TB children <15 years in 6 tertiary hospitals from 4 TB, TB/HIV high-burden countries (India, Uganda, South Africa and Zambia). Each participant gave at least one respiratory sample and one stool. We assessed the sensitivity and specificity of each method and the percent agreement on positive and negative results using culture-confirmed TB or Ultra positive result from a respiratory sample as a reference standard.

Results: Between December 2019 and February 2021, we enrolled 513 children and 409 (Median age: 2.2 years; 20% HIV-infected) with a stool sample tested with at least two methods were included in the analysis. Sensitivities of SOS, SPK and OSF were respectively 50% (95% CI; 37 - 63), 52% (38 - 66) and 45% (32 - 59) and specificities were 98% (95 - 99), 97% (94 - 98) and 98% (95 - 99). The proportion of indeterminate results was 9.6% for SOS, 11.5% for SPK and 12% for OSF (Table).

	Ultra/SOS	Ultra/SPK	Ultra/OSF
Sensitivity (% 95CI ; n/N)	50% (37 - 63) 25/50	52% (38 - 66) 23/44	45% (32 - 59) 22/49
Specificity (% 95 CI ; n/N)	98% (95 - 99) 275/282	97% (94 - 98) 263/271	98% (95 - 99) 260/266
Trace among positive (n/N ; %)	6/25 (24%)	7/23 (30%)	5/22 (23%)
Invalid (n/N ; %)	30/405 (7.4%)	32/390 (8.2%)	25/391 (6.4%)
Error (n/N ; %)	9/405 (2.2%)	13/390 (3.3%)	22/391 (5.6%)

Table: Performance of each stool processing method compared to culture and Ultra as reference standard

Amongst 368 children having a stool tested with the 3 methods, 37 (10%) samples were positive by at least one method, and 19 (5.1%) were positive in all.

Conclusions: The three centrifuge-free methods showed similar diagnostic accuracy. Further larger studies to confirm these findings and assess feasibility and costing are ongoing.

EP-24-331 Utility of Xpert MTB/RIF Ultra, digital chest radiography and urine LAM in the diagnosis of TB in HIV-positive individuals: a randomised controlled trial

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Background: Tuberculosis (TB) is a leading cause of mortality among HIV positive individuals. Accurate algorithms are needed to achieve early TB diagnosis and reduce mortality. We investigated the use of chest radiography (with computer-aided diagnosis software [CAD]) in combination with Xpert MTB/RIF ultra and urine lipoarabinomannan (LAM) for diagnosis of TB in ambulatory HIV positive individuals.

Design/Methods: This was an individually-RCT with a 2 by 2 factorial design (XACT-TB trial, registration number ISRCTN77241966). Participants were randomly assigned to four arms; Arm 1 - "No-Xpert-Ultra/No-chest radiography", Arm 2 - "No-Xpert-Ultra/Chest radiography", Arm 3 - "Xpert-Ultra/No chest radiography" and Arm 4 - "Xpert-Ultra/Chest radiography". Qure.ai qXR CAD software was used for interpreting x-rays. All trial arms received urine LAM testing for TB. Participants were followed up at day 28 and 56 to assess for TB treatment initiation, hospital admissions and vital status.

Results: We randomised 640 participants. Bacteriological TB treatment initiations at day 28 by individual arm were Arm-1 (7.1% [11/154]), Arm-2 (6.5% [10/154]), Arm-3 (7.1% [11/154]) and Arm-4 (5.2% [8/154]) and between Xpert group (6.2% [19/309]) vs Xpert-Ultra group (6.8% [21/308]), risk ratio 0.90 (95% CI:0.49-1.64, p=0.736). By day 56, there were higher all TB treatment initiations in the x-ray group (14.0% [43/309]) compared to the No-Xray group (9.4% [29/309]), risk ratio

1.49 (95% CI: 0.95-2.32, p=0.079). Qure.ai software identified more bacteriologically confirmed TB cases 19/24 (79.2%) than human readers 14/24 (58.3%). Urine LAM contributed additional to 6% (5/83) to all patients treated for TB. By day 56 there were 8/640 (1.3%) deaths overall and 26/640 (4.3%) hospitalisations and there was no difference in the arms, p=0.417.

Conclusions: The Xpert MTB/RIF Ultra performed similar to GeneXpert. X-rays are useful for TB screening and CAD software out-performed human readers, but impact of x-rays on probable false positive TB treatment initiation should be mitigated by additional use of host response markers to TB disease.

EP-24-332 Pooling sputum for Xpert MTB/RIF and Xpert Ultra testing during the Covid-19 pandemic in Lao People's Democratic Republic

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Background: The world is facing an unprecedented health crisis due to the Covid-19 pandemic. Due to lockdowns, quarantines and diversion of resources worldwide, National Tuberculosis Control Programmes need to be innovative to maintain continuity of essential services for people affected with TB during the pandemic.

Design/Methods: Four sputum samples were pooled together and tested with a single test using the GeneXpert® system (Cepheid Sunnyvale, CA, United States). We tested samples using Xpert MTB/RIF assay and repeated the survey using Xpert Ultra assay. The pool results were compared with the individual MTB/RIF results to determine if the pool result were in agreement with individual samples. We explored changes in the CT values of the tests and whether discrepant results were more/less associated with high CT values (low DNA load).

Results: For the Xpert MTB/RIF survey we included 840 samples of which 12.3% (95% CI:10-14.5%, n=103/840) were Xpert-MTB detected and tested them in 210 pools. There was 36.7% (95% CI:30.1-43.2%, n=77/210) of the pools reported as Xpert-MTB detected and 63.3% (95% CI:56.8-69.8%, n=133/210) as MTB not detected.

There was 98.1% (95% CI:96.2-100%, n=206/210) of the pools in agreement with the individual test results, with 1.9% (95% CI:0-3.7%, n=4/210) being false negative. The pooling method identified correctly 96.1% (95% CI:92.4-99.8%, n=99/103) of the patients with TB and all patients without TB using 518 cartridges instead of 840, translating into 38.3% savings in time and money. Xpert Ultra results are expected to improve the sensitivity and data will be presented.

Conclusions: The pooling strategy is a promising method, with high sensitivity, reducing time and resources compared to the individual testing method. In a context where countries may experience stock out or delay in laboratory commodities procurement due to the lockdown, the pooling can be considered to ensure every TB patient receives the best option for TB diagnosis.

EP-24-333 Sustained impact of decentralised molecular testing for TB in Uganda

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Background: Data on how well interventions are sustained as part of routine care following interventional trials are limited. Here, we report on the ongoing uptake and impact of onsite molecular testing for TB using the GeneXpert Edge platform at health centers randomized to the intervention arm of a completed trial.

Design/Methods: The XPEL TB trial (October 2018-March 2020) evaluated a multi-component intervention strategy including onsite Xpert Ultra testing, restructuring of clinic workflows, and monthly performance feedback at 20 health centers in Uganda. After the trial was completed, monthly performance feedback was stopped but intervention health centers continued to offer onsite Xpert testing. We conducted a pre-post analysis comparing selected outcomes between the trial (October 2018 – March 2020) and post-trial (March 2020 – February 2021) periods.

Results: 5,572 adults (59.4% female, 41.3% HIV positive, and median age 40 years) were enrolled in the intervention arm during the trial period, as compared to 3,462 adults (55.6% female, 29.6% HIV positive, and median age 42 years) in the post-trial period. Among all adults, the proportion treated for confirmed TB on the same-day (4.5% vs. 4.7%, p=0.59) and within 14 days (6.1% vs. 7.0%, p=0.11) were similar in the trial and post-trial periods. Among adults with confirmed

TB, the proportions treated on the same-day (63.5% vs. 57.5%, p=0.12) and within 14 days (86.3% vs. 84.6%, p=0.53) were also similar.

Conclusions: The impact of onsite molecular testing for TB was sustained for 12 months following the end of XPEL TB trial, even in the absence of performance feedback. These data further support scale-up of decentralised molecular testing for TB to improve case detection and linkage to care.

EP-24-334 How do healthcare workers manage TB patients with MTB-positive, Rif-indeterminate Xpert results? Study of practices in a South West State in Nigeria

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Background: The diagnosis of MTB detected Rif-indeterminate GeneXpert results could lead to delay and uncertainty in clinical decision-making. In Nigeria, the national policy for the management of MTB detected Rif-indeterminate GeneXpert results is prompt initiation of patients on first-line TB medicines, while samples are taken for repeat GeneXpert testing to ascertain the RIF-resistance status. Culture analysis is recommended in persistent Rif-indeterminate results. There is insufficient data on the adherence to this algorithm. The objective was to determine the prevalence of MTB Rif-indeterminate results and adherence to recommended management algorithm among health care workers (HCWs) in Oyo State, South West Nigeria

Design/Methods: A retrospective cross-sectional analysis of GeneXpert tests performed between July-December, 2020 among presumptive TB patients in five health facilities, Oyo State, Nigeria. Information on samples tested, indeterminate results, indeterminate with repeat Xpert or culture test, outcomes, treatment status of patients with indeterminate results etc. were extracted from laboratory Xpert, presumptive and TB treatment registers. Descriptive data analysis was done on Microsoft excel to determine proportions of each outcome.

Results: Of the 1911 samples analyzed, 12 (0.6%) were indeterminate results. 3 (25%) of the 12 indeterminate samples were immediately started on first line anti-TB drugs. 10 (83%) of the indeterminate samples had repeat Xpert of which 4 (40%) returned as MTB detected Rif-sensitive, 3 (30%) as persistent MTB detected Rif-indeterminate and 3 (30%) with pending results. None of the samples, including those with persistent indeterminate results were repeated for culture.



Figure. Cascade of GeneXpert tests with MTB detected Rif-indeterminate outcome, Oyo state, Nigeria

Conclusions: We found 0.6% prevalence of MTB detected Rif-indeterminate results in Oyo State, Nigeria. HCWs in the State are not adhering to the National algorithm in the management of TB patients with MTB detected Rif-indeterminate results, as many patients with indeterminate results were not placed on first-line anti-TB treatment, while patients with persistent indeterminate results did not have samples taken for culture tests.

EP-24-335 Sample pooling for TB diagnosis: Xpert MTB/RIF and Xpert Ultra assay

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Background: World Health Organization (WHO) recommend the use of tuberculosis (TB) molecular assays, such as Xpert MTB/RIF assay, which will be replaced with Xpert ULTRA. Recently, studies demonstrated sputum pooled strategy has the potential to reduce diagnostic cost and improve diagnostic efficiency. Therefore, we aimed at demonstrating the performance of Xpert TB tests using the pooling method.

Design/Methods: We enrolled adults with presumptive TB attending TB clinics in Nigeria. Participants provided one sputum sample (4ml), tested within 24h with Xpert MTB/RIF or ULTRA MTB/RIF assay according to manufacturer's guideline. Remnant specimens were pooled in pools of four before the results of the individual sample are known, to avoid bias. The diagnostic performance of the individual or pooled tests determined at 95% confidence intervals, with the test agreement (kappa ratio).

Results: One thousand persons were recruited with individual Xpert result showing positive (detected) in 88 (61%) males and 57 (39%) females. The individual test findings were 14% MTB detected each for Xpert MTB/RIF and Xpert Ultra. The trace grading was 13 (18%) for Xpert Ultra, and intermediate RIF resistance 15 (21%). For the pooled tests, MTB detected was 40% and 37% each. The trace grading was 10 (22%) for Xpert Ultra, and intermediate RIF resistance 11(24%). The overall agreement of the each 125 pooled for Xpert MTB/RIF and Xpert Ultra with at least one positive individual test was 93.2% with a kappa ratio of 0.86, and 91% (83%, 96%) sensitivity and 95% (90%, 98%) specificity.

Conclusions: Xpert MTB/RIF or Xpert Ultra for TB pooling shows almost similar outcomes individually, though slightly better with Xpert Ultra assay due to relative increased sensitivity, with a strong agreement (Kappa ratio=0.86) and high sensitivity (91%) and specificity (95%), which will support its potential use in pooling strategy.

EP-24-336 Xpert MTB/RIF Ultra cycle threshold values as predictors of sputum culture conversion during TB treatment

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Background: The Xpert MTB/RIF Ultra (Xpert Ultra) assay offers a rapid diagnosis of tuberculosis (TB) and quantitative estimation of bacterial burden through Cycle threshold (Ct) values. We assessed the association of Xpert Ultra Ct values at the time of TB diagnosis in predicting sputum culture conversion at month 2 and 6 post TB treatment initiation among adult pulmonary TB (PTB) patients in Mbeya Tanzania.

Design/Methods: Information was obtained from adults PTB patients participating in the NAC-TB sub-study of TB Sequel cohort, which examine if oral N-acetylcysteine (NAC) could restore Glutathione and prevent lung injury in TB patients. Participants were enrolled at the time of TB diagnosis and were followed up for at least 2 years. About half of the participants received NAC in addition to standard TB and HIV therapy. Information on demographics, HIV status, Xpert ultra, and culture results at enrollment, and subsequent culture results at month 2 and 6 were extracted from the NAC-TB database. The association between Xpert Ultra Ct values and culture conversion at month 2 and 6 were determined using multivariable logistic regression.

Results: Between March 2019 and August 2020, 90 participants were enrolled. The median age was 34 (IQR: 28-40) years, 64(71.9%) were male, and 23(25.6) were HIV positive. The median Xpert Ultra Ct values were 16.2 (IQR; 16.1-16.3). At month 2 and month 6 (end of TB treatment), 45/87 (51.7%) and 5/73(6.9%) participants remained culture-positive respectively. Xpert Ultra Ct values at the time of TB diagnosis showed no association with sputum culture conversion at month 2 and 6 during TB treatment.

Variable	Number or Mean of MONTH 2 culture Neg (n=42)	Number or Mean of MONTH2 culture Pos (n=45)	AOR, 95% CI	Number or Mean of MONTH 6 culture neg (n=68)	Number or Mean of MONTH 6 culture Pos (n=5)	AOR, 95% CI
Baseline CT values						
Mean (SD)	16.37 (0.65)	16.31 (0.63)	0.91 (0.45-1.82)	16.35 (0.65)	16.12 (0.11)	0.01 (0.0008-23.63)
Sex						
Male	24 (58.5)	37(82.2)	Ref	48 (71.6)	3(60)	Ref
Female	17 (41.5)	8(17.8)	0.28 (0.11-0.78)	19 (28.4)	2(40)	1.82 (0.25-13.43)
HIV results						
Negative	30 (71.4)	34(75.6)	Ref	52 (76.5)	4(80)	Ref
Positive	12 (28.6)	11(24.4)	0.96 (0.34-2.71)	16 (23.5)	1(20)	1.40 (0.13-15.26)
Age						
<30yrs	14 (34.1)	18(40)	Ref	22 (32.8)	3(60)	Ref
>30yrs	27 (65.9)	27(60)	0.65 (0.25-1.68)	45 (67.2)	2(40)	0.44 (0.06-3.11)

Conclusions: Over half of adult TB patient remain culture positive at the end of the intensive phase of TB treatment. Xpert Ultra Ct values at the time of TB diagnosis shows no association with sputum culture conversion during TB treatment.

EP-24-337 Diagnostic algorithm for improved TB case yield in outpatient screening: a pilot study in Nigeria

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Background: Nigeria remains one of the countries with the highest burdens of TB, DR-TB and TB/HIV coinfection with an estimated gaps of 323,000 unreported TB cases annually. We trialed two new algorithms to enhance TB screening among patients attending outpatient departments (OPDs) in urban Nigeria.

Design/Methods: In two separate public health facilities in the federal capital territory (Maitama District Hospital; MDH and Nyanya General Hospital; NGH) OPD patients reporting i) a cough of two or more weeks (algorithm 1) or ii) a cough of any duration (algorithm 2) were referred for chest radiography and Xpert MTB/Rif testing. Individuals whose chest X-ray were suggestive were reviewed by the clinician and upon diagnosis were referred to the DOTS clinic for treatment.

Results: Over a six weeks period, 106 patients were screened across both OPDs, of which 88 (83%) were identified as presumptive TB though 63 (73%) were tested using different algorithms and 17 were (16%) confirmed as suffering of TB. A greater proportion of presumptive cases were identified among patients screened using the second algorithm (any cough) compared to the first (cough >2w; 73.8% vs 66.6% respectively). The second algorithm (any cough) also resulted in higher yield of TB cases among those screening (21.3% with any cough vs 14.8% with cough >2w - p-value: 0.177). All 17 identified cases initiated TB treatment.

Conclusions: This pilot study showed that TB screening in OPD is feasible and is effective compared to other TB screening strategy and that instituting an algorithm that includes symptomatic screening of cough of any duration can increase case detection. Ensuring that effective linkage and follow up of identified presumptive cases to diagnostic services is critical to minimize losses along the patient pathway. The full study is now being finalized of which the results will inform national efforts to improve case detection in Nigeria.

EP-24-338 Diagnostic network optimization and integration of TB and HIV testing on GeneXpert can benefit TB programmes: a Zambia case example

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Background: Diagnostic network optimization (DNO) can improve access to diagnostics and reduce costs while informing policy makers' decisions on diagnostic network changes. Until now, DNO has mostly been a manual exercise and conducted in a siloed, disease-specific way. We modelled the impact on the TB programme in Zambia of integrating priority HIV viral load and early infant diagnosis (priority HIV) testing with TB testing on GeneXpert platforms.

Design/Methods: Using OptiDx, an open-source modelling platform, we first established the baseline diagnostic network based on historical 2020 testing demand, referral linkages, testing sites, platforms, and costs for TB and HIV testing respectively. Next, we integrated priority HIV testing on GeneXpert platforms, historically only utilized by the TB programme, while optimising device placement. We calculated the annualized device cost, per test cost, and sample referral cost for each scenario.

Results: 212,797 TB tests were conducted on GeneXpert devices and 168,224 priority HIV tests on centralized Roche/Hologic devices in 2020. Currently, mean GeneXpert utilization is 10%, a TB sample travels on average 15km to a testing site and priority HIV tests travel 82km. With integration, the distance travelled on average priority HIV samples decreased 7-fold to 12km and the proportion tested onsite increased from 8% to 47%. There were potential benefits to the TB programme: onsite testing increased to 66% (from 59%) alongside savings in annualized GeneXpert costs of \$910,451 (49%) through cost-sharing with the HIV programme. The total cost of the combined testing programme can be reduced by 3% through integration and optimization.

Scenario	Baseline		Integrated		Difference	
	TB	Priority HIV	TB	Priority HIV	TB	Priority HIV
Average GeneXpert device utilization		10%		21%		11%
1. Annualized device fixed cost	\$1,840,364	\$92,671	\$929,913	\$545,686	-\$910,451 (-49%)	+\$453,015 (+489%)
2. Annual test cost (reagents/consumables)	\$2,470,090	\$2,214,181	\$2,470,090	\$2,891,400	\$0	+\$677,291
3. Annual transport cost	\$77,204	\$345,240	\$42,997	\$92,477	-\$34,207	-\$252,763
Non-priority HIV viral load testing cost				\$11,505,012		-\$554,980
Total cost of combined programmes		\$19,099,742		\$18,477,575		-\$622,167 (-3%)
Average distance travelled per sample (km)	15km	82km	7km	12km	-8km	-60km
Proportion of tests performed on-site	59%	8%	66%	47%	+7%	+39%

Table 1: Comparison of scenarios

Conclusions: DNO modelling predicts that integration of HIV testing on GeneXpert platforms currently only used for TB in Zambia will be cost-saving while improving the performance of the diagnostic network as measured by device utilization and a higher proportion of samples tested closer to the patient.

TB diagnostics: innovation, the host and the bacterium

EP-27-359 Diagnostic accuracy of the TB Molecular Bacterial Load Assay among presumptive pulmonary TB adult patients

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Background: Patient tuberculosis (TB) bacillary load is an established marker for disease severity and treatment response. We evaluated the accuracy of the culture-free Tuberculosis- Molecular Bacteria Load Assay (TB-MBLA) for detection and quantification of TB bacterial burden among presumptive pulmonary TB participants in a resource constrained-high-burden setting.

Design/Methods: Three serial spot sputa per patient were pooled, homogenised, and then tested for TB using fluorescent smear microscopy, GeneXpert MTB/RIF Ultra (Xpert Ultra), culture and TB-MBLA. Sensitivity, specificity, and percent agreements (Cohen's kappa coefficient, κ) were calculated using STATA version.15.1.

Results: The study has so far enrolled 150 presumptive TB participants of whom 73 were included in the preliminary analysis. Cohort median age was 35 years. 46(63%) were male, and 26 (36%) were living with HIV-infection. Using MGIT culture as a reference test, 34 (47%) of the participants were confirmed TB positive of whom 29(85%) were positive by TB-MBLA with mean bacterial load of $4.8 \pm 1.3 \text{Log}_{10} \text{ eCFU/mL}$. Sensitivity and specificity at 95%CI were 85% (69-95) and 97% (85-100); 100% (90-100) and 92% (79-98); and 77% (59-18) and 97% (87-100) for TB-MBLA; Xpert Ultra; and smear microscopy respectively. Overall TB-MBLA-Xpert Ultra concordance was 88%; $\kappa = 0.8$. TB-MBLA and MGIT culture concurred on the TB negativity of 3/5 participants who were diagnosed as 'trace positive' by Xpert Ultra.

Conclusions: We show that TB-MBLA is a sensitive and specific method for determining the presence of viable bacteria in sputum samples with high potential to enhance assessment of patient TB disease severity and response to anti-TB therapy.

EP-27-360 Diagnostic accuracy of computer-aided chest X-ray screening in the Kenya National TB Prevalence Survey

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Background: Community-based screening for tuberculosis (TB) could improve diagnosis and reduce transmission but is resource intensive. We set out to evaluate the accuracy of computer-aided TB screening using digital chest X-ray (DCXR-CAD), which may be an accurate and efficient approach to mass screening in low-resource settings.

Design/Methods: Chest X-ray images from participants in the 2016 Kenya National TB Prevalence Survey were evaluated using CAD4TBv6 (Delft Imaging), giving a probabilistic score for pulmonary TB ranging from 0 (low probability) to 99 (high probability). We constructed a Bayesian mixed model to estimate the latent sensitivity and specificity profile of DCXR-CAD screening against microbiologically-confirmed TB across CAD4TBv6 threshold cut-offs, incorporating data on Clinical Officer CXR interpretation, participant demographics (age, sex, TB symptoms, previous TB history), and sputum culture and Xpert results.

We additionally compared model-estimated sensitivity and specificity of CAD4TBv6 to target product profiles (TPP) for community screening tests.

Results: Of 63,050 prevalence survey participants, 61,848 (98%) had analysable chest X-ray images, and 8,966 (14.5%) underwent sputum microbiological testing; 298 had microbiologically-confirmed pulmonary TB. Median CAD4TBv6 scores for participants with microbiologically-confirmed TB were significantly higher (72, IQR: 58-82.75) compared to participants with microbiologically-negative sputum results (49, IQR: 44-57, $p < 0.0001$). Overall, with the CAD4TBv6 threshold set to achieve a model posterior mean sensitivity of 90% (minimum TPP), specificity was 91.6% (95% CrI: 91.1%-92.0%) (CAD4TBv6 thresholds: 36). There was substantial variation in modelled estimates by participant characteristics, with sensitivity highest among older individuals, those with previous TB or with cough of greater than two weeks; specificity was lowest in older participants (Figure 1).

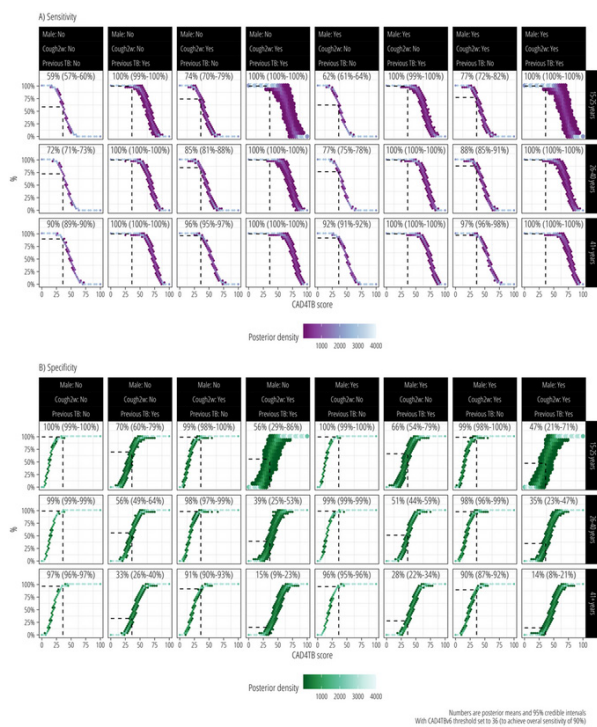


Figure 1.

Conclusions: In this analysis, TB screening with CAD4TBv6 met the minimum TPP for community screening. High accuracy can be achieved within population subgroups.

EP-27-361 Novel point-of-care urine FujiLAM test to detect TB in HIV-positive patients: how feasible and acceptable is it in primary care settings?

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Background: The novel FujiLAM test is a promising TB diagnostic tool but may be complex to use. We aimed to assess the feasibility and users' acceptability of the FujiLAM test in 4 African countries.

Design/Methods: Mixed-methods study in primary care settings in Kenya, Uganda, Mozambique and South Africa. Procedures:

1. Direct observations on the health facilities' organization including space, human, and logistics requirements;
2. Standard questionnaires and individual interviews with test users (16 and 6 participants respectively);
3. Focus group discussions with program/laboratory managers (14 participants).

Results: FujiLAM test was performed by laboratory technicians, nurses, clinicians, and community health workers (CHWs) in the clinic laboratory or the consultation area using already existing infrastructure. A 2-4 hours training was conducted prior. Most of the users (15/16; 94%) reported that the test was easy to perform. Users and stakeholders asserted that with proper training, the test could be performed by anyone in a health-care setting, including lay health workers.

The main concerns raised were the multiple timed steps involved, including long urine incubation period. Some users (5/16, 31%) reported that the test would be difficult to integrate into their daily workload.

Other challenges included test cartridge fragility and susceptibility to the characteristics of the urine sample used (invalid results were obtained when test cartridges were dropped, or tests were performed on blood stained or cloudy urine). There was consensus that the test was suitable to be implemented as point-of-care at primary care level, but opinions differed on where in the facility (clinic laboratory versus consultation area).

Conclusions: Implementing the FujiLAM test in primary care settings is feasible using existing infrastructure. The test is perceived as easy to perform by users (including lay health workers) and acceptable as a point-of-care test. Drawbacks are the test fragility and the multiple timed steps involved to perform the test.

EP-27-362 Comparison of C-reactive protein and symptom screening as TB screening tools among outpatients in a high TB burden setting

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Background: World Health Organization(WHO) recently recommended C-Reactive Protein(CRP) as a screening tool for TB among adults and adolescents living with HIV. Using a cut off of 5mg/L, its sensitivity and its specificity are similar to or higher than WHO recommended four symptom screen(W4SS).

Additional research to evaluate accuracy and predictive value of measuring CRP above any cut-off higher than 5 mg/L for TB screening is recommended by WHO. There is no WHO recommendation on use of CRP among HIV negative individuals.

Design/Methods: At a primary health care facility in Lusaka Zambia, we evaluated the screening value of Alere Determine CRP rapid test in consecutive adult outpatients presenting for TB screening and compared it to W4SS(any symptom) using a composite reference(culture, Xpert or smear) as the reference standard. CRP level of <10mg/l signified a negative result. HIV status was determined by both self-report and testing.

Results: Of 753 participants, 436 (57.9%) were male, median age was 38(29-47), 324(43.0%) were HIV positive, 546(72.5%) had any TB symptom, 516(68.5%) had a CRP \geq 10mg/L and 99 were diagnosed with TB bacteriologically. Overall sensitivity of W4SS and CRP were 91.4(84.7- 96.4)% and 91.9(84.7-96.4)% while overall specificity was 30.4(26.9-34.1)% and 35(31.4-38.8)% respectively. Among HIV positive, sensitivity of W4SS and CRP were 95(83.1-99.5)% and 97.5%(86.8-99.9)% while specificity was 36.3(30.7-44.2)% and 26.8(21.7-32.3)% respectively. Among HIV negative, sensitivity of W4SS and CRP was 89.8(79.2- 96.2)% and 88.1 (77.1-95.1)% while specificity was 25.9(21.6-30.7)% and CRP was 41.4(36.3-46.6)% respectively.

Conclusions: At a cut off of 10mg/L, sensitivity and specificity of CRP was similar to W4SS in HIV positive outpatients. However, among HIV negative individuals, while sensitivity was similar, CRP had higher specificity. Use of CRP as an adjunct screening tool in HIV negative sub-populations should be explored further.

EP-27-363 Integrating artificial intelligence-supported radiology in active case-finding in rural Bihar, India

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Background and challenges to implementation: Accessibility to quality radiology reporting for tuberculosis (TB) diagnosis processes is limited in remote settings for people with TB symptoms. Artificial Intelligence (AI) for radiograph interpretation can potentially improve the processes and supplement the case finding efforts when used as a part of screening to help radiologists or physicians.

Intervention or response: We used qXR (qure.ai) a chest X-ray screening tool, from July 2020 onwards in four digital X-ray centers catering to patients seeking care for TB symptoms in the public health system (PHS). Community health workers screened people with the help of a questionnaire and referred those with symptoms to the PHS. Physicians advised chest X-ray and genexpert (Gx) tests for patients. X-ray was read by the qXR and a radiologist. Gx test was requested by physicians irrespective of qXR interpretation.

Results/Impact: In a set of 693 patients, qXR suggested 64% positive TB screens compared to 44% suggested by radiologists. We assessed the sensitivity and specificity of qXR and the radiologist, using a positive Gx test as a base. The cutoff score for qXR was set at 0.5. We subsequently calculated the positive and negative predictive values of the qXR and radiologist's reading. 64 chest X-rays interpreted as normal by radiologists and as suggestive of TB by qXR turned out to be Gx positive. There was 71% concordance in qXR and radiologist reports on the level of TB presence.

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
qXR	74%	44%	49%	70%
Radiologist	59%	66%	55%	69%

Conclusions: Understanding AI tools' performance in remote rural areas with high TB prevalence rates and consequentially using the data to strengthen the algorithm is the way forward. It is also crucial to understand the role of AI in existing community health workers driven active case finding projects for optimum integration in the workflow.

EP-27-364 First clinical evaluation of QIAreach™ QuantiFERON-TB for TB infection and active pulmonary disease

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Background: Diagnosis and treatment of tuberculosis (TB) infection are core conceptual elements of the TB elimination strategy. Recently, the portable QIAreach™ QuantiFERON-TB (QIAreach QFT) test was developed. This is novel digital fluorescence lateral flow immunoassays uses nanoparticle technology to measure the levels of IFN- γ in plasma released from both CD4 and CD8 T cells, thus doing not need for enzyme-linked immunosorbent assay. QIAreach QFT has advantages in use as point-of-care-test in low-resource countries.

Design/Methods:

1. to compare the QIAreach QFT vs. QuantiFERON®-TB Gold Plus assay (QFT-Plus) to detect tuberculosis (TB) infection;
2. to evaluate the clinical performance of QIAreach QFT as a screening tool for TB disease;
3. to preliminarily evaluate QIAreach QFT in immunocompromised individuals.

Methods: QIAreach QFT measures the level of interferon- γ in plasma specimens from blood stimulated by ESAT-6 and CFP-10 peptides in one blood collection tube (equivalent to the TB2 tube of the QFT-Plus). QIAreach QFT was applied to plasma samples from 41 patients with pulmonary TB (median age: 82 years) and 42 healthy or low-TB-risk individuals (median age: 39.5 years).

Results: Sensitivity and specificity of QIAreach QFT vs. QFT-Plus were 100% (41/41) and 97.6% (41/42), respectively; total accuracy was 98.8% (82/83). All of each sample were measured within 20 minutes. The higher the interferon- γ level of the sample was, the shorter the time to result. Seven cases in the active TB group were immunocompromised (CD4 T-cells <200/ μ L) and tested positive by QIAreach QFT.

Conclusions: QIAreach QFT provides an objective readout with a minimum blood sample volume (1 mL/subject), potentially being a useful point-of-care screening test for active TB in high-TB-burden, low-resource countries and for immunocompromised patients.

EP-27-365 Impact of pregnancy on latent TB diagnostics using QuantiFERON Gold In-Tube assay and tuberculin skin testing in a food-insecure population in Haiti

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Background: Pregnancy is a high-risk time to develop active TB. It is unknown how food insecurity affects latent TB diagnostics in pregnant women. We conducted a study comparing the tuberculin skin test (TST) and QuantiFERON Gold-in-tube (QGIT) in pregnant and non-pregnant women in Haiti, where 40% of people are food insecure.

Design/Methods: We conducted a longitudinal study of pregnant women and age-matched non-pregnant women at GHESKIO in Port-au-Prince, Haiti. At enrollment, food insecurity was measured using the Household Food Insecurity Access Scale. All women underwent TST and QGIT testing at enrollment and 9 months later, after delivery. Test positivity was compared using chi-square.

Results: We enrolled 53 pregnant and 51 non-pregnant women with a median age of 25.5 and 25 years, respectively ($p=0.47$). The median gestational age for pregnant women was 20 weeks (IQR:16-24). The median BMI for pregnant women was significantly lower than in non-pregnant (11 vs. 23, $p<0.01$). Over 90% of all women had moderate to severe food insecurity.

Compared to non-pregnant women, pregnant women had similar TST positivity (51% vs. 63%, $p=0.33$) and significantly lower QGIT positivity (38% vs. 76%, $p<0.01$). At follow-up, TST positivity was significantly higher than in pregnancy (78% vs. 51%, $p<0.01$) but similar to non-pregnant (78% vs. 74%, $p=0.48$). QGIT positivity did not significantly increase postpartum (38% vs. 43%, $p=0.60$) and remained lower than non-pregnant (43% vs. 67%, $p=0.06$). In the non-pregnant cohort, TST and QGIT positivity remained similar between visits (see Figure). A positive correlation between BMI and IFN-g was observed ($r=0.36$, $p<0.01$).

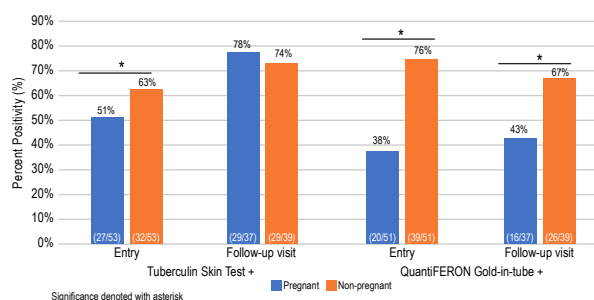


Figure 1a. Longitudinal comparison of latent TB diagnostics in pregnant and non-pregnant women

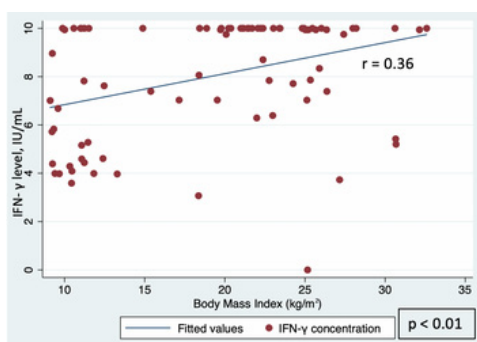


Figure 1b. Body mass index versus IFN- γ response in pregnant and non-pregnant women.

Conclusions: We found that TST results fluctuate more than QGIT in pregnant women. However, postpartum QGIT results remained lower than in non-pregnant women. Poor nutrition and increased food insecurity in Haiti may contribute to the persistent immune dysfunction postpartum. Further research should address how the burden of malnutrition during pregnancy affects TB.

EP-27-366 Perspectives and perceptions of urine sampling and urine-based TB testing among patients in Kenya and Uganda

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Background: Despite the advent of novel urine-based assays to diagnose tuberculosis (TB), evidence on their acceptability by patients remains limited. The objective of the study was to describe patients' experiences, perspectives and perceptions of urine sampling and urine-based TB testing.

Design/Methods: For this qualitative descriptive study, 32 HIV-positive adult patients from Kenya and Uganda, enrolled in the FujiLAM diagnostic study, were selected purposively and proposed participation. Consenting participants were interviewed using a semi-structured interview guide. Each interview was audio-recorded, translated and transcribed. Textual data were analyzed using content analysis.

Results: We identified three domains, including a) urine sampling perspectives and urine-based TB testing perceptions, b) enabling factors of urine-sampling and c) motivational determinants of urine sampling acceptance. Most participants viewed urine sampling positively and easier than sputum provision. Trust in the

relevance and accuracy of urine-based TB testing was associated with beliefs on TB's etiology and the function of the urinary system. Toilets' cleanliness, perceived privacy, and proximity influenced participants' experience, and for some, willingness, to submit urine. Participants reported preferring same-day results, willing to wait from 30mins to three hours for their TB diagnosis. Acceptance of urine-based TB testing was motivated by participants valuing their health, especially if experiencing symptoms, as well as their trust in, and quality of communication with the medical team. Urine based-TB testing acceptance stems from a combination of individual perceptions, positive perspectives based on experience, and external, supportive environmental factors affecting motivation to engage in urine sampling.

Conclusions: This study indicates that among participants, urine sampling is well accepted and often preferred to sputum provision. Education on the biological pertinence of the test, adequate sampling environments, collaborative patient-provider interaction, and same-day result reporting can improve patient's experiences and promote their uptake of urine-based testing. These results encourage the future broad implementation and use of urine-based assays.

EP-27-367 Novel bioelectronic assay for the detection and quantification of Mycobacterium tuberculosis antigen CFP-10 in serum and urine for rapid diagnosis of active TB disease

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Background: The World Health Organization estimates that over 10 million individuals become infected with *Mycobacterium tuberculosis* annually, and of those, approximately 1.4 million individuals die of tuberculosis disease. Currently however, there are no commercially available point-of-care diagnostics that are rapid, inexpensive, and highly sensitive for the diagnosis of active tuberculosis disease, contributing both to ongoing transmission and delayed tuberculosis care.

Design/Methods: We describe the development, optimization, and evaluation of a novel bioelectronic tuberculosis antigen (BETA) assay to detect tuberculosis-specific antigen, CFP10, in small-volume unprocessed serum and urine samples. The performance of the BETA assay was assessed using biobanked clinical serum and urine specimens from three tuberculosis diagnostic studies.

Results: Circulating CFP10 antigen was detected in all serum (n=19) and urine (n=3) samples from bacteriologically confirmed tuberculosis patients who were untreated or had been treated for less than one week at the

time of serum collection. CFP10 antigen was undetectable in serum (n=7) and urine (n=6) samples collected from individuals who were at risk of having tuberculosis but were determined to be clinically and bacteriologically tuberculosis negative. Paired urine and serum samples collected from presumptive tuberculosis patients (n=10) produced highly correlated amperometric responses, Pearson's $r=0.95$, $p<0.01$. Additionally, antigen quantification of serially collected serum samples from drug resistant tuberculosis patients (n=8) collected both before and after treatment initiation, demonstrated consistently declining within-person levels of CFP10 antigen concentration during treatment.

Conclusions: This novel, low-cost prototype BETA assay successfully detected CFP10 antigen in serum and urine samples from all culture positive tuberculosis patients, demonstrating not only significant promise as a rapid, non-sputum-based, point-of-care tool for the diagnosis of active tuberculosis disease but also as a potential treatment response monitoring tool.

EP-27-368 A systematic review of biomarkers to replace the four-symptom screen for active TB disease

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Background: The standard TB four-symptom screen does not meet the ideal screening criteria for having >90% sensitivity to identify active TB disease, regardless of HIV status. We conducted a systematic review to identify potential screening biomarkers for active TB. **Design/Methods:** We performed a systematic review of any cohort or case-control study reporting associations between screening biomarkers and active TB disease. We searched PubMed and Embase for articles published before January 28th, 2021; search terms included tuberculosis, screening, and a list of TB-endemic countries. We evaluated articles that reported an association between a screening biomarker and active TB. We excluded articles focusing on C-reactive protein and lipoarabinomannan. For all included biomarkers, we calculated sensitivity, specificity and 95% confidence intervals, and assessed study quality using a tool adapted from the QUADAS-2 risk of bias.

Results: From 8,003 abstracts screened, we included 72 articles. The articles described 268 unique biomarkers, including host antibodies, host proteins, TB antigens, microRNAs, whole blood gene PCRs, and combinations of biomarkers. Of these, 21 biomarkers had sensitivity greater than 90% and specificity greater than 70%,

meeting World Health Organization (WHO) criteria for an ideal screening test. This included 9 antibody tests and 12 non-antibody tests such as host proteins, TB proteins, and microRNAs. Among the nine biomarkers described in people living with HIV, only one had a sensitivity greater than 90% and specificity greater than 70% for active TB.

Conclusions: Twenty-one biomarkers of active TB infection exceed the WHO's criteria and may be superior to TB symptom screening alone. Further evaluation of biomarkers of active TB should be pursued to accelerate identification of TB infections.

Mycobacterial epidemiology, vaccines, and the interaction with other diseases

EP-28-369 Contrasting virulence properties of drug-resistant *Mycobacterium tuberculosis* strain clusters in Siberia, Russia

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Background: *Mycobacterium tuberculosis* Beijing genotype is subdivided into modern and ancient sublineages. The former is globally spread and includes known drug resistant strains while the latter is mainly drug susceptible and have not been much studied to date.

We aimed to study biological properties of the two recently identified multidrug-resistant clusters of ancient Beijing sublineage emerging in Siberia and Far East, Russia.

Design/Methods: Strains were studied in the in vitro model to assess their growth rate (7 isolates of each cluster) and in the in vivo C57BL/6 mouse model (one isolate from each cluster) to assess their virulence. Laboratory strain H37Rv served as reference. Genetic analysis of the strains was performed using VNTR typing and whole genome sequencing.

Results: *M. tuberculosis* genotypes 1071-32 and 14717-15 (defined as such according to the MIRU-VNTRplus.org classification) belonged to the ancient sublineage of the Beijing genotype. All studied strains were MDR. No significant differences were found in the growth rate characteristics except for longer lag phase for the isolates of the Beijing 14717-15 cluster. In contrast, these clusters differed dramatically in the murine model. Strain of the cluster 1071-32 was low virulent in terms of weight loss, bacterial load and lung pathology. Strain of the cluster 14717-15 showed exceptionally high mortality, that was higher than that recorded for the notorious Russian epidemic strain Beijing B0/W148.

Conclusions: This study highlighted that large phylogenetic lineages and genetic families such as Beijing genotype are heterogeneous both genetically and pathogenetically, and strains within the same sublineage (ancient Beijing sublineage) may differ considerably not only in their capacity to acquire drug resistance but in virulence and lethality. This should be taken into account by the local and global molecular surveillance programs in order to trace possible dissemination of these clusters outside Russia.

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EP-28-370 Latent *M. tuberculosis* co-infection is associated with heightened levels of humoral, cytokine and acute phase responses in seropositive asymptomatic SARS-CoV2 infection

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Background: Latent *Mycobacterium tuberculosis* infection (LTBI) is postulated to modulate immune responses and alter disease severity in SARS-CoV2 co-infection. However, no data exist on the effect of LTBI on the immune responses in SARS-CoV2 co-infected individuals.

Design/Methods: Consenting individuals with age range among 60 - 80 years of age, living in hotspots for SARS-CoV2 infection. IgM and IgG positivity diagnosed sARS-CoV2 infection. LTBI was determined on the basis of positivity for QuantiFERON TB Gold in tube (QGIT) test. We examined the SARS-CoV2 specific antibody responses, plasma cytokines, chemokines, acute phase proteins and growth factor levels in LTBI positive (n=61) and negative individuals (n=72) with SARS-CoV2 infection.

Results: Our results demonstrated that individuals with LTBI (LTBI+) and seropositive for SARS-CoV2 infection were associated with elevated SARS-CoV2 specific IgM, IgG and IgA antibodies, as well as enhanced neutralization activity compared to those negative for LTBI (LTBI-) individuals.

Our results also demonstrate that LTBI+ individuals exhibited significantly higher plasma levels of IFN γ (p<0.0001), IL-2 (p<0.0001), TNF α (p<0.0001), IL-1 α (p<0.0001), IL-1 β (p=0.0007), IL-6 (p<0.0001), IL-12 (p<0.0001), IL-15 (p=0.0007), IL-17 (p<0.0001), IL-3 (p=0.0003), GM-CSF (p<0.0001), IL-10 (p=0.0213), IL-25 (p=0.0056), IL-33 (p<0.0001), CCL3 (p<0.0001) and CXCL10 (p=0.0077) compared to LTBI- individuals.

Finally, our results show that LTBI+ individuals exhibit significantly higher levels of C-reactive protein, alpha-2 macroglobulin, VEGF and TGF α compared to LTBI- individuals.

Conclusions: Thus, our data clearly demonstrates that individuals with LTBI and seropositive for SARS-CoV2 infection exhibit heightened levels of binding and neutralizing antibodies, cytokine and acute phase responses. Thus, LTBI is associated with modulation of antibody and cytokine responses as well as systemic inflammation in individuals seropositive for SARS-CoV2 infection.

Nevertheless, our data provide a plausible mechanistic explanation for a positive protective effect of LTBI on SARS-CoV2 infection and call for more clinical and basic research studies on this interaction.

EP-28-371 A nationwide molecular survey of pre-extensively drug-resistant TB identifies distinct clades and resistance patterns across India, 2019–2020

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Background: Pre-extensively drug-resistant tuberculosis (preXDR-TB) — resistance to first-line drugs rifampicin, isoniazid and second line fluoroquinolones is an advanced form of drug-resistant tuberculosis. Treatment for preXDR-TB is difficult and requires appropriate drug selection for treatment success. Thus, simultaneous detection of resistance-conferring mutations across antituberculosis medicines and identification of genetically-related clusters may improve treatment management and aid in outbreak detection.

Design/Methods: During 2019–2020, a representative survey of persons with presumed drug-resistant tuberculosis from 29 states and territories of India resulted in 1,827 *M. tuberculosis* isolates. Cultured isolates underwent whole genome sequencing (WGS).

WGS data characterized isolates to predict published resistance-conferring mutations for first- and second-line antituberculosis drugs, *M. tuberculosis* phylogeny, and strain relatedness. MTBseq aligned sequences and a maximum likelihood phylogenetic tree was built in RAxML v8.2.12 using the GTRGAMMA option with 1000 bootstraps.

Results: A total of 231 strains (13%) harboured single nucleotide polymorphisms (SNPs) and insertions/deletions associated with preXDR resistance. All four phylogenetic lineages were identified; Lineage 2 was predominant (64%; 150/231) among the preXDR-TB isolates. Phylogenetic analysis and pairwise SNP difference of Lineage 2 preXDR-TB isolates, yielded 9 clades, including a unique clade comprising 17% (25/150) with pairwise SNP differences ranging from 1 to 31.

This preXDR-TB clade had a distinctive pattern of nine mutations associated with resistance to rifampicin, isoniazid, ethambutol, pyrazinamide and kanamycin, and simultaneously shared 11 unique SNPs in genes associated with bacterial growth and development.

Conclusions: A predominance of Lineage 2 genotypes, distinct phylogenetic clades, and a unique resistance- and growth-associated genomic signature were associated with preXDR-TB across India. These data may inform national treatment guidelines and influence tailored individualized treatment regimens.

Furthermore, understanding the genomic diversity and evolution of TB resistance mechanisms will be useful to establish epidemiological links between patients and inform outbreak detection in India.

EP-28-372 Building a national TB cohort from routine laboratory data: record linkage in South Africa

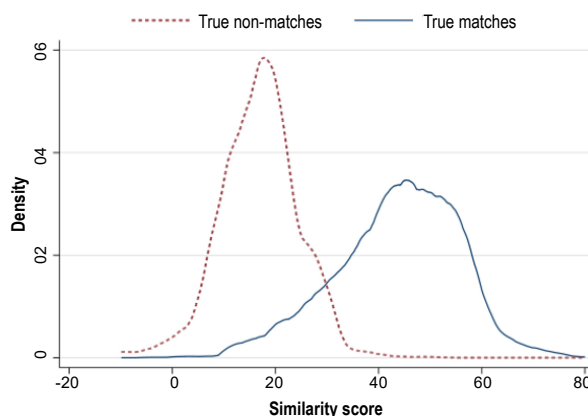
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Background: Laboratory testing is used to diagnose tuberculosis (TB), to determine drug susceptibility, and to monitoring for treatment response and cure. South Africa's National Health Laboratory Services (NHLS) conducts all laboratory testing for South Africa's public

sector national TB programme. However, the absence of a unique patient identifier has constrained the use of the NHLS database for longitudinal analysis.

Design/Methods: We developed and validated a record linkage algorithm and applied it to all TB laboratory results in the NHLS database, collected January 2011 – March 2017. The linkage approach combined Fellegi-Sunter probabilistic record linkage with methods from network analysis. Records were linked probabilistically on name, date of birth, gender, and facility, accounting for transcription errors and movement across facilities. We previously used this approach to link HIV-related laboratory results in the NHLS database. The algorithm was validated through manual review of 9548 “candidate matches” for a random sample of 999 laboratory specimens. Each candidate match was reviewed by at least two members of the study team, with disagreements resolved through discussion.

Results: A total 30,147,523 specimens collected for TB-related testing during the study period were linked. The linkage algorithm was able to distinguish most “true matches” from “true non-matches” (Figure). Our validation exercise indicated that the algorithm correctly identified 92% of true matches (Sensitivity) and that 91% of matches identified were correctly assigned (Positive Predictive Value). By comparison, “exact matching” correctly identified just 34% of true matches. The algorithm identified 11,630,589 unique patients with TB tests, of whom 1,555,244 (13.4%) had microbiologic evidence of TB. Men represented 56% of people diagnosed with TB.



Conclusions: With a validated patient identifier, the NHLS database can be analyzed as national TB cohort. The database can be used to assess treatment outcomes, re-engagement with care, policy impacts, and co-infection with HIV and other laboratory-monitored conditions.

EP-28-373 The impact of Covid-19 on TB diagnosis in The Gambia, West Africa: a cross-sectional survey

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Background: The Covid-19 pandemic has reversed global TB progress by 12 years with nearly 25% decrease in TB diagnosis and treatment. The Gambian Government declared lock-down from 31 March until 19 September 2020.

Our aim was to determine the notification rates for presumed TB and smear positive pulmonary TB at DOTS centers in Gambia before and during the lock-down.

Design/Methods: We retrospectively review TB registers of five DOTS centers (Brikama, Serrekunda, Sukuta, Bundung and Fajikunda) in the Greater Banjul Area (GBA) of The Gambia from January 2019 to September 2020. We analyzed data from presumed TB and confirmed smear positive patients' registers. Trained healthcare workers at the selected DOTS centers were interviewed (by phone) about their experiences during the lock-down about TB diagnosis and plausible reasons for the decrease in TB notification rates during the period. The quantitative data are presented in proportions and percentages with 95% confidence intervals (CI) and thematic analysis for the qualitative data.

Results: Patients with TB-like symptoms seeking care at GBA health clinics from January to September 2019 was 3555/6458 (55%), reduced to 2903/6458 (45%) in 2020. There was reduction in the proportion of symptomatic individuals seeking care during the lock-down period (April to September 2020) 1725/4350 (39.7%), 95% CI 0.38- 0.41 compared to the same period in 2019, 2625/4350 (60.3%), 95% CI 0.59- 0.62.

The confirmed smear positive TB during these periods 132/476 (27.7%) 95% CI 0.24- 0.32 in 2020 and 344/476 (72.3%), 95% CI 0.68- 0.76 in 2019. There was a significant drop in smear positive TB notified by 212/476 (44.5%), 95% CI 0.04- 0.07.

Conclusions: Covid-19 lock-down has significantly reduced smear positive TB notification rates in The Gambia. The fear of being tested for COVID-19 was thought to be responsible. Public enlightenment activities about TB and COVID-19 needful in The Gambia.

EP-28-374 Metformin as enhancer of anti-TB drug efficacy in diabetes mellitus-TB coinfection patients

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Background: Metformin is the most commonly prescribed drug for type 2 diabetes mellitus. Nowadays metformin (MET) is also use for efficacy in diabetes mellitus-tuberculosis coinfection patients through several mechanisms, such increasing superoxide production therefore activation isoniazid is increasing; inducing adeno-monophosphate kinase (AMPK) associated autophagy process; and regulating inflammation cytokines. Metformin associated lactic acidosis during this study was also not occurred.

Design/Methods: For the purpose of understanding the MET effect as an adjuvant therapy in TB therapy and insulin simultaneous therapy, an observational clinical study was done in type 2 DM newly TB coinfection outpatients at Surabaya Paru Hospital. Patients were divided into two groups.

First group was MET group, in which the patients were given MET accompanying insulin and TB treatment regimens, the golden standard therapy of DM-TB coinfection. MET therapy was given for at least 2 months. Second group was non-MET group, in which the patients were given insulin and TB treatment regimens. The Acid-Fast Bacillus (AFB) smears, microtubule-associated Protein1 Light Chain 3B (MAP1LC3B) level, as the presentation of autophagy, Superoxide Dismutase (SOD) level, Interferon (IFN)-g and Interleukin (IL)-10 levels in both groups were measured before and after two months MET additional therapy. While, the lactate levels was measured once, after two months MET additional therapy.

Results: From 42 participants in this study, 22 participants of observation group that received additional MET therapy, 100% had sputum smear reversion after 2-months intensive phase of anti-TB therapy. Whereas 25% of 20 participants of comparison group did not undergo reversion inserts sputum smear.

Conclusions: MET has the potential of being an additive combination therapy to enhance the bactericidal effect of anti-TB on DM-TB coinfection patients. MET enhances the effects of anti-TB and insulin therapy in increasing the smear reversion by increasing autophagy. MET also increased both pro-inflammatory and anti-inflammatory cytokines.

EP-28-375 Potential implementation strategies, acceptability and feasibility of new and repurposed TB vaccines

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Background: Recently, two TB vaccine trials reported positive efficacy results in adolescents and adults. The coming years will be crucial in terms of strategy for these vaccines to move forward in an efficient manner. Adolescent and possibly adult vaccination will be required for the implementation of this vaccine.

We explored potential implementation strategies for the M72/AS01_E vaccination and BCG revaccination-like candidates, and their acceptability and feasibility.

Design/Methods: We conducted in-depth semi-structured interviews among key decision makers/actors from three high TB burden countries (South Africa (SA), India and China). We used thematic analysis with deductive coding based on the interview guide. We summarized strategies per suggested target group, accompanied by narrative where needed.

Results: Adolescents in schools and high risk groups were named most often as key target groups. In China and India, elderly were also seen as a target group. Routine vaccination was preferred in all countries due to stigma and logistical issues related to mass campaigns. Perceived benefits for implementation of M72/AS01_E were its efficacy in persons infected with TB, and potential safety among people living with HIV (PLHIV). Perceived challenges for this vaccine for adults were building new infrastructures and double dosing which could decrease coverage. Requirements opted were clinical trials in local context and specific age groups, TB epidemiological data and addressing vaccine. Stakeholders valued BCG's familiarity, but disliked the adverse effects it can have in PLHIV which was especial-

ly a concern among SA respondents. Testing for Mtb or HIV infection status was thought not feasible regarding logistics and finance.

Conclusions: Our study provides context-specific implementation scenarios for TB vaccines targeted and adolescents and adults. Stakeholders considered the implementation of TB vaccines targeting adolescents and adults feasible within the local health care system if efforts are undertaken to address vaccine acceptance and scale up of infrastructure, human resources, and monitoring systems.

EP-28-376 Impact of Covid-19 on TB diagnosis in an Indian tertiary care setting

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Background: The recent COVID-19 pandemic became a looming catastrophe over global public health and severely disrupted essential healthcare services like tuberculosis (TB). This study estimated the impact of the COVID-19 in the diagnosis of TB, a microbiology laboratory-based overview.

Design/Methods: This ambispective observational study was conducted at the Department of Microbiology in a tertiary care hospital in South Karnataka from January 2019 to December 2020. A standardized data collection sheet was prepared to collect the month-wise total number of suspected TB and confirmed TB samples. Data were analyzed using EZR 3.4.3 (R, open-source). Categorical variables were expressed in frequency and percentage. The Chi-square test was performed to test the difference in proportions and $p < 0.05$ indicated statistical significance.

Results: Overall 49.4% decrease in tuberculosis suspected samples was observed (13,747 in 2019 vs 6,948 in 2020), along with a 49.1% decrease in confirmed TB samples (1,173 in 2019 vs 597 in 2020). In 2020, month-wise a sharp decline was noted for the confirmed TB cases, with a maximum 89.9% and 88.1% decrease in April and August respectively, compared to the same periods in 2019 [Fig 1].

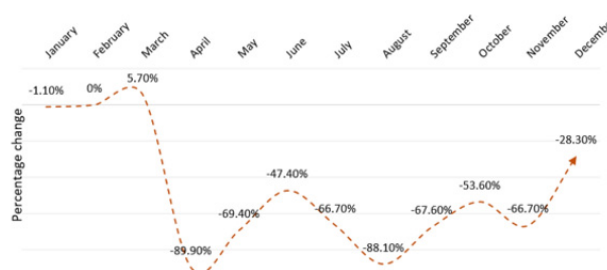


Figure 1. Comparison of confirmed TB cases in 2020 vs 2019

Another major finding from this study reveals the PTB: EPTB proportion changed from 2.7:1 in 2019 to 2.1:1 in 2020, divulging an overall increase in EPTB sample proportion in 2020 ($p=0.0385$).

Conclusions: The COVID-19 pandemic adversely impacted the TB diagnostic services, resulting in a significant reduction of active TB case detection. Delayed detection of active TB cases might act as a new source of infections and increase TB transmission, along with prolonged lag in treatment. The development of new strategies to control and eliminate TB should be the utmost priority in this hour of the pandemic crisis.

EP-28-377 Directory of TB vaccine clinical trial sites in sub-Saharan Africa: results from a comprehensive inventory of clinical trial sites

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Background: There are currently approximately 14 vaccine candidates for TB in the clinical pipeline. These vaccine candidates need to be tested in TB prevalent populations over the coming years and rely on clinical trial sites and capacity around the globe. In order to sustain the clinical pipeline for TB vaccines, we developed a directory of clinical trial sites in sub-Saharan Africa and provide an overview of capacity for performing clinical trials for TB vaccine candidates.

Design/Methods: We identified key parameters for the trial site directory by a desk literature review and discussion with key experts. Trial sites in sub-Saharan Africa were identified by using information from pre-existing public databases. Sites were included in the directory if they had experience with TB vaccine trials, or experience with TB trials and experience with vaccines. Sites were invited by email to participate and complete an online survey on their capacity. We present summarized characteristics of the clinical trial sites.

Results: In this assessment 91 sites were shortlisted and 45 sites provided information. The majority of sites (24) were in South Africa, followed by Tanzania (5), and Kenya (4). The remaining other 12 countries had one site. In terms of TB clinical trial endpoint experience, 18 sites had conducted doing prevention of disease trials, 15 sites prevention of infection trials and 17 sites had no experience. Tuberculin skin testing was available at 38 sites, interferon gamma release assay at 26 sites and HIV testing at 41 sites.

Conclusions: Our directory provides relevant information on clinical trial sites for TB vaccines in sub-Saharan Africa. Capacity was self-assessed which could introduce bias. Language barriers may have introduced bias in our data collection. Our assessment can serve as a basis for further comprehensive assessment of clinical trial sites and expansion to include trial sites in other countries and continents.

EP-28-378 C-di-AMP as adjuvant enhanced BCG-induced trained immunity and provided protection against *M. tuberculosis* infection in mice

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Background: BCG is a live attenuated vaccine approved for prevention of tuberculosis (TB), which is caused by infection of *Mycobacterium tuberculosis* (Mtb). Though adaptive immunity plays a pivotal role in controlling Mtb infection, more evidence suggests that BCG induces trained immunity, which contributes to host defense against Mtb infection. In our previous work, we constructed a recombinant BCG (rBCG) by overexpressing diadenylate cyclase of *M. tuberculosis* (DisA). rBCG-DisA could produce more c-di-AMP, a bacterial second messenger regulating bacteria processes and host immune responses, which acted as an endogenous adjuvant. rBCG-DisA immunization subcutaneously (s.c) elicited elevated immune response as well as enhanced trained immunity in mice.

However, the protection efficiency of rBCG-DisA immunization was not superior to that of BCG in mice after intravenous infection of Mtb.

Design/Methods: Mice were vaccinated intravenously (i.v) with rBCG-DisA and challenged with Mtb intravenously.

Results: rBCG-DisA induced lower antibody response and reduced proportion of CD4⁺ T cells in splenocytes ($P<0.001$) than BCG. Splenocytes from rBCG-DisA-immunized mice produced slightly higher Th1/Th2 cytokines than that induced by BCG. Noticeably, splenocytes from rBCG-DisA-immunized mice produced more IL-1 β ($P<0.05$), IL-6 ($P<0.001$), and TNF- α ($P<0.01$), and exhibited enhanced response to heterologous re-stimulation using *S. aureus* and LPS. Bone marrow-derived macrophages (BMDMs) from rBCG-DisA-immunized mice showed more lactate production than those isolated from BCG-vaccinated animals ($P<0.05$). rBCG-DisA-immunized mice showed lower Th2 immune responses in spleen, but exhibited stronger distribution of H3K4 trimethylation in lung after Mtb challenge. rBCG-DisA and BCG-vaccinated mice showed similar bacteria reduction in spleen after Mtb infection ($P<0.01$).

Interestingly, rBCG-DisA-vaccinated mice displayed $\sim 1.5 \log_{10}$ CFU reduction in lung compared with both un-immunized ($P<0.05$) and BCG-vaccinated groups ($P<0.01$).

Conclusions: rBCG-DisA with c-di-AMP as endogenous adjuvant inoculated intravenously induces enhanced trained immunity, which provides additional protection against Mtb infection in mice.

EP-28-379 Preventive effects of *M. tuberculosis* DNA vaccines on latent TB infection in a mouse model

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Background: To understand the effects of *M. tuberculosis* latent infection-associated proteins against latent tuberculosis infection (LTBI), and to provide candidate targets for the construction of DNA vaccine anti-LTBI.

Design/Methods: A mouse LTBI model was established. At 16 weeks after infection, the mice were immunized respectively with PBS, pVAX1 vector DNA, *Vaccae* vaccine, *ag85ab* plasmid DNA and 7 kinds of plasmid DNAs encoding LTBI-associated proteins (including Rv2660c, Rv1733c, Rv1813c, Rv2628, Rv2029c, Rv2659c, and Rv3407) once every two weeks for three times. At 3 weeks after stopping prednisone injection, the mice were killed for tissue colony count and immunological evaluation.

Results: The lung CFUs of mice in each vaccine group were significantly lower than those in the PBS group and vector group ($P < 0.05$), but there was no significant difference in the liver CFUs of mice in each group.

The number of effector T cell spots secreting IFN- γ in splenic lymphocytes was significantly higher in the *ag85ab* DNA group than those in PBS, vector, and *vaccae* groups ($P < 0.05$). But the number of lymphocyte spots from 7 LTBI-associated DNA groups had no significant difference with the vector group. IFN- γ /IL-2 and IL-17A levels in the supernatant of splenocyte culture significantly increased in *ag85ab*, *rv2659c*, and *rv2029c* DNA groups ($P < 0.05$). There was no significant difference in IL-6 and IL-10 among DNA groups, PBS and vector groups.

The percentages of CD4⁺CD25⁺FOXP3⁺ regulatory T cells in spleen cells of *ag85ab*, *rv2660c*, *rv2029c*, and *rv3407* DNA groups were significantly lower than those of the PBS and vector groups.

Compared with the PBS group, the proportion of living cells was significantly decreased, while the proportion of late apoptotic cells was significantly increased in *ag85ab*, *rv1733c*, *rv1813c*, and *rv2659c* DNA groups ($P < 0.05$).

Conclusions: *M. tuberculosis* *ag85ab* and 7 LTBI-DNA vaccines had preventive effects on the mouse LTBI model.

Optimising TB diagnostics

EP-29-380 Mobile van TB screening at Blantyre Bus Station, Blantyre City, Malawi

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Background: Malawi National TB Control Programme introduced Mobile Van TB Diagnostic Units (MDU) in 2018. The MDUs are equipped with digital X-ray and gene X-pert machines to complement TB case detection effort, finding and treating missed cases in high-risk populations in hard-to-reach areas.

The aim was to fulfill the WHO End TB Strategy (2016–2035) which focuses on systematic and active screening of high-risk groups and to promote early diagnosis of TB. Identification of high-risk communities in hard-to-reach areas such as bus terminals is more likely to aid in the detection of missing TB cases and improve TB control. Such places harbor different kinds of people who always are immobile and work in overcrowded conditions. Their mobile lifestyle exposes them to respiratory infections including TB. Therefore, the aim of the study was to screen all people in Blantyre bus station.

Design/Methods: A mass TB screening exercise was organized targeting the drivers, bus conductors, passengers, vendors, bus cleaners, hawkers, mechanics, and traders within the Blantyre bus station. Community mobilization was done. The screening was conducted by the MDU team using a structured questionnaire and chest X-ray.

Those who had presumptive TB were asked to submit sputum for gene X-pert examination and were evaluated for TB. The activity was conducted from July to October 2020.

Results: A total of 2005 people were screened, 307/2005 (15.3%) were presumptive TB cases, 22/307 (7.1%) were confirmed to have TB. A total of 10 (45.5%) of the 22 TB cases were biologically confirmed cases and 12 (54.5%) were diagnosed through chest X-ray.

Conclusions: Targeted screening in high-risk populations is a strategy for finding the missing TB cases and systematic screening using the MDU is an effective strategy for increasing TB case notification.

Such screening exercises should be conducted routinely to improve TB case notification and should be replicated in other towns.

EP-29-382 Kazakhstan's experience with the introduction of the Xpert MTB/RIF assay at the primary health clinic level

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Background and challenges to implementation: The WHO estimates Kazakhstan among the 20 countries with high levels of RR/MDR-TB. A pilot project for the introduction the GeneXpert MTB/RIF ("GeneXpert") for rapid TB identification in primary health clinics (PHCs) was launched in 2017 in 3 regions of Kazakhstan following the 2014-2020 Complex Plan against TB with Global Fund support.

Intervention or response: Fifty-six GeneXpert-machines were available in TB dispensary till 2017, which did not meet the country needs given the long distances between human settlements. GeneXpert was expanded to 33 PHCs. We compared the number persons with suspected TB examined with the GeneXpert test, the number of tests performed, and the proportion of smear-negative pulmonary bacteriologically confirmed cases before 2017 - 979 and after 2017 - 827.

Results/Impact: Following GeneXpert expansion to PHCs, the number of persons with suspected TB tested with molecular diagnostics increased 2.8 times (6 986 tests per year to 19 262 tests per year).

Furthermore, 62.3% of the total number of the GeneXpert tests was performed at the PHC level. With the introduction of GeneXpert MTB/RIF at the PHC level, the coverage of newly detected TB cases using GeneXpert increased by 16.1% (from 84.6% before to 98.2% after).

Among new smear-negative pulmonary TB cases bacteriological confirmation improved by 88.1% (from 36.1% before to 67.9% after) and RR/TB detection increased by 51.7% (from 14.9% before to 22.6% after).

Conclusions: All regions have an access to the Xpert at the PHC level now. Based on this pilot data and with further expansion of GeneXpert throughout the country, a diagnostic algorithm has been revised by the Ministry of Healthcare and examination of sputum samples using Xpert is the priority TB test. Microscopy is performed only when the GeneXpert is positive to define an epidemiological status of a TB case and to implement infection control.

EP-29-383 Decentralising rapid TB diagnosis: Truenat implementation experience at sub-district microscopy centres in Uttar Pradesh, India

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Background and challenges to implementation: Centre for Health Research and Innovation (CHRI), PATH India affiliate and National TB Elimination program (NTEP) deployed rapid molecular diagnostic test Truenat, here we are sharing experience of deployment.

Intervention or response: Truenat deployment was done in October 2019 at sub district Designated Microscopy Centres (DMC). Selection of DMCs were based on higher foot fall. A list of DMCs with high OPD load were prepared, DMCs with CBNAAT facility and state's identified Truenat sites was excluded from the list, remainder were considered. Five sites in two districts (3 in Bahraich and 2 in Sambhal) were selected in consensus of state TB cell. Total 2019 presumptive TB cases (65% male, 35% female, 98% adults and 2% paediatric age group) were tested across the five sites.

Results/Impact: Of the presumptive cases tested, 770 (38.0%, 95% CI 36.28-40.56) were found as MTB positive and 100% (95% CI 99.5-100) were offered on Rif resistance assay, compared to Rif assay offered, 41% in base line year (2018) of the 5 sites. Of the MTB positive cases 96% (95% CI 93.2-96.34) were Rifampicin sensitive and 16 (1.7%, 95% CI 1.0-2.9) were Rifampicin resistant.

Of the sample collected 99%, (95% CI 98.69-99.5) were tested within 0 to 1 days. TB Treatment in 95% (95% CI 93.2-96.34) diagnosed cases were initiated within 7 days, compared to 70.8% in base line year. Verbal interaction with patients during site visit indicates high satisfaction with the service.

Furthermore, deployment of Truenat at the sub-district level yielded 20-25% more cases in comparison with baseline data of microscopy performance (10-15% microscopy positivity).

Conclusions: Deploying rapid molecular test at sub-district level will accelerate rapid, accurate early diagnosis of Rifampicin assay and appropriate treatment initiation. NTEP should consider replacing microscopic method to molecular testing method in a phased manner to achieve the end TB.

EP-29-384 Determinants of the gap between the diagnosis and treatment of multidrug-resistant TB in Cameroon: a mixed-method study

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Background: Multi-drug resistant tuberculosis (MDR-TB) continues to be a global public health threat. Unfortunately, a persistently high proportion (>12%) of patients diagnosed with MDR-TB in Cameroon do not initiate treatment despite efforts by the government and international partners. This study reported the determinants of the gap between MDR-TB diagnosis and treatment.

Design/Methods: This was a mixed-method study implemented between January and April 2021 in the 11 MDR-TB treatment centers in Cameroon. A structured questionnaire was administered to patients who initiated treatment in 2020 and in-depth interviews (IDIs) were conducted with 14 patients (8 who initiated treatment and 6 who never initiated treatment) and 15 health personnel at the different levels of MDR-TB care cascade (treatment and diagnostic clinics staff, laboratory, and regional MDR-TB focal persons) to understand their perspectives on the barriers to treatment initiation.

Results: One-hundred and fourteen (121) MDR-TB patients were enrolled. The mean age (years) was 37±12, majority (66.3%) were males, 21.1% were HIV positive. 28% had a history of smoking and 30% initiated treatment >14 days following diagnosis. About (12%) 15/121 never initiated treatment. Of the patients who initiated treatment, 78% reported difficulties in treatment engagement. The main barriers were multiple drugs (75%) and long hospitalization period (55%). The patients who never initiated treatment (during in-depth interviews) reported long hospitalization period, stigmatization and long distance between home and treatment centers as the factors that stopped them from initiating treatment. Refusal of hospitalization by patients, long-distance of the treatment center from patients home, lack of nutritional support to patients were main barriers reported by health personnel.

Conclusions: Both patient and health system barriers determined the gap between diagnosis and treatment of MDR-TB. Enforcing patients counselling, taking treatment closer to patients, improving hospitalization conditions and nutrition support could reduce the diagnosis-treatment gap. Community based MDR-TB treatment models should be investigated.

EP-29-385 Diagnostic accuracy of Truenat TB and rifampicin resistance assays in microscopy centres in Addis Ababa, Ethiopia

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Background: Rapid and sensitive Tuberculosis (TB) diagnosis closer to patients is a key global TB control priority. Molbio Diagnostics, Bangalore, India has developed new molecular TB and RIF (Rifampicin)-resistance diagnostic tool Called Truenat assays. The assays utilize chip-based real-time micro-PCR. This study aimed to evaluate the diagnostic accuracy of the Truenat assays (Truenat MTB, MTB Plus and MTB-RIF Dx) for TB and RIF-resistance detection; and to compare the assays to that of Xpert MTB/RIF assay.

Design/Methods: A prospective evaluation study was conducted in three microscopy centers in Addis Ababa, Ethiopia from May 2019 to February 2020 and enrolled 200 presumptive TB adults. Both solid and liquid culture were used for isolation; and phenotypic liquid method was used for drug susceptibility testing (DST) as reference standard.

Results: Of 200 adult participants, culture confirmed TB cases were 25 (12.5%), and only one isolate was resistant to RIF by phenotypic DST. The sensitivity of Truenat MTB was 88.0% [95% CI 70.1, 95.8], while 94.0% [95% CI 93.3, 98.9] for Truenat MTB Plus assay at the microscopy centers. The specificity of Truenat MTB was also 97.2% [95% CI 93.1, 98.9], while for Truenat MTB Plus assay was 97.2% [95% CI 93.0, 99.0]. Of 19 results of Truenat MTB-RIF Dx assay and phenotypic DST, 18 were concordant susceptible and one was concordant resistant. The assays were compared to Xpert MTB/RIF assay and the sensitivity of Truenat MTB was 90.5% while for MTB Plus, 100% and for Xpert, 100% for TB detection at the reference laboratory. The overall non-determinate rate for Truenat assays was 14.5%, whereas 3.7% for Xpert MTB/RIF assay.

Conclusions: Truenat assays were found have high diagnostic accuracy. The assays have the potential to be used as a point of care TB diagnostic tests though more data is required to increase confidence on the estimated diagnostic accuracy.

EP-29-386 TB diagnosis: time series of health system dynamics in a city of northeast Brazil

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Background: Tuberculosis (TB) is a disease that should be treated in Primary Health Care (PHC), therefore the aim was to investigate the behavior of the incidence of TB according to the place of diagnosis in the city of São Luís/Maranhão - Brazil.

Design/Methods: Ecological study that considered the notified cases of TB of residents in São Luís, from 2010 to 2019. The cases were grouped according to the place of diagnosis (PHC and hospital environment) and the monthly incidence rates were calculated. The Prais-Winsten regression model was used, followed by the Seasonal and Trend decomposition using Loess method, finishing with the four-year forecast of the temporal trend (until 2023) using the forecast function. The tests were conducted using the STATA and RStudio software, considering a significance level of 5%.

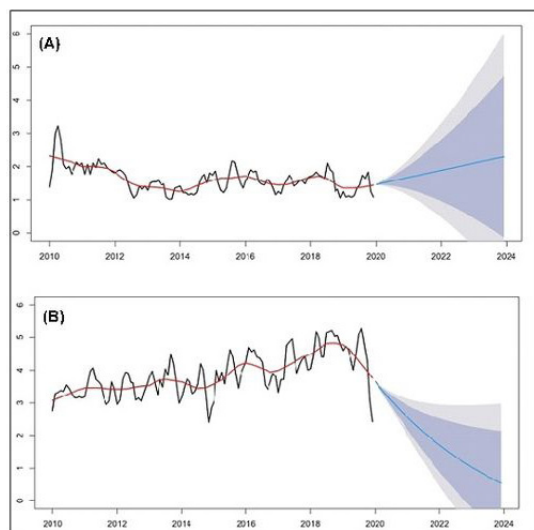


Figure 1. Time series and forecast of the trend of tuberculosis cases diagnosed in PHC (A) and in hospitals (B) São Luís - Maranhão, Brazil

Results: A total of 7,958 TB cases were identified, 1,286 (16.16%) of which were discarded because no diagnosis site was reported; of those remaining, 4,706 (59.14%) were diagnosed in the Hospital environment and 1,966 (24.70%) in PHC. The regression model classified a de-

creasing temporal trend for the diagnosis of TB in PHC (-0.91%/month (95%CI: -0.22 - -1.82)) and increasing in the hospital environment (+2.56%/month (95% CI: 1.39 - 3.75)). The forecast showed a slight increase in the rate of diagnoses of TB cases in PHC and a decrease in the hospital environment (Figure 1).

Conclusions: The decreasing temporal trend of TB diagnosis in PHC shows the difficulties faced for its early diagnosis and treatment, while the increasing trend in the hospital context demonstrates the worsening of the disease and the integrity of its chain of transmission. Despite the forecasts indicating a decrease in TB diagnosis in the hospital environment, with a slight increase in the diagnosis in PHC, it must be considered that with the pandemic scenario of COVID-19 this could be even worse.

EP-29-387 Aspects associated with the site of TB notification in people deprived of liberty

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Background: This study aimed to describe the sociodemographic, diagnostic, and clinical aspects associated with the notification of inmates with tuberculosis outside the prison system.

Design/Methods: A case-control study, whose data used were collected from the information system of tuberculosis cases in the state of São Paulo and included new cases of tuberculosis in prison units in the state from 2015 to 2017. The variable dependent consisted of the site of notification (prison system x outside the prison system). The exposure variables included: sociodemographic, diagnosis, and clinical data, which were analyzed through frequency distribution and bivariate analysis.

Results: 7,559 people took part in the study, of which 5,764 were notified in the prison system. Evidence was identified that people of white (OR 1.43; CI 95% 1.27-1.61) and black (OR 1.37; CI95% 1.14-1.65) race/color were a risk factor for notification outside the prison system compared to brown people. Other factors associated with notification outside the prison system were: diagnosis during hospitalization (OR 1.37; CI 95% 1.01-1.86) compared to diagnosis at an outpatient clinic; negative sputum culture OR 1.65; CI 95% 1.41-1.92) and not performed (OR 1.25; C I95% 1.09-1.44) compared to positive; extrapulmonary (OR 2.84; CI95% 2.12-3.81) and pulmonary + extrapulmonary (OR 3.20; CI 95% 1.78-5.75) clinical form compared to pulmonary TB; diabetes

mellitus (OR 2.03; CI 95% 1.19-3.47) and drug use (OR 1.66; CI 95% 1.47-1.88). The normal X-ray (OR 0.46; CI 95% 0.30-0.70) and not performed (OR 0.45; CI 95% 0.40-0.52) were protective factors for the notification of tuberculosis outside the prison system compared to those with a suggestive image of TB.

Conclusions: The identification of aspects associated with the site of notification of tuberculosis in inmates shows the difficulties faced by the prison system in the diagnosis of tuberculosis of specific groups, requiring articulation with community services for the detection of cases.

EP-29-388 Quality assurance practices of TB diagnostic health facilities laboratory in Ethiopia

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Background and challenges to implementation: Ensuring the quality of laboratory test results is a mandatory component in the diagnosis and treatment of tuberculosis (TB). Therefore, this study was aimed to assess the quality assurance practices in tuberculosis diagnostic health facilities of Ethiopia.

Intervention or response: A cross-sectional study was conducted from October 2018 to March 2019 at nine governmental TB-culture laboratories and 34 randomly selected GeneXpert® MTB/RIF (Xpert® MTB/RIF) testing health facilities of laboratory in Ethiopia. We reviewed the last one year of records and interviewed the laboratory focal. Prior to the data collection, training was given for the data collectors. Descriptive statistics were used to produce results and presented with tables and graphs.

Results/Impact: From a total of 34 Xpert®MTB/RIF testing laboratories 17 (50%) of them were run Internal quality control (IQC) for Acid-Fast Bacillus (AFB) Microscopy and 23/34 (67.6%) of them had lot-to-lot verification of staining reagents. For Xpert® MTB/RIF assay, a lot-to-lot verification of cartridge and method validation practiced performed only in 3/34 (8.8%) and 7/34 (20.6%) of Xpert® MTB/RIF testing laboratories respectively. All TB-culture laboratories were included in the study run start and end IQC (negative control) during TB-culture sample processing and were performed lot-to-lot verification for Mycobacteria growth Indicator Tube (MGIT) in 8/9 (88.9%) of TB-culture laboratories.

External Quality Assessment (EQA) Proficiency Testing (PT) for AFB microscopy practiced in 27/34 (79.4%) of Xpert® MTB/RIF testing laboratories and 34 (100.0%) for Xpert® MTB/RIF assay. TB-Culture PT participation practice among TB-culture laboratories were 8/9(88.9%). A major challenge of health facilities dur-

ing PT participation were AFB PT-sample transportation delay 11/27(40.7%) and Xpert® MTB/RIF assay EQA-PT feedback missing 13/34 (38.2%).

Conclusions: This assessment reveals lot-to-lot verification and method validation were not well-practiced. Most TB diagnostic health facilities laboratory had EQA-PT participation practice while a major gap was identified in PT samples-transportation and feedback missing.

EP-29-389 The role of private healthcare providers in the detection of people with TB during the Covid-19 pandemic in the Kyrgyz Republic

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Background and challenges to implementation: The number of TB cases detected in 2020 decreased by 28% compared to the previous year due to the COVID-19 pandemic. Due to closure of public health centers, people go to Private Health Care Facilities (PHF) to see a doctor. Some TB patients are diagnosed there but not officially registered as it is not allowed by the law.

Intervention or response: To address the issue MoH established a working group with TB specialists, lawyers, doctors from private clinics and laboratories to see a possibility to involve PHF to detect TB cases and refer them to the state system for registration and treatment. 50 PHF facilities were accessed in terms of ability to start detection of TB patient.

Due to various factors, instruction for PHF were adapted accordingly. Followed by assessment, series of off-line, on-line and on-job trainings on TB were conducted. All detected TB cases should refer to state TB centers for registration and treatment

Results/Impact: In the first four months of 2021, 10,500 patients were screened for TB symptoms in 38 actively working private clinics. Sputum samples of 200 presumptive TB cases were collected and tested for microscopy and Gene-Xpert.

As a result, TB was detected in 40 people, including 12 DR TB patients. Although, it is a not big figure but it is promising and shows impact of PHF in detection of TB cases.

Conclusions: In the era of COVID-19 pandemic when state health system is under pressure and TB is not a priority, involving PHF is necessary to detect TB. It eases the financial burden to the state system as some patients

could afford service. The project is planning to propose to MoH to work on the legislation of TB management in PHF under private-governmental partnership condition and to motivate PHF to work on TB to achieve End TB.

EP-29-390 Diagnostic network optimisation: a data-driven approach to increasing access and network efficiency of programmatic management of drug-resistant TB in India

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Background: India is expanding access to Programmatic Management of Drug Resistant TB (PMDT) towards its vision to eliminate TB by 2025. Diagnostic Network Optimization, a modelling-based approach, was utilized to assess and inform the capacity and location of Culture/Drug susceptibility testing/Line Probe Assay testing sites and inform scale-up of Xpert XDR.

Design/Methods: We used a supply chain optimization software (Supply Chain Guru) to map India's TB diagnostic network using available data sources, such as laboratory and programme reports and health and demographic surveys. We analyzed various scenarios including current network configuration, model recommended addition and placement of testing instruments and applying service distance/ time constraints. We modelled testing demand at three time points (2018, 2021, 2025) based on trajectory of current testing volumes and National Strategic Plan (NSP) targets and analyzed the outputs to provide optimal access to services, maintain or reduce turnaround time and minimize costs

Results: Demand for culture tests was expected to increase 5-8 times by 2021 to meet targets and then substantially reduce towards 2025 as caseload reduces. To meet peak testing demand in 2021, the model indicated a need for 108-164 MGIT instruments spread over nearly all states. Necessary testing capacity could be added through public sector equipment procurement, or engagement of private sector labs at lower long-term costs. Current state (2018) of utilization of LPA (line probe assay) instruments was very low (13%). Existing LPA footprint was thus found largely sufficient to meet near term demand but 70-79 GT Blots or 168- 444 GeneXpert XDR machines (to reduce service distance) were recommended.

Conclusions: Analysis of TB diagnostic networks using existing sources of data highlighted key gaps and opportunities to inform procurement and placement of instruments. Network mapping and optimization should be considered an integral part of strategic planning and monitoring progress towards case notification and testing targets.

Tailored care: the way forward

EP-30-391 Digital adherence technology for self-administered TB preventive therapy

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Background: Strategies to support and monitor adherence to tuberculosis (TB) preventive therapy (TPT) are urgently needed, particularly in the context of scale-up of short-course regimens including weekly isoniazid- rifapentine (3HP). Digital adherence technologies (DATs) have been evaluated in active TB but have not been used to facilitate self-administered TPT.

Design/Methods: We used human-centered design (HCD) to co-design a contextually adapted version of the commercially available 99DOTS platform for delivery of 3HP with routine HIV/AIDS care. 99DOTS uses pill-pack envelopes that reveal a toll-free number when pills are removed that a patient calls to report dosing. We conducted semi-structured interviews and workshops with 30 people living with HIV (PLHIV) and 9 providers at the Mulago AIDS clinic (Kampala, Uganda) to develop 6 insights to guide the HCD process. We then conducted 2 focused brainstorming sessions to generate ideas for prototypes, and iteratively tested and refined these prototypes with 20 PLHIV for the final adapted version of 99DOTS.

Results: Based on our 6 HCD insights, we expanded the 99DOTS system for patients to include a waterproof, handheld, zipper-secured fabric pouch in masculine and

feminine designs, with 5 internal pockets, each carrying one week of 3HP pills in a plastic bag, card inserts containing pictorial instructions to report dosing with motivational messages, and a clinic contact information card.

We developed weekly dosing reminder phone calls that allow for self-reporting of adverse events and educational and motivational audio recordings when patients call to report dosing.

For health care workers we redesigned the online platform with a weekly calendar and dosing window that allows for patient choice of dosing day and delivery strategy as well as a task-list of missed doses.





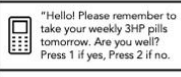
Insight	Design Opportunity	99DOTS Redesign
HIV is a disease, not an identity, and treatment options must honor diverse individuals and needs.	Provide a suite of options for different treatment modalities.	For patients on SAT, they can choose the type of fabric pouch they wanted to use with distinct male and female designs in many colors and patterns. 
Patients compare healthcare options based on a unique application of their personal values.	Allow for facilitated decision making and honor autonomy.	Patients may choose their dosing date and time. For acute concerns, patients can call or drop into clinic as needed.
PLHIV are excited about the new opportunity to prevent TB for themselves and their families and thus motivated to engage with TPT.	Tailor education and messaging to PLHIV's needs and concerns.	We included a card insert with motivational messages and 99DOTS instructions as well as motivational audio messaging when calling in. 
In contrast to novice pill takers, experienced PLHIV have well defined medication routines and are more confident and capable of incorporating TPT into their lives.	Ensure any new interventions fits well into patient routines.	We utilized well-known plastic pill bags and pill blister packs with educational and motivational messaging. 
The introduction of a new medication for PLHIV prompts an increased desire for provider contact.	Provide easy to access contact information for providers and allow for ample in person touchpoints.	We included a clinic contact information card with information about their drugs. 
The fear of side effects is deeper with PLHIV and brings back old fears about new side effects.	Address this fear of side effects openly and transparently.	We included weekly automated check-in phone calls and targeted clinician follow-up. Pharmacy technicians screen side effect concerns and refer to a clinician when needed. 

Table 1. Human-centered redesign of 99DOTS system for weekly tuberculosis preventive therapy.

Conclusions: Using HCD, we co-designed a contextually adapted version of 99DOTS with end users that can be further evaluated as part of 3HP scale-up.

EP-30-392 Patient acceptance of video-observed therapy: a narrative review

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Background: Virtual modes of tuberculosis (TB) treatment monitoring are increasingly relevant. We conducted a scoping literature review on TB patient acceptance towards video directly observed therapy (VDOT).

Design/Methods: We searched MEDLINE and EMBASE for studies published prior to November 3rd, 2020, where video-based technology was used to supervise or support treatment for TB infection or disease, and where data was collected from patients about their related experience, perspective, and/or utilization. A narrative synthesis was performed, drawing on a theoretical framework of acceptability.

Results: Of 2483 articles identified in MEDLINE, 22 were included. (EMBASE search is in progress.) Studies were conducted in 14 countries (five high-income, nine upper and lower-middle-income).

Video-based technology was used to monitor treatment intake for TB disease; other reasons were not specified. The taxonomy VDOT or video-/based observation was universal. Acceptance, assessed via surveys or in-depth interviews, was quantitatively and qualitatively assessed as high, and built upon:

1. Convenience: VDOT was easily integrated into patients' daily routines and removed stressors related to weather, transportation, and health system scheduling.
2. Privacy: patients appreciated controlling when, where, and by whom they were seen taking treatment, though possible intrusion into their home environment or risk of TB disclosure to household members deterred some patients.
3. Technology literacy: familiarity and comfort with any technology, facilitated acceptance to VDOT; clear, repeat instruction was crucial to building acceptance among new users. In twelve studies, a preference for VDOT over in-person directly observed therapy was voiced.

Conclusions: By facilitating patient autonomy, VDOT has the potential to be an empowering and person-centered treatment monitoring strategy. However, more robust evaluations are needed; scales were not employed and often only a single question was asked.

The role of social determinants such as place of residence, access to technology, and patient-provider communication requires further exploration.

EP-30-393 Using digital technology on improving TB treatment adherence, Khartoum State, Sudan

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Background: Tuberculosis continues to be a major global cause of morbidity and death. Although tuberculosis is a treatable disease, the high frequency of treatment non adherence remains a challenge. The use of mobile phones structurally in a TB program has the potential to improve the nonadherence.

However, its impact on treatment outcome in Sudan has not yet been evaluated.

Objective: To assess the potential use of digital technology (cell phones) for enhancing TB treatment adherence.

Design/Methods: We conducted a controlled intervention pilot study during the period from 1st of May 2017 to 31st of March 2018, in eight TB treatment units in Khartoum state, Sudan. Newly diagnosed patients with positive sputum smear on DOTS therapy were enrolled in intervention and control groups. SMS reminders were sent to the intervention group and telephone calls if needed. Assessments were done at the beginning and at the end of the treatment.

Results: One hundred and forty-eight patients were enrolled, seventy-four patients in each group. The participants in the two groups were similar in demographic characteristics and behavioral and knowledge related factors about TB disease at baseline. The patients in the intervention group had a lower default rate (6.8%), higher documented cure rate (78.4%), better knowledge e.g. when to stop treatment (OR: 2.261; 95% CI: 1.050-4.870; $P < 0.037$) compared to control group who had default rate of (10.8%) and cure rate of (59.5%). SMS reminder was useful and facilitated good interaction between patients and health personnel.

Conclusions: The study shows promising results that the use of mobile texting seemed useful in improving the treatment adherence, lowering default and was highly accepted by participants. Further evaluation of its potential benefit was warranted.

EP-30-394 Reasons and timing of loss to follow-up outcomes among patients on first-line anti-TB medicines in South West Nigeria

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Background: Loss to follow-up (LTFU) along the TB care cascade are barriers to TB control because of sustained TB transmission including resistant strains, high mortality and increased spread of DRTB strains. Understanding common reasons for LTFU and their timing could help target interventions to improve adherence to TB treatment. We aimed to highlight common reasons for LTFU among patients on first line anti-TB medications in 3 states implementing USAID-funded LON 3 project in Nigeria.

Design/Methods: A cross-sectional study, using pre-tested questionnaires, were administered by phone interviews to 90 TB patients receiving treatment between January and December 2020 who were LTFU while on TB treatment in 31 health facilities across three States in South West Nigeria. The focus of the interview was to find out the reasons why they were LTFU. Interviewers contacted treatment supporters when patients could not be reached. Clinical and sociodemographic information, such as age, sex and HIV status were extracted from treatment registers.

Results: The mean age was 43 years. Majority 73 (81%) of LTFU were male, while Ogun State had the highest number of 35 (38.9%), LTFU was highest during the first month on treatment, 60 (66.7%), amongst HIV negative, 63 (70%) and those that had not been treated for TB before 85 (94.4%). The commonest reason for LTFU among TB patients on treatment was death, 23 (25.6%), followed by lack of transport, 16 (17.8%) and religious beliefs, 12 (13.3%).

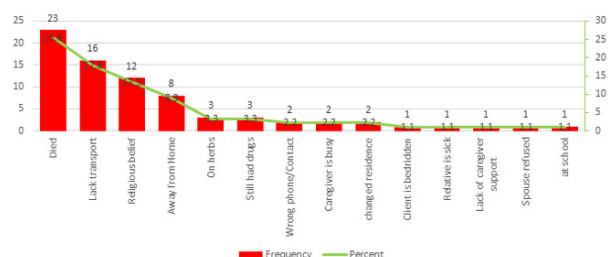


Figure. Reasons for LTFU while on TB treatment, n=90

Conclusions: The study suggests a high mortality among patients on treatment who may have been classified as LTFU. Interventions to reduce mortality and increase coverage of TB treatment facilities, thus bringing care closer to patients is necessary. We suggest the use of 30-day adherence calendars to improve adherence counselling in the first one month on treatment to minimize LTFU.

EP-30-395 Factors associated with TB treatment loss to follow-up in Napak District, Karamoja Sub Region, North Eastern Uganda

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Background: Across the Karamoja sub-region, only 65% of TB patients successfully completed TB treatment in 2019. Loss to follow-up (LFU) was the major cause of treatment non-completion. Napak district contributed 29% of TB cases notified by the sub-region that year. We sought to examine the factors associated with loss to follow-up while on TB treatment in this district.

Design/Methods: We extracted demographic and routinely collected data on patients initiated on TB treatment from January 1st to December 31st, 2019 from the unit TB registers. LFU was defined as missing two or more consecutive months of TB treatment. Factors associated with LFU were examined using a multilevel logistic regression model accounting for clustering by health facility.

Results: A total of 956 patients were started on TB treatment in Napak district between January 1st and December 31st 2019. Most of the patients (56.4%) were male. Majority (91.6%) of patients were HIV negative, and (55.8%) were diagnosed with bacteriologically confirmed TB. Of the 956 patients, 28.2% were LFU during TB treatment. Residing outside Napak district (aOR= 2.67; 95% CI: 2.38-2.99, p<0.01) and starting treatment during the planting season -April to June (aOR= 2.44; 95% CI: 1.76-3.40, p<0.01) increased the odds of being LFU whereas being in the 35-44 age category (aOR=0.81; 95% CI: 0.69-0.96, p=0.01), receiving care from a hospital (aOR=0.81; 95% CI: 0.69-0.96, p=0.01) and having been previously treated for TB (aOR= 0.29; 95% CI: 0.18-0.47, p<0.01) decreased the odds of being LFU.

Conclusions: A significant proportion of patients started on TB treatment in Napak district were LTFU. Provision of client-focused differentiated services including tailoring interventions seasonally; provision of TB medicine refills closer to patients' homes either through community TB treatment points or home-based drug deliveries by community-owned resource persons may reduce the number of TB patients who experience LFU while on treatment.

EP-30-396 Community-based care and management of TB patients: a pilot project

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Background: The study aims to identify the association of the baseline vulnerability with treatment outcome and the impact of community-based care and management for more vulnerable group on treatment outcome.

Design/Methods: The study was designed a cross-over study that A region was designated as an intervention group and B region was a control group during the first phase of the study. At the second phase of the study, the intervention was conducted in the B region where was previously a control group.

During the study period, all notified tuberculosis patients were assessed baseline vulnerability consisting of 20 questions, and categorized as low vulnerable group and high vulnerable group. In the intervention group, case manager met patients identified as the high vulnerable group, and supported them according to their needs.

The supporting packages included administrative assistance to get an entitlement of social benefits and long-term care services, financial incentive, connecting to long-term care facility, and directly observed therapy. We constructed a vulnerability-stratified multivariate logistic regression model.

Results: According to the baseline vulnerability assessment, 561 patients (87.4%) were identified as the low vulnerable group and 81 patients (12.6%) as the high vulnerable group. High vulnerable group was likely to be unfavorable outcome compared with the low intervention group, and the ORs were 3.9 (95% CI 1.8-8.4) within strata of intervention group and 9.3 (95% CI 3.6-24.2) within the strata of control group.

The control group was unlikely to be favorable outcome compared with the intervention group, and the ORs were 1.2 (95% CI 0.8-1.8) within the strata of low vulnerable group and 1.7 (0.5-5.3) within the strata of high vulnerable group.

Conclusions: The study identified the baseline vulnerability was associated with favorable treatment outcome. The community-based care and management according to patients vulnerability is likely to increase treatment success rate, but it was statistically insignificant.

EP-30-397 Exploring the effect of patient support group meetings on improving TB treatment outcomes in selected districts of South India

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Background: Participation in Patient Support Groups (PSG) has demonstrated improved quality of life for persons with cancer and diabetes. We explored the impact of participation of TB patients in PSG on TB treatment outcomes in selected five districts of Karnataka and Telangana states in India.

Design/Methods: Field level staff of Tuberculosis Health Action and Learning Initiative (THALI) project, funded by USAID, organised PSGs once a month on a regular basis, for patients recently initiated on treatment.

Patients, most likely to have poor TB treatment outcomes (ex. Elderly, alcohol consumption, co-morbid, re-treatment and DR-TB), were encouraged to participate in the PSGs. We extracted TB treatment outcomes and other variables from official Nikshay data for patients who had initiated TB treatment in 2019.

We compared treatment outcomes by participation in PSG and used multivariate logistic regression models to analyse outcomes by socio-demographic and other risk characteristics.

Results: Twelve percent of 30,706 TB patients from five districts of Karnataka and Telangana attended PSGs. Participation in PSG was higher among re-treatment patients (16% vs 11%), diabetes patients (21% vs 11%) and patients who consumed alcohol (20% vs 11%) than among those without these characteristics. Overall, successful treatment outcomes were significantly higher among patients who attended PSG (94%) as compared to patients who did not attend PSG (88%) [AOR: 2.44, 95% CI: 2.10-2.82].

The effect was significant for Bengaluru Urban, Bellary and Hyderabad. Similarly, the difference in treatment outcome according to PSG attendance persisted across different characteristics including age (60+ AOR: 3.2), gender (female AOR:3.3), type of TB (retreatment AOR:1.7), presence of co-morbidity (Diabetes AOR: 3.0); HIV AOR: 3.7), alcohol consumption (AOR: 1.8) and DR-TB status (AOR: 1.9).

Conclusions: Participation in PSGs was instrumental in improving the successful TB treatment outcomes. It is imperative to enhance the coverage of patients' participation in the PSGs to achieve higher population level impact.

EP-30-398 TB management and referral practices among traditional medicine practitioners in Lagos, Nigeria

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Background: Despite the potential role of Traditional Birth Attendants (TBAs) and Traditional Healers (THs) in tuberculosis management and referral practices in Nigeria, little is known about their knowledge of tuberculosis management and referral practices.

The study's aim was to determine traditional birth attendants' and traditional healers' knowledge and self-reported practices in managing tuberculosis in Lagos, Nigeria.

Design/Methods: A cross-sectional study of 120 THs and TBAs from three high-TB-burden Local Government Areas (LGAs) in Lagos, Nigeria. Data were collected using interviewer-administered questionnaires from April to September 2018. For data analysis, we used the Statistical Package for Social Sciences (SPSS) software. Independent predictors of being TBA or TH were determined using logistic regression at the statistical significance of $p < 0.05$ and 95% confidence interval.

Results: TB knowledge increased from 52.7% on the pretest to 61.7% on the post-test, with no differences between TBAs and THs 70% (84) of the 120 Traditional Medical Practitioners (TMPs) studied had never treated TB; 57.3% (69) had never referred a chronic cough patient to a health facility; 90% (108) were willing to collaborate with NTBLCP; and 85% (102) attached monetary and token incentives as a condition for collaboration. THs had a lower likelihood of ever referring a TB patient to the hospital (AOR: 0.3, 95% CI:0.14-0.64, $p=0.002$), currently referring TB patients (AOR: 0.06, 95% CI:0.02-0.17, $p0.0001$), and consulting 40 patients in a year (AOR: 0.22, 95% CI:0.09-0.53, $p0.0001$).

Conclusions: The majority of THs and TBAs were willing to work with NTBLCP to identify and refer Presumptive TB patients. We propose that the NTBLCP empower TBAs and THs to assist in the early referral of TB patients.

EP-30-399 Effectiveness of e-learning curriculums in educating healthcare professionals on obstructive lung diseases in low-middle-income countries

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Background and challenges to implementation:

To upgrade knowledge of healthcare professionals (HCPs) in Obstructive Lung Diseases (OLDs) using e-learning curriculums and to review their effectiveness in urban and rural areas of Pakistan

Intervention or response:

The Lung Health Program (LHP) developed e-curriculums for HCPs working at various sites of the Indus Hospital and Healthcare Network (IHHN), Pakistan. We used <https://canvas.instructure.com> an online platform for educators, to develop curriculums relevant to OLDs and their management.

Each course is spread on a four-week format and includes updated information from guidelines (for example GOLD COPD 2021) and pre- and post- course assessments. Currently available courses are Asthma, COPD, and Inhalers. STATA was used for statistical analyses.

Results/Impact: Between October 2020 and April 2021, 21 HCPs (20 doctors and 1 nurse) enrolled and completed 36 courses. Overall, 67% resided in urban areas while 33% in rural areas. Pre-course tests demonstrated that there was some knowledge of OLDs as the mean pretest score was 6.37 (SD 1.69).

After going through the courses, the mean score increased to 8.50 (SD 1.50). A statistically significant improvement of 34% (99% CI; 1.35-2.92; $p=0.000$) was thus observed.

This training pilot can now be expanded to include other public health initiatives in lung health and can be a valuable resource especially in rural communities.

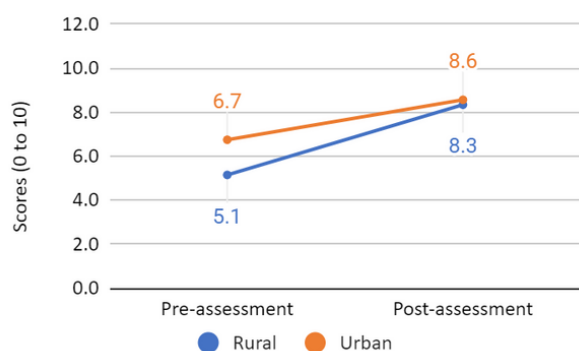


Figure. Pre- and post-assessment scores of HCPs in rural and urban areas.

Conclusions: E-curriculums are innovative tools to augment basic information on a diverse range of diseases. They provide distant training now that internet connectivity and smartphones are widely available.

Accessing rural communities is crucial as over 60% of the population reside here. OLD and other areas of lung health can benefit by keeping HCPs updated with international guidelines using a cost effective and sustainable model of education.

EP-30-400 A structured assessment of patient-centred care services for drug-resistant TB clients in the Philippines

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Background and challenges to implementation: In a high DRTB-burden country like the Philippines (14th globally), patient-centered care (PCC) is a critical intervention for DRTB control. Studies show that PCC can increase TB diagnosis by 40% and treatment success by 10%.

However, the inadequate provision of PCC services contributes to high LTFU rates of 40%. Structured assessments are needed to assess the implementation of PCC in TB health facilities and improve execution.

Intervention or response: We surveyed 16 DRTB satellite treatment centers (STCs). The survey assessed 71 items across 4 PCC domains:

1. Respect to patient autonomy and support efficacy,
2. Maximize physical comfort, safety, and wellness,
3. Provision of psycho-emotional support and protection from social isolation or discrimination and,
4. Prevention of catastrophic costs.

We calculated composite scores as the total of all weighted scores from each survey item, with a maximum score of 100%.

We performed multiple regression analyses to identify individual PCC components that contribute to improving treatment outcomes.

Results/Impact: The average PCC score was 64%. By domain, STCs scored the highest (82%) for patient autonomy and support efficacy, followed by 66% for physical comfort, safety, and wellness and 62% for psycho-emotional support and protection from social isolation or discrimination. The lowest-performing domain was the prevention of catastrophic costs (44%).

Regular monitoring and treatment of mental health conditions affecting patient's ability to reach cure ($\beta=10.81$), reduction of social isolation and provision of emotional support and encouragement ($\beta=8.48$), and regular monitoring and treatment of comorbid physical conditions ($\beta=8.45$) were the top 3 elements affecting treatment outcomes.

Conclusions: Implementation of PCC must be strengthened, with focused efforts on improving specific components. These include mental health care provision, providing psychosocial and emotional support, and managing comorbid physical conditions. Supportive interventions such as financial support for families and patients will reduce out-of-pocket expenditure, facilitate treatment completion, and achieve EndTB and UHC goals.

TB in children and adolescents 1

EP-33-422 Surveillance of childhood TB and drug resistance in the Covid-19 era

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Background: To determine the prevalence of drug resistance in children with bacteriologically-confirmed tuberculosis in the context of routine Xpert MTB/RIF Ultra (Xpert) use during the COVID-19 era.

Design/Methods: Prospective surveillance conducted from March 2019 through February 2021 in all children (<13 years) diagnosed with bacteriologically-confirmed tuberculosis (culture and/or Xpert) at Tygerberg Hospital, Cape Town, South Africa. Xpert was done on at least one specimen per child. Drug susceptibility testing (DST) was done using line-probe assay (GenoType MTBDRplus) for isoniazid (INH) and rifampicin (RIF); further DST only if RIF resistance identified.

Results: 418 children, 206 (49.3%) boys, median age 32 months (IQR 13-62) had bacteriologically-confirmed tuberculosis; 35/405 (8.6%) tested for HIV were positive. Overall, 259 (62.0%) had culture-confirmed tuberculosis: 26 (10.0%) had any INH or RIF resistance; 6 (2.3%) multidrug-resistant tuberculosis (MDR-TB) and 5 (1.9%) RIF-mono-resistant tuberculosis. 159/418 (38.0%) were Xpert-positive only; 6/159 (3.8% - all CSF) had no culture done and the remainder were culture-negative. Xpert-positive only DST results were: 4/159 (2.5%) RIF-resistant, 57 (35.8%) RIF-susceptible and 98 (61.6%) RIF-unsuccessful. Of children only Xpert-positive, 55 (34.6%) were currently receiving or had previous tuberculosis treatment. Comparing March 2020-February 2021 to the preceding year, the total number of bacteriologically-confirmed cases declined from 276 to 142 (45% reduction) and culture-positive cases declined

from 167 to 92 (49.5% reduction). Compared to the average number of culture-confirmed cases over the three preceding years (2017-2019), the reduction was 47.7%. A comparison of DST results to 8 previous 2-year surveillance periods is presented in figure 1.

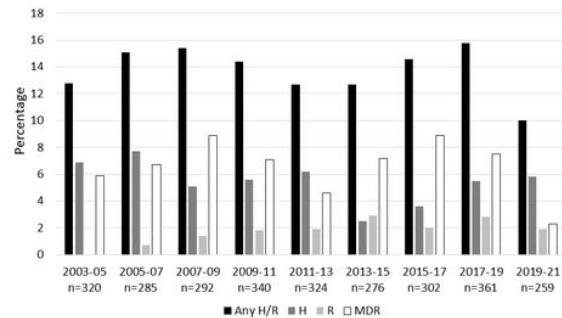


Figure 1. Prevalence of drug resistance in children with TB at Tygerberg hospital 2003-2021 in 2-year periods.

Conclusions: There was a dramatic decline of almost 50% in children diagnosed with bacteriologically-confirmed tuberculosis following COVID-related lockdown in Cape Town. The prevalence of any drug resistance/MDR-TB was the lowest ever compared to previous periods. Successful RIF DST was obtained in <40% of children who were only positive on Xpert.

EP-33-423 Strengthening data collection in children and adolescents with TB

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Background and challenges to implementation: The *Roadmap towards ending TB in children and adolescents*, launched in 2018, highlights gaps related to data collection, reporting and analysis. These include inconsistent reporting of TB cases in children and adolescents to National TB Programmes, a lack of data on TB in adolescents (10-19 years), as well as on multi-drug and rifampicin resistant TB (MDR/RR-TB) in children and adolescents.

Intervention or response: To address these gaps, from 2020, WHO has requested countries to report disaggregated data on notifications for more age groups (0-4, 5-9, 10-14 and 15-19 years, compared with 0-4 and 5-14 years previously), the number of patients aged 0-14 years enrolled on treatment for MDR/RR-TB, and treatment outcomes for this age group.

Results/Impact: In 2020, 95 countries reported data disaggregated into the four age categories for children and adolescents, including 10 high TB burden countries (HBC). In 2019, 396,000 cases among children and adolescents aged 10-19 years were reported, equivalent to 10% of total notifications in these countries. The number and proportion of children and young adolescents

treated for MDR/RR-TB was 5,588 (3.2%) in 2019. 123 countries reported the treatment success rate among children and young adolescents, including 19 TB HBC. The overall figure was 85%, ranging from 73% in Papua New Guinea to 97% in Bangladesh. In line with the commitments of the Rome Action Plan on Paediatric HIV & TB, data on TB/HIV co-infection in children and young adolescents will be requested for the Global TB Report 2021.

Conclusions: The WHO global data collection system can play a pivotal role in catalysing collection, review, analysis and reporting of data for key TB vulnerable populations, which is crucial for informing policy and programmatic action. Implementation of case-based TB recording and reporting system provides a platform for more targeted and responsive programming.

EP-33-424 Clinical presentation and risk factors for extrapulmonary TB disease in children in Pakistan

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Background: The clinical presentation for extrapulmonary tuberculosis (EPTB) in children can be variable and non-specific. This leads to delays in diagnosis, which contributes to increased morbidity and mortality. We aim to describe the clinical presentation and risk factors for EPTB in children in four facilities in Jamshoro district, Sindh, Pakistan.

Design/Methods: We conducted a prospective intensified screening program in Pakistan (2015-2016). TB disease was diagnosed through either bacteriologic confirmation or clinically. EPTB was defined as having any form of TB disease that did not involve the lungs, including abdominal, lymph node, CNS, bone, and pleural effusion. We report the proportion of site of EPTB by age group. We conduct regression analysis to identify factors associated with being diagnosed with EPTB for children 0-14 and also disaggregated in 0-4, 5-9, and 10-14 years age groups.

Results: A total of 1,163 children were diagnosed with TB, of which 157 (13.5%) had EPTB. Of those, 46 (29.3%) were 0-4, 53 (33.8%) were 5-9, and 58 (36.9%) were 10-14 years old. The most frequently reported types of EPTB were abdominal TB (2.7%; 3.5%, 0.9%, and 3.2% in the 0-4, 5-9, and 10-14 age groups) and

lymph node TB (9.8%; 4.1%, 12.6%, and 18.3% in the 0-4, 5-9, and 10-14 age groups). Type of EPTB varied by age (Figure 1). Ages 5-9 (RR: 1.88) and 10-14 (RR: 2.83), fever (RR: 1.96), and weight loss (RR: 2.04) increased risk of EPTB while being below the 5th weight percentile (RR: 0.29), cough (RR: 0.17), and family history of TB (RR: 0.50) decreased risk of EPTB (all $p < 0.05$).

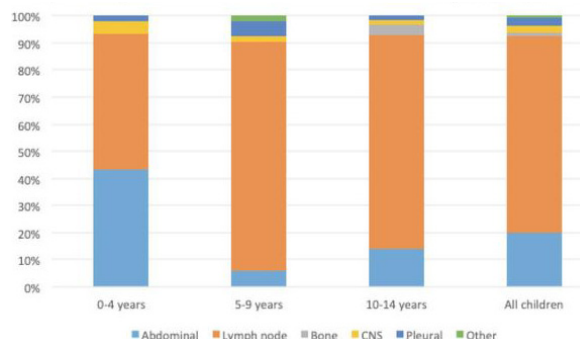


Figure 1. Proportion of EPTB site in all children with EPTB, by age group (N=157)

Conclusions: This study adds important knowledge about clinical presentation of EPTB disease in children in a rural setting in Pakistan and can help to optimize clinical algorithms to ensure that children with EPTB receive a timely diagnosis and have successful outcomes.

EP-33-425 Key to finding missing childhood TB cases in Nigeria: community-based contact investigation

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Background and challenges to implementation: According to WHO, the urgency of the problem of tuberculosis (TB) in children, whose full scope is still not fully known, cannot be underestimated. Multiple interventions exist to find TB cases with more attention on adult compared to children. USAID-funded TB LON 1&2 project, implemented by KNCV Nigeria reviewed the TB case yield and paediatric to adult TB ratio from facility and community-based interventions to prioritize areas for high yield for paediatric TB to improve on Paediatric TB case finding within the project.

Intervention or response: The project collects routine primary data from patients and service delivery points following the cascade of care. We reviewed secondary data reported over 26 weeks (between September 2020 and March 2021) across 840 facilities and their

surrounding communities in 14 states of Nigeria. The summary data includes number of clients screened, presumptive TB identified, presumptive TB evaluated, and TB patients diagnosed. Data were analyzed to compare results from both facility and community interventions.

Results/Impact: In facility-based intervention 2,601,003 clients were screened, 183,855 presumptive were identified, 147,378 evaluated, 13,738 TB patients diagnosed with 759 (6%) as children. From the communities, 92,851 clients were screened, 28,003 presumptive TB identified, 23,369 were evaluated and 2,123 (9%) TB cases diagnosed with 232 (11%) being children. Further analysis shows that 14% of childhood TB cases across all interventions and 59% from communities are solely from contact investigation with a 12% yield from evaluated presumptive TB.

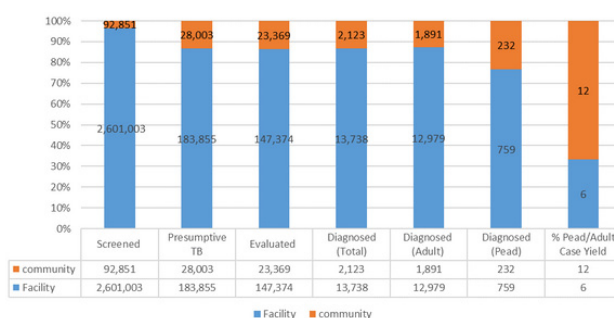


Figure. Contribution by intervention to Paed TB case finding.

Conclusions: Paediatric-to-Adult TB case proportion is higher in community (12%) compared to facility (6%) interventions. Contact investigation should be prioritized due to its high yield and relatively larger contribution to childhood TB cases. With good referral systems, community interventions including contact investigation present a good opportunity for improved childhood TB case finding.

EP-33-426 TB in children during the Covid-19 pandemic: analysis of the epidemiological situation in Siberian and Far Eastern federal districts of Russia

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Background: Until 2020, tuberculosis (TB) was the infectious “killer No.1”, annually about 1.5 million people die from TB in the world. However, the implementation of national health programs and joint international efforts made it possible to achieve in 2019 the lowest TB mortality rate in the last 10 years. At a time when the

COVID-19 pandemic swept the whole world, consuming global economic and health system resources, providing care to TB patients may be belated and incomplete.

Design/Methods: Epidemiological situation of TB among children and adolescents has always been and remains an indicator of entire situation with regard to TB. The purpose of our study was analysis of epidemiological data collected in the regions of the Siberian (SFD) and Far Eastern (FEFD) federal districts of Russia, where the highest incidence of TB and TB/HIV co-infection is registered.

Results: Compared to 2019, a significant decrease in the TB incidence among children under 14 years old (-20% in SFD and -35.8% in FEFD) was identified. The most significant decrease in the incidence rate was recorded in the Republics of Altai (-90.9%) and Khakassia (-77.1%). Considering that in 2019 the decrease rate of TB incidence among children was 13.6% in SFD and we registered increase of TB incidence by 6.2% in FEFD, it becomes apparent that such rapid decrease is due to insufficient identification of TB patients. We also noted deterioration in the clinical structure of tuberculosis among children, which indicates late diagnosis and initiation of anti-TB therapy.

Conclusions: Extremely unfavorable trends in the development of TB epidemic in Siberia and Far East of Russia were identified. On this basis, we can predict TB incidence increase not only among children, but also among adult population already in 2021 and, as a result, an increase in the number of TB deaths in 2021-22.

EP-33-427 Using DHIS2 TB case-based surveillance to describe the epidemiology of childhood TB in Tanzania

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Background and challenges to implementation: Globally, children (0-19 years old) are at an increased risk of developing Tuberculosis (TB). Household sputum positive cases are an important contributor to TB infection among children. Limited diagnostic capacity and inability to produce sputum for laboratory examination limits the capacity to diagnose TB in children in Tanzania.

Intervention or response: To measure a true burden of TB disease among children, Tanzania adopted a case-based surveillance system as recommended by the World Health Organization. A tracker module was adopted and customized on the already existing DHIS2 platform. In-depth analysis of available case-based childhood TB data

from 2017 to 2019 was conducted to describe the epidemiology, identify the gaps and highlight lessons learnt.

Results/Impact: There has been an increase in diagnosis and notification of children from 10% in 2015 to 15% in 2019. From 2017 to 2019, a total of 30,932 childhood TB patients have been diagnosed, 85% through clinical methods and 15% through bacteriological confirmation. A major proportion of all notified childhood TB patients were among under 5 years old with the ratio of 0-4 to 5-14 at 1.3, followed by those aged 15-19 years old. There is a gap in identifying TB among those aged 10-19 years. Among those initiated on treatment (n=21,465), 14.6% were cured, 80.7% completed treatment and 3.4% died. 35% (n=211) of deaths occurred within 10 days of treatment initiation, mostly from HIV negative children and showing regional disparities.

Method of diagnosis	Number	Percentage (%)
Score Chart	7,186	25.4
Sputum Microscopy	6,812	24.1
Chest Xray	10,720	37.9
GenXpert	3,588	12.7

Table.

Conclusions: Case-based surveillance provides a platform to understand TB burden and factors associated with care and outcome of treatment. This review is an essential component for sustaining interventions that help to increase childhood TB diagnosis and notification and create a platform for focused national and sub-national strategic planning, resource allocation and activity implementation.

EP-33-428 About one fourth of TB cases in Ethiopia are in the adolescent population

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Background and challenges to implementation: In Ethiopia, one in four persons is an adolescent (age 10-19 years), and this age group is potentially exposed to risk factors for tuberculosis (TB) such as stigma, HIV, alcohol & substance abuse, and tobacco use. Despite this, current models of care have gaps in meeting their needs. Hence, Ethiopia developed a child and adolescent TB roadmap in 2019 to emphasize TB among the adolescent.

However, there is limited data on the magnitude of TB among adolescent in Ethiopia. We computed the proportion of adolescent TB among all TB cases in selected health facilities found in four regions of Ethiopia.

Intervention or response: Age disaggregated data were collected using a standardized tool as part of the supportive supervision in the USAID/ Eliminate TB project intervention regions. The data was collated from 692 health facilities from July-December 2020.

Results/Impact: There were a total of 6258 new and relapsed cases of TB notified in the assessed health facilities, of which 1,416 (22.6%) were TB among the adolescent age group. There is a regional variation, where the highest proportion was in Sidama (35.4 %) and the lowest was in Amhara (11.1%).

#	Region	Total TB cases	TB in Adolescent	% adolescent TB cases
1	Amhara (N=221 health facilities (HFs))	1911	212	11.1
2	SNNP (N=81 HFs)	680	178	26.2
3	Sidama (N=23 HFs)	562	199	35.4
4	Oromia (N=286 HFs)	3105	827	26.6
5	Total (N=692 HFs)	6258	1416	22.6

Table: Proportion of TB among Adolescent age at demonstration zones and regions, July-December 2020

Conclusions: A quarter of TB cases in Ethiopia are among the adolescent age groups. Hence, a routine data collection and monitoring mechanism for adolescent TB should be instituted as part of the national health management information system. survey among adolescent might be undertaken to estimate the TB prevalence.

EP-33-429 TB issues in children and adolescents in the Russian Federation

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Background: Since 2014 in Russia for the early diagnosis of tuberculosis an annual screening of the child population is carried out with modern immunological tests in vitro and in vivo in combination with computer diagnostics of respiratory lesions and accelerated methods of bacteriological confirmation of tuberculosis.

Design/Methods: Assessment of the current state and dynamics of the epidemic situation of tuberculosis of the child population in Russia amid the introduction of innovative technologies for providing anti-tuberculosis care to children.

Results: The current epidemiological situation of tuberculosis among children and adolescents in Russia during the introduction of screening tests is evaluated with positive tendencies.

The rate of new tuberculosis in children aged 0-14 years decreased by 49.4% from 16.1 per 100,000 children in 2012 to 7.7 per 100,000 children in 2019; at the age of 15-17 years it decreased by 55.1% from 39.0 per 100,000 children in 2006 to 16.8 per 100,000 children in 2019.

This is also reflected in the decrease of the new tuberculosis in young people (older 18 years) from 54.2 per 100 thousand of population in 2014 to 35.7 per 100 thousand of population in 2018. Clinical forms of tuberculosis in children are characterized by predominance of lesions of the intrathoracic lymph-nodes without involvement of lung tissue in the process. The secondary forms of tuberculosis with characteristic radiological changes prevail in 15-17 years old adolescents; often they are confirmed by bacterial excretion.

Also, a decrease in the death rate of children from tuberculosis is recorded in the last 10 years: in children of 15-17 years old from 0.1 to 0.02 per 100,000 children, and in children 0-14 years old from 0.09 to 0.03 per 100,000 children.

Conclusions: The obtained results show the viability of introducing modern methods of screening, which allows to significantly improve the quality of diagnosis of tuberculosis infection and epidemiological situation.

EP-33-430 Local geographic heterogeneity of TB infection in children exposed at home to TB

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Background: Each year millions of children with tuberculosis (TB) or sub-clinical TB infection are not identified by TB services, have delays in diagnosis, and never receive life-saving treatment. We sought to assess the geographic heterogeneity and to identify local hot spots of TB infection in children to inform spatially tailored interventions for children at high risk of TB.

Design/Methods: We conducted a prospective household contact cohort study in Lima, Peru (2009-2012). Residential locations of child household contacts <15 years old were linked to the Carabayllo district census data. Children were tested for TB infection at baseline using tuberculin skin tests (TST). We calculated the percentage of TST+ children out of all child contacts

per census tract, then visualized the geographic heterogeneity through heat maps. We calculated localized Moran's *I*s to test whether each census tract's percentage of TST+ children was spatially independent from that of neighboring tracts. Cluster maps were produced to visualize neighborhoods with a statistically significant Moran's *I* ($p < 0.05$) and to indicate the type of spatial association observed—either a spatial cluster (hot or cold spots) or spatial outliers (high or low).

Results: We identified 685 child contacts in the Carabayllo district, of which 146 (21.3%) were TST+ at baseline. The median percentage of TST+ children by tract was 20.0% (IQR: 0-35.4%; range: 0-100%). The Moran's *I* for the study area was 0.276 ($p = 0.002$). Few tracts were identified to have significant spatial dependency with neighboring tracts; of those, most were classified as hot spots.

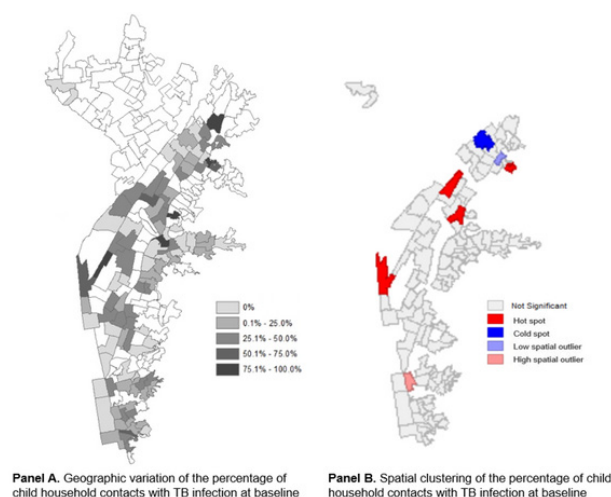


Figure 1. Heat and cluster maps of the percentage of TB infection in children in the study area.

Conclusions: There is significant local geographic heterogeneity in the proportion of children with TB infection and evident hot spots within the study area. Characterization of the spatial distribution of these proportions and local hot spots may be one practical tool to inform spatial targeting of interventions to improve TB care for children.

TB in children and adolescents 2

EP-34-431 Decentralising paediatric TB detection efforts increases case-finding in nine sub-Saharan countries

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Background: The capacity to diagnose pediatric TB is often centralized at the highest healthcare structure levels. A previously described, multi-pronged case-finding intervention improving pediatric TB case detection across the network is now evaluated across each healthcare structure level to identify where its implementation is the most impactful.

Design/Methods: We purposively sampled 144 health facilities across all healthcare levels in Cameroon, Côte d'Ivoire, Democratic Republic of Congo, Kenya, Lesotho, Malawi, Tanzania, Uganda, and Zimbabwe. All sites are part of a multi-pronged intervention, which includes training on pediatric TB, systematic TB screening in child health entry points, improved access to sample collection and molecular testing, and intensified household contact investigation.

Using a pre-post intervention design, pre-intervention data (12 months) were retrospectively collected from facility registers. Intervention data of varying periods per site (mean= 20 months) were collected prospectively in the same facilities and aggregated per tier levels.

Averages, proportions, and monthly rates were calculated using descriptive statistics. Pre- and post-intervention comparisons of tier-level monthly rates was done using T-Test for two dependent means.

Results: The average monthly rate of pediatric TB case identification/site significantly increased by 1.43-fold within the entire study site network, increasing from 1.33 (pre-) to 1.90 (post-intervention).

This was mostly driven by lower-tier facilities (health centers/clinics/dispensaries) with a significant 1.91-fold increase during (1.70) compared to pre-intervention (0.89). No significant change in the average monthly rate/site was observed in higher tiers.

Consequently, the relative contribution of lower-tier facilities to the total cases detected within the study network improved from 38% (861/2,295) pre- to 50% (2,930/5,866) post-intervention, showing a greater intervention impact in lower-tier facilities than other tiers.

Conclusions: Decentralizing pediatric TB case finding to the Health centers/Clinics/Dispensaries level is feasible and showed greater impact than higher tiers. Future efforts in closing the pediatric TB detection gap should therefore prioritize decentralized models of care.

	Number of sites	Pre-intervention (n=144)	Intervention (n=144)	Fold increase	P-value
Central / Reference Hospitals	2 (1%)	1.42 (0.83-2.00)	0.62 (0.04-1.19)	0.43	N/A
Provincial / Regional Hospitals	2 (1%)	2.29 (0.50-4.08)	2.49 (0.15-4.83)	1.09	N/A
Small Hospitals (District or lower)	59 (41%)	1.90 (0.00-14.42)	2.21 (0.13-16.82)	1.17	p=0.1821
Health centers / Clinics / Dispensaries	81 (56%)	0.89 (0.00-6.58)	1.70 (0.05-9.92)	1.91	p<0.0001
All sites combined	144 (100%)	1.33 (0.00-14.42)	1.90 (0.04-16.82)	1.43	p<0.0001

Table. Site-level average in monthly case detection rates (range)

EP-34-432 Age-specific effectiveness of a TB screening intervention in children

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Background: Existing cascades of care delivery for children with tuberculosis (TB) disease identified through active-case finding interventions do not examine differential effectiveness by age. We assessed whether a TB patient-finding intervention varied in effectiveness according to the age of the child screened.

Design/Methods: We conducted a prospective intensified screening program in Pakistan (2014-2016). We constructed a care cascade consisting the following steps per the Zero TB Initiative framework: screened for TB, positive screen, evaluated for TB, diagnosed with TB, started TB treatment, and successful treatment outcome. We evaluated the cascade by year of age by calculating the percentage of children completing each step among those eligible, then calculating the mean and standard deviation (sd) across each age for all steps.

Results: Of 105,338 children who were verbally screened, 5,880 (5.6%) had a positive TB screen. A total of 5,162 (mean: 87.5%; sd: 1.9%) were evaluated for TB. Of these, 1,417 (mean: 26.8%; sd: 5.5%) were diagnosed with TB disease; 1,404 (mean: 99.1%; sd: 1.0%) initiated treatment and 1,311 (mean: 93.3%; sd: 3.3%) had a successful treatment outcome. An average of 31.9% (sd: 4.8%)

of children 0-4 were diagnosed with TB, followed by a decline in children 5-9 (mean: 22.4%; sd: 2.2%), and another increase in children 10-14 (mean 26.0%; sd: 5.4%). Other steps had little variability across ages. An average gap of 12.5% (sd: 2.0%) was identified for children who screened positive but were not evaluated for TB.

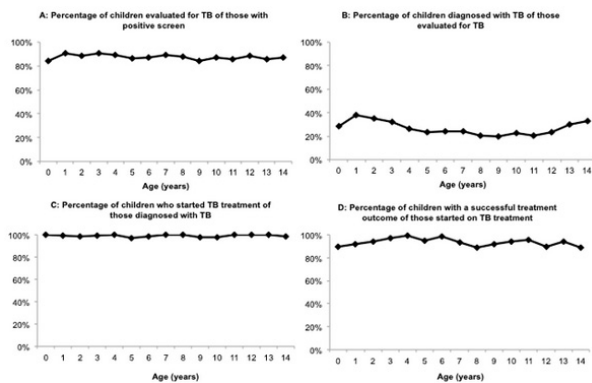


Figure 1. Percentage of children completing each step of the care cascade, by age

Conclusions: Across all ages this intervention was highly effective. Facility-based strategies may be essential to increase the percentage of children getting evaluated for TB. Our study illustrates the utility of applying operational analyses of age-stratified cascades of TB care for children to identify age-specific gaps and to guide novel interventions to close these gaps.

EP-34-433 Effect of Covid-19 on paediatric TB diagnosis, treatment and prevention cascades in CaP TB Project-supported facilities in Cameroon

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Background: The CaP TB model of care aims to improve pediatric TB diagnosis, treatment and prevention by integrating TB screening in all routine pediatric entry points, increasing access to molecular diagnosis and to more effective pediatric TB drug formulations and TB preventive therapy. We describe the impact of COVID-19 on these targets in Cameroon.

Design/Methods: We analyzed data from 21 facilities implementing CaP-TB six months pre-COVID-19 (September 2019-February 2020), and six months during COVID-19 pandemic (March 2020-August 2020: Covid-19 period). We compared cascade yields in detection, treatment and prevention before and during COVID-19, using a Z-score test for two population proportions (two-tailed, $p < 0.05$).

Results: Among 2,216 and 2,361 children screened for TB during pre-COVID-19 and COVID-19 periods, respectively, the relative proportion of < 5 y/o screened dropped from 55.9% to 32.1%. Similarly, the relative proportions of those screened across outpatient, pediatric inpatient and contact tracing services combined, significantly decreased from 71.8% (1,591/2,216) to 31.5% (743/2,361), whereas a significant increase in pediatric TB screening was observed in HIV clinics (from 27.0% to 68.4%). The proportion of children identified as presumptive TB during pre-COVID-19 (63.8%) was significantly lower during COVID-19 period (24.8%), and fewer children (from 125 to 81) were diagnosed with TB. TB treatment initiation rates did not significantly change. Despite a significant increase in the proportion of children for whom TB diagnosis was ruled out (37.2% pre-COVID vs 75.2%, during COVID-19 period), the proportion of children identified as eligible for TPT among the < 5 y/o contacts and among children living with HIV significantly decreased (60.6% pre-COVID vs 29.8% during COVID-19 period). TPT initiation rates among those identified as eligible decreased from 99.1% to 96.6%.

Variables	Pre-Covid (09/2019 - 02/2020)	Covid (03/2020 - 08/2020)	P-value (* = significant)
% of < 5 y/o screened for TB among all children 0-14 y/o screened (num/denom)	55.9% (1 238/2 216)	32.1% (757/2 361)	$< 0.001^*$
% of screened in HIV clinic among all children screened for TB (num/denom)	27.0% (599/2 216)	68.4% (1 614/2 361)	$< 0.001^*$
% of TB presumptive identified among screened (num/denom)	62.8% (1 392/2 216)	24.8% (585/2 361)	$< 0.001^*$
Number of TB cases identified (% among presumptives)	125 (9.0%)	81 (13.8%)	$< 0.001^*$
% initiated on DS-TB treatment among TB cases identified (num/denom)	86.4% (108/125)	88.9% (72/81)	0.596
% of screened where TB was excluded among total screened (num/denom)	37.2% (824/2 216)	75.2% (1 776/2 361)	$< 0.001^*$
% of identified as eligible for TPT among those potentially eligible** (num/denom)	60.6% (469/774)	29.8% (503/1 688)	$< 0.001^*$
% initiated on TPT among those identified as eligible (num/denom)	99.1% (465/469)	96.6% (486/503)	0.007*

** based on WHO TPT eligibility recommendations which includes any child contacts < 5 y/o and PLHIV irrespective of age

Table.

Conclusions: COVID-19 negatively affected both TB detection and prevention services. Additional strengthening effort are urgently needed to restore capacity and to ensure continuity of essential TB services.

EP-34-434 Comparing childhood TB outcomes in rural vs. urban settings during the CaP TB intervention in Cameroon: a programmatic outcome evaluation

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Background: Access to pediatric TB services remains challenging, especially in rural settings. The CaP-TB project aimed to decentralize pediatric TB care in order to address those gaps. We compared TB cascade of cares for children 0-14 years old in urban versus rural settings in project-supported facilities in Cameroon

Design/Methods: Data from 17 rural and 33 urban CaP-TB-supported facilities, collected between January-2019 and December-2020, were analyzed. The project implemented a multi-pronged approach, supporting pediatric TB case finding, TB treatment and TB prevention. TB cascades of care for children 0-14 years old were compared in urban versus rural settings using Z-score test for two population proportions (two-tailed, $p < 0.05$).

Results: Coverage of TB screening among pediatric attendees was higher in rural compared to urban facilities (73.9% vs 63.6% $p < 0.0001$), but capacity to identify children with presumptive TB among those screened was lower in rural compared to urban settings (1.0% vs 2.2% $p < 0.0001$). Among children with presumptive TB, 87% (375/431) accessed Xpert testing in rural settings compared to 94.4% (3,572/3,785) in urban settings ($p < 0.0001$).

However, no significant difference was observed in the proportion of children diagnosed with TB among those identified as presumptive (8.1% in rural vs 10.3 in urban settings $p < 0.1645$) nor in the proportions of children initiating TB treatment among those diagnosed (100% in rural vs 98.5% in urban settings $p < 0.4593$). Similar TB treatment success rates were achieved in the two settings. In contrast, a higher TB preventive treatment (TPT) completion rate was observed in rural compared to urban settings (96.6% vs 92.4% $p < 0.0226$).

Variables	Rural	Urban	P-value (* = significant)
% of screened among attendees (num/denom)	73.9% (42 645/57 706)	63.6% (171 199/269 242)	<0.0001*
% of TB presumptive identified among screened (num/denom)	1.0% (431/42 645)	2.2% (3 785/171 199)	<0.0001*
% of TB presumptive identified accessing Xpert MTB/RIF testing (num/denom)	87.0% (375/431)	94.4% (3 572/3 785)	<0.0001*
% initiated on DS-TB treatment among TB cases identified (num/denom)	100.0% (35/35)	98.5% (382/388)	0.4593
% successfully treated children among those with an expected outcome at time of data collection	90.5% (19/21)	90.1% (245/272)	0.9522
% initiated on TPT among those eligible** (num/denom)	96.0% (308/321)	96.7% (1799/1861)	0.5157
% children completing TPT among those with an expected outcome at time of data collection (num/denom)	96.6% (227/235)	92.4% (904/978)	0.0226*

** based on WHO TPT eligibility recommendations which includes any child contacts <5 y/o and PLHIV irrespective of age

Table.

Conclusions: While capacity to identify children with presumptive TB and access to Xpert testing remains more challenging in rural compared to urban settings, our data show that capacitating rural facilities to provide pediatric TB services is feasible with comparable key cascade outcomes can be achieved in the 2 settings.

EP-34-435 Awareness raising and capacity building to improve diagnosis and care for childhood multidrug-resistant TB in Myanmar during the Covid-19 pandemic

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Background and challenges to implementation: Globally, half a million people developed MDR/RR-TB in 2019 and approximately 5% - 7% (25,000-32,000 cases) of them were children. About 5,500 of these cases were started second-line treatment for drug-resistant TB. Diagnosing MDR/RR-TB in children is a challenge due to difficulty in collecting samples and pauci-bacillary nature of disease. As a result, there is a gap in diagnosis and initiation of correct TB treatment regimen.

In Myanmar, similar challenges exist. Amongst all MDR/RR-TB cases on treatment, children were about 1%, during 2017-2019. Performing gastric aspiration to test with Xpert MTB/RIF for the diagnosis of childhood TB/MDR-TB was a rare practice outside two major cit-

ies of the country. Awareness about probable/possible childhood MDR/RR-TB among health care professionals was limited and children received second-line treatment only by microbiological confirmation. More sensitive molecular diagnostic platforms are being expanded which are far from being universally accessible in Myanmar.

Intervention or response: Low rates of childhood MDR/RR-TB detection is a major concern for National TB Programme, WHO and partners. Only limited planned activities could be conducted because of the pandemic. Nevertheless, awareness raising for childhood MDR/RR-TB targeting patients on treatment, and family members, by using a three-year calendar with health information was held; the childhood MDR/RR-TB treatment guidelines was disseminated; virtual orientation on Childhood TB/MDR-TB were organized through rGLC mechanism targeting pediatricians and MDR-TB clinicians all over the country.

Results/Impact: The approach was successful in identifying twenty-four childhood MDR/RR-TB patients (1% of total MDR/RR-TB cases) on whom treatment was initiated in 2020 at a time when access to TB services were disrupted. Furthermore, five probable MDR/RR-TB cases were identified and put on treatment who otherwise would have been missed.

	2017	2018	2019	2020
Total TB case notification	132025	136039	134120	103012
% decline in case notification of DS-TB due to Covid in 2020 compared to that of 2019				-23%
Total childhood DS-TB case notification	28723	26235	23678	13217
% decline in Childhood DS-TB case notification due to Covid in 2020 compared to that of 2019				-44%
Total number of MDR/RR-TB cases detected	3197	3479	3205	2368
% decline in case detection of MDR/RR-TB due to Covid in 2020 compared to that of 2019				-26%
Total number of MDR/RR-TB patients initiated on treatment	2691	2802	2891	2359
Gap between Case detection and treatment initiation	16%	19%	10%	0.4%
Number and proportion of < 15-year (Childhood) MDR/RR-TB cases initiated on treatment amongst total MDR/RR-TB cases	18 (0.7%)	17 (0.6%)	38 (1.3%)	24 (1.02%)

Conclusions: Awareness raising and capacity building activities must continue during Covid pandemic. One case of TB detected, and cured means five to seven new cases averted.

EP-34-436 Generating evidence for improved childhood TB care: assessing the gaps in childhood TB service delivery in the Philippines

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Background and challenges to implementation: The Philippines' population is young, with 52% aged <25 versus 43.2% in the Western Pacific Region. Among TB clients notified, 9-12% are aged 0-14 - lower than expected from TB high-burden areas, where children constitute 15-20% of all TB clients. Childhood TB is a marker of ongoing community TB transmission and an indicator of TB control within the population. We assessed the childhood TB situation in the 3 highest-burden regions to understand gaps in childhood TB management.

Intervention or response: We surveyed 220 health facilities using an adapted childhood program assessment questionnaire by WHO. The questionnaire explored 4 thematic areas:

1. Policy environment,
2. Provider capacity to provide TB services,
3. Access to childhood TB services, and;
4. Quality of care for children.

We synthesized information by triangulating data extracted from the national TB information system with survey respondent perspectives, National TB guidance, and evidence from technical reviews, surveillance reports, and peer-reviewed literature.

Results/Impact: There were significant gaps in childhood TB diagnosis, treatment, and reporting. Despite chest x-ray (CXR) not being recommended for diagnosis, 43-50% of facilities use CXR to diagnose childhood TB; only 35-37% conduct sputum testing. Only 11% cited extrapulmonary signs and symptoms; studies suggest that extrapulmonary TB among children may be underdiagnosed. Fixed-Dose Combinations (FDCs) of TB drugs to reduce medication errors and improve treatment adherence are available in 33-57% of facilities. Half of the respondents cited treatment success rates to be >90%. There are weak data systems to track childhood TB notification and treatment outcomes in the private sector, TB contact investigation, and preventive treatment.

Conclusions: Significant gaps in childhood TB management exist, warranting immediate action, including capacity-building and more robust engagement of private sector providers. Health policy actions are also needed to promote the availability of FDCs. Childhood TB data gaps must be addressed within the national TB information system.

EP-34-438 Standardised childhood TB case notification in limited-resource settings: experience from Afghanistan

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Background and challenges to implementation: In Afghanistan, children under the age of 15 make 47.7% of the total general population. According to the 2019 WHO report, Tuberculosis (TB) new/existing cases among children under the age of 15 year were estimated to be 15,624. However, in 2014, the NTP notified 4,451 (49%) of it. The aim of this assess was to explore the role of new approach to diagnose TB among children.

Intervention or response: The National TB Program (NTP) in partnership with local stakeholders developed standard operation procedures (SOP) to diagnosis childhood TB and trained healthcare providers on it. The NTP revised guidelines for testing and diagnosis and used combination of clinical signs & symptoms, Tuberculin Skin Test (TST) readings, and chest X-rays (CXRs) findings. The diagnostic criteria contains signs and symptoms of TB, skin reaction to TST above 10 mm and CXR suggestive of TB. The NTP made available Xrays, TST availability in health facilities and trained the staffs on SOP for children. Furthermore, in each health facility one pediatrician was hired to provide quality TB service and facilitate the recording report among children.

Results/Impact: The number of children diagnosed with TB increased from 4,451 in 2014 to 9,371 in 2020 (110.5% increase). The proportion of children out of all TB cases notified was 14% in 2014 and increased to 20.7% in 2020. The male to female ratio of children under 5 was almost 1:1 in every year [see Table 1]

Conclusions: According the WHO estimate of childhood TB for 2019, the country notified almost 96% all childhood TB cases. In 2020, the national target set was to notify 12,186, which achieved only 9371 (76.8%) the target due to Covid 19 impact on TB case notification.

EP-34-439 Community-based stool specimen collection, storage and transport to improve TB diagnosis in children

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Background and challenges to implementation: Only 1,688 of the estimated 10,000 cases of pediatric tuberculosis (TB) were notified to the National TB Program of Vietnam (NTP) in 2019. Most notified cases were clinically diagnosed due to difficulty of collecting viable sputum specimens from children.

Intervention or response: The Breath4Life project supported the NTP's pediatric TB working group to update guidelines to include stool for pediatric TB diagnosis

and, the Infectious Disease Detection and Surveillance project supported the Nghe An Provincial TB Program to review the new procedures in the province. Per the new procedures, caregivers of children with presumptive TB collected stool specimens; irrespective of location-home, health facility or hospital-the same procedure was used. Specimens were packaged and transported for molecular testing by GeneXpert. The Provincial TB Program synthesized collection data and compared stool specimen results against respiratory specimen results for concordance.

Results/Impact: Stool specimens can easily be collected from children of any age, by anyone, anywhere. Among the 122 stool specimens reviewed, 74 were collected in the provincial hospital, 30 in primary and secondary health facilities, and 18 in homes of patients. Turn-around times from home-collected samples were one day – the same as for hospital collected samples, and GeneXpert results on stool specimens were concordant with sputum specimens.

Conclusions: As a rule-in test for pulmonary TB, stool-based GeneXpert testing can quickly and accurately provide bacteriological confirmation for children with presumptive TB. Decentralized stool specimen collection increases the number of children able to access molecular testing and when linked with a reliable specimen transport system, can speed diagnosis and treatment initiation compared to extensive clinical reviews at specialized facilities. Health care worker and patient acceptability of stool collection appears to be high and requires little training compared to gastric aspirate collection. Rapid adoption of this method would reduce the number of children with TB who go undetected in Vietnam.

EP-34-440 The socio-economic burden of TB on children and adolescents

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Background: Approximately 12% of the world's tuberculosis burden is among children under the age of 15. The socioeconomic burden of tuberculosis on affected households is well established and includes catastrophic tuberculosis-related costs and stigma.

However, little is known about how the socioeconomic impact of tuberculosis on children and adolescents. We conducted a scoping study on the socioeconomic impact of tuberculosis among children and adolescents.

Design/Methods: We searched Pubmed, CINAHL, Proquest, Scopus, Google Scholar and Opengrey for primary studies and reviews on the socioeconomic impact on children and adolescents.

We found 11,391 citations of which we selected 124 articles for full text independent assessment. Of these, we located 120 that underwent independent analysis. Our final data consisted of 50 articles that met inclusion criteria and underwent data extraction.

Results: The articles came from all WHO regions, with the highest representation (n=18) from the African region. Most (n= 31) used qualitative methods, with interviews and focus group discussions. Few articles had the socioeconomic impact of children and adolescent as their main focus with most reporting socioeconomic impacts on children and adolescents as part of the wider impact on families and households in general.

We found that the impacts of TB were social, including stigma, social exclusion and separation from parents, relating to relationships between parents and children including the need for childcare arrangements and children's separation from their parents. Financial issues also arose as impacting on household spending, and no-

tably nutrition. Research on children also suggested that they suffered from cognitive and behaviour challenges after treatment, with and challenges to school success.

Conclusions: Children and adolescents are an overlooked group among people with tuberculosis. Further study is needed for a holistic understanding of TB's social and economic impacts on children and adolescents.

TB and important comorbidities

EP-35-441 Extent of pulmonary TB disease in HIV-positive and -negative patients in four African countries: the TB Sequel Project

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Background: HIV increases risk of progression to active TB and is associated with higher mortality, but whether HIV status influences extent of disease, particularly lung pathology, and long-term consequences of TB disease is not known.

Design/Methods: The TB Sequel cohort of recently diagnosed pulmonary TB patients from four African countries namely Mozambique, Gambia, South Africa and Tanzania was examined. HIV status was determined using history (if HIV positive), or test result at enrolment. Baseline clinical characteristics including symptoms, chest x-ray scores and spirometry readings. Lung function was assessed using spirometry (both FVC and FEV/FVC values) according to Global Lung function Initiative and American Thoracic Society/European

Respiratory Society guidelines. Ralph and Falk scoring systems measured of extent of disease on chest radiographs. A regression model evaluated the effect of HIV on lung functional impairment.

Results: Of 1429 (65.2% male, mean age 35.9 years) patients enrolled, 825 (57.8%) were HIV positive (median CD4 count 208, 60.7% on antiretroviral therapy). BMI, Karnofsky score, and number of symptoms did not vary by HIV status. There was reduced extent of disease in HIV-infected patients: duration of symptoms (mean 9.3 for HIV+ vs 7.7 weeks for HIV-); lung function impairment (spirometry using FVC and FEV1/FVC; 33.6% vs 21.0%, $p<0.001$), cavitation on x-ray (45.5% vs 21.1%, $p<0.001$) and extent of lung involvement on x-ray (Ralph score: median 50 vs 20, Falk score advanced 78.77% vs 61.18%, $P<0.001$). Extent of disease also reduced by increased immunosuppression as measured by CD4 count category. Regression analysis (Table) showed that the influence of HIV on lung impairment was evident after adjusting for relevant covariates.

Variable	Lung function impairment (n/N, %)	Unadjusted OR (95% CI)	HIV effect Adjusted OR for the Covariate
HIV			
Negative	277/345 (61.6%)		0.46 (0.34 – 0.62)
Positive	127/404 (42.5%)		
Age category			
≤30 years	169/250 (67.6%)	1.00	0.55 (0.40 – 0.76)
31 – 40 years	135/261 (51.7%)	0.51 (0.36 – 0.74)	
41 – 50 years	58/143 (40.6%)	0.33 (0.21 – 0.50)	
>50 years	42/95 (53.9%)	0.38 (0.23 – 0.62)	
Site			
Mozambique	122/221 (55.2%)	1.00	0.65 (0.47 – 0.91)
Tanzania	74/143 (51.8%)	0.87 (0.57 – 1.32)	
The Gambia	139/200 (69.5%)	1.85 (1.24 – 2.76)	
South Africa	69/185 (37.3%)	0.48 (0.32 – 0.72)	
Gender			
Female	108/227 (47.6%)	1.00	0.48 (0.35 – 0.65)
Male	296/522 (56.7%)	1.44 (1.06 – 1.97)	
Past TB			
No	356/664 (53.6%)	1.00	0.45 (0.33 – 0.61)
Yes	48/85 (56.5%)	1.12 (0.71 – 1.76)	

Regression model evaluating HIV infection effect on spirometry outcome for lung function impairment (N=749 with acceptable spirometry results)

Conclusions: HIV infection is associated with less severe lung pathology and functional impairment in patients with recently diagnosed pulmonary. This most likely reflects reduced inflammation due to loss of CD4+ T cells.

EP-35-442 Factors associated with HIV and TB co-infection among adult patients in Engela District, Oshana Region, Namibia

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Background: Tuberculosis is the leading cause of death in people living with HIV/AIDS. In Namibia, tuberculosis is the fourth leading cause of death, and HIV/AIDS is the leading cause of death. It is critical to obtain information on the prevalence of HIV-TB co-infection to plan and evaluate HIV-TB control measures. The objective of this study is to identify factors associated with HIV-TB co-infection in Engela district.

Design/Methods: A retrospective case-control study among adult HIV patients in Engela district from January 2018 to December 2018. We used data from the Engela district on HIV and TB notification. To identify associated risk factors for TB-HV co-infection, we performed bivariate and multivariate logistic regression analyses. The odds ratio with 95% confidence intervals was calculated, and the statistical significance was set at a p-value of 0.05.

Results: Of 264 records reviewed, 90 (34.09%) were between 40-49 years. The proportion of HIV/TB co-infected patients was 88 (33.46%) and 80 (90.91%) patients had pulmonary TB. Male had the highest HIV-TB co-infection rate 42.35%. Single patients accounted the larger proportion 58(65.91%) of HIV-TB co-infection compared to married 24 (27.27%) and widowed 6 (6.82%). HIV-TB co-infection was significantly associated with sex (COR=1.78; 95% CI 1.04-3.05; P=0.03); age group (AOR=0.61; 95% CI 0.31-1.170; P=0.013); marital status (COR=0.20; 95% CI 0.05-0.84; P=0.016), alcohol intake, (AOR 4.49; 95% CI 1.02-19.71; P=0.047); smoking status (COR=4.23; 95% CI 2.09-8.55; P=0.002); HIV treatment outcome (COR=0.08; 95% CI 0.009-0.709; P=0.004), TB prophylaxis (AOR=0.16; 95% CI 0.04-0.64; P=0.009), and WHO HIV clinical stage (AOR=0.02; 95% CI 0.01-0.06; P=0.001).

Conclusions: HIV-TB co-infection was high and found to be significantly associated with the male productive age group, being single, drinking, smoking, and being in the final stage of WHO HIV clinical status. We recommend continuous health education on tuberculosis among HIV patients, treatment and prevention, including lifestyle changes, are required, particularly among men.

EP-35-443 Prevalence and characteristics of TB among young children living with and those without HIV in sub-Saharan Africa

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Background: Children living with HIV (CLHIV) are at greater risk for rapid progression of TB. Limited data are available on TB/HIV co-infection among CLHIV. We assessed the TB/HIV co-infection rate and compared TB presentation between CLHIV and HIV-negative children in Cameroon and Kenya.

Design/Methods: This study was a sub-analysis of a cluster-randomized trial evaluating the integration of pediatric TB services in 32 facilities in Cameroon and Kenya. From May 2019 to March 2020, we enrolled children under five years old with presumptive TB. Clinical and diagnostic characteristics between CLHIV and HIV-negative children were compared using the Fisher exact test.

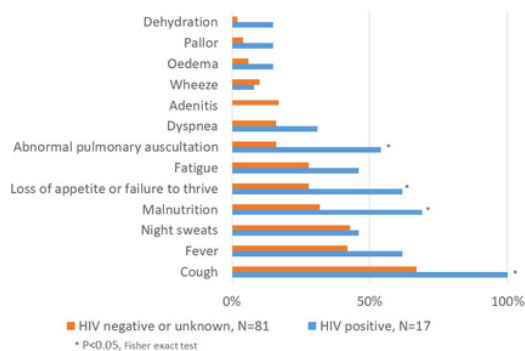


Figure 1. Signs and symptoms among children with confirmed TB, according to HIV status.

Results: We enrolled 275 TB presumptive children, 55% (n=151) were male and mean age was 22.9 months (SD 16.1). 149 out of the 275 children with presumptive TB were tested for HIV and 18% (n=27) were CLHIV, 74% (n=20) of whom were on antiretroviral therapy. Overall 34% (94/275) of the TB presumptive were diagnosed with TB, of whom 14% (13/94) were CLHIV. The proportion of children diagnosed with TB tended to be higher among CLHIV (48%; 13/27) than children with a negative or unknown HIV status (33%; 81/248), p=0.067. The following symptoms were more frequent among CLHIV: cough (100% vs 67%; p=0.017), appe-

tite loss (62% vs 28%; p=0.018), malnutrition (69% vs 32%; p=0.014), and abnormal pulmonary auscultation (54% vs 16%; p=0.002) (Figure 1).

Most diagnoses were made clinically (90%; 85/94). Bacteriologic confirmation was more frequent in CLHIV (31%; 4/13, all with positive urine Alere LF-LAM test) compared to HIV-negative children (6%; 5/81, all with positive Xpert test), p=0.02. Pulmonary TB was the most common form in both groups (85% in CLHIV vs 72%), p=0.5.

Conclusions: TB/HIV coinfection rate was high in children and CLHIV had worse clinical presentations than HIV-negative children. CLHIV had more bacteriologic diagnoses, via the use of LF-LAM in this population.

EP-35-444 The MOCT II study: a collaborative mobile health-based programme to expand patient-centred care for people living with HIV with or without TB in Irkutsk, Siberia

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Background: Human immunodeficiency virus (HIV)/tuberculosis (TB) co-infection remains a concern in Irkutsk, Siberia. A pilot study demonstrated improved outcomes for a cohort of people living with HIV (PLWH)/TB using a smartphone platform called MOCT (Russian for 'bridge').

Design/Methods: We have formed a multi-organization effort to integrate HIV/TB care and promote a patient-centered approach to engage PLWH throughout Irkutsk. Testing, early antiretroviral (ART) initiation and linkage coordination to the Irkutsk AIDS Centre were performed for patients recruited from the Irkutsk TB Referral Hospital and 4 affiliated clinics. We performed 75 mobile screening/outreach events to perform counseling, HIV testing, status notification and referral to the AIDS Centre. The MOCT platform was offered to PLWH at the AIDS Centre starting January 2019. We examined platform-collected data including usage of app features and HIV-related labs.

Results: A total of 4,640 people attended outreach events, and 849 patients from the TB Referral Hospital/affiliated clinics received testing and linkage services. In total, 1,426 patients were started on ART, and 2,005 people are enrolled in MOCT. A minority of the cohort used the app features (\geq once per month) by month 6 post-download. However, those who used the app maintained robust engagement despite an early decline. After

month 4, usage stabilized. Available lab data (N=627 enrolled) demonstrated improvement in viral suppression between download and 6 months (78% versus 54%, $p < 0.001$). The proportion converting from unsuppressed to suppressed was higher in the subgroup with any active feature use over 6 months compared to those who did not (29% versus 18%, $p = 0.03$).

Conclusions: Status notification, referral to outpatient HIV care and ART initiation occurred for a broad, under-engaged population in Irkutsk, including those with TB otherwise at high risk of mortality. Without providing incentives, smartphones, or data plans, continued MOCT usage was observed for a large 'real-world' population of PLWH in Irkutsk.

EP-35-445 In-hospital TB diagnostic cascade among people living with HIV in the Greater Accra Region, Ghana

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Background: To describe the routine in-hospital tuberculosis (TB) diagnostic cascade among people living with HIV (PLHIV), recruited in the TBPOC study (NCT04122404) in Ghana with specific focus on timing of the TB diagnostic cascade and to identify gaps in the pathway towards TB treatment initiation.

Design/Methods: We conducted a prospective study including adult PLHIV admitted at three major hospitals in Ghana (Korle Bu teaching hospital, Lekma hospital, Tema general hospital); with either ≥ 1 TB symptom, serious illness, or advanced HIV disease; and not on TB treatment. Participants were recruited between October 2019 and March 2020. Presenting signs and symptoms, HIV and TB status, timing and results from TB diagnostics were recorded at baseline and at follow-up including 8 weeks outcomes. Descriptive statistics were used.

Results: We included 143 patients (median age 42 years, 70.6% female) in the study. Of these, 57.3% were not on antiretroviral treatment and the median CD4 count was

64 (IQR 22-175) cells/mm³. All patients reported ≥ 1 TB symptom, including cough (81.1%). Of participants, 42.7% had a sputum GeneXpert MTB/Rif result after a median 4 days and 32.2% had a chest X-ray after a median 1 day. Overall 25 (17.7%) were referred for TB treatment and 16.3% (confirmed TB (9) and presumptive TB (14)) initiated TB treatment after a median 7 days. The overall 8 weeks-mortality was 27.7% and higher in patients with presumptive TB (57.1%, 0.047). Lost to follow up was low at 2 participants (1.4%).

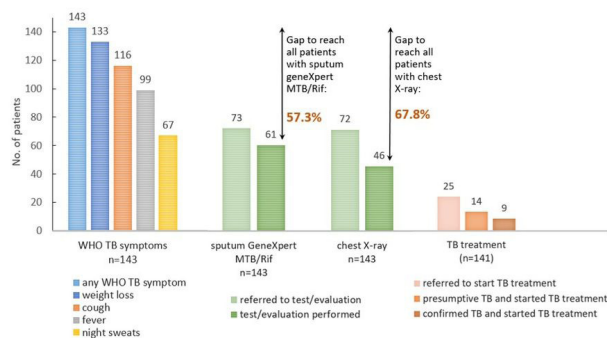


Figure. The routine TB diagnostic cascade among 143 PLHIV on admission with a positive WHO TB symptom screening.

Conclusions: All PLHIV had clinical features suggestive of TB but only half were referred for TB investigation. The delay from admission to TB diagnostics and treatment may be critical in this population with high early mortality. There is an urgent need for implementation of add-on rapid TB diagnostic tests to detect all forms of TB and guide timely TB treatment among PLHIV on admission.

EP-35-446 Probability of TB or cryptococcal meningitis being screened among newly diagnosed HIV patients presenting with advanced HIV disease in Uganda

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Background: Almost one in three patients present to care with Advanced HIV Disease (AHD). These patients are at high risk of death, even after initiating Anti-Retroviral Therapy (ART), with Tuberculosis (TB) and cryptococcal meningitis (CCM) being the commonest causes of death.

We set out to find the cumulative conditional probability that a newly diagnosed HIV patient presenting with AHD were screened for either TB or CCM.

Design/Methods: We conducted a retrospective records review of the 2020 data for newly diagnosed HIV-positive patients > 15 years using the District Health Information System-II (DHIS-II).

All new HIV-positive patients presenting with a Cluster of Differentiation 4 (CD4) < 200 cells/mm³ were considered to have AHD. For each new patient, we extracted data on numbers, with a baseline CD4, a CD4 < 200 cells/mm³, a Lateral Flow urine lipoarabinomannan assay (LF-LAM), and a serum cryptococcal antigen (CRAG) test. Data were analyzed using Stata 16 and summarized into proportions and percentages.

The cumulative conditional probability that a newly diagnosed HIV patient presenting with AHD was screened for either TB or CCM was determined using the Cascade Analysis Tool.

Results: In 2020, there were 136,931 newly diagnosed HIV patients >15 years. Of these 31.03% (42487/136,931) had a baseline CD4, with 35.22% (15,493/42,487) having a CD4 < 200 cells/mm³ (AHD), 42.01% (6,509/15,493) and 54.17% (8,393/15,493) of these patients did either LF-LAM or serum CRAG respectively.

The cumulative conditional probability that a newly diagnosed HIV patient with AHD would complete screening for either TB or CCM was 5% or 6% respectively.

Conclusions: The probability that a newly diagnosed AHD patient would be screened for either TB or CCM is very low in this setting.

We recommend that all newly diagnosed AHD patients be screened for TB or CCM in order to manage those with disease effectively to avert mortality.

EP-35-447 Diabetes and HIV comorbidity among TB patients and their impact on treatment outcome in Odisha: a registry-based cohort study

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Background: Effective treatment for tuberculosis (TB) is provided free of cost under the National Tuberculosis Elimination Program (NTEP), India. However, co-existence of HIV and diabetes with active TB have been associated with unfavorable TB treatment outcome. Also, HIV and diabetic patients are more susceptible to contract and develop TB.

The aim of this study was to analyse the burden and influence of diabetes and HIV on the treatment outcome of new cases of tuberculosis in the state of Odisha, India.

Design/Methods: A retrospective study was conducted using registry-based secondary data (sociodemographic, comorbidity and treatment outcomes) of new TB

patients of Odisha of 2018 from Nikshay, a web-enabled patient management system under the NTEP in India.

Results: A total 42145 new TB cases, having a mean age 39 years, were included in the study. 55.7% (23464/42145) and 81.8% (34457/42145) new TB patients were screened for diabetes and HIV respectively. Of the screened population, 7.3% (1714/23464) and 1.2% (413/34457) were found to have diabetes and HIV respectively. The mean age of TB patients with diabetes and HIV patients were 49 and 38 years respectively.

The overall treatment success rate was 90%, whereas 5%, 2.5%, 1.1%, 0.3% patients died, were lost to follow up, not evaluated and had treatment failure respectively. The mortality rate was 1.7 times and 2.3 times higher in TB patients with diabetes and HIV respectively, compared to patients without any comorbidity.

There was no significant difference in treatment failure in patients with comorbid conditions compared to those without any comorbidity. However, lost to follow up cases were 8.9% and 33% higher in TB patients with diabetes and HIV respectively.

Conclusions: Both diabetes and HIV influence TB treatment outcome. Hence, the bidirectional screen of these diseases and their management are crucial to achieve higher treatment success of TB.

EP-35-448 The detection and the co-management of TB and diabetes comorbidity in Jakarta, Indonesia: a mixed-method study

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Background: Indonesia has initiated a national program of co-management of tuberculosis (TB) and diabetes mellitus (DM) since 2017. This study investigates the detection and co-management of TB-DM in Jakarta in 2017-2019 and explores health system challenges during the implementation.

Design/Methods: A mixed-method approach was used. TB registry in two districts, East and South Jakarta from late 2017 to 2019 was used for a 4-step cascade analysis: TB patients with DM test records, diagnosed as TB-DM, received and completed TB treatment, and logistic regression was used explore the associated factors. Individual in-depth interviews with TB professionals at primary and district health office were conducted to explore their views of challenges of implementing the co-management of TB-DM.

Results: Since late 2017 50.8% of the new pulmonary TB patients aged over 15 had DM test records, and this percentage increased from 41.7% before 2019 to 60.1% in 2019. Over 90% of the detected TB-DM patients received standard TB treatment, and 86.3% of those completed treatment. Bacteriologically negative TB patients and those who were not registered resident in the study region were less likely to be tested for DM, receive TB treatment or complete treatment ($P < 0.01$). Qualitative results showed that there was almost no training on implementing TB-DM program till a recent year. There was often lack of coordination between TB department and noncommunicable diseases (NCDs) department at the primary healthcare center.

Conclusions: The TB-DM case detection has been largely improved after the introduction of TB-DM program in Jakarta. The training and coordination between TB and NCD department at all levels should be strengthened to improve performance of co-management of TB and DM.

EP-35-449 Barriers to diabetes screening and care among patients receiving pulmonary TB treatment in public health facilities in Uganda

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Background and challenges to implementation: The World Health Organization (WHO) recommends that all patients initiating treatment for Tuberculosis (TB) be screened for diabetes (DM). We sought to understand barriers to patient-centered diabetes screening and care for patients receiving treatment for pulmonary TB (PTB) at public health facilities in Uganda, a high HIV-TB burden country with a growing diabetes epidemic.

Intervention or response: We nested a qualitative study of patients at high risk for DM into an ongoing prospective cohort study of treatment outcomes among PTB patients at two public primary health facilities in Kampala, Uganda. We purposively sampled 12 patients with $HbA1C \geq 6.1\%$ from a cohort of 66 patients. In-depth interviews were conducted by a doctor and community health worker in the local language, Luganda, with patients with double- (TB-DM) and triple-burdens (TB-HIV-DM). Interviews were recorded, transcribed verbatim, translated, and analyzed with Atlas.ti 9 using inductive content analysis to identify themes.

Results/Impact: Twelve participants were interviewed. Eleven were male and 3(25%) newly diagnosed HIV patients. One had initiated oral hypoglycemics. Participants described clinic-based and personal challenges to engaging in screening and care for TB and DM or pre-DM. Clinic-based challenges included insufficient communication from health workers regarding the purpose or outcome of DM screening and lack of health education materials or programming focused on DM for patients with TB and TB-HIV. Some TB patients were unaware they had been diagnosed with DM. Participants also described concerns about pill burden, anxiety during diagnosis process, and misperception of diabetes as an infectious disease. They were motivated to engage in screening and care for DM by support and counseling from health workers, family, and friends.

Conclusions: TB patients at high risk of DM lacked access to information about DM. There is need to develop education materials for patients who learn they may have DM during WHO-recommended screening at TB treatment initiation.

EP-35-450 Investigating models of integrated TB respiratory care: a systematic review

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Background: Chronic respiratory diseases (CRDs) are relevant to patient wellbeing across the TB care cascade: patients with respiratory symptoms may present through TB services; harmful respiratory exposures including tobacco use, air pollution, and occupational exposures are common among people with TB; and pulmonary TB may lead to post-TB lung disease. Despite growing calls for integrated, patient-centred TB care, we are not aware of any models for the delivery of integrated TB-CRD care.

Design/Methods: We conducted a systematic review to identify models of integrated care for TB-comorbidities in low- and middle-income countries (LMICs). PUBMED, SCOPUS and Google Scholar were searched to identify relevant qualitative and quantitative studies published since 2003, with no language limits. Search terms were included for TB, integrated care, CRDs, post-TB conditions, and other TB-comorbidities. Title and abstract screens, and full text reviews were completed by two authors. Data were extracted on models of

care using the WHO Health System building blocks, and on barriers and facilitators for implementation.

Results: We identified 15,050 individual records. Twenty-nine studies were included in the final analysis. There were no studies describing the provision of integrated screening or care for TB and CRDs. The majority of studies addressed a single TB-comorbidity, including diabetes (n=10), tobacco use (n=5), alcohol use disorders (n=3), and opioid dependency (n=1). Seven studies addressed multiple comorbidities, but did not include CRDs. We identified only one study addressing comorbidities amongst TB survivors, but this also did not address CRDs.

Conclusions: Despite growing emphasis on the need for patient-centred TB care, there are few data on health system models through which integrated care for TB-comorbidities can be achieved. In particular, studies describing the design or delivery of integrated TB-CRD services in LMICs remain scarce. Further work is needed to develop and evaluate models of integrated TB-CRD care.

Local champions of health for all

EP-41-499 Integrated approach to communication skilling and community engagement: a pilot project in India

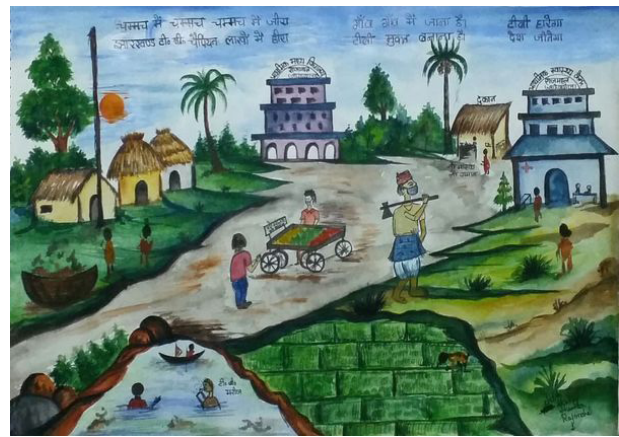
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Background and challenges to implementation: In the wake of the COVID-19 pandemic - strategic efforts were required to enable TB Champions to continue community engagement activities such as psycho social counselling and referrals. Communication skilling through a virtual training was undertaken to accelerate strategic dissemination of information on TB and COVID-19.

Intervention or response: A specific communications curriculum that improved and enhanced the communication skills of TB Champions which could be delivered on a virtual platform was co-created with TB Champions to ensure enhanced use of communication channels as part of their established roles and responsibilities.

(REACH has trained TB Survivors through a standardized curriculum that helps them advocate better. Those who complete the training are called TB Champions). During October 2020, the REACH ALLIES project identified and trained 89 TB Champions from four states of India in slogan, poem and song writing, wall painting, photos and videos and public speaking. In a subsequent two-month period, 28 TB Champions undertook community engagement activities filling in a simple reporting format.

Results/Impact: A total of 438 communication materials created sought to accelerate strategic dissemination of information on TB and COVID-19. A majority of their work was directed towards awareness generation in local dialects as well as Hindi, Tamil and Odia. Most of the slogan writing were converted to wall paintings in the immediate community of the TB Champions.



Conclusions: The TB Champions were able to provide improved community awareness on TB and COVID-19. The opportunity allowed the TB Champions to improve their communication skills and use their creativity to disseminate correct messages on TB and COVID-19. It also provided a platform for the TB Champions to express their communication skills and creativity.

EP-41-500 Engaging self-help groups for TB identification and awareness: experience from rural India

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Background and challenges to implementation: Intersectoral collaboration and social mobilisation are pivotal to achieving the End TB targets. There is a robust network of women self-help groups (SHGs) in rural India that address economic empowerment, health and nutrition. Equipped with TB knowledge, these SHGs have the potential to improve the healthcare seeking behaviour in women and address stigma, cultural and financial barriers faced by female TB patients.

Intervention or response: Supported by TB REACH Wave 7 funding, Innovators in Health (IIH) piloted a programme to involve SHGs in TB response in 3 blocks (population 1 million) of Samastipur, Bihar. This was a part of an ongoing active case finding programme that provided end-to-end TB care, while emphasising women's empowerment. The engagement process involved liaising with existing SHG network in the district; identifying a cadre of 262 female SHG leaders; providing them with training on TB symptoms, transmission, prevention, diagnosis, and treatment; supporting them to conduct TB awareness sessions with their groups; and following up with them to collect referrals of presumptive TB cases.

Results/Impact: Between March 2020 and March 2021, SHG leaders conducted 891 sensitization meetings with their groups. These resulted in 725 referrals (62% female). Of these, 642 people were screened by IIH programme staff using a symptom-based screening tool and 253 were found to be symptomatic (59% female). Diagnostic procedures were undertaken for 132 symptomatic cases (54% female), resulting in the identification of 50 people with TB (50% female). The SHG leaders supported in follow-up with patients who were reluctant for diagnosis as well as during treatment adherence of positive patients.

Conclusions: Community structures such as SHG networks are a critical resource for TB identification and prevention, especially in vulnerable populations, including women. Capacity building and engaging with SHGs could prove to be effective in promoting TB control efforts.

EP-41-501 The "TB storyteller": ZMQ's women's empowerment initiative leads to increasing TB awareness, testing and notification in Mewat, India

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Background and challenges to implementation: Mewat is one of 117 aspirational districts of India; having the lowest development indicator. TB case notification in the district is 289/100,000 population as estimated as 392/100,000 population and; literacy levels in women at 32.6%, are less than half that of men, at 69%. The TB case notification gap is primarily attributed to low literacy levels and poor socio-economic conditions of rural women. In response, ZMQ developed innovative localised knowledge tools, including digital talking comics to raise TB awareness.

Intervention or response: ZMQ developed six TB digital comics (stories) with local language voice-overs. The intervention was disseminated through house-to-house

storytelling sessions and through women's group sessions in communities. The stories are designed to address topics like TB awareness, signs and symptoms, screening and diagnostics, and; adherence and treatment. Each story has a pre-test and post-test questionnaire that captured the change in TB-related knowledge and attitudes.

Results/Impact: Over 431 women (out of 468) participated in 52 story-telling community sessions and over 215 individual women were engaged by Maternal and Child health peer counselors in house-to-house storytelling sessions. TB knowledge among women increased from 54% (pre-test score) to 82% (post-test score).

Of the 646 women who participated in the storytelling session, 42 women were screened for presumptive TB, 28 women were tested for TB and of which 7 bacteriologically confirmed new cases were notified.

Conclusions: The result of the study strongly supports the use of innovative and localised knowledge tools like 'Digital Talking Comics' for building knowledge, attitudes, and practices in the communities leading to demand for health-seeking behaviors & services.

Storytelling in local languages is a powerful tool that is effective in engaging communities, especially low-literate rural women.

EP-41-502 Engaging TB survivors as Champions for empowered communities: an experience from India

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Background and challenges to implementation: Empowered communities are critical for an effective TB response and TB elimination, in the long-term. Active participation of TB-affected communities including TB survivors and families is crucial, given their unique abilities to draw on personal experiences to support people with TB (PWTB) and mobilise communities.

Intervention or response: Between January and September 2019, 229 TB survivors were engaged as TB Champions (TBCs) through a structured six-month Mentorship Programme across 126 districts in 6 states during which TB survivors provided psychosocial-support to PWTB, organised community meetings and advocated with stakeholders for increased attention to TB.

The TBC engagement was designed with the dual purpose of positively impacting lives of PWTB as well as that of TBCs themselves, through capacity-building, mentorship and public acknowledgement of their identities as Champions. They worked in close coordination with NTEP and received a monthly honorarium for time

and effort. At the end of mentorship, structured questionnaire was used to capture their perceptions on engaging in TB care activities

Results/Impact: Of 229 TBCs, 66% responded to the questionnaire. 70% TBCs reported better understanding of health issues; 93% felt more confident accessing health services.

They reported that their standing in the community had evolved; 70% reported being approached for health issues beyond TB; 65% felt their involvement extended to other social issues. A majority acknowledged personal growth; 92% felt mentorship enhanced their ability to use technology, particularly mobile phones; 79% expressed improved confidence in public speaking. Overall, 95% reported receiving respect and recognition from their communities.

Conclusions: The mentorship was aimed at building capacity of TB survivors to address TB related challenges. TBCs expressed overall personal empowerment and increased respect/standing in their communities, which were significant collateral benefits of the mentorship program.

The findings have highlighted that mentorship could help pave their journey towards becoming champions of Community Health in their local communities.

EP-41-503 What do women think about gender and TB? Dialogues during the implementation of a TB project in Uganda

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Background and challenges to implementation: Tuberculosis disease is a common condition among women in low resource settings in Kampala and Wakiso Districts. PRES-TB project was a research based project aimed at improving TB case notification by engaging private health providers.

The project had a community engagement model aimed at training healthcare workers in community pharmacies and drugs shops to screen patients for TB and collect or refer sputum samples to public facilities for TB diagnosis.

Intervention or response: Dialogues were designed to enhance community sensitisation for early diagnosis and appropriate, timely intervention. Three meetings with a total of 150 women (50 per dialogue) were implemented with community women in poorly planned and congested areas around the shores of Lake Victoria. Topics covered community perceptions on tuberculosis diagnosis and management; nutrition; gender-based violence; and barriers to tuberculosis care.

Results/Impact: Women expressed lack of TB knowledge. Suggesting the need for information at the community level through direct education and dialogue interactions with established community leadership.

They reported the importance of male involvement due to men's perceived lack of information, poor health seeking behaviour, and unwillingness to take infection control measures, like wearing masks when infectious. Women further felt that better male involvement and TB knowledge would reduce gender-based violence on women because it would create awareness. The dialogues further identified numerous gendered barriers to care access, including, pervasive stigma (linked to HIV) and drug use.

Conclusions: Given the poor levels of knowledge about TB in-community, the differential knowledge about TB and different ideal training methods, TB interventions need to start by assessing gendered knowledge gaps, and designing their training content and structure to meet the specific, local needs of men and women. The effects of TB education on levels of gender-based violence experienced by women affected by TB should be further explored for instance divorce and separation, domestic violence, poor adherence.

EP-41-504 Best practices and challenges in community based approach to TB case finding in Nasarawa State, Nigeria

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Background and challenges to implementation: The World Health Organization (WHO) advocates community active case finding as a panacea to finding the missing TB cases especially in low income countries like Nigeria. TB case detection remains low in Nigeria despite improvement in TB services facility coverage.

With the impact of COVID-19 on facility attendance leading to a decline in access to healthcare services especially TB services, the focus has shifted to the community to find the missing TB cases.

Intervention or response: Community ACF was carried out using a targeted approach with focus on TB hot spot analytics through the EWORS alerts from BI Portals, an innovative approach to track clusters of TB cases in the community and alert service providers to follow up with community based interventions.

Entry advocacy visits were conducted to community gate keepers to help mobilize dwellers while community mobilizers were deployed to create awareness and encourage persons with signs and symptom of TB disease to turn up for screening and sample collection from presumptive TB clients done under strict infec-

tion control protocols and transported for GeneXpert. Clients unable to produce sputum were referred for Chest Xray.

Results/Impact: A total of 1521 persons were clinically screened for TB across 10 communities within 5 LGAs identified by the EWORS system within a two month period. Seven hundred and nine (779) (51%) presumptive TB were identified with 99% (774) successfully evaluated and 50 new (6%) confirmed TB cases detected (94% bacteriological) out of which 48 (96%) persons were commenced on treatment. The Number needed to screen to find one TB case was 30 and number needed to test to find one TB case was 15.

Conclusions: The use of the hot spot analytics for targeted TB case finding in the community presents one of the best practices in improving TB yield in community based ACF interventions in Nigeria

EP-41-505 Working with civil society organisations to minimise TB diagnostic delays In Kampala Capital City, Uganda

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Background and challenges to implementation: In Uganda, more than 30% of TB patients go undetected either because of missed opportunities at health facilities or failure to access information and diagnostic services by the community. USAID Defeat TB project has since September 2018 been working with Civil Society Organizations (CSO) to provide TB services at the community level. CSOs through community volunteers and in collaboration with health facilities offer TB services. While executing their roles, CSOs noticed delays and or failure in the testing of presumptive TB patients.

Intervention or response: TB care data analysis conducted in Feb 2020 revealed that; sputum samples collected in the community were inadequate and thus rejected by laboratories. In addition, some presumptive TB patients when referred could not access health facilities or delayed, and TB testing services were not consistently available at some health facilities. Interventions were executed to address the noted gaps while monitoring the proportions of presumptive TB patients from community activities that were evaluated for TB within 7 days. CSOs reoriented community volunteers on sputum sample collection procedures to avoid sample rejection at the laboratories, Lab personnel were coopted on the community TB outreach teams to support sputum sample collection and bi-weekly meetings were held between CSO staff, volunteers, health facilities staff to review progress and address barriers.

Results/Impact: The proportion of presumptive TB cases from community interventions evaluated within 7 days of identification increased from 23% at 3 health facilities to 87% by the 5th week (end of Feb 2020) of the intervention and remained high thereafter. The number of identified TB case also raised during the intervention period compared to the preintervention period.

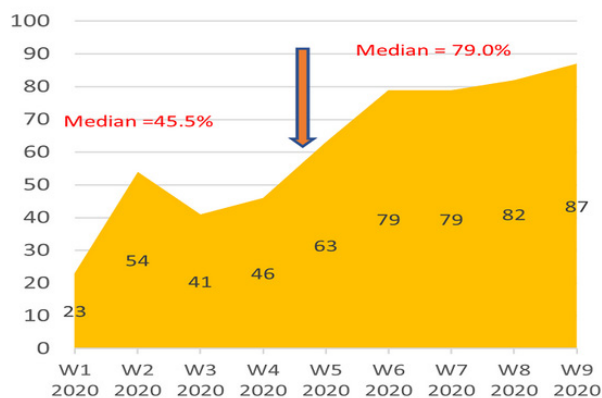


Figure. % of presumptive TB evaluated within 7 days at 3 intervention HFs in Kampala City, Jan - Feb 2020.

Conclusions: Coordination of community TB services by CSOs promotes timely access to TB diagnosis through reducing barriers to TB testing.

EP-41-506 Achieving End TB Strategy in Nigeria: the role of health system governance

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Background: Nigeria is committed to achieving the END TB Strategy. One of the pillars of the strategy is bold policies and supportive systems with components as political commitment and adequate resources. Global Fund and USAID provide major resources through many Implementing Partners (IPs). There is a multiplicity of partners and activities posing significant challenges to effective coordination which further weakens the health system. We examine the existing governance structure for stakeholder management and propose ways to maximize it.

Design/Methods: Desk review of existing TB policy documents and charters, review of existing coordination mechanisms/platforms, and 52 key informant interviews were conducted with NTP, TB IPs, Civil Society, Private and Public providers to elicit information on the availability and functionality of coordination mechanisms. Interviews were transcribed, and analysis done using

WHO Health Systems Governance(HSG) framework: Policy guidance, intelligence and oversight, Accountability, Collaboration and coalition building, Regulation, and System design.

Results: Policy documents exist for effective TB control; Coordination mechanisms exist mainly at the National level- Planning cell meetings, zonal review meetings; Platforms at the subnational levels are used for data collation without coordination functions; Strong Governance Functions at National level are Policy guidance, Intelligence and oversight and regulation. Weak functions are Programme accountability, Collaboration and system design. Reported challenges that contribute to weak functionality are a federation system with autonomy of sub national government, independent statutory professional bodies, managing the growing private sector, array of national and international organizations working in the TB space. Suggested ways to multisectoral collaboration and accountability framework are building coalition across NTP, other government, private and civil society organizations, and holding all system actors publicly accountable.

Conclusions: Capacity building among NTP on the role of HS governance for TB control at all levels will crystallize efforts and resources of stakeholders and ensure a synergistic drive towards achieving the END TB strategy.

EP-41-507 The Wellness on Wheels mobile unit: an excellent tool for advocacy and community mobilisation

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Background and challenges to implementation: The increasing funding gap for the TB program in Nigeria had impacted program ownership and the scale-up of key TB control interventions. Strategic advocacy for increased domestic resources mobilization will be essential in ensuring increased funding and sustainability of the TB program.

Intervention or response: The WoW truck (fig 1) with its inbuilt diagnostic unit and X-ray with AI commenced integrated COVID-19 TB testing with flag-off ceremonies attended by high profile government officials, including a state governor. The trucks had continued since the start of the KNCV USAID funded TB LON project to support community TB case finding. At these events, government officials appreciated its usefulness in TB and COVID diagnosis. In the communities where the trucks were deployed, it became a cynosure of all eyes and awakened the communities' interest in care-seeking for TB.



Fig 1. The WoW Truck and its diagnostic components- X-ray with CAD4TB and the 8 modular GeneXpert section.

Results/Impact: The WoW deployment to the states and engagement of high-profile government officials in the flag off ceremonies catalyzed an unprecedented interest in the TB program. In one of the States, the governor keyed into the WoW COVID TB integrated community intervention to procure Xpress SARS COV 2 cartridges, ordered similar WoW trucks and GeneXperts. The WoW community outreaches continued to attract an increasing number of community members to access TB services. In Kano state, between April 2020 to March 2021 across 128 communities, the truck enrolled 18,840 clients and diagnosed 459 TB cases. Health facilities in these locations had continued to see an increasing number of clients seeking care for TB even after the truck had left.

Conclusions: The WoW truck in addition to improving access to TB services, has become a good tool for advocacy and awareness creation for TB. The continued deployment of the WoW trucks to more states with sustained advocacy would ensure increased commitment and political will from government to improve funding for TB control.

ABSTRACT PRESENTATIONS FRIDAY 22 OCTOBER 2021

ORAL ABSTRACT SESSION (OA)

OA-26 Challenges for programmatic management of drug-resistant TB

OA26-775-22 Comparison of time to culture conversion in multidrug-resistant TB regimens including bedaquiline vs. high-dose isoniazid

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Background: High-dose isoniazid (INH) is not included in the current World Health Organization (WHO) MDR-TB treatment guidelines, yet may have benefit. We retrospectively examined time to culture conversion in HIV-negative adults with MDR-TB who received regimens including bedaquiline (Bdq) vs. high-dose INH vs. neither drug at GHESKIO, in Haiti.

Design/Methods: Patients with MDR-TB at GHESKIO are treated according to WHO and Haitian guidelines. From 2008 – 2011, patients initiated treatment on a fluoroquinolone (FQ) and second-line injectable-based regimen including p-aminosalicylic acid (PAS), cycloserine, ethionamide, and pyrazinamide.

Between October 2011 – October 2014, high-dose INH (16-18 mg/kg) replaced PAS. Bdq was prescribed for newly diagnosed patients starting in 2018. Culture was performed monthly (intensive phase), every other month (continuation phase) then monthly (final 3-5 months of treatment).

Culture conversion was defined as 2 consecutive negative cultures ³⁰days apart. Patients were grouped for analysis based on drug regimen: regimens with Bdq, with

high-dose INH or with neither drug. Time to culture conversion was evaluated using Kaplan-Meier survival analysis and log-rank test for comparison.

Results: Between June 2008 - December 2020, 364 HIV-negative adults were diagnosed with MDR-TB and initiated treatment. Seventy-seven patients (21%) received Bdq and 99 (27%) received high-dose INH; 188 (52%) received neither drug. Patients receiving Bdq or high-dose INH had similar time to culture conversion (Bdq: median 54 days, 95% CI: 50, 57; high-dose INH: median 49 days, 95% CI: 44, 58) followed by those receiving neither drug (median 60 days, 95% CI: 51, 65). There was no significant difference in time to culture conversion between regimens with Bdq or high-dose INH ($p=0.35$), but occurred later in patients who received neither drug ($p<0.01$).

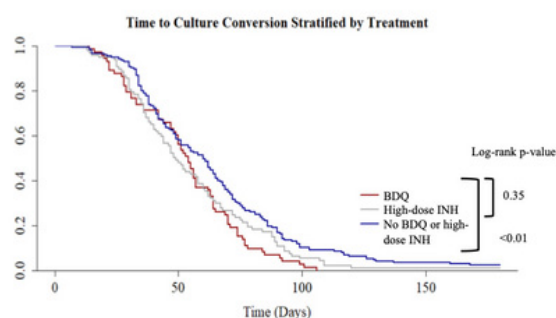


Figure 1. Time to culture conversion (in days) between regimens containing Bdq vs high-dose INH vs neither drug.

Conclusions: High-dose INH may provide clinical benefit for the treatment of MDR-TB. Further data on the potential efficacy of high-dose INH in MDR-TB are needed.

OA26-776-22 Interim treatment outcomes of patients with drug-resistant TB on standard short and long all-oral regimens in the Philippines

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Background and challenges to implementation: The treatment outcomes of patients with rifampicin-resistant/multi-drug resistant tuberculosis (RR/MDR-TB) continued to be unsatisfactory despite the use of a 9-month treatment regimen containing injectable (9-MTR) in the Philippines. Among the 2018 cohort of patients with RR/MDR-TB, 75% were treated with 9-MTR with treatment success rate (TSR) of only 69% and high loss to follow-up (LTFU) at 20%, mainly due to adverse events.

Intervention or response: To improve the RR/MDR-TB TSR, the National Tuberculosis Control Program (NTP) rapidly adopted the World Health Organization-recommended bedaquiline-containing standard long and short all oral regimens (SLOR and SSOR) in 2019 and 2020, respectively. The NTP with the support of its partners developed RR/MDR-TB guidelines and conducted training including active drug safety monitoring and management (aDSM) for staff involved in RR/MDR-TB care, with virtual training for SSOR in 2020 after the COVID-19 pandemic erupted. Flexible supervised treatment by family members was also allowed.

Results/Impact: By the end of 2020, 1143 and 1646 patients were treated with SLOR and SSOR, respectively. The interim outcomes of these patients showed 66% and 63% culture conversion and 2.8% and 3.5% LTFU for SLOR and SSOR, respectively. In comparative sub-analysis of 9-MTR from March-June 2019 and SSOR from March-June 2020 cohorts, there was no statistically significant difference in age distribution, with a mean age of 43 for both groups (SD 14.3 vs 14.9, p=0.32). The proportion of males was significantly higher in SSOR over 9-MTR with 74.1% vs 68.9% (p=0.02), respectively. Deaths were more common in 9-MTR with 8.0% vs 3.8% (OR=2.2; p=0.001), especially in males (OR=1.7; p=0.028) and those >65 years (OR=2.08; p=0.007). Importantly, LTFU was higher in 9-MTR with 12.9% vs 3.3% (OR 4.4, p=0.001), especially among those >55 years (OR=1.76, p=0.0003).

Treatment outcomes at 6 months of treatment	SSOR (N=553)	9-MTR (N=1,384)	p-value ^a
Positive culture	10 (1.8%)	18 (1.3%)	0.398
Negative culture	363 (65.6%)	867 (62.6%)	0.216
Died	21 (3.8%)	110 (8.0%)	0.001
Lost to follow-up (LTFU)	18 (3.2%)	178 (12.9%)	<0.001
Failed	3 (0.5%)	16 (1.2%)	0.216
Not evaluated (NE)	138 (25.0%)	195 (14.1%)	<0.001 ^b

^aUse of Pearson's chi test

^bThe imposition of enhanced community quarantine in the Philippines from March 15, 2020 may have significantly limited transportation of sputum samples from health facilities to culture laboratories.

Table 1: Comparison of the interim outcome categories between standard short all oral regimen (SSOR), March-June 2020, and 9-month treatment regimen containing an injectable agent (9-MTR), March-June 2019, Philippines

Conclusions: Having patient friendly treatment regimens along with flexible provision of supervised treatment and proper aDSM systems can significantly improve treatment success.

OA26-777-22 Month 24 outcomes after initiating short bedaquiline- or injectable-containing rifampicin-resistant TB treatment: a retrospective study in South Africa

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Background: We compared outcomes for rifampicin-resistant tuberculosis (RR-TB) patients treated with a short, all-oral bedaquiline-containing regimen or a short, injectable-containing regimen 24 months after treatment initiation in South Africa.

Design/Methods: RR-TB patients treated from 1 January to 31 December 2017 using a bedaquiline- or injectable-containing short treatment regimen of 9 to 12 months registered in the national drug-resistant TB database (EDR Web), with known age, sex, HIV status, and regimen meeting WHO recommendations were included.

We did logistic regression using generalized linear mixed models to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95%CI) for successful outcome (survival with recurrence-free cure/completion at 24-months).

We matched on age, sex, HIV, previous treatment with first-line drugs, isoniazid resistance, smear positivity, and culture positivity between patients receiving bedaquiline- or injectable-containing regimens.

Results: Of the 10,152 RR-TB patients treated during the year 2017, 1,387 met inclusion criteria. There were 688 patients who received an all-oral short, bedaquiline-containing regimen and 699 patients who received a short, injectable-containing regimen. Characteristics are in Table 1.

	Bedaquiline-Based Short Regimen (n=688)	WHO Short Regimen (n=699)	p-value
Median (IQR) Age	42 (33 to 51)	34 (28 to 42)	<0.001
Male	423 (61.5%)	389 (55.7%)	0.03
HIV Infection	493 (71.7%)	474 (67.8%)	0.13
Previously Treated for TB	274 (39.8%)	286 (40.9%)	0.72
Final Treatment Outcomes at 24 Months Post-Initiation			
Number with Treatment Success	478 (69.5%)	396 (56.7%)	--
Number with Treatment Failure and Recurrence	4 (0.6%)	17 (2.4%)	--
Number Dying	162 (23.5%)	199 (28.5%)	--
Number Lost to Follow-up	44 (6.4%)	87 (12.4%)	--

Table 1: Characteristics of the included population.

24-months after initiating treatment, 478/688 (69.5%) of patients were successfully treated in the bedaquiline group with 396/699 (56.7%) in the injectable group. Treatment failure and recurrence were 4/688 (0.6%) in the bedaquiline group and 17/699 (2.4%) in the injectable group. The aOR for treatment success was 1.8 (95% CI 1.4 to 2.4) times higher among the bedaquiline vs. injectable group. This effect was maintained in analyses stratified on HIV status, AFB smear positivity, and previous treatment history.

Conclusions: The short all-oral, bedaquiline-containing regimen was associated with higher odds of successful outcome 24-months post-treatment initiation compared to a short, injectable-containing regimen. The analysis supports the use of short bedaquiline-containing regimens in eligible patients.

OA26-778-22 Treatment outcomes with the shorter treatment regimen for multidrug-resistant TB in Uganda

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Background: In April 2018, Uganda adopted the shorter multi-drug resistant TB regimen (STR) and patients were enrolled based on the WHO eligibility criteria. The rest of the patients were enrolled onto the longer regimen. USAID Defeat TB sought to compare treatment outcomes (cure, completed, death, failure and lost to follow up) among patients enrolled onto the two regimens.

Design/Methods: We conducted a retrospective cohort study of 492 MDR-TB patients treated with STR or longer regimen during 2018. The STR comprised of 4-6Km-Mfx-Pto-Cfz-Z-Hhigh-dose-E/5Mfx-Cfz-Z-E while the longer regimen had 6-8Km-Eto-Cs-Lfx-Z/14Eto-Cs-Lfx-Z. Data was extracted from the electronic TB case based surveillance system. We analyzed the cohort with respect to treatment outcomes for bacteriologically confirmed rifampicin resistant (RR-TB) and MDR-TB patients and compared findings among patients on STR and longer regimen.

Results: 492 patients were diagnosed with drug-resistant TB and started on treatment. Of 492 patients who started treatment; 51.8% (255/492) were treated with the longer regimen and 48.2% (237/492) with the STR. Patients characteristics were similar regardless of the regimen, with a median age of 36 years in both groups. The overall cohort TSR was 77.2% (380/492). The TSR was higher 78.8% (201/255) among the STR patients compared to 75.5% (179/237) for patients on the longer regi-

men. The overall outcomes were cure 64.7% Vs 53.2%, completed 14.1% Vs 22.4%, death 11.8% Vs 13.1%, LTF 5.9% Vs 8.0% and failure 3.5% Vs 3.4%, among the STR and longer regimen, respectively. STR patients were twofold more likely to get a cure outcome compared to patients on the longer regimen (OR:1.61;95% CI:1.12, 2.32, $p = 0.01$).

Conclusions: In Uganda, patients treated with the STR were more likely to have a cure outcome than those treated with the longer regimen. Mortality and lost to follow-up were higher in patients on the longer regimen while treatment failure was similar in both groups.

OA26-779-22 Limited sampling strategies and probability of target attainment for linezolid in patients with multidrug-resistant TB

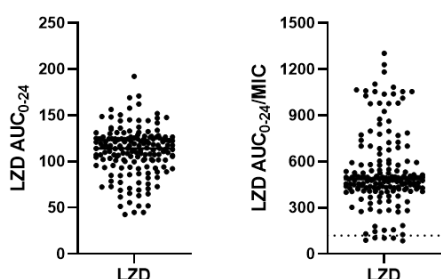
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Background: Therapeutic drug monitoring (TDM) of linezolid in multidrug-resistant tuberculosis (MDR-TB) treatment can help to maximize the therapeutic effect. This study aims to develop a feasible limited sampling strategies (LSSs) for linezolid in programmatic setting, along with an evaluation of probability of target attainment under current doses.

Design/Methods: A prospective cohort of MDR-TB patients was conducted in China between 2016 to 2019. Drug concentrations of linezolid were measured after intensive blood sampling and minimum inhibitory concentration (MIC) was determined for *Mycobacterium tuberculosis* isolates. Bayesian approach and multiple linear regression were used to develop LSSs with the acceptance criteria of root-mean-square error (RMSE) <15%, mean prediction error (MPE) <5% and $R^2 > 0.95$. The evaluation of probability of target attainment was based on an $AUC_{0-24}/MIC > 119$.

Results: In total, 168 patients with pulmonary MDR-TB received linezolid-containing regimen with a median age and weight of 41 years and 53 kg, respectively. The Bayesian LSS using 2- and 6-h post-dose samples adequately estimated the area under the concentration-time curve (AUC) for linezolid (MPE = 4.5%, RMSE = 5.8%, $R^2 = 0.955$) while multiple linear regression LSS using 0- and 6-h post-dose samples was most predictive of AUC for linezolid (MPE = 2.8%, RMSE = 3.4%, $R^2 = 0.978$). The median values for AUC_{0-24} and AUC_{0-24}/MIC were 114.1 (IQR, 99.8-125.0) mg^*h/L and 485.7 (IQR, 422.2-593.9), respectively. The proportion of patients reaching target attainment of $AUC_{0-24}/MIC > 119$

was over 97%. When considering a dose reduction to decrease toxicity, 92.9% (156/168) of the patients were eligible for dose reduction as they had an $AUC_{0-24}/MIC > 238$.



Conclusions: Clinically feasible LSSs were successfully developed for linezolid. Current doses for linezolid had a high probability of target attainment, potentially allowing for a dose reduction to increase tolerability.

Funding: NSFC (No. 81874273)

†: Equally contributed

OA26-780-22 Leveraging a private provider interface model to measure the burden of drug-resistant TB in the private sector of Vietnam

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Background: In Vietnam a substantial number of persons with tuberculosis (TB) seek health in the private healthcare sector. However, studies have shown the variable quality of care among private providers. This has been hypothesized to sustain the development of multi-drug resistant TB (MDR-TB).

Design/Methods: With support from TB REACH, we established a private provider interface agency (PPIA) through which we have collected data on referral and treatment notifications, including for drug-resistant TB. Since Jan-2020, we have collected data through the PPIA in 19 districts across three provinces of Viet Nam (Ha Noi, Hai Phong and Ho Chi Minh city). We present the TB care cascade of referred and notified persons with TB from the private sector, and describe the prevalence of drug-resistance.

Results: In total, private providers referred 160,544 persons for chest X-ray screening, which resulted in 14,823 persons (9.2%) with GeneXpert test conducted. Among these, we detected 2,230 persons with bacteriologically-confirmed TB (2,230/14,823=15.0%), including 5.2% (116/2,230) with drug-resistant TB (MDR/RR TB). In

addition, private providers reported 3,049 persons on private TB treatment of whom 2,599 persons (85.3%) had sputum test results and 1,522 persons with bacteriologically-confirmed TB (1,522/2,599=58.6%). The rate of drug-resistance in this group was 3.6% (55/1,522).

Conclusions: Implementation of PPIA model leads us to detect 171 drug-resistant TB cases among 3,752 persons bacteriologically-confirmed TB from the private health-care sector. Further studies are needed to understand the role and contribution of private providers to Vietnam's MDR-TB burden.

OA26-781-22 Integrating palliative care within a drug-resistant TB model of care in Mumbai, India

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Background and challenges to implementation: In India, less than one percent of population has access to pain relief and palliative care. There are no palliative healthcare services dedicated to DR-TB patients, and those who need long term oxygen therapy (LTOT) or facing stigma at home are hospitalized at central TB hospitals.

Intervention or response: The Médecins Sans Frontières clinic in Mumbai provides free of cost multidisciplinary care to DR-TB patients with advanced resistance profiles. Palliative care is integrated with curative care since day of initiation of treatment. Palliative care is continued for patients whose anti-tuberculosis treatment (ATT) is ceased due to failure on treatment. For medical management, physicians give symptomatic management in-person or via telemedicine in monthly appointments. Clinic provides oxygen concentrators at home for LTOT. Mobile health team comprising of nurse and counsellor make monthly visits to patient's home to teach and encourage non-pharmacological care. Trained nurses do IPC assessment of the home and structural modifications are done on case by case basis for ventilation, along with masks. Contact tracing of target groups is done. Psychologist and counsellor provide psychosocial support and establish referral to psychiatrist if required. Healthcare workers are being trained in generalized palliative care. Limited access to opioids is a challenge.

Results/Impact: Use of oxygen concentrators at home and mobile health teams decrease need for hospitalization and reduce burden on inpatient healthcare facilities. As of 03rd May 2021, clinic is providing DRTB treatment to 103 patients and palliative care to 12 patients whose TB treatment was ceased due to failure on treatment. In 2020, fourteen patients received LTOT at home.

Conclusions: Our implementation strategy provides an ambulatory and patient-centric model of palliative care, which should be adopted by national TB programmes to ensure quality of life for DR-TB patients. We advocate for access to Opioids for DRTB patients on palliative care.

OA-27 Spotlight on HIV-TB

OA27-782-22 The effect of HIV coinfection on the pharmacokinetics of the components of the new child-friendly, dispersible, fixed-dose combination tablet in children with TB

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Background: Children with TB/HIV coinfection have a higher risk of lower antituberculosis drugs concentrations than those with TB alone treated with previous pediatric formulations. The new child-friendly (isoniazid/rifampin/pyrazinamide 50/75/150mg) formulation developed in line with revised WHO dosing guidelines is expected to improve adherence and drug pharmacokinetics (PK). This study compared the PK and C_{max} targets (3mg/L for isoniazid, 8 mg/L for rifampin, 20 mg/L for pyrazinamide and 3 mg/L for ethambutol) of the drugs in children with TB/HIV coinfection to those with TB alone who were treated with the new formulation.

Design/Methods: Children with TB with or without HIV coinfection on recommended first-line antituberculosis therapy for at least 4 weeks had blood samples collected at pre-dose, 1, 2, 4, 8 and 12 hours post-dose. Drug concentrations were measured using validated LCMS/MS and PK parameters calculated by noncompartmental analysis. Differences in PK parameters for each drug were compared by HIV status.

Results: Of the 68 study participants, 34 (50%) had HIV infection. The baseline characteristics and drug dosages for the two groups were similar except HIV/TB co-infected patients were more likely to have a lower weight-for-age and height-for age z-scores. The median plasma

area under the concentration-time curve from 0-12 hours for isoniazid in the children with TB/HIV coinfection and TB alone were (22.7 vs. 28.0 mg*hr/L; $P=0.227$), rifampin were (27.2 vs. 33.6 mg*hr/L; $P=0.394$), pyrazinamide (252.5 vs. 296.7 mg*hr/L; $P=0.034$) and ethambutol (10.6 vs. 13.3 $\mu\text{g}^*\text{hr}/\text{mL}$; $P=0.012$), respectively. There was no significant difference in C_{max} or T_{max} between the two groups. The proportion of children who achieved drugs C_{max} targets was not different between the two groups.

Conclusions: The new water-dispersible FDC tablet for tuberculosis treatment in children achieved similar target concentrations in children irrespective of HIV coinfection. Our data support similar dosing recommendations of the new tablet irrespective of HIV infection status.

OA27-783-22 Treatment and safety outcomes in patients with multidrug-resistant TB and diabetes mellitus comorbidity from STREAM Stage 1

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Background: Recent meta-analyses concluded that diabetes mellitus (DM) is associated with adverse treatment outcomes in patients with drug-susceptible TB (DS-TB), and significantly increases the odds of developing multidrug-resistant TB (MDR-TB). However, there is limited evidence regarding effect of DM on patients with MDR-TB. We report trial/treatment outcomes and safety events in participants with MDR-TB and DM comorbidity enrolled in STREAM Stage 1 – a randomized, phase 3 trial that compared short and long regimens for MDR-TB.

Design/Methods: Analyses were performed on the modified-intention-to-treat (mITT) population. Participants who self-reported DM status or had non-fasting blood glucose $\geq 200\text{mg}/\text{dl}$ at baseline were classified as the DM group. Summary statistics for trial-defined outcomes, WHO-defined outcomes, as well as safety outcomes are reported. Associations between DM status and baseline characteristics were assessed for adjustment in Cox-proportional hazard models for time-to-event outcomes.

Results: A total of 357 participants were included in the analyses (n=35 DM, n=322 non-DM). The DM group were significantly older, more likely to have higher BMI and less likely to have HIV co-infection or acquired PZA resistance. The proportion with an unfavourable outcome (trial primary endpoint) was higher in the DM group (26% vs. 19% non-DM) and this difference was seen in both regimens. There was some evidence that

time to unfavourable outcome was faster in the DM group (HR 1.84, 95% CI: 0.80 to 4.20) and that they were less likely to culture convert (HR 0.87, 95% CI: 0.58 to 1.29) compared to the non-DM group. There were no significant differences in WHO treatment outcomes between groups. A higher proportion of DM patients experienced grade 3–5 safety events (63% vs. 46%), serious adverse events (43% vs. 29%), and deaths (11% vs. 7%) compared to the non-DM group.

Conclusions: Overall, patients with MDR-TB and DM comorbidity performed poorer on trial outcomes and experienced more safety events.

OA27-784-22 Using the TB lipoaribomannan assay to accelerate TB diagnosis among people with advanced HIV disease in the Democratic Republic of Congo

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Background and challenges to implementation: Tuberculosis (TB)/HIV coinfection remains a major challenge in the Democratic Republic of the Congo (DRC). HIV-positive TB mortality is 11 per 100,000, with TB being the primary cause of death among people living with HIV (PLHIV). Novel approaches to rapidly identify and link people with TB/HIV coinfection to treatment are essential to improving PLHIV health outcomes.

Intervention or response: PATH, through the USAID-funded Integrated HIV/AIDS Project, integrated use of TB-LAM at project-supported facilities and during household TB/HIV screening campaigns in seven health zones of Haut-Katanga, to accelerate TB/HIV diagnosis. Under this strategy, people who screened with presumptive TB at facilities or households were screened for HIV using a Determine rapid test. Those who screened HIV positive were assessed for advanced HIV disease (World Health Organization clinical stage 3 or 4) and then offered TB-LAM at either community or facility-level, and then referred to facilities for confirmatory diagnosis and treatment initiation for HIV and/or TB.

We analyzed 2 months (December 2020–January 2021) of programmatic data using descriptive and inferential statistics.

Results/Impact: TB prevalence among the 1,570 PLHIV diagnosed using TB-LAM was 18% (282), with greater prevalence among sicker PLHIV (Stage 4) and among those reached through household screening campaigns (see table). PLHIV with presumptive TB identified in communities were 1.77 times more likely to be confirmed with active TB than those in facilities (OR=1.77; 95% CI: 1.36–2.30). All 282 people with confirmed TB/HIV coinfection were initiated on HIV and TB treatment.

	PLHIV offered TB-LAM	Active TB prevalence (combined Stage 3 & 4)	Active TB prevalence (Stage 3)	Active TB prevalence (Stage 4)
Community household screening campaigns	770	22% (171/770)	21% (112/532)	25% (59/238)
Health facilities	800	14% (111/800)	11% (67/605)	23% (44/195)
Total	1,570	18% (282/1,570)	16% (179/1,137)	24% (103/433)

Table.

Conclusions: Proactively offering TB-LAM to people with presumptive TB who screen positive for advanced HIV disease at both facility and household levels enabled rapid diagnosis and linkage to treatment for PLHIV with active TB. We plan to extend the use of TB-LAM in household TB/HIV screening campaigns to other underserved areas of DRC to facilitate rapid TB/HIV diagnosis and linkage to treatment during COVID-19.

OA27-785-22 Sensitivity of community-based symptom and chest radiography screening for TB in a high HIV prevalence setting

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Background: The World Health Organization recommends routine screening for Tuberculosis (TB) in high-incidence settings and among those infected with HIV, with symptom screening more widely used. Where resources permit, chest radiography is also recommended. We analysed data from Namibia’s first national TB prevalence survey (2017–2018) to determine the sensitivity of symptom and chest radiography screening.

Design/Methods: The national survey sampled 68 clusters of 500 adults each. Participants were screened for symptoms (cough, weight loss, fever and night sweats) and were offered CXR, sputum testing using Xpert MTB/RIF, and either culture or another Xpert MTB/RIF using two sputa. Cases were defined as any person with a positive culture result or a positive Xpert MTB/RIF result, and a CXR consistent with TB interpreted by a radiologist. All participants were offered an HIV test. Data analysis was based on pooled data.

Results: In total, 29,495 participants were screened; 29,494 had symptom screening and among these, 27,617 (93.6%) had valid CXR results. Among the participants screened, 2,934 (9.9%) had prolonged cough, 4,670 (15.8%) any cough, and 7,740 (26.2%) any symptoms. A total of 122 participants had laboratory-confirmed TB. The sensitivity of prolonged cough in detecting laboratory-positive TB was 35% (95% CI 26.6–44.1), any

cough 48.8% (95% CI 39.7-58.0) and any symptoms 60.2% (95% CI 50.9-68.9). Radiography had a sensitivity of 91.0% which increased to 98.4% when combined with any symptoms, with a negative predictive value of 100%. Of the 23,378 participants with HIV results, 3,174 (13.6%) were HIV positive.

Conclusions: Symptom screening alone or as part of community-based screening may miss over 30% of laboratory-positive TB cases. CXR alone or in combination with symptom screening improves the sensitivity of TB Diagnosis. Screening programmes should invest in introducing rapid CXR techniques, to improve TB case finding, especially in high-HIV prevalence settings.

OA27-786-22 Longitudinal QFT-Plus and TST positivity and IFN- γ responses during pregnancy and postpartum in women with and without HIV in Kenya

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Background: HIV and pregnancy may affect latent tuberculosis (LTBI) diagnostics. Large longitudinal studies of pregnant women living with (WLHIV) and without HIV (HIV-) evaluating newer generation interferon gamma-release assay (QFT-Plus) and tuberculin skin test (TST) are lacking.

Design/Methods: WLHIV and HIV- women enrolled from antenatal clinics in Kenya underwent QFT-Plus and TST in pregnancy, 6-weeks (6wkPP) and 12-months postpartum (12moPP).

Results: We enrolled 400 pregnant women (200 WLHIV/200 HIV-) at median 28 weeks gestation (IQR 24-30). All WLHIV were on antiretroviral therapy; median CD4 was 464 cells/mm³ (IQR 325-654). QFT-Plus positivity was similar between WLHIV and HIV- women at baseline (31.5% vs. 33.2%, $p=0.72$) and subsequent postpartum timepoints (**Figure A**). In pregnancy, QFT-Plus had higher sensitivity for LTBI than TST, identifying 3-fold more women (32.3% vs. 11.6%, $p<0.0001$). QFT-Plus/TST discordance was greatest in HIV- women during pregnancy (QFT+ 33.2% vs. TST+ 4.6%, agreement 61.9%, kappa 0.07, $p=0.022$) with similar discordance through 12moPP.

Among 115 women who were QFT-Plus positive in pregnancy, 34.8% (40/115) reverted to negative or indeterminate at anytime during postpartum. Among 254 women who were QFT-Plus negative or indeterminate in pregnancy, 14% (36/254) converted to QFT-Plus positive. Conversions and reversions were similar among WLHIV and HIV-.

Among women who were QFT-Plus positive in pregnancy, median mitogen and nil IFN- γ responses increased from pregnancy to 6wkPP ($p=0.0016$ and $p<0.0001$, respectively) and then decreased from 6wkPP to 12moPP ($p=0.003$ and $p=0.02$, respectively) (**Figure B** by HIV status). TB-specific TB1 (CD4) and TB2 (CD4 & CD8) responses decreased from pregnancy to 12moPP ($p=0.01$ and $p=0.02$, respectively).

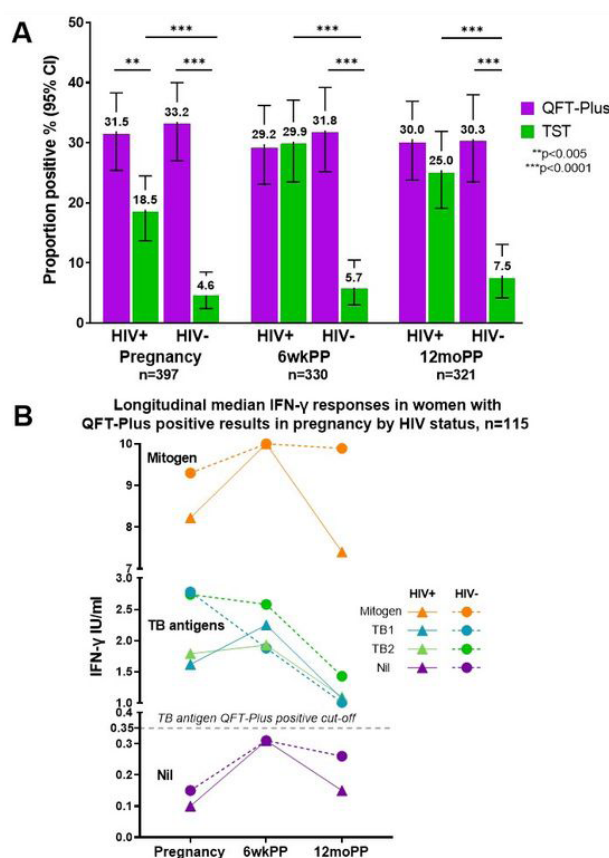


Figure. QFT-Plus and TST positivity and longitudinal IFN- γ responses in pregnancy and postpartum in women with and without HIV.

Conclusions: In one of the largest QFT-Plus and TST evaluations to-date in pregnancy/postpartum including women with/without HIV, QFT-Plus positivity was similar irrespective of HIV and pregnancy status, though dynamic changes in IFN- γ responses occurred. Conversions and reversions were common which has implications for clinical use and research studies.

OA27-787-22 Intensified case finding and TB preventive therapy initiation in people living with HIV in Kampala, Uganda

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Background: To reduce TB/HIV burden, the World Health Organization (WHO) recommends systematic TB screening followed by:

1. Confirmatory testing for screen-positives (intensified case finding [ICF]); or
2. Consideration of TB preventive therapy (TPT) for screen-negatives.

However, ICF and TPT scale-up has been unacceptably low in Africa, where symptom screening is the standard-of-care. C-reactive protein (CRP) is a promising alternative screening approach recently endorsed by WHO, though its clinical impact remains unclear.

Design/Methods: TB SCReening Improves Preventive Therapy Uptake (TB SCRIPT) is an ongoing randomized trial evaluating the impact of point-of-care CRP (POC-CRP)-based TB screening on 2-year clinical outcomes among Ugandan adults with CD4≤350 cells/uL initiating routine antiretroviral therapy (ART).

Participants are randomized to POC-CRP- or symptom-based TB screening. Screen-positive participants (POC-CRP≥8 mg/L or ≥1 TB symptom in the past month) undergo confirmatory testing (urine LAM ± sputum Xpert Ultra MTB/RIF).

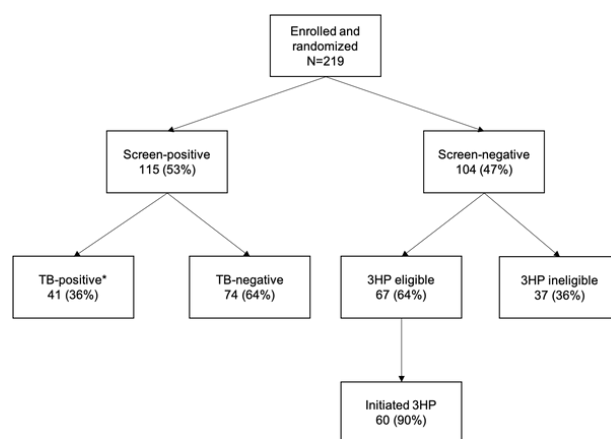
Screen-negative participants without contraindications are referred for 3HP (3 months of weekly isoniazid and rifapentine) two weeks following ART initiation.

This preliminary analysis includes participants enrolled during the first five months of the trial to determine the:

1. Proportion that screened positive;
2. Prevalence of microbiologically-confirmed TB; and,
3. Proportions eligible for and initiating 3HP.

Results: Among 219 participants, 56% were female, median age was 30 [IQR 26-38], and median pre-ART CD4 was 171 cells/uL [IQR 71-264]. Of these, 115 (53%) screened positive, and 41/219 (19%) were diagnosed with prevalent TB.

Among the 104 (47%) participants that screened negative, 37 (36%) were 3HP-ineligible (29 [78%] due to pregnancy). Of the 67 eligible participants, 60 (90%) initiated 3HP.



Legend:
*TB-positive defined as a positive urine LAM and/or sputum Xpert Ultra MTB/RIF result

Conclusions: Even in the universal test-and-treat era, TB prevalence is extremely high among PLHIV initiating ART, highlighting the need for rigorous ICF in this population. Attention must be paid to preventing TB among pregnant women and others with short-course TPT contraindications.

OA27-788-22 Sub-optimal pharmacokinetic exposures of anti-TB medications in people with HIV and critical illness

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Background: Critical illness from tuberculosis (TB) bloodstream infection like sepsis or meningitis is common among people living with HIV (PLWH) in TB prevalent settings, and results in high case fatality ratios. Such patients with critical illness from TB may have altered pharmacokinetics (PK) leading to suboptimal drug exposures.

Design/Methods: We enrolled PLWH hospitalized with sepsis and/or meningitis in Mbarara, Uganda who were starting first-line anti-TB therapy. We collected serum two weeks after enrollment at 1-, 2-, 4-, and 6-hours post-dose and quantified drug concentrations by validated LC-MS-MS methods. Non-compartmental analyses were used to determine total drug exposures over 24 hours (AUC₀₋₂₄), and population pharmacokinetic (PopPK) modeling and simulation were performed for the drug with lowest serum target attainment.

Results: A total of 81 participants were enrolled. Given that 18 (22%) died and 13 (16%) were lost to follow-up prior to PK testing, and one had incomplete serum

collection, 49 completed week-two PK testing. Of these 49, 17 (35%) were women, the median age, weight, and CD4 count were 36 years, 53 kgs, and 169 cells/mL³, respectively. For rifampin, only 8.2% attained a target serum concentration (C_{max}) of 8 mg/L and 16.3% attained target AUC₀₋₂₄ of 35 mg^{*}h/L, despite appropriate weight-based dosing. Simulation for higher doses of rifampin is shown in the figure, and at a median dose of 1800 mg (35 mg/kg), 88% had attained target C_{max} and 80% had reached target AUC₀₋₂₄ levels.

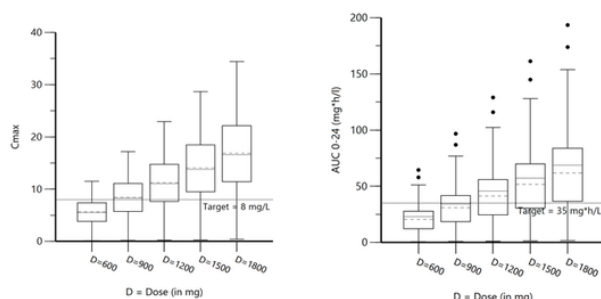


Figure. Box and whisker plots for simulated C_{max} and AUC₀₋₂₄

Conclusions: A majority of PLWH who survived the first two weeks of suspected TB-related critical illness did not reach target serum exposures for rifampin. Given the high case fatality ratio of TB-related critical illness among PLWH, empirical and higher dose anti-TB therapy, and/or early drug concentration monitoring and personalized dose adjustment should be trialed.

OA-28 Innovations in diagnostics

OA28-789-22 The impact of cash transfers on TB diagnostic evaluation outcomes (ExaCT TB): a stepped-wedge, cluster randomised controlled trial

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Background: Mitigating financial barriers to obtaining tuberculosis (TB) diagnosis and treatment is core priority of the global TB agenda. We evaluated the impact of a cash transfer (CT) intervention on improving completion of TB testing and treatment initiation outcomes in Uganda.

Design/Methods: We conducted a pragmatic complete stepped wedge randomized trial of a one-time unconditional CT intervention at ten health centers (HC) in Uganda between September 2019-March 2020. Patients referred for sputum based TB testing were enrolled to receive a CT of 20,000 Uganda Shillings (~US\$5.34) at the time of sputum submission. We defined the primary outcome as the number of patients who initiated treatment for micro-bacteriologically confirmed TB within two weeks of initial evaluation. Secondary outcomes included process metrics related to steps in diagnostic evaluation. We performed cluster-level intent-to-treat (ITT) and per-protocol (PP) analyses using negative binomial models to assess the effect of the CT on trial outcomes.

Results: 4,288 patients were eligible for the intervention according to trial criteria. Although more patients diagnosed with TB initiated treatment in the ITT analysis, the result was not statistically significant (aRR=1.34, 95% CI: 0.62-2.91 (p=0.46).

However, a greater number of patients were referred for and completed TB testing per Ugandan National TB Guidelines (aRR=2.60, 95% CI: 1.86-3.62; p<0.001; aRR=3.22, 95% CI: 1.37-7.60; p=0.007, respectively (Table)).

These results were similar in the PP analysis. More patients diagnosed with TB who received the intervention had treatment success than those who did not (PP: aRR=1.96, 95% CI: 1.02-3.75 (p=0.04)).

N	Outcome	Unadjusted Rate Ratio (uRR)	uRR 95% Confidence Interval (CI)	p-value	Adjusted Rate Ratio ¹ (aRR)	aRR 95% CI	p-value
Intent-to-Treat†	Primary outcome: Initiation of treatment within 14 days of tuberculosis (TB) testing	1.17	(0.80-1.70)	0.42	1.34	(0.62-2.91)	0.46
	Secondary outcome: Referred for TB testing	2.75	(2.13-3.55)	<0.001	2.60	(1.86-3.62)	<0.001
	Secondary outcome: Completion of TB testing per Uganda National Guidelines	2.88	(1.98-4.18)	<0.001	3.22	(1.37-7.60)	0.007
	Secondary outcome: Diagnosed with micro-bacteriologically confirmed TB	1.20	(0.83-1.74)	0.32	1.50	(0.80-2.79)	0.21
	Secondary outcome: Favorable treatment outcome among those treated for micro-bacteriologically confirmed TB	1.31	(0.86-2.00)	0.21	1.42	(0.59-3.43)	0.44

1. Adjusted for mean age, proportion male (log transformed), proportion HIV positive (log transformed), health center location (peri-urban vs. rural), and trial month
 † Comparison population is control period patients
 TB: tuberculosis; CI: Confidence Interval

Table. Cash transfer impact on primary and secondary trial outcomes.

Conclusions: While a single unconditional cash transfer did not increase the numbers of patients diagnosed and treated for TB, it did support more patients in completing diagnostic evaluation and completing treatment a programmatic setting. These results further highlight the potential role of social protection interventions in improving TB diagnosis and testing outcomes.

OA28-790-22 Results from an independent field evaluation of CAD4TB software versions in Vietnam

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Background: CAD4TB (Delft Imaging, The Netherlands) was one of the first artificial intelligence (AI) software solutions to become commercially available for TB screening. New software versions are regularly released, which purport to have improved performance characteristics. However, there is a dearth of independent field evaluations confirming these assertions.

Design/Methods: A chest X-ray (CXR) test library was created using data from a community-based CXR screening initiative in Ho Chi Minh City, Viet Nam between December 2017 and October 2019. The test library was blindly re-read by an Intermediate Human Reader (IHR, 5yrs of experience) and an Expert Human Reader (EHR, >30yrs of experience). In addition, the library was processed using CAD4TB software versions 6 and 7. The areas under the receiver operating characteristic curve (ROC AUC) and precision-recall curve (PR AUC) were calculated and compared for each software version, using Xpert MTB/RIF results as the reference standard. Abnormality score cut-off thresholds were then selected for each software version to match the sensitivity of the IHR and EHR so that specificity could be calculated and compared.

Reader	Cut-Off Score	Sensitivity	Specificity
Expert Human Reader	N/A	97.2% (94.4-98.9)	25.3% (23.5-27.3)
CAD4TB v6	55	97.6% (94.9-99.1)	13.4% (12.0-15.0)
CAD4TB v7	46.74	97.2% (94.4-98.9)	35.3% (33.2-37.5)
Intermediate Human Reader	N/A	90.1% (85.8-93.5)	29.9% (27.9-31.9)
CAD4TB v6	64	90.9% (86.7-94.1)	30.6% (28.6-32.6)
CAD4TB v7	61.88	90.1% (85.8-93.5)	56.6% (54.4-58.7)

Results: The final test library contained CXR images from 2,265 participants, 253 of whom were Xpert-positive (11.2%). CAD4TB v7 showed significant improvements over v6 on both the ROC AUC (0.84 vs. 0.67; p<0.001) and PR AUC (0.39 vs 0.15; p<0.001). When matching the sensitivity of human readers, CAD4TB v7 achieved a significantly higher specificity than both the EHR (35.3% vs 25.3%) and IHR (56.6% vs 29.9%).

Whereas, CAD4TB v6 only achieved a specificity significantly lower than the Expert Reader, yet on par with the Intermediate Reader.

Conclusions: CAD4TB v7 has significantly better performance characteristics than v6. The software performs significantly better than an expert reader in our setting, and would be a valuable decision support tool for TB screening initiatives.

OA28-791-22 Optimising the use of mobile digital X-ray with CAD4TB among populations at increased risk for TB to increase TB case detection in Uganda

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Background and challenges to implementation: TB treatment coverage in Uganda stands at 76% of incident TB cases. Use of chest X-ray (CXR) to screen patients for TB has the potential to increase TB case identification and improve TB treatment coverage. We present findings from initial efforts by the Uganda Ministry of Health to scale-up use of CXR for TB screening.

Intervention or response: Five portable digital X-ray machines with (CAD4TB) software for automated results interpretation were placed at five health facilities serving high burden communities. Clinicians were trained to use the X-ray equipment and mentored on eligibility and interpretation of CAD4TB output to facilitate TB diagnosis.

Patients were eligible for X-ray screening if they belonged to a high-risk group e.g., PLHIV, prisoners and TB contacts or presumptive TB patients with initial negative laboratory test.

Patients with CAD4TB score of 60% or more were considered to have abnormal X-ray and referred for GeneXpert test. All confirmed TB patients were initiated on standard TB treatment while those with negative result were managed per the national guidelines.

Results/Impact: At health facility settings, 1,308 individuals (96% >14 years and 56% females) were screened with X-ray between June 2020 and May 2021. Of these, 281 (21%) had abnormal X-ray and 243 (86%) were tested with GeneXpert. Of these, 35 patients (14%) were confirmed with TB (71% males, 51% HIV positive and 54% TB contacts). (Table 1).

Meanwhile, 1,403 clients were screened with X-ray at community settings, in March 2021, of these, 189 (13.5%) had abnormal X-ray and were tested with GeneXpert and 12 (6.3%) were confirmed with TB.

Conclusions: TB screening using digital X-ray had a higher yield of TB at health facilities compared to community settings, especially among PLHIV and TB contacts. National TB programs and partners should scale up use of CXR for TB screening targeting high-risk groups, to increase TB case detection.

	Age		Sex		HIV status			Patient category	
	0-14 years	>14 years	Male	Female	HIV positive	HIV negative or unknown	Contact of index TB patient	Other risk groups (health workers, diabetic patient, prisoners)	Unknown (non-risk groups)
Number screened with X-ray (n=1,308)	51	1257	575	733	448	860	593	87	628
%	4%	96%	44%	56%	34%	66%	45%	7%	48%
Number with abnormal X-ray (n=281)	11	270	153	128	81	200	112	12	157
%	4%	96%	54%	46%	29%	71%	40%	4%	56%
Number tested with GeneXpert (n=243)	4	239	133	110	67	176	87	12	142
%	2%	98%	55%	45%	28%	72%	36%	5%	58%
Number TB positive (n=35)	1	34	25	10	18	17	19	0	16
%	3%	97%	71%	29%	51%	49%	54%	0%	46%

OA28-791-22 Table.

OA28-792-22 Development of artificial intelligence for active TB screening using CT images

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Background: CT has been installed in almost all hospitals in rural area for diagnosis and screening tuberculosis (TB) in China. The diagnosis of TB on CT requires a doctor with a certain diagnostic ability, which is a difficult task for TB prevalent locations in which experienced radiologists are lacking. We develop an automated detection system based on artificial intelligence (AI) following with a self-organized clustering (SOC) algorithm in this study to improve the diagnostic accuracy for active tuberculosis (ATB) in multi-slice spiral CT images.

Design/Methods: 846 CT studies (476 ATB, 150 non-TB pneumonia, and 220 normal) confirmed with sputum smear, cultures or diagnostic reports were collected as training set from multiple hospitals to train a U-Net based deep learning AI algorithm to segment and recognize ATB lesions in each slice. A SOC algorithm is then developed to consolidate lesions in consecutive slices into lesion in volumetric 3D study and to eliminate any false positive. The independent test data containing 530 ATB, 40 pneumonia, and 100 normal cases, retrospectively collected from 4 different hospitals are then used to test the AI SOC algorithm.

Results: In an independent test, the sensitivity and specificity for artificial intelligence are 0.935 and 0.971, respectively, which show that the AI tool performs well for diagnosis of ATB and differential diagnosis of ATB and pneumonia. Among patients that have a series of CT scan, AI-SOC can detect ATB during the first scan while lesions are vague and subtle.

Conclusions: An AI-SOC algorithm for automatic detection of ATB in chest CT is successfully developed in this study. The AI-SOC can accurately diagnose ATB during their earlier stage, and distinguish between ATB and non- ATB (i.e. pneumonia and normal cases), which simplifies the diagnosis process and lays a solid foundation for AI in CT diagnosis of ATB in a large-scale clinical application.

OA28-793-22 Mechanisms by which social and structural determinants act as barriers or enablers to TB diagnostic evaluation in Uganda

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Background: Social and structural determinants of health (SDoH) are associated with tuberculosis (TB) outcomes, but are often unaddressed in TB care programs. We sought to describe the mechanism by which SDoH affect completion of TB diagnostic evaluation in Uganda using an implementation science framework rooted in behavioral theory

Design/Methods: Trained research staff interviewed 24 purposively sampled adult patients who were undergoing TB diagnostic evaluation at six community health centers in Uganda between February-August 2019. Framework analysis was used to extract themes linked to SDoH across the TB diagnostic evaluation cascade of care.

Themes were then mapped to domains of the capability, opportunity, and motivation behavior change model (COM-B).

Results: Barriers related to SDoH were noted across the diagnostic evaluation cascade of care (Table). These included: limited knowledge about TB diagnosis and treatment (psychological capability); low socioeconomic status and competing financial priorities (physical opportunity); internalized and anticipated stigma of TB diagnosis, lack of social support programs and limited social support/social capital (social opportunity); trust or distrust in the government health facility to provide quality care (reflective motivation); and fear and shame about worsening poverty (automatic motivation).

Representative quotes demonstrate these themes: "I failed to make it [to the hospital] because I did not have transport and the money I got [by digging] I used to buy the children food."

"I do not bother them [community] with the knowledge that maybe I am a TB patient. I do not want to be the laughing stock."

Cascade of Care	Seeking care	Testing	Treatment Initiation	Cross-cutting
Capability	Psychological +Facilitator: Knowledge of TB symptoms		Psychological +Facilitator: Knowledge/understanding that about the risks and benefits of treatment	Psychological +Facilitator: Knowledge/understanding of TB
	Physical -Barrier: Ability to reach the clinic if ill			
Opportunity	Physical opportunity -Barrier: High cost of accessing the clinic -Barrier: Lost income by not working while care-seeking -Barrier: Competing financial needs in the household leads to deprioritizing seeking care +Facilitator: Seeking care for multiple reasons in one visit	Physical -Barrier: Long waiting time at the clinic to be tested	Physical -Barrier: High (actual) cost of medications -Barrier: Out of stock medications -Barrier: Limited access to food/diet to support continuation of medication	Physical -Barrier: Low socio-economic status -Barrier: Lack of awareness of social support programs
	Social opportunity -Barrier: Anticipated stigma of a positive TB diagnosis	Social opportunity -Barrier: Internalized stigma of being seen taking medications in the community	Social opportunity -Barrier: Perception HCW is skilled and acting in patient's best interest	Social opportunity -Barrier: Stigma +Facilitator: Belief that someone will take care of them for the duration of their illness
	Social opportunity -Barrier: Women must rely on men for money or approval to seek care			
Motivation	Automatic +Facilitator: Family and friends' encouragement to seek treatment +Facilitator: Positive prior experiences with the healthcare system	Reflective -Barrier: Fear TB diagnosis implies HIV positive status -Barrier: Expectation to receive medication without diagnosis	Reflective +Facilitator: Fear of spreading disease Automatic +Facilitator: Support network to help consistent medication taking	Reflective -Barrier: Limited social support networks outside immediate family -Barrier: Distrust that healthcare worker (HCW) has ability to correctly treat
				Automatic -Barrier: Fear, shame and worry about worsening poverty

Conclusions: Biomedical interventions alone are unlikely to address the spectrum of SDoH-related barriers to completion of TB diagnostic evaluation. Linking these barriers to a behavior change model may help guide the design and evaluation of appropriate people-centered social protection interventions.

OA28-794-22 Accuracy of the Simple One-step stool method with Xpert MTB/RIF Ultra assay for the diagnosis of *M. tuberculosis* in children

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Background: Young children with presumptive tuberculosis (TB) cannot produce sputum spontaneously, hindering the bacteriological diagnosis of TB. Stool is easily obtained from children and can be tested for TB detection with Xpert MTB/RIF Ultra (Xpert Ultra). The recently published Simple One-step (SOS) stool processing method provides a very simple method for processing stool in any Xpert laboratory. We assessed the sensitivity of stool Xpert testing using the SOS stool processing method compared to Xpert and culture on a nasogastric aspirate (NGA).

Design/Methods: We enrolled children aged up to 10 years investigated for presumptive TB in 26 health care facilities in Addis Ababa, Ethiopia for whom an NGA sample was requested. Written parent consent was obtained. Children were asked to also submit a stool sample. Xpert on both samples was done on-site. NGA was also cultured using liquid and solid culture at the national TB reference laboratory. We collected data on general characteristics, symptoms and signs of TB, Xpert and culture test results, and final diagnosis.

Results: Until March 2021, 637 children had been enrolled, of whom 636 provided NGA and 609 also provided stool. A total of 48 (7.5%) children tested positive: 15 (31%) tested positive on both samples on culture and Xpert; 20 (42%) tested positive on Xpert on both samples, and 5 tested positive on Xpert stool only. The sensitivity and specificity of Xpert stool testing against NGA culture and NGA Xpert were 56.3%, 98.3%, and 64.1% and 98.7% respectively.

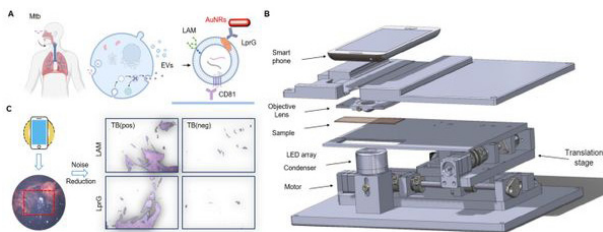
Conclusions: Xpert stool testing using the SOS stool method provides a good alternative to NGA testing, which is a more invasive sample that cannot be obtained in all health facilities. Further studies are needed to assess if and how the sensitivity of Xpert stool testing can be further optimized.

OA28-795-22 Detection of M. tuberculosis-specific extracellular vesicles in peripheral blood for paediatric TB diagnosis

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Background: Timely diagnosis of tuberculosis remains urgent for positive patient outcomes. However, traditional techniques suffer limitation including poor sensitivity and delayed diagnosis. We identify several Mtb-derived antigens that selectively present on the extracellular vesicles (EVs) that purified from TB-infected patient blood samples. We develop nano plasmonic-enhanced immunoassay (NEI) to enable multiple, wash-free probing and quantification of the markers identified from EVs.

Design/Methods: EVs are captured directly from serum by an EV-specific antibody, then hybridized with gold nanorods conjugated with two TB-specific antigen antibodies, after which nanorod light scattering is captured using a benchtop-based or portable smartphone-based dark-field microscope (DFM) and specific signal from target EVs is quantified by image processing.



Results: NEI results showed similar sensitivity for unconfirmed TB cases with and without clinical TB diagnoses, and detected 90.9% confirmed TB case, as well as 78.2% of TB cases missed by microbiological assay. NEI also identified a majority (52.7%) of children with unlikely TB who had at least one criteria required for unconfirmed TB diagnosis. Successful ATT response rates were high in children with confirmed and unconfirmed TB (87.2% vs. 66.7%). Mortality was higher in children with confirmed vs. unconfirmed TB (33.3% vs. 8.5%) after ATT initiation. NEI also enabled early detection of TB diagnosed by further clinical algorithm.

Conclusions: The nano plasmon-enhanced scattering approach described offers an attractive means for the rapid, purification-free and ultrasensitive measurement of circulating EVs in small sample volumes. Through the detection of pathogenic antigens on extracellular vesicles, our assay realizes enhanced sensitivity and specificity for Mtb diagnosis/treatment monitoring especially in HIV negative pediatric patients.

OA-29 Public awareness and capacity building for TB elimination

OA29-796-22 The “Ek Pahal” Online online TB awareness campaign amongst school children in India during the pandemic lockdown

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Background and challenges to implementation: Pediatric Tuberculosis is amongst 10 major causes of mortality in children globally (Pediatric Tuberculosis: Global Overview and Challenges). ~700 children succumb to TB everyday. In India, Pediatric TB accounts for 6% of total TB burden while actual pediatric burden is closer to 8%. In 2018, 1,32,711 pediatric TB patients (59% of estimated) were notified in India (TBC India Report 2019). TB in a child or a family member of school-going children impacts the continuity of child’s education and lack of TB education in curriculum unable to generate TB awareness amongst children.

Intervention or response: To address the above challenges, GLRA India with FICCL implemented one of its kind awareness intervention ‘Ek Pahal’ in north India (Delhi and four districts of Uttar Pradesh). The intervention is designed to enhance awareness about TB, WASH, and COVID amongst children, school personnel, families, and community members by engaging schools in activities like health talks, painting, essay, quiz competitions, infotainment game (snake and ladder), comics, pamphlets, and pre-and-post questionnaires to assess the level of awareness of students.

Children as peer educators act multiplier to sensitize further in community for identification of TB presumptive, thus support in TB care and prevention.

Results/Impact: Out of 478 schools visited (Feb2020-Mar2021) by counselors in target districts, 383 agreed to project intervention. 1,34,046 children out of total 1,79,512 children in 383 schools were sensitized on TB, COVID-19 prevention, and hygiene practices through offline activities and virtual in-house developed animation video on TB. Children act as peer educators and have started increasing awareness in community and identifying presumptive for further diagnosis and treatment. Due to COVID crisis, 80% (n=106991) students were sensitized through the animation video during their online classes.

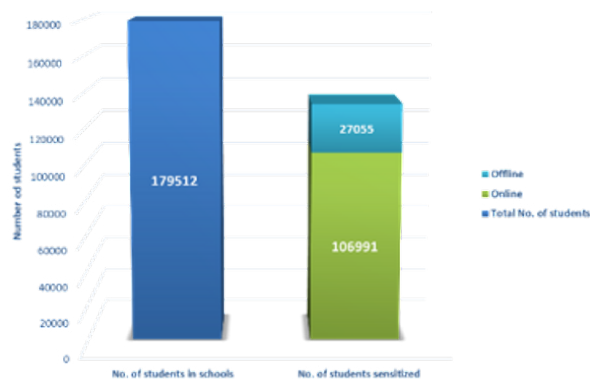


Figure. Students sensitized on TB (Feb 2020 - Mar 2021)

Conclusions: The intervention has improved TB awareness amongst school children who are acting as multiplier in the community to identify presumptive TB patients, facilitating TB care and prevention.

OA29-797-22 TB knowledge among community members without TB and people with TB diagnosed through active vs. passive case-finding in Nepal

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Background: In Nepal, 15 people-per-day die from TB and one in two cases are not diagnosed or treated. Active case finding (ACF) increases case detection but its impact on TB knowledge is unknown. Enhancing TB knowledge amongst people with TB (PWTB) and their households can increase their agency to make informed health choices. ACF represents a unique opportunity to improve people's TB knowledge and potentially their TB treatment outcomes.

Design/Methods: Using prospective cohort study data from four districts of Nepal, we compared TB knowledge amongst 111 adult PWTB diagnosed by ACF, 110 PWTB diagnosed by passive case finding (PCF), and 119 adult community members without TB. Associations of TB knowledge with being a PWTB versus community member or being a PWTB diagnosed by ACF versus PCF were assessed using adjusted multivariable ordinal logistic regression analyses. Independent variables included age, sex, education, multidimensional poverty index,

and participant group (e.g. ACF, PCF, community member). The outcome variable was composite TB knowledge of TB symptoms, TB services, and availability of TB preventive therapy. Participants' TB knowledge was graded low, medium, or high disaggregated by the entire cohort and PWTB only.

Results: Community members were more likely to have low TB knowledge than PWTB (aOR=3.5, 95% CI=2.2-5.7). There was no difference in TB knowledge of PWTB diagnosed by ACF versus PCF (aOR 1.3, 95% CI=0.68-1.9, Table). Amongst both the community members and PWTB, being female or in most poor quintile were independently associated with low TB knowledge (Table).

TB Knowledge of People with TB diagnosed by ACF vs PCF (n=221) ¹	
Independent Variable	Adjusted Odds Ratio (95% CI)
Poverty	
Least poor (n=42)	Ref
Poor (n=53)	1.3 (0.58-2.8)
Poorer (n=57)	1.8 (0.84-3.9)
Most poor (n=69)	2.1 (0.97-4.5)*
Sex	
Male (n=147)	Ref
Female (n=74)	1.8 (1.0-3.2)**
PWTB diagnosed by PCF or ACF	
PCF (n=110)	Ref
ACF (n=111)	1.1 (0.68-1.9)
TB Knowledge of People with TB vs Community Members (n=340) ²	
Independent Variable	Adjusted Odds Ratio (95% CI)
Poverty	
Least poor (n=85)	Ref
Poor (n=85)	1.0 (0.56-1.8)
Poorer (n=85)	1.4 (0.78-2.5)
Most poor (n=85)	1.9 (1.1-2.8)**
Sex	
Male (n=207)	Ref
Female (n=133)	1.8 (1.1-2.8)***
PWTB or community member	
PWTB (n=221)	Ref
Community members (n=119)	3.5 (2.2-5.7)****

Legend: abridged to show statistically significant associations and participant groups only. Abbreviations: ACF = Active case-finding; CI = Confidence Interval; PCF = Passive case-finding; PWTB = People with Tuberculosis; Ref = Reference

¹Adjusted for study population (ACF vs PCF), age, sex, education, poverty level

²Adjusted for study population (PWTB vs Community), age, sex, education, and poverty

*p=0.06 **p=0.04 ***p=0.01 ****p<0.001

Table. Ordinal logistic regression of factors associated with low TB knowledge score.

Conclusions: In four districts of Nepal, community members had lower TB knowledge than PWTB. Across PWTB and community members, underserved people including the most highly impoverished and females, had lower TB knowledge. Amongst PWTB, ACF was not associated with greater TB knowledge. Integration of TB education with ACF interventions could increase TB knowledge of vulnerable TB-affected households in Nepal.

OA29-798-22 Empowering women as community health mentors using interactive voice response-based training during Covid times: experiences from Tamil Nadu, India

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Background and challenges to implementation: Women are proven community resources to address public health challenges such as TB, immunization, HIV counselling and family welfare. In resource constrained settings like India, empowering communities, especially women, with basic health knowledge is imperative to improve health-seeking behaviour and lifestyle habits of the community

Intervention or response: Through Wave 7 TB REACH grant, we enrolled women across 4 districts of Tamil Nadu, India into basic health-skills training, to develop them as health point-persons in their communities. We delivered this training over Interactive Voice Response (IVR)-based community media platform specifically meant for rural communities. IVR technology does not require users to own smartphones and no call charges are incurred. The audio modules published were identified through needs-assessment among female health-care workers.

The training included modules on TB, HIV, non-communicable diseases, first aid, menstrual disorders, common gynaecological issues, assisting a loved one to quit smoking/alcohol, domestic violence, and financial literacy besides COVID. The trainees could access dramatized content on different topics, listen to experts and consume content in an accessible format, especially during the COVID pandemic when in-person training was not feasible. The system conducted surveys to assess knowledge and document module completion. Certificates and incentives were provided to trainees.

Results/Impact: Over a six month period, we registered 606 users, of whom 374 were consistently engaged. The IVR system acted as a mechanism for delivering training in a colloquial, regionally relevant and humorous manner. The participants reported that the training was useful to bring about lifestyle modifications in their families and immediate neighbourhood and equipped them to conduct community meetings for finding people with TB

Conclusions: From the service-delivery perspective, IVR is an interactive medium which is easy to develop and deliver training on health; from the user's perspective it is a convenient and effective medium to receive training remotely in an easily understandable format.

OA29-799-22 Innovative thinking regarding TB recovery in the midst of Covid-19: TB health promotion in Khayelitsha, South Africa

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Background and challenges to implementation: COVID-19 has had a sustained impact on TB diagnosis globally. In South Africa, there has been a 48% decline in TB testing, including in Khayelitsha, a low-income community with a high TB prevalence. As part of an innovative TB recovery plan, Médecins Sans Frontières (MSF) and the City of Cape Town (COCT) Health Department collaborated in conducting a community TB outreach campaign including:

1. Health promotion;
2. Education about overlapping signs and symptoms between COVID-19 and TB as well as awareness of the availability of TB Preventive Therapy (TPT); and
3. Community-based TB testing.

Here we describe a community level TB-related health promotion campaign.

Intervention or response: The TB outreach campaign was organized with multiple stakeholders: MSF, COCT Health Department, TB HIV Cares, University of Witwatersrand, St Luke's Hospice, and TB survivors.

As build-up to the campaign, training workshops were held for community care workers (CCWs) and the other stakeholders on TPT. An event was facilitated in an outdoor setting following COVID-19 infection control protocols. At the site, community members were educated about TB, TPT, and COVID-19 and TB survivors shared their personal experiences.

On site screening and testing for TB/HIV, family planning, and deworming services were provided. On the same day as the campaign, MSF health promoters and CCWs combined door-to-door TB screening, including the distribution of sputum jars for TB case detection, and community level health promotion.

Results/Impact: Eighty-three community members attended the campaign and 250 sputum jars were distributed. Successes, challenges, and lessons learnt are highlighted in the Table.

Successes	Challenges	Lessons Learnt
The event, which was 4 hours long, was well attended (n=83 community attendees)	Activities started later than planned	Ensure timeous arrival of all stakeholders that will be part of the outreach
Attendees arrived throughout the day (staggered attendance)	The time taken for the event was insufficient – attendees still arrived as event was closing	Conduct door-to-door outreach / health promotion a day before the event to better sensitize the community as to timing
Range of clinical and testing services provided on-site as a part of health promotion	Insufficient clinical staff for the number of attendees thus long waiting times for health services	Make necessary provision to have more clinic staff on hand at specific community events
Engaging question and answer game session with prizes	Very few attendees were English speaking	The game session allowed for further engagement on the educational content/ materials shared
Youth friendly event: DJ playing music Pamphlets provided in English and isiXhosa		Youth friendly activities is imperative in engaging youth It is essential to develop content in the relevant language of the community
Collaborative event led by various community level stakeholders	Different targets across stakeholders; some stakeholders did not want event to close on time as their targets were not met	All stakeholders involved should have similar targets and a good understanding of their respective targets
Door-to-door outreach/health promotion combined with sputum jar distribution	The door-to-door outreach/ health promotion took as long as the event; this meant most of the CCWs were in the field instead of attending the event	Should consider conducting door-to-door health promotion a day before the campaign
The venue chosen accommodated the community that will mostly benefit from the campaign	The first venue identified did not accommodate the target audience and had to be changed	The venue chosen is important in order to accommodate the target audience

Conclusions: TB outreach campaigns, including health promotion, are an important way to engage the community regarding public-health concerns and to improve education regarding TB. These campaigns can have impact when they are conducted in collaboration with other stakeholders in the community to provide a variety of services.

OA29-800-22 Feasibility of having a toll-free helpdesk platform to support health worker use of digital adherence technology for TB treatment in Uganda

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Background: 99DOTS is a digital adherence technology that enables health workers to monitor patient adherence to TB medication in real-time using a smartphone app. We aimed to assess the feasibility of utilizing a helpdesk platform to mentor and support health workers using 99DOTS.

Design/Methods: As part of scaling-up 99DOTS in Uganda to 30 health facilities, we set up a toll-free Helpdesk Platform to receive calls from health workers and redirect calls to local support staff (one staff member per 10 facilities). We evaluated the volume of calls received from TB care providers between January-March 2021 and analyzed call transcripts to characterize issues reported.

Results: The majority of health workers using 99DOTS (94/100, 94%) contacted the Helpdesk Platform with a median of 3 calls per provider and a mean length of 106 seconds per call. Of 520 support calls made to the Helpdesk Platform, 349 (67%) were connected directly to support staff and 291 of 349 (83%) had meaningful transcripts extracted from the recordings.

There were 360 issues reported including 138 (38.3%) issues with 99DOTS (application crashes, unexpected dashboard or task list displays), 52 (14.4%) enrollment issues (challenges enrolling a new patient on 99DOTS), 54 (15%) administration issues (scheduling training), 86 (24%) logistics issues (questions about the supply of 99DOTS envelopes and phones to be given to patients), and 30 (8.3%) other issues. After communication with 99DOTS support staff via the Helpdesk, 312 (86%) issues were resolved (Table).

	Issues Presented	Issues Resolved
Total Issues	360	312 (86%)
99DOTS issues	138 (38.3%)	111 (80%)
Logistics issues	86 (24%)	79 (92%)
Administrative issues	54 (15%)	47 (87%)
Enrollment issues	52 (14.4%)	52 (100%)
Other issues	30 (8.3%)	23 (77%)

Table. Helpdesk Support Calls Resolution Cascade Results.

Conclusions: Remote support of TB care providers with a Helpdesk Platform is feasible and may ease the adoption of 99DOTS among TB care providers as well as limit the need for onsite re-trainings.

OA29-801-22 Alternative models of web-based training and education of laboratory staff adapted to the Covid-19 pandemic: an experience from Kazakhstan

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Background and challenges to implementation: The COVID-19 pandemic has disrupted the conventional education, training, and support of healthcare workers and created a need for innovative solutions to address this problem. Training laboratory specialists requires not only theoretical but also practical sessions. Here we share the experience of alternative training models delivered utilizing information technology (IT) for tuberculosis (TB) laboratory staff in Kazakhstan.

Intervention or response: Despite COVID-19 restrictions, the response against TB continued in Kazakhstan partially using information technology applications such as Zoom, Teams, and Skype for both training of HCWs and teleconsultations for patients. The USAID Eliminating Tuberculosis in Central Asia project provided IT equipment to the National Reference Laboratory, assisted with its commissioning and conducted practical training and real time monitoring sessions of laboratory staff in different parts of the country.

Results/Impact: New online models of training and support enabled the NTP to build theoretical and practical knowledge and skills for DST and quality control for new and repurposed TB drugs - bedaquiline, delamanid, clofazimine and linezolid in 2020. The training sessions delivered on web-based audio-visual applications allowed fully interactive live bi-directional communication between mentors and trainees. The compact size and portability of the IT equipment which enabled the training allowed moving it to all parts of the laboratory to demonstrate multi-step procedures greatly enhancing the learning process. Also, the recording of the whole training can be used for future troubleshooting and analysis of complicated steps.

Conclusions: New technologies allowed the implementation of training, education, and support from a distance addressing the needs of the laboratory services of the TB program in a time of quarantine restrictions.

Beyond the pandemic, this could be utilized routinely as a complementary and low-cost alternative model for capacity building and support of HCWs and patient care.

OA29-802-22 Blended online approach for urgent technical laboratory training courses in response to the Covid-19 pandemic

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Background and challenges to implementation: The introduction and the need for rapid deployment of the Xpert Xpress SARS-CoV-2 Assay as diagnostic tool option for the COVID-19 in the Philippines has presented an opportunity for the National TB Reference Laboratory (NTRL) to develop an alternative training approach leveraging the use of existing online platforms that enabled distance learning in light of the restrictions in place for face-to-face trainings due to the pandemic.

Intervention or response: The training intervention adopted included a blended learning approach consisting of:

1. Self-paced but time-limited modules in the form of reading materials and videos distributed through a shared folder, and;
2. A competency assessment on good laboratory practices and biosafety, done on-site at NTRL during the initial roll-out and mostly by remote observation at the participant's facility through teleconferencing in succeeding batches.

Pre- and post-tests were similarly administered via electronic forms; only those who passed the post-test proceeded for the hands-on competency assessment.

Results/Impact: The blended learning approach delivered all requested training efficiently, as it can be readily given anytime the need arises and allows engaging a larger number of participants in a shorter amount of time while not requiring trainers to be physically present.

This design provided adequate knowledge in performing Xpert Xpress as reflected by the improvement of post-test scores and competency assessment, which led to the operationalization of Xpert Xpress SARS-CoV-2 in 56 sites all over the country, greatly improving the laboratory access and diagnosis of patients with COVID-19 in places with no RT-PCR laboratory.

Conclusions: The blended approach used for Xpert Xpress SARS-CoV-2 training proved effective and expedited the deployment of the test. The same method may be adopted and lessons learned from its implementation can be used for training programs for other diseases.

	Pre-test	Post-test	Competency Assessment
Total participants		430*	255**
Total passed (85% passing grade for pretest and posttest) (90% passing grade for competency assessment)	80	392	255
Total failed (85% passing grade for pretest and posttest) (90% passing grade for competency assessment)	350	38	0
Average score	75.37%	93.64%	94.38%
Modal score	73.33%, 84.44%	100%	90%
Highest score	100%	100%	100%
Lowest score	42.22%	68.89%	90%

*-include participants without competency assessment, does not include participants who did not complete posttest

**-does not include participants who have yet to complete competency assessment

Table 1. Summary of Xpert Xpress SARS-CoV-2 Knowledge and Skills Evaluation

OA-30 Exposing the fingerprints of the tobacco industry

OA30-803-22 Time taken by tobacco companies to comply with notified rotational public health and well-being regulations in India: results from a nationally representative cross-sectional survey

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Background: In 2014 the Ministry of Health & Family Welfare, Government of India notified larger pictorial health warnings (PHW) covering 85% of the principal display area of all tobacco packs. These 2014 rules allowed a grace period of two months for the tobacco companies to clear the old stock and specified that no products must be sold post-moratorium with old PHWs. We monitored compliance with the new PHW rules of July 21, 2020, for the warnings which became effective from December 1, 2020.

Design/Methods: We selected one prominent tobacco point-of-sale (PoS) in 18 cities from eight states to monitor all tobacco products available in that PoS. A 'saturation technique' was employed i.e. assessing the number of weeks taken for all products to have the newly notified PHWs.

Results: Our survey finds that tobacco companies take an average of 12 weeks to comply with the regulations (as against two months or 8 weeks specified under the rules). Nine cities from the states of Gujarat, Jharkhand, and Rajasthan complied with the regulation within the mandated two-month period, with Ahmedabad in the 5th week, Bhavnagar, Chittorgarh, Kota, Jodhpur, Jhunjhunu in the 7th week, and Vadodara, Ranchi, and Ramgarh in the 8th week had the newly notified PHWs.

The remaining nine cities took 13-18 weeks to comply with the regulations. Different brands and types of products complied with the new PHWs in different weeks or different cities.

Conclusions: In India, tobacco companies are taking more than two months to comply with the PHW regulations, and different cities have different saturation points for the new PHWs. There is a need to strictly enforce the regulations to ensure that the grace period is not violated by the tobacco companies.

OA30-805-22 Effectiveness of Turkish plain packaging for tobacco products

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Background: Turkey, while implementing plain packaging in the beginning of 2020, chose not to standardize pack sizes.

This study was carried out to identify the deviations from the internationally accepted plain packaging concept and their effect on public.

The aim was to investigate:

1. The various applications on unstandardized plain packs.
2. The level of compliance with legislation in terms of labeling and packaging features of cigarette packs on the market.
3. Industry interference to point of sales (POS) display methods.
4. The perception of the unstandardized packs by the public.

Design/Methods: 1. 105 different sub-branded packages from 22 brands were evaluated in terms of deviation from international norms and compliance with Turkish law.

2. POS at the 6 trade-dense districts of Istanbul were visited and the pattern of displays were recorded.

3. A sample of smokers were interviewed by showing a set of differently designed products and asked to evaluate each package.

Results: Packs came in various size and did not meet the criteria of standard pictorial health warnings. Brands that may describe sweeteners, additives, flavors, cosmetics, textile were used.

A consistent pattern of stacking that made the pictorial warning invisible was noted in the majority of the POS in various districts of the city, indicating orchestrated industry interference.

The standard pack was stated to have an unattractive design. Most preferred narrow and long designs with a flip lid. The women defined such packages as “stylish” and “pretty”, men convenient for carrying in the pocket.

Conclusions: Turkey has legislated plain packaging without standard shapes. Non-standard plain packs still appeal to the consumer through pack designs and do not have a deterrent effect on smoking. The displays of plain packs at POS indicated to the interference of the industry. Countries implementing plain packaging must be warned against industry tactics.

OA30-806-22 Tobacco vendor density in Ranchi and Siliguri, India

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Background: High tobacco vendor density is directly associated with high rates of tobacco use. The Cigarettes and Other Tobacco Products Act (COTPA) prohibits the sale of tobacco within 100-yards of any school in India. Local government in two Indian cities, Ranchi and Siliguri, is implementing policies to strengthen enforcement of COTPA and reduce tobacco vendor density through tobacco vendor licensing, which includes limiting licenses to specific vendor types. The following tobacco vendor density estimates are made off of a study conducted to capture a census of tobacco vendors in 3 wards in Ranchi (Jharkhand), and 5 wards in the city Siliguri (West Bengal).

Design/Methods: Data collectors traversed all roads within the selected wards and identified the geocoordinates of all tobacco retailers and schools. Based on

physical features, tobacco vendors were classified as a permanent vendor (supermarkets/independent grocery stores, permanent kiosks), or a temporary vendor (street vendors, temporary kiosks). GIS was used to estimate vendor density per square kilometer.

Results: In Ranchi, across the 3 wards, there were 68 tobacco vendors/km²[range: 37-195]; in Siliguri, across the 5 wards, there were 99 tobacco vendors/km²[range: 43-237]. Eliminating tobacco vendors within 100-yards of schools would result in a vendor density reduction of approximately 19% in Ranchi and 23% in Siliguri. A strategy that restricts the sale of tobacco to only permanent vendors may reduce the vendor density by approximately 20% in Ranchi and 40% in Siliguri. Coupling these two strategies would have a projected reduction in density of 37% in Ranchi and 56% in Siliguri.

Conclusions: Tobacco vendor density could be greatly reduced by effectively enforcing COTPA. Limiting tobacco vendors, based on the retailer type, could further reduce the number of vendors. Proven density reduction strategies such as vendor licensing could be used to achieve these goals.

OA30-807-22 Tobacco industry strategies for tobacco sale and promotion in the context of Covid-19 in Argentina

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Background: The TI has diversified sales systems and marketing strategies for its products, even in times of COVID-19. The privileged outlets for sales are kiosks and mobile applications, and its target audience continues to be children and adolescents despite being forbidden by the National Tobacco Control Law (NTCL)

Design/Methods: The research has been implemented in Argentina from March to November 2020. The study describes the actions deployed by the TI in the context of the COVID-19 pandemic, including marketing actions in mobile applications and actions aimed at front groups such as retailers. We conducted a survey with retailers on TI attitude during the pandemic. In addition, we made an observational study in mobile applications in seven argentinian cities to evaluate the purchase operation and marketing strategies on tobacco products.

Results: Among mobile applications, we found violations of the NTCL regarding the commercialization of tobacco products: in 100% of cases children and adolescents could buy and receive tobacco products, and in 27% we detected promotions that could tempt them

such as cigarettes with sweets. The TI developed lobbying actions in order to establish alliances with retailers: 41% received information from the TI promoting flavoured cigarettes, and 12% mentioned that the industry requested support for the authorization of production during the quarantine

Conclusions: The TI developed a strong strategy during the pandemic with the aim of continuing to sell its products, promote tobacco initiation in adolescents, improve their image, influence public opinion and interfere in the progress of tobacco control policies.

We recommend: to ban all forms of advertising, promotion, sponsorship and display of tobacco products; a better State control over violations of the current regulatory framework; and to strengthen transparency and conflict of interest measures at all governmental levels.

OA30-808-22 The tobacco industry supply chain database: extending tobacco control from demand to supply

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Background: Tobacco control research and advocacy has yet to capitalise on understanding the tobacco industry supply chain. The objective is to build a database to expose the processes, actors and supporting industries involved in tobacco production, laying the groundwork to expand the scope of tobacco control beyond the transnational tobacco companies (TTCs).

Design/Methods: Systematic search of the academic literature and tobacco industry documentation (industry magazine advertisements) were used to build a model of the tobacco industry supply chain. These findings were updated with web searches and broadened via data from the United Nations, World Health Organisation and Global Burden of Disease are sources for the Tobacco Industry Supply Chains database. The database provides country-level information on supply chain companies, tobacco growing and trade, supplemented by health and environmental implications of involvement in the tobacco industry supply chain.

Results: We identify five major processes in tobacco production:

1. Growing tobacco,
2. Primary processing the tobacco leaf,
3. Secondary processing into manufactured products,
4. Logistics – moving and distributing tobacco leaf and manufactured products, and;
5. Selling the tobacco products. Supporting industries supply machinery, chemicals (for example pesticides and flavourings), other product components (paper filters and packaging) and buildings (curing barns and

warehousing). Our database includes 195 jurisdictions; approximately half of these host at least one of the 1000 supply chain companies or subsidiaries recorded in the database.

Conclusions: Researchers and campaigners seeking to design effective policy preventing the expansion of this industry and the health harms it produces, need to look beyond the TTCs to identify under-exploited leverage points along the entire tobacco supply chain.

OA30-809-22 An assessment of violations of tobacco product laws in West Bengal, India

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Background: The prevalence of currently using any kind of tobacco among the adults in West Bengal is 33.5% and which is higher than the national average (28.6%) (GATS-2, 2017). The state is regarded as the high burden state.

The present study was aim to assess violations to restrictions on tobacco advertising, promotion and sponsorship at Point of Sales (POS) in West Bengal.

Design/Methods: The present study was conducted in purposively selected three cities of West Bengal (Kolkata, Siliguri, Asansol) and were further divided into three categories as per the socio-economic status i.e. SES-1 (High), SES-2 (Medium), SES-3 (Low).

From each SES zone one market area was purposively selected based on the available information and by keeping in mind its popularity, access to the place and visibility. Transect survey was conducted to cover all tobacco shops within 3 kilometres of long stretch road in each zone.

Results: A total 514 tobacco shops were covered (Asansol- 36.9%; Kolkata-36.8% and Siliguri-26.3%) and out of these- 99.8% vends were found at least one violation, and of them 93.8% with SLT product violations such as product displayed, advertisement through posters, stickers, bill boards, banner/flex, danglers etc. were found. Tobacco shops within 100 yards of Schools were observed in Kolkata and Siliguri.

It was also revealed that vendors were selling tobacco products in front of the main gate of Government hospitals in all three cities. Tobacco vendors had lack of awareness regarding POS advertisement and storage of tobacco products.

Conclusions: Wide-spread violations, lack of awareness and limited enforcement promoted and proliferate a large number of attractive advertisements by tobacco companies in all cities. Strict adherence to tobacco vendor licensing, prohibition of tobacco shops within 100 yards area of any educational institutions are needed.

OA-31 Ground realities: challenges with Xpert

OA31-810-22 Health worker perspectives on uptake of on-site molecular testing for TB at community health centres in Uganda

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Background: The XPEL TB trial demonstrated that an intervention strategy including onsite Xpert Ultra MTB/RIF (Xpert) testing using the GeneXpert Edge platform increased the number of patients diagnosed and treated with confirmed TB within 14 days at community health centers in Uganda. Here, we report health worker perspectives on successes and challenges in implementation of onsite Xpert testing.

Design/Methods: Between January and April 2021, we conducted an explanatory qualitative assessment guided by the Consolidated Framework of Implementation Research at the 10 intervention health centers. We conducted in-depth semi-structured interviews with 2-3 health workers involved in TB-related activities at each health center. Interviews were conducted by phone in English and Luganda by experienced research staff, audio recorded, and transcribed to English following a naturalistic approach. Transcripts were coded for thematic analysis.

Results: We conducted 25 interviews with 4 clinicians, 3 nurses, 14 laboratory staff, and 4 other health center staff involved in TB work. Providers at all health centers reported that onsite Xpert testing enabled same-day testing and treatment initiation, provided reliable results, and eased workload relative to sputum smear microscopy (Table 1). Reported challenges included power interruptions and malfunctioning of external batteries at 9 health centers, increased workload due to more patients being referred for TB testing and limited computer literacy of laboratory staff. Health workers at high-volume health centers (>5 patients tested per TB daily) also expressed concerns about the GeneXpert Edge platform including only one testing module, which limited the number of samples that could be processed each day.

CFIR Domain/ construct	Facilitators	Barriers
Intervention Characteristics	<p><u>Relative advantage:</u></p> <ul style="list-style-type: none"> • Detected drug resistant TB • Reduced patient waiting time to diagnosis • Eased workload relative to smear microscopy. • Enabled laboratory staff to work on sputum samples while also processing other test samples. • Provided health worker safety in terms of infection control relative to smear microscopy. • Increased screening from all patient entry points at the health center. • Health workers without specialized training were able to operate testing platforms with minimal training. • Improved service delivery that contributed to better health center performance at district level. 	<p><u>Complexity:</u></p> <ul style="list-style-type: none"> • Increased workload due to more patients being referred for TB testing • Limited knowledge on computer use by laboratory staff <p><u>Adaptability</u></p> <ul style="list-style-type: none"> • One module testing platform limited daily testing volume, timely results reporting. • Health workers transfers affected implementation • Disproportionate increase in testing volumes relative to staffing levels.
Characteristics of individuals	<p><u>Knowledge and beliefs about intervention</u></p> <ul style="list-style-type: none"> • Improved health worker knowledge of TB diagnosis using Xpert testing and treatment. • Provided reliable results because it's not dependent on human interpretation. • Health workers were made more aware and curious to investigate TB <p><u>Self-efficacy</u></p> <ul style="list-style-type: none"> • Improved health worker confidence as reported by a nurse "before we could treat clients with doubt". 	<ul style="list-style-type: none"> • Insufficient continuous training, information, education and communication materials for health workers.
Inner setting	<p><u>Available Resources</u></p> <ul style="list-style-type: none"> • Regular supply of cartridges, drugs and other laboratory commodities <p><u>Leadership engagement</u></p> <ul style="list-style-type: none"> • Actively involve health center directors to support health center staff in addressing challenges and provision of resources. • Integrated TB diagnostics and treatment in health center priorities. 	<ul style="list-style-type: none"> • Electricity interruptions and malfunctioning external batteries delayed testing

Conclusions: Onsite molecular testing was feasible and considered to be highly acceptable at community health centers. However, testing volume and infrastructure requirements (such as need for replacement batteries) should be considered when decentralizing molecular diagnostics platforms.

OA31-811-22 Dual detection of TB and SARS-CoV-2 disease from sputum among in-patients with pneumonia using the GeneXpert® system

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Background: Shared symptoms between tuberculosis (TB) and SARS-CoV-2 disease warrants co-testing in high-incidence settings. Co-testing on a single sputum specimen may maximize the diagnostic outcome and reduce turnaround time.

We developed a laboratory-based swab capture (SC) testing workflow and investigated proof-of-concept on sputum specimens received from in-patients with x-ray confirmed pneumonia.

Design/Methods: Adult patients ≥ 18 years admitted to hospital were routinely tested for SARS-CoV-2 using nasopharyngeal (NP) swabs tested on the 2019-nCoV RT-PCR assay (TIB MOLBIOL, Roche). Paired raw sputum was split for sediment processing (SP) and routinely tested for TB using Cepheid's Xpert MTB/RIF Ultra (Ultra). Post-TB testing, residual raw split sputum (1ml, n=71) was stored (-70°C). A nylon flocked swab was then inserted into the thawed sputum, washed to re-suspend in PBS and the eluate was tested for SARS-CoV-2 on the Xpert Xpress SARS-CoV-2 cartridge. A second Ultra test was performed on the residual sputum post-SC.

Results: TB-testing post-SC revealed 73% (46/63) concordance when compared to SP-results. Moreover, SP detected 8% (5/63) (qualitative results: very low or 'trace') that were reported as negative for SC. For SARS-CoV-2 testing, concordance of 80% (57/71) was observed between NP- and SC-results and 100% (71/71) SC generated a SARS-CoV-2 result with 9.9% (7/71) specimens having Ct values <30 (high viral load).

Overall, moderate agreement was observed between gold standard tests (SP/NP) and the SC with Cohen's kappa coefficient of 0.46 (95% CI, 0.23-0.67) and 0.52 (95% CI, 0.31- 0.73) for TB and SARS-CoV-2 detection respectively.

Conclusions: Swab-capture appears feasible to identify both SARS-CoV-2 and TB-disease off a single tested sputum. The method is not aimed to be a replacement

of current gold-standard methods for diagnosis of TB (sputum) and SARS-CoV-2 (NP swabs) but may be considered an added benefit of SARS-CoV-2 diagnosis among patients investigated for suspicion of co-infection.

OA31-812-22 Interpreting Xpert MTB/RIF Ultra Trace results: a prospective comparison of children with Ultra Trace results and unlikely TB

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Background: Xpert MTB/RIF Ultra provides a trace semi-quantitative category, but clinically there is concern for false-positive results. We characterized children with trace results at a pediatric TB clinic in Kampala, Uganda.

Design/Methods: We prospectively enrolled children under 15 years who presented for TB evaluation from November 2018 to December 2020. Clinical history and exam were performed and patients were investigated with two-view chest X-ray, Tuberculin Skin Test (TST), urine Determine TB LAM, fluorescent sputum smear microscopy, sputum Xpert MTB/RIF Ultra, and mycobacterial culture.

All children were followed for two months, and children treated for TB for six months. TB status was classified as Confirmed, Unconfirmed or Unlikely TB per NIH classification.

We determined the outcome of children with Trace results at 2 and 6 months of follow-up, and compared their clinical and laboratory characteristics to children with Unlikely TB.

Results: Of 463 children enrolled, 21 (5%) had Trace results and 140 (30%) were classified as Unlikely TB. Trace results represented 36% of all Ultra-positive results and 3 of 21 (14%) were confirmed by culture. There were no differences in prevalence of TB symptoms between children with Trace results vs. Unlikely TB.

However, children with Trace results were more likely to have a known TB contact (71% vs 32%, p=0.001), and to have a positive TST (76% vs 29%, p<0.001).

All children with Trace results were initiated on anti-TB therapy and had clinical improvement at 2- and 6-month follow-up.

Characteristics	Unlikely TB n/N (%) or Median (IQR)	Xpert Ultra Trace n/N (%) or Median (IQR)	Chi2 test p-value
Age in years	3.6(1.5-6.3)	2.4 (1.0-5.2)	
Fever	119/140 (85.0%)	19/21 (90.5%)	0.74
Weight loss or failure to thrive	30/140 (21.4%)	5/21(23.8%)	0.81
Unexplained cough ≥2weeks	138/140 (98.6%)	21/21 (100.0%)	1.0
Under weight	47/140 (33.3%)	6/21 (28.6%)	0.55
TB contact	45/140 (32.1%)	15/21 (71.4%)	0.001
Past history of TB disease	1/140 (0.7%)	0/21 (0%)	1.0
Positive TST	40/140 (28.6%)	16/21 (76.2%)	<0.001
Determine TB LAM	4/63 (6.3%)	3/17 (17.7%)	0.16

Conclusions: Trace results represented a large proportion of positive results in children. Children with Trace results were more likely to be exposed to TB and have a positive TST. All improved on treatment. These findings support initiation of TB treatment in children with Trace results to prevent treatment delays.

OA31-813-22 Prevalence of Ultra Trace call results and associated risk factors during active TB case-finding in Vietnam

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Background: The Xpert MTB/RIF Ultra assay is a second-generation molecular diagnostic test which has a higher sensitivity than its predecessor. A semi-quantitative MTB burden category, called Trace Call, has been added as a result for extremely low bacillary loads. The prevalence and interpretation of Trace Call results is poorly understood in the context of community-based active case finding (ACF).

Design/Methods: We organized 56 days of mobile chest X-ray (CXR) screening across three districts of Ho Chi Minh City, Viet Nam between October 2020 and March 2021. Participants were verbally screened for TB symptoms and by CXR in parallel. Individuals with an abnormal CXR were tested using the Ultra assay; those with a Trace Call result were re-tested in line with national policy. We extracted data for all Ultra-positive participants from the ACF database, calculated descrip-

tive statistics and fitted a multivariate logistic regression to identify factors associated with an initial Trace Call result.

Results: 17,015 people were screened by CXR, resulting in the detection of 186 Ultra-positive participants. 71 (38.2%) of these positives were Trace Call results. 61 (85.9%) participants with an initial Trace Call result were re-tested and 33 (54.1%) had a negative second Ultra test. The multivariate logistic regression showed that having no cough (aOR = 2.40 [1.11-5.19]), a low Qure.ai abnormality score for your CXR (aOR = 3.98 [1.60- 9.92]) and a past history of TB (aOR = 3.66 [1.80- 7.46]) were independent factors for an initial Trace Call result.

Factors	Ultra(+)*	Trace Call(+)	aOR (95% CI)	P-Value
Cough	Yes	47 (70.1%)	20 (29.9%)	Ref
	No	68 (57.1%)	51 (42.9%)	2.40 (1.1-5.2) 0.025
TB History	Yes	40 (50.0%)	40 (50.0%)	3.66 (1.8-7.5) <0.001
	No	75 (70.8%)	31 (29.2%)	Ref
Qure.ai Score	<0.60	13 (38.2%)	21 (61.8%)	3.98 (1.6-9.9) 0.003
	0.60-0.80	21 (67.7%)	10 (32.3%)	0.88 (0.4-2.2) 0.79
	>0.80	81 (66.9%)	40 (33.1%)	Ref

* All Ultra(+) results, except for Trace Call

Conclusions: Community-based CXR screening initiatives are likely to mobilize the kinds of participants who are most at risk for Trace Call results. Consequently, these results can comprise a large proportion of an ACF initiative's initial testing yields. Further prospective studies are warranted to follow people with discordant Trace Call results to measure TB outcomes and inform policy.

OA31-814-22 Equivalence of the GeneXpert® and GeneXpert Omni Systems for TB and rifampicin resistance detection

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Background: The new GeneXpert Omni is a mobile, single-module, battery-powered, near-patient system with cloud-based connectivity for data transfer and device management, designed to withstand challenging environmental conditions. We set out to demonstrate equivalence for Xpert MTB/RIF Ultra and Xpert Omni MTB/RIF Ultra cartridge testing on the GeneXpert Omni and GeneXpert Systems, respectively, including whether the presence of environmental stressors (e.g. high temperature and humidity) influence assay performance on GeneXpert Omni, given the intended use of the device for decentralized environments.

Design/Methods: In this prospective laboratory validation, we assessed the concordance between Ultra testing on the GeneXpert Omni and GeneXpert Systems. The validation consisted of two parts.

Study 1: Equivalence assessment at normal ambient conditions using 200 well-characterized tuberculosis (TB) -negative and -positive clinical specimens from biorepositories, including a wide range of rifampicin (RIF) resistance-conferring mutations.

Study 2: Environmental equivalence assessment with control materials tested on GeneXpert Omni either at 20-25°C, 50% relative humidity or 35°C, 90% relative humidity and GeneXpert at 20-25°C, 50% relative humidity.

Results: In Study 1, 100% (40/40) of TB-negative sputum specimens and 99.4% (158/159) of TB-positive sputum specimens were accurately characterized by both devices (Figure 1A).

In addition, 92.9% (145/156) of tested RIF-resistant specimens were accurately characterized by both devices (Figure 1B).

In Study 2, all TB-negative, wildtype and RIF-resistant controls were accurately characterized by each device for all replicates regardless of tested environmental condition. Equivalence of the Cts for all Xpert MTB/RIF Ultra probes was demonstrated based upon prospectively set, pre-defined equivalence limits, and all *rpoB* probe melt temperature variations were within 1°C between the two devices.

		Omni		
Result of Test		TB+	TB-	Total (%)
Gene Xpert	TB+	158 (79.8%)	1 (0.5%)	159 (79.9%)
	TB-	0 (0.0%)	40 (20.1%)	40 (20.1%)
	Total (%)	158 (79.4%)	41 (20.6%)	199 (100%)

Figure 1A

		Omni			
Result of Test		RIF-R	RIF-S	RIF-Indet.	Total (%)
Gene Xpert	RIF-R	145 (92.9%)	0 (0.0%)	2 (1.3%)	147 (93.1%)
	RIF-S	1 (0.6%)	1 (0.6%)	1 (0.6%)	3 (1.9%)
	RIF-Indet.	2 (1.3%)	2 (1.3%)	2 (1.3%)	6 (3.8%)
	Total (%)	148 (94.9%)	3 (1.9%)	5 (3.2%)	156 (100%)

Figure 1B

Conclusions: We have demonstrated equivalence for Xpert MTB/RIF Ultra testing on GeneXpert Omni and GeneXpert Systems for detection of TB and RIF resistance for a range of specimens and extreme environmental conditions.

OA31-815-22 Diagnostic performance of Xpert MTB/RIF Ultra for the detection of tuberculous meningitis using cerebrospinal fluid in Bangladeshi adults

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Background: Rapid, sensitive, and accurate diagnostic tool for detection of tuberculous meningitis (TBM) using cerebrospinal fluid (CSF) is still scarce. We evaluated the diagnostic performance of Xpert MTB/RIF Ultra (Xpert Ultra) for detection of TBM in adult patients.

Design/Methods: We prospectively enrolled presumptive TBM adults from three tertiary hospitals in Dhaka, Bangladesh. CSF collected from the patients were tested by the Xpert Ultra, Xpert MTB/RIF (Xpert), Lowenstein Jensen (L-J) culture, and acid-fast bacilli (AFB) microscopy. The diagnostic performance of each test was assessed against the uniform case definition of probable or definite TBM and composite microbiological reference standard.

Results: A total of 157 presumptive TBM adults were enrolled between the period of December 2019 to February 2021. Uniform clinical case definition classified 61 patients as having probable or definite TBM. Against this uniform case definition, Xpert Ultra had 83.6% sensitivity (95% CI, 71.9-91.9; 51 of 61), and a negative predictive value (NPV) of 90.6% (84.5-94.4; 96 of 106), compared with 34.4% sensitivity (22.7-47.7; 21 of 61), and NPV of 70.6% (6.7-74.2; 96 of 136) for Xpert, 29.5% sensitivity (18.5-42.6; 18 of 61) and NPV of 69.1% (65.5-72.4; 96 of 139) for L-J culture, and 1.6% sensitivity (0.04-8.8; 1 of 61) and NPV of 61.5% (60.8-62.3; 96 of 156) for AFB microscopy.

Against the composite microbiological reference standard, Xpert Ultra had a sensitivity of 100% (93.02-100; 51 of 51 patients) which was higher compared with Xpert at 41.2% (27.6-55.8; 21 of 51), L-J culture at 35.3% (22.4-49.9; 18 of 51), and microscopy at 2% (0.1-10.5; 1 of 51). Xpert Ultra detected 28 TBM cases which were missed by other tests.

Conclusions: Xpert Ultra detected TBM with higher sensitivity compared with Xpert, L-J culture, and AFB microscopy, and therefore, can be used for rapid detection of TBM among adults in clinical settings.

OA31-816-22 High concordance between stool processing using Xpert Ultra and gastric aspirate for TB diagnosis in young children

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Background: Bacteriological confirmation of tuberculosis (TB) in young children is hampered by their inability to produce sputum, necessitating an invasive procedure to collect gastric aspirate (GA). It is imperative to investigate new specimen types and testing methods that increase the availability of pediatric diagnostic services.

We compared performance of Xpert MTB/RIF Ultra using stool processed by two methods with GA Xpert and culture.

Design/Methods: Cross-sectional study of children 0-5 years-of-age presenting with presumptive TB at University Teaching Hospital, Lusaka, Zambia. Stool and GA were collected. GA was tested using Xpert Ultra and MGIT culture. Before testing using Xpert Ultra, stool was processed by two simple methods:

1. Simple One-Step (SOS), adding ~1g stool to 8mL of Xpert reagent and,
2. PrimeStore® MTM Molecular Transport Media (PS-MTM), 150mg stool collected on a swab and placed into 1.5mL of PS-MTM, which inactivates MTB and stabilizes DNA, permitting storage and transport at ambient temperatures.

Results: 116 children were enrolled: median age 17 months (IQR 7-30); 56.1% male; 21.6% reported a close TB contact; 36.2% with severe acute malnutrition; 23.3% HIV-infected and 17.2% HIV-exposed. From 116 GA collected: 12/116 (10.3%) were Xpert-positive and 7/100 (7.0%) were culture-positive. 114 children submitted stool: 11/114 (9.6%) were Xpert-positive using SOS and 10/114 (8.8%) using PS-MTM.

Concordance between available testing results was high (figure 1), with 9/13 MTB cases detected by all 3 methods. Of the 116 children enrolled, 79 (68.1%) were diagnosed with TB (13 bacteriologically-confirmed and 66 clinically). The study will continue until 150 children are enrolled.

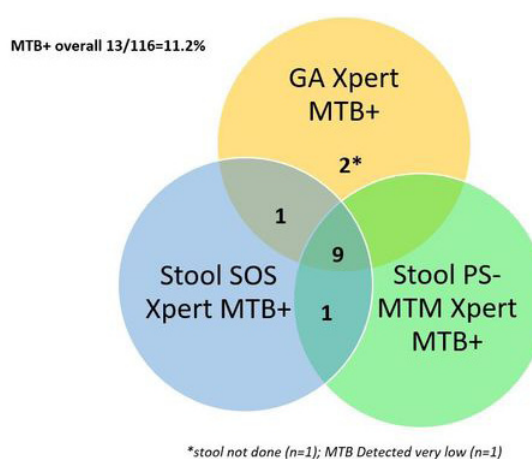


Figure 1. Concordance between Xpert Ultra results performed on stools using SOS stool method and PS-MTM compared with GA Xpert Ultra and culture.

Conclusions: Xpert Ultra using stool processed by the SOS and PS-MTM methods showed high concordance with gastric aspirate for diagnosis of tuberculosis in young children. Stool collection is non-invasive and can be performed almost anywhere, increasing access to a bacteriologically-confirmed TB diagnosis.

OA31-817-22 Implementing a systematic and rapid Xpert® MTB/RIF Ultra TB detection using nasopharyngeal aspirates in children with severe pneumonia

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Background: Nasopharyngeal aspirate (NPA) was recently recommended by WHO for Xpert tuberculosis (TB) testing in children. The TB-Speed Pneumonia study assessed systematic early TB detection among young children with severe pneumonia.

We describe the implementation of Xpert MTB/RIF Ultra (Ultra) on NPA in 15 reference hospitals of 6 high TB incidence countries participating in the study.

Design/Methods: Implementation followed a site assessment in term of infrastructure, electricity, staff availability, and bio-risk management. For hospitals

with limited access to GeneXpert, a battery-operated GeneXpert Edge system (G-Edge) was installed in or close to the ward to allow testing by nurses. We measured the turnaround time (TAT) as the time between sample collection and result delivered to the clinician and assessed nurses' opinion on Ultra feasibility using a self-questionnaire. We implemented an external quality assessment (EQA) using proficiency testing panels.

Results: 4 hospitals implemented Ultra testing in/close to the ward by the nurses and 11 used hospital laboratories. A total of 1229 Ultra tests on NPA were performed. The median (interquartile range) TAT was 2 hours [1.5, 2.9] in/close to the ward vs 2.8 hours [2.0, 4.7] for hospital laboratories. In five sites using hospital laboratories, TAT was above 3h mainly due to high workload, laboratory closing hours and sample transportation challenges.

Overall 2.2% of invalid/error results were reported and EQA was above 87.5% for all the sites. Testing inward required infrastructure renovation, training of nurses on basic computer and laboratory skills and regular instrument troubleshooting. Nurses reported that 4.7% (7/150) of the tests were difficult or impossible to perform.

Conclusions: Implementation of high-quality Ultra testing and delivery of results within 3-hours of sample collection was feasible in/close to the ward using a G-Edge by nurses but requires substantial and continuous support that should be considered for future implementation.

OA-33 Resistance Ground Zero

OA33-825-22 Seq&Treat Phase I: an analytical evaluation of three targeted next-generation sequencing solutions for the detection of drug-resistant TB

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Background: The use of culture-free, targeted next-generation sequencing (tNGS) for detection of drug resistant tuberculosis could offer higher throughput, greater accuracy, and more comprehensive antimicrobial resistance profiles across more anti-tuberculosis drugs than current WHO endorsed molecular assays, with significantly faster time-to-result than phenotypic drug susceptibility testing (DST). As a first stage in a larger clinical evaluation study of tNGS, we evaluated the ana-

lytical performance of three end-to-end tNGS solutions to determine if they met the sequencing Target Product Profile (TPP) for clinical evaluation.

Design/Methods: A blinded, manufacturer laboratory-based analytical validation study utilizing contrived samples and strains was conducted on the tNGS solutions. The accuracy of phenotypic drug resistance prediction and specific mutation detection was evaluated using three blinded replicates of 111 highly characterized and globally diverse clinical *Mycobacterium tuberculosis* strains representing a variety of phenotypic resistance profiles to rifampin, isoniazid, pyrazinamide, fluoroquinolones, and second-line injectables driven by a diversity of drug resistance associated mutations. Detection of heteroresistance was evaluated using three blinded replicates of contrived mixtures of mutant to wildtype strains at 0.1%, 1%, 10%, 20%, and 50%.

Results: All three manufacturer solutions performed extremely well identifying mutations with 98-100% sensitivity for SNP identification on 79-96% of the mutations examined across the three solutions. Additionally, all solutions were able to meet or exceed the TPP criteria for identification of mixtures down to 10% or lower, demonstrating the depth of resolution offered by sequencing approaches.

Conclusions: These findings illustrate the reproducibility and accuracy of three tNGS solutions for drug resistance detection on a diverse strain set. The current study is part one of a two-phase clinical study to assess performance of culture-free, end-to-end tNGS solutions for drug resistant TB diagnosis. The data collected demonstrate tNGS solutions' technical performance prior to further clinical assessment.

OA33-826-22 Resistance to new TB drugs in *Mycobacterium tuberculosis* clinical isolates from the Republic of Tajikistan

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Background: New MDR-TB treatment regimens using bedaquiline (BDQ) were introduced in Tajikistan in 2016-2017. In 2018 the WHO released a new „Technical manual for drug susceptibility testing (pDST) of medicines used in the treatment of tuberculosis“, including updated critical concentrations (CC) for new and repurposed drugs like BDQ, clofazimine (CFZ), linezolid (LZD) and delamanid (DLM).

In the same year National Reference Laboratory (NRL) of Tajikistan has implemented pDST for BDQ, CFZ, LZD and DLM. In 2019, totally 34 MDR isolates were tested to be resistant against BDQ.

Design/Methods: In order to confirm resistance, all 34 isolates were sent by NTP to Supranational TB Reference Laboratory (SRL) for rechecking. The pDST was conducted to CC of BDQ, CFZ, LZD and DLM as well as low concentrations of BDQ to detect low-level resistance. The USAID Eliminating Tuberculosis in Central Asia project supported analysis of discrepant results as well as whole genome sequencing (WGS) and cluster analysis.

Results: Of the 34 isolates, 12 were found to be truly resistant to the critical BDQ concentration (1 µg/ml) and 3 to the low BDQ concentration (0.5 µg/ml). With an exception of one phenotypically resistant isolate, all, including those resistant to low concentrations of BDQ (0.5 µg/ml), carry characteristic mutations in the *mmpR* gene (Rv0678) and one in the *atpE* gene. All BDQ-R strains were also cross-resistant to CFZ. Six isolates were resistant to LZD with confirmed Cys154Arg *rplC* mutation. Three strains were DLM-R with confirmed *ddn* mutations. One strain was resistant against all 4 new drugs. Beijing lineage was the most prevalent among BDQ-R strains, but other lineages like LAM and Ural were also prominent.

Conclusions: The emerging drug resistance to new TB drugs among multidrug-resistant tuberculosis (MDR-TB) isolates poses a serious threat to healthcare delivery to patients with MDR-TB and threatens to undermine global TB control efforts.

OA33-827-22 Evaluation of the compatibility of a bio-safe filter paper-based sputum transport kit with line-probe assay for diagnosing drug-resistant TB

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Background: Near-patient access to appropriate tests is a major obstacle for the efficient diagnosis of Tuberculosis (TB) and associated drug resistance. Drug susceptibility testing (DST) is a major challenge in primary healthcare centres (PHCs), particularly in remote geographical areas of India and other high-burden countries, where DST facilities are restricted to centralized laboratories. At present, DST services are extended to

patients residing in remote areas by sample transport under temperature-controlled and bio-safe containment conditions.

Design/Methods: We recently developed the 'TB Concentration & Transport' kit for bio-safe, ambient-temperature transportation of dried sputum on *Trans-Filter*, and the 'TB DNA Extraction' kit for DNA extraction from *Trans-Filter* for DST. In the present study, we evaluated the compatibility of Kit-extracted DNA with Hain's Line Probe Assays (LPAs), which are endorsed by National TB programmes for the detection of drug resistance in sputum collected from presumptive Multi-drug resistant TB patients (n=207).

Results: *Trans-Filter*-extracted DNA was seamlessly integrated with the LPA protocol (Kit-LPA). The sensitivity of Kit-LPA for determining drug resistance was 83.3% for rifampicin (95% Confidence Interval [CI]: 52, 98%), 77.7% for isoniazid (95% CI: 52, 94%), 85.7% for fluoroquinolones (95% CI: 42, 100%) and 66.6% for aminoglycosides (95% CI: 9, 99%), with a specificity range of 93.7% (95% CI: 87, 97) to 99.1% (95% CI: 95, 100) using phenotypic drug susceptibility testing (DST) as a reference standard. A high degree of concordance was noted between results obtained from Kit-LPA and LPA [99% to 100% (value: 0.83-1.0)].

Conclusions: This study demonstrates successful integration of our developed kits with LPA. The adoption of these kits across Designated Microscopy Centres in India can potentially overcome the existing challenge of transporting infectious sputum at controlled temperature to centralized testing laboratories and can provide rapid near-patient cost-effective 'Universal DST' services to TB subjects residing in remote areas.

OA33-828-22 Cost-utility of first- and second-line line-probe assay for the diagnosis of multidrug- and extensively drug-resistant TB

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Background: Shorter regimens for multidrug-resistant tuberculosis treatment has been proposed based on fluoroquinolones as backbone. In this context, newest molecular assays for laboratorial detection of multidrug/extensively tuberculosis (MDR-XDR-TB) should be evaluated at country level through economic analysis. The aim of study was to assess the cost-utility of line probe assay first line (LPAfl) and second line (LPAsl) for laboratorial detection of MDR/XDR-TB in the Brazilian Public Health System (SUS).

Design/Methods: Decision tree analysis comparing LPAfl and LPAsl with phenotypic drug susceptibility test was performed. We considered TB patients detected by XPERT-MTB-Rif or acid fast bacilli positive or positive culture; SUS perspective; time horizon of 18 months with discount rate.

In the model were assumed direct costs (diagnosis, assays and antimicrobial drugs) and effectiveness parameters: drug-resistance incidence; patient outcome; and LPAfl and LPAsl sensitivity for quality-adjusted life-years (QALY).

Results: LPAfl and LPAsl were cost-effective compared with phenotypic drug susceptibility test. Incremental cost effectiveness ratio (ICER) was -R\$ 1.750,37/QALY. Sensitivity analysis showed that the MDR-TB incidence and MDR-LPA cost influenced more significantly the model. Limitations of study were related to extrapolated utility data from others countries besides exclusion of another costs like human resources, insumes, equipments, TB complications and adverse events of therapeutic regimens.

Conclusions: LPAfl and LPAsl were cost-effective in Brazilian Public Health System scenario allowing reduce the interval until MDR/XDR-TB resistance diagnosis and adjusted therapeutic.

OA33-829-22 A multicentere evaluation of the Nipro Genoscholar PZA-TB II line line-probe assay to detect pyrazinamide resistance in Mycobacterium tuberculosis isolates

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Background: The WHO supports the use of high complexity hybridisation-based NAAT's such as line probe assays (LPA) for pyrazinamide (PZA) resistance detection on isolates. Ideally performed directly on sputum these could improve patient management, avoiding culture-based testing.

This study evaluated the genetic accuracy of the Nipro Genoscholar PZA-TB II line probe assay (PZA-LPA) for *M. tuberculosis* isolates, which allows detection of mutations in the full length *pncA* gene, including its promoter region, based on absent probe binding to the wildtype sequence.

Design/Methods: We conducted a prospective, multi-center study (three sites), coordinated by the SRL Antwerp and supported by FIND. It included blinded testing of 100 isolates representing a variety of *pncA* polymorphisms. All SRLs used the Hain Lifescience Twincubator platform, with additional parallel testing on the Nipro MultiBlot device by the SRL Antwerp. Aliquots of thermolysates were distributed to all participating sites and the PZA-LPA instructions were followed with an adapted program for hybridization on the Twincubator. Resistance calling by PZA-LPA was compared to *pncA* sequencing results as reference standard, to calculate sensitivity and specificity.

Results: At SRL Antwerp, the average sensitivity for the detection of PZA-resistance was higher for the Twincubator (84.2%) compared to the MultiBlot (78.1%), with 100% specificity for both devices. Comparing the results of all three sites using the Twincubator, the average sensitivity for PZA-resistance was 89.5% with a specificity of 92.3%. Percentages differed by operator and site. The individual probe specificity ranged from 91.2% to 100% and the sensitivity from 0.0% to 100%. Two probes consistently failed to detect the presence of a mutation.

Conclusions: Our data support the use of the Nipro Genoscholar PZA-TB II assay using the Twincubator hybridisation platform to assess the PZA resistance profile in MTBC isolates, acknowledging shortcomings in the design of specific assay probes.

OA33-830-22 Assessing pyrazinamide resistance: a comparative study between the Nipro Genoscholar PZA-TB II line-probe assay and whole-genome sequencing in cultured Mycobacterium tuberculosis isolates

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Background: Pyrazinamide (PZA) remains an important component of anti-tuberculosis regimens. The Nipro Genoscholar PZA TB II line probe assay (PZA-LPA2) indirectly detects mutations in *pncA* by targeting the wild-type sequence. We compared results obtained by PZA-LPA2 with whole genome sequencing (WGS) as reference standard to assess PZA resistance in *Mycobacterium tuberculosis* (*Mtb*) isolates.

Design/Methods: PZA-LPA2 and WGS were performed on multidrug-resistant *Mtb* isolates from the STREAM stage I clinical trial. DNA extracts were subjected to PZA-LPA2 and Illumina WGS. Probe profiles were interpreted by two operators for PZA-LPA2 and WGS data were analyzed using TB-Profler. We compared overall genotypic agreement on PZA resistance calling.

Non-synonymous mutations and insertions/deletions in *pncA* identified by WGS were interpreted as resistant (R) and the wildtype sequence as susceptible (S). For LPA an absent probe was interpreted as R and the presence of a probe as S.

Results: Of 323 isolates with PZA-LPA2 and WGS results, 54 (16.7%, 95% CI 12.6-20.8) were invalid and 4 negative by PZA-LPA2 (). Interpretable results by both methods were obtained for 265 isolates, of which 242 were concordant (91.3%, 95% CI 87.9-94.7). For 21 isolates with PZA-LPA2-S/WGS-R results, the discordance may be explained partly by undetected heteroresistance (n=7) and undetected mutations in the *pncA* promotor region (n=4) by PZA-LPA2. For two isolates PZA-LPA2-R was reported while WGS showed *pncA* wild-type (WGS-S). Of the 242 isolates with concordant resistance calling, the mutation position (n=142) or wild-type sequence (n=88) detected in 230 (95.0%, 95% CI 92.3-97.8) isolates corresponded to the absent or present PZA-LPA2 probe, respectively.

PZA-LPA2	WGS (n=323)	
	R (n=212)	S (n=111)
R (n=156)	154	2
S (n=109)	21	88
Invalid (n=54)	34	20
Negative (n=4)	4	NA

R=resistant, S=susceptible

Table 1

Conclusions: The concordance between PZA-LPA2 and WGS to detect PZA resistance was high (>90%). Most discordances were observed in the PZA-LPA2-S/WGS-R group; the current design of the PZA-LPA2 does not allow heteroresistance detection and hinders the detection of *pncA* promotor mutations upstream of the *pncA* gene.

OA33-831-22 Monocyte miRNA as biomarker for drug-susceptible and -resistant individuals infected with *M. tuberculosis*

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Background: The biomarker and therapy quest for tuberculosis (TB) is rapidly evolving towards micro RNAs (miRNA) due to their regulatory and immunomodulatory functions. Deep sequencing enables better understanding on mycobacterium survival and could reveal

potent biomarker signature for TB. We aimed to study the differential expression of monocyte miRNAs among healthy and diseased individuals through NanoString nCounter technology.

Design/Methods: FACS sorted monocytes (HLA-DR+ CD14+ CD16+), (N=24) were subjected to Nano string nCounter miRNA profiling assay, representing four groups [healthy individuals (HC), latently infected (LTB), drug sensitive TB (DS-TB) and single or multi-drug resistant TB (DR-TB)] with 6 samples each. Differentially regulated miRNAs and their targeted mRNAs and pathways were identified using nSolver, miR-DB and Webgestalt softwares.

Results: Differentially regulated miRNAs were identified with p values <0.05 and fold changes >= 1.2 and <=-1.2 for all possible comparisons: 11 (LTB vs HC), 23 (DS-TB vs HC), 56 (DR-TB vs HC), 31 (DS-TB vs LTB), 83 (DR-TB vs LTB) and 6 (DR-TB vs DS-TB). miRNAs from LTB group are involved in regulating IL-1 induced NF-KB activation, IRAK1 recruits IKK complex and TRAF6 mediated IRF7 activation in TLR 7/8/9 signaling and PI3K/AKT/mTOR-VitD3 signaling. Among which, miR-146b-5p/miR-146a-5p and miR-486-3p were upregulated in LTB and downregulated in DS-TB. miR-19a-3p, miR-219a-1-3p and miR-506-5p from DS-TB group regulates macrophage markers, p53, mTOR, FoxO, IL-11, IL-23 and IL-27 signaling pathways. miR-1298-5p from DR-TB group regulates interferon gamma signaling pathway. Both DR-TB and DS-TB has upregulated miR-132-3p compared to HC and LTB and DR-TB has strong upregulation of miR-150-5p compared to HC, LTB and DS-TB groups.

Conclusions: Novel miRNAs identified in the study should be validated further in a separate cohort for its potential diagnostic utility in differentiating TB disease spectrum from latency, drug sensitive and resistance conditions.

OA-34 Tobacco/nicotine use and marketing

OA34-832-22 Influence of cigarette smoke on *Mycobacterium tuberculosis* mutagenesis and transcriptional response

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Background: Smoking is a risk factor for tuberculosis (TB), with a five-fold increase in the risk of active TB in smokers compared to non-smokers. The respiratory tract microbiota differs between smokers and non-smokers, indicating that in addition to the effect of cigarette smoke on the host cells and immune response, bacteria in the host are also affected by cigarette smoke. Despite this, no studies have investigated the effect of cigarette smoke on *Mycobacterium tuberculosis* (*Mtb*), the causative agent of TB.

Design/Methods: This study aimed to investigate the effect of cigarette smoke condensate (CSC) on the in vitro survival, mutation frequency and gene expression of *Mtb*. Survival assays were done and rifampicin resistance mutation frequency was monitored to determine the mutation frequency in *Mtb* exposed to CSC in vitro. The transcriptional profile of *Mtb* upon CSC exposure was investigated by RNA-sequencing.

Results: *Mtb*'s survival was not affected when exposed to CSC. A two-fold higher mutation frequency was observed in *Mtb* exposed to CSC versus unexposed, which could likely be biologically significant. *Mtb* upregulated the expression of 59 genes within the first three hours of exposure to CSC. The expression of the global stress-response regulator, *sigH*, which enables response to oxidative stress and increases virulence in *Mtb*, and part of the SigH regulon increased upon initial CSC exposure. *MmpL6*, encoding a protein also involved in oxidative stress response and virulence was upregulated upon initial as well as prolonged (24h) exposure to CSC.

Conclusions: CSC induces *Mtb*'s oxidative stress response and virulence genes in vitro. This may contribute to the increased mutation frequency observed following CSC exposure. CSC may also affect *Mtb* within the host environment. The effect of cigarette smoke on *Mtb* itself, instead of only the host, may therefore be contributing to the associated TB risk in smokers.

OA34-833-22 Point-of-sale tobacco advertising and promotions, and tobacco product display in Ranchi and Siliguri, India

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Background: In India, the Cigarettes and Other Tobacco Products Act (COTPA, 2003) restricts tobacco advertising and product display at the point-of-sale (POS). COTPA further prohibits tobacco promotions at POS and requires vendors to display the appropriate warning signage to limit minors from accessing tobacco products. The extent to which these provisions are implemented is not well documented.

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 and 47 wards in Siliguri. The geographic location of each tobacco vendor was recorded. For each POS data collectors noted the presence of tobacco advertisements, tobacco product display if tobacco products were within reach of minors, and the presence of health warning signage.

Results: The study conducted observations in N=982 locations including n=374 in Ranchi and n=608 in Siliguri. Approximately one-third of tobacco vendors (Ranchi, 31%, n=115; Siliguri, 36%, n=218) had some form of tobacco advertising. In Ranchi, 14% (n=54) of vendors had tobacco products on display, and of those, 89% (n=48) were placed within reach of minors. In Siliguri, 81% (n=493) of vendors had tobacco products on display and of those, 68% (n=334) were within the reach of minors. Across the two cities, only three vendors displayed the required COTPA health warning signage.

Conclusions: Tobacco advertising is common at POS settings in the two cities included in this study. Tobacco products are commonly displayed and accessible to minors. Required health warning signage is almost completely absent. Eliminating tobacco advertisements and restricting the visibility of and access to tobacco products at the POS, perhaps through vendor licensing, are effective strategies for reducing tobacco use and initiation.

OA34-834-22 Protecting minors from tobacco use and exposure: COTPA Section 6 compliance assessment in five districts of Karnataka, India

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Background: India's Cigarettes and Other Tobacco Products Act (COTPA) 2003 prohibits sale of tobacco products to and by a person below the age of 18 years and sales within 100 yards of educational institutions. Tobacco vendors are required to display the 60x30 signage against sale to minors and educational institutions are required to display mandatory signage against sale within 100 yards. Tobacco industry adopted key strategies to increase new recruits and also to retain their existing consumers. Point of sale (PoS) promotion is an effective means to communicate with underage potential and current tobacco users. Youth experimenting with tobacco are more likely to have reported seeing tobacco advertisements at points of sale. This study presents a compliance assessment with COTPA section-6 from 2013 to 2020 in Karnataka.

Design/Methods: This comparative Study was done in five out of 30 Districts of Karnataka State in India. The study investigators made a direct observation of points of sale in the five Districts to assess the Tobacco Industry tactics by using a structured, pre-tested checklist.

Results: In 2013 Out of the total 2019 PoS observed for section 6(a), 20% had displayed section 6(a) signages and out of the total 1826 education institutions observed for section 6(b) 30% displayed the statutory signage. In 2020 out of the total 985 points of sale observed in the five districts for section 6(a) only 12% PoS had displayed section 6(a) signages i.e. 8% less institutions; whereas out of the total 1018 education institutions observed for section 6(b) 43% education institution displayed section 6(b) signage i.e. 13% increase in compliance. Although, there is increase in signage compliance by educational institutions the compliance at point of sale has declined in 2020 when compared to 2013.

Conclusions: There is urgent need to strengthen effective implementation of COTPA at all levels and in all districts.

OA34-835-22 Covid-19 measures to curb threats of emerging trends in tobacco use: a case study from Chandigarh, India

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Background and challenges to implementation: Chandigarh is a Union Territory that shares its borders with the state of Punjab and Haryana. Punjab has been successful in amending the Central law and banning Hookah (Waterpipe) Bars in the state in the year 2018. The same resulted in mushrooming of numerous cafes serving Hookah in the city.

Intervention or response: During the outbreak of COVID 19, a new direction has been seen in Public Health measures and Tobacco Control interventions have played a pivotal role in the same. Chandigarh, which was struggling from few years have seen an opportunity to put forward the nuisance of waterpipes.

The city government and Civil Society Organizations advocated of putting a ban on the same to prevent spread of COVID and also to reduce the harm of tobacco use in COVID.

The intervention included consultations, representations and mapping of cafes serving Hookahs. The resistance from front groups was also faced and resolved collectively.

Results/Impact: The consultations resulted in the administration putting a temporary ban on these cafes on serving Hookah.

It paved a way to bring the discussion of a complete ban post COVID also.

The counter consultations with the cafe owners and the administration strengthen the advocacy for a complete ban.

The prevailing COVID situation brought restrictions that stayed for almost a year which made many cafe owners to move away from their business of serving Hookah.

Strict implementation of the ban resulted in booking of 26 such cafes representing an approximate of 80% of such cafes.

Conclusions: Synergy among health programs and emergencies with tobacco control can help in coming up with measure and strengthen the tobacco control initiatives.

It verified that tobacco use lies in the heart of public health threats and for a country to be ready for health emergencies need stringent measures of curbing causes of preventable death and health harms.

OA34-836-22 Increased severity of Covid 19 among users of tobacco and nicotine in any form, including electronic cigarettes

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Background and challenges to implementation: More than 157 million COVID-19 cases and 3.2 million deaths are reported worldwide. Tobacco is a risk factor for all non-communicable diseases. The comorbidity influenced the severity of COVID-19. Nicotine, tar, and other chemical toxins present in tobacco have immunosuppressive effects. Smoking (cigarette, e-cigarette, bidi, hookah) and smokeless tobacco damage the lungs.

The aim of this study was to find out the recent consensus among the scientific & medical community about tobacco consumption in any form and nicotine as a risk factor for COVID severity.

Intervention or response: We have conducted a PubMed search with keywords (tobacco OR smoking OR nicotine OR paan masala OR khaini OR hookah OR electronic cigarette) AND (SARS COV 2 OR COVID 19 OR novel coronavirus). We selected article type as “systematic review” and “meta-analysis”, language as “English”, species as “human” and studies published between December 2019 to May 2021. A total of 31 studies were retrieved through the search. Irrelevant studies (six) were excluded.

Results/Impact: The majority of systematic reviews were in consensus that tobacco is a risk factor for the severity of COVID-19. One systematic review recommended pharmaceutical nicotine as a treatment option for treating covid-19. A single meta-analysis study concluded smoking as a protective factor against covid-19 hospitalization. Studies questioning, recommending, or non-conclusive about tobacco as a risk factor in COVID-19 severity are either improperly designed or used low sample sizes or influenced by the tobacco industry. A study claiming a protective role of smoking is now retracted from the European Respiratory Journal as one author was associated with the tobacco industry.

Conclusions: Methodological robust studies have reported smoking as a risk factor in the progression of COVID-19. While assessing the effects of tobacco we must keep in mind the history of the tobacco industry's scientific manipulation and planting flawed research findings.

OA34-837-22 Tobacco advertising, promotion and sponsorships in international cricket venues, 2015–2020

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Background: Tobacco companies realize the significance of one of the most intense sports-cricket, for the increased brand visibility during cricket tournaments. This study examines the frequency and nature of Tobacco advertising, promotion and sponsorships (TAPS) in a set of televised cricket matches representing the main highlight hours of network programming broadcast.

Design/Methods: Highlight recordings of 552 telecasts (on official cricket championship websites and media channels) were monitored for tobacco product or brand or company names for all forms of international cricket matches (Test, One Day International, T-20, domestic cricket leagues) played by:

- (i) any major cricketing nations (Australia, Bangladesh, England, India, New Zealand, Pakistan, South Africa, Sri Lanka, West Indies and Zimbabwe) on Indian grounds, and
- (ii) Indian cricket team elsewhere (January 2015–January 2020).

Results: All the Indian Premiere League (IPL) seasons (240) and 89.7% (253/282) of major tournament highlights ranging from 30 seconds to 4 minute were successfully analyzed. Out of the 253 telecasts, 22.5% glamorized sponsorships and 33.6% showcased in-stadia TAPS (India-Sri Lanka majorly) as compared to any other innings. The audience was found to be exposed to Indian Pan Masala advertising through the appearances of stadium signs such as boundary wall, LED visuals and other on-site promotions

Conclusions: Tobacco companies exploit multiple legislations and lacunae in international broadcast and consumer laws to continue advertising their products. TAPS is banned in India's tobacco control legislation and Article 13 of WHO Framework Convention on Tobacco Control (WHO-FCTC). Major smokeless tobacco products and their surrogate brands (pan masala) were found to be the most prevalent advertisers. Ban enforcement on brand stretching and surrogate tobacco advertising

(including pan masala and like products) is necessary to mitigate the problem permanently. A new system of regulation-by engaging national and international cricket bodies and officials-is required to reduce this unacceptable level of exposure to tobacco brands.

OA34-838-22 Understanding knowledge of tobacco shop vendors on tobacco control in Indore City, India

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Background: Indian Government has enacted Tobacco Control Act, COTPA in 2003. Its Section 4 prohibits smoking at public places, section 5 prohibits advertisements of tobacco products, section 6a prohibits sale of tobacco to minors, 6b prohibits sale of tobacco within 100 yards of educational institutions, section 7 mandates 85 percent pictorial warning. The government of Madhya Pradesh also banned Gutka in the state. The study was done in order to know the awareness level of tobacco shop vendors about various tobacco control efforts.

Design/Methods: Study was conducted in Indore city. Total 8 different geographical areas comprising of slums, residential, dense market were selected and 10 point of sale from each were taken for interview. A total of 80 shop owners or head of point of sale (vendors) were interviewed. All the shops were selected randomly.

Results: Only 41% knew about Ban on Gutka, 58% vendors knew that government of India has made Tobacco Control Act, 86% vendors well aware about smoking is prohibited in public places, 55% knew about the ban on tobacco related advertisements, 51% knew that sale of tobacco to minors is prohibited.

Only 45% knew that sale of tobacco by minors is prohibited. 64% knew that sale of tobacco products without pictorial warning is prohibited. 59% knew that sale of tobacco within 100 yards of educational institutions is prohibited. Least awareness of ban on Gutka was observed in slum area, only 18.2% tobacco vendors knew that Gutka is banned.

Conclusions: The awareness level of tobacco shop owners was on an average around 50 to 60 percent. Most of the vendors still violate the rules due to poor monitoring, poor retention of act and influence of the suppliers and advertisements. The lack of awareness among the backward and slum area was a cause of concern. From time to time awareness drive needed.

E-POSTER SESSION (EP)

COVID-19: challenges for TB care?

EP-01-100 Community actors and sustaining access to TB treatment during Covid-19 lockdown

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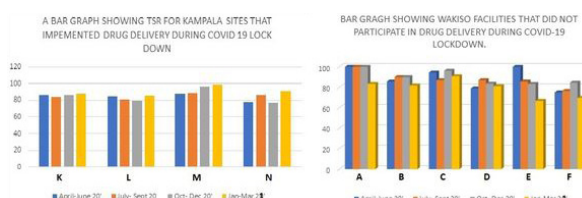
Background and challenges to implementation: The national lockdown measures to contain the spread of the Corona virus instituted in March 2020 created disruptions in Tuberculosis (TB) service delivery. Due to traffic restrictions, patients were unable to attend clinic refill visits which compromised adherence to TB treatment. We describe innovations implemented by the USAID Defeat TB project to minimize disruptions in TB service delivery and compare treatment success across intervention and non-intervention sites; to ensure continuity of care in urban and peri-urban facilities in Uganda.

Intervention or response: In April – May 2020, the project collaborated with facility healthcare teams to line-list patients on TB treatment and contact them on phone to agree on preferred drug delivery model.

Project technical officers trained community linkage facilitators (CLFs) on COVID-19 infection prevention and control (IPC) measures, paired them with facility health workers, issued introductory letters, N95 masks and alcohol hand-sanitizers. Drugs were prepacked using paper bags and labeled for each patient and delivered directly by the team or using pre-authorized motorcycles to patients' homes or preferred community locations. Physical locator forms were used to document patients' physical addresses and enable home drug delivery. Drugs were accounted for using a community drug delivery form signed by the patient or their designee.

Results/Impact: There was an increase in treatment success rate for the Jan-Mar.20 compared to the Oct-Dec.2019 cohorts for four sites that implemented community drug delivery. Six control facilities that did not implement community interventions witnessed a decline in treatment success.

Conclusions: A community-based intervention was useful in mitigating the effect of COVID-19 lock down measures to ensure continuity of care among patients diagnosed with TB; and also led to increased treatment success rate.



EP-01-101 Maintaining TB care during COVID-19 pandemic

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Background and challenges to implementation: COVID-19 pandemic had a major impact on the TB program implementation in Georgia. The rapid spread of virus put a major pressure on the health system and COVID-19-related restrictions affected patients' mobility and care seeking behavior.

Intervention or response: The country made significant efforts to maintain access to TB services during the pandemic, adopting new modes of service provision: daily DOT was substituted by monthly provision and home delivery of medications to limit patients' need for travel. All patients were offered to video-supported treatment (VST) and more patients were enrolled on VST. Georgia has become one of the first countries in the region to introduce molecular test for detection of SARS-CoV-2 using Xpert® Xpress SARS-CoV-2 cartridges. The existing GeneXpert machines that had been used for TB diagnosis were reallocated to serve both TB and COVID-19 diagnostics.

Results/Impact: In 2020, case notification rate decreased by 25% compared to 2019. As Figure 1 shows, during 2020, the lowest TB case notifications in Georgia (April-May, November-December) coincide with the surge of COVID-19 and corresponding restrictions as reflected by high score of the Oxford Stringency Index.*

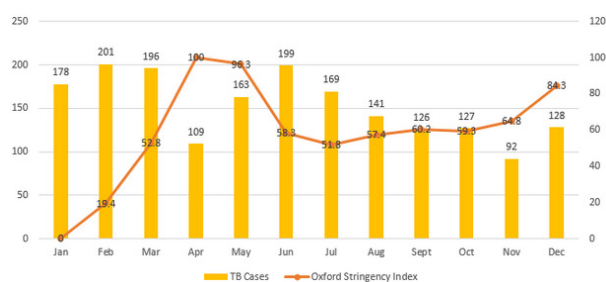


Figure. Oxford Stringency Index and notified TB cases, Georgia 2020

Country's timely implemented activities helped TB program to continue TB services without interruption and prevent spread on infection in healthcare settings.

GeneXpert machines enabled decentralization of PCR testing regions, including high-mountain areas. All newly diagnosed TB patients were also tested for COVID-19. VST was well received and country plans to expand using digital health care systems.

*The Oxford Stringency Index uses several indicators about common policy responses governments have taken and aggregates these scores into a Stringency Index.

Conclusions: Program modification gave the opportunity to TB program to maintain essential services for TB patients. However, pandemic halted active case finding and as the case notification rate decreased rapidly in 2020, efforts should be made to get back on track.

EP-01-102 Women "iddirs" as resilient Covid-19 partners in improving TB preventive treatment in three Ethiopian zones

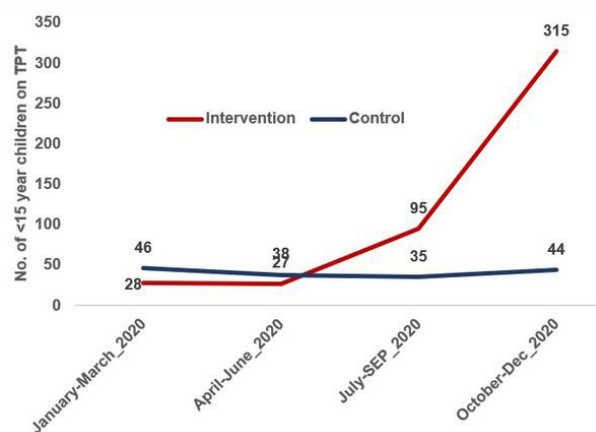
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Background and challenges to implementation: The Corona Virus Disease 2019 (COVID-19) pandemic has further slowed TB preventive treatment (TPT) uptake worldwide. In Ethiopia, the first wave of COVID-19 which ran from March-December 2020 affected TPT uptake rates, but some local actions helped deter its worst consequences. We report on a successful model of TPT delivery through volunteer women groups called Iddirs in Ethiopia.

Intervention or response: *Iddirs* are membership-based local associations of people who have voluntarily entered an agreement to help each other during times of adversities. Between January and December 2020, in two remote zones in southern Ethiopia and in a slum sub-city in Addis Ababa, we trained 120 volunteers from 67 Iddirs, equipped them with personal protective materials, provided monthly stipends, and supervised and mentored them regularly. Volunteers conducted weekly home visits to the households with known index TB patients, verified if they were screened for TB, linked them to the nearby health facility, and monitored adherence and side effects. Children who completed $\geq 95\%$ of the recommended regimen received certificates of completion from the district health office. We analyzed and compared quarterly TPT data with two non-intervention zones.

Results/Impact: Volunteers identified 470 eligible under-five children of whom 397 (84%) initiated TPT, accounting for 91% (397/437) of <15 year children put on TPT in the intervention zones. The number of <15

started on TPT increased from 20 to 315 per quarter in the intervention zones while there was no change in the control zones (Figure). TPT initiation rate among <15 year children increased from 51% to 72% in the intervention zones while it increased from 28% to 32% in control zones.



Conclusions: There was demonstrable increase in TPT enrollment rate in the intervention zones despite the impact of COVID-19, suggesting the added value of the intervention. Further work is needed to sustain and scale-up the approach in similar settings.

EP-01-103 Perspectives of healthcare providers on the integration of Covid-19 and TB screening at a national referral hospital in Uganda

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Background: Following the COVID-19 outbreak, Uganda experienced a 40% drop in TB screening between April and June 2020. We explored healthcare providers' (HCP) perspectives on TB screening in the context of COVID-19 at a National Referral Hospital.

Design/Methods: In this formative cross sectional study, we conducted in-depth interviews with HCP involved in TB activities at outpatient and emergency departments from January 2021- March 2021, at Kiruddu National Referral hospital, Kampala, Uganda. We explored HCP' work experience in the setting of COVID-19, perceived effect of COVID-19 on TB screening and perceptions about social and contextual factors that might influence their willingness to screen for both diseases. We analyzed the data using an inductive thematic approach, aligned the emergent themes to the Capability,

Opportunity, Motivation and Behavior (COM-B) model (Table1), to denote the barriers to and facilitators of COVID-19-TB integrated screening.

Results: A total of 12 HCP (3 Nurses, 7 doctors, 1 Clinical Officer and 1 TB community linkages Social worker) were interviewed. Barriers and facilitators of the integration of COVID19 and TB screening appeared in all three COM-B domains.

The barriers included; HCPs' inadequate knowledge on how to integrate screening of TB and COVID-19, absence of simple standard operating procedures and data collection tools, inconsistent supply of personal protective equipment (PPE), under staffing, and fear of contracting COVID-19 infection.

The facilitators included; HCPs have knowledge of how to separately screen for TB and COVID-19, availability of TB focal persons and interest in learning how to provide integrated screening for TB and COVID-19.

COM-B constructs	Health provider Barriers	Health provider Facilitators
Psychological capability	lack of knowledge on how to integrate screening of TB and COVID-19	Healthcare providers have knowledge of how to screen for TB and COVID-19 as independent diseases
Physical capability	There were no barriers in this domain	Healthcare providers have adequate skills to screen for TB and COVID-19
Physical Opportunity	Lack of simple Standard operating procedures for integrated screening of TB and COVID-19	Potential TB and COVID-19 patients are received through the same units in the hospital TB focal persons are available to support other healthcare providers to provide integrated screening for TB and COVID-19
	Inconsistent supply of personal protective equipment (PPE)	
	Understaffing at the outpatient and emergency departments	
Social Opportunity	Lack of data collection tools and databases for integrated screening of TB and COVID-19	
Social Opportunity	There were no barriers in this domain	
Reflective Motivation	Healthcare providers fear contracting COVID-19 infection during integrated screening	Healthcare providers are interested in learning how to provide integrated screening for TB and COVID-19
Automatic Motivation	Lack of risk allowance for healthcare providers who conduct integrated screening of TB and COVID-19	There were no facilitators in this domain

Table 1. Barriers and facilitators of integrating TB and COVID-19 screening at Kiruddu National Referral Hospital

Conclusions: These findings provide a basis for designing contextually appropriate interventions targeting factors that are likely to influence HCP's decisions and willingness to conduct TB screening in the context of COVID-19.

EP-01-104 Maintaining TB case notifications in the Covid-19 era: the case of Lango sub-region in Northern Uganda

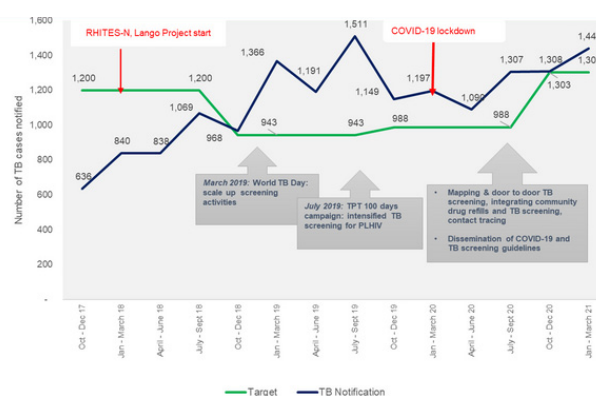
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Background and challenges to implementation: According to the World Health Organization, Uganda's national TB incidence is 200/100,000 (Global TB Report, 2019). In November 2019, Uganda's Ministry of Health (MOH) declared TB a national public health emergen-

cy. However, the COVID-19 pandemic and subsequent restrictions interrupted continuity of essential TB services.

Intervention or response: The USAID Regional Health Integration to Enhance Services-North, Lango project, led by John Snow, Inc. supports high-impact facility and community TB case finding interventions in the Lango sub-region in Northern Uganda. The project supports systematic contact-tracing, TB hotspot screening, capacity building for lay health workers on basic TB basic facts, use of intensified case finding guides, registers of presumptive cases, TB infection control, and sputum collection techniques, and community drug refills. The project supports community interventions by engaging community support organizations, village health teams and community linkage facilitators to reach marginalized and remote populations, and strengthening access to TB diagnostics (X-rays, geneXpert and TB LAM tests). Between January – March 2020 when the Government of Uganda instituted a lockdown, the project disseminated the MOH's COVID-19 and TB screening guidelines to the health facilities. These guidelines included information on innovative interventions such as mapping of community hotspots, door-to-door TB screening in hotspots, and systematic contact tracing.

Results/Impact: While the rising COVID-19 cases may have affected TB case identification, the project continued to identify more than the quarterly target of new cases. Through the project's support, there has been a steady rise in the TB case notification from 638 (January - March 2018) to 1,197 cases (January – March 2020) during the lockdown. This rise has been sustained post lockdown period.



Conclusions: Intensification of community-based responses for TB services during the COVID-19 pandemic is key in maintaining TB services. They will also be vital for longer term management of people with post-COVID or post-tuberculosis lung disease and complications.

EP-01-105 The impact of Covid 19 on National TB Elimination Programme in Uttarakhand, India: a mixed-methods operational research study

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Background and challenges to implementation: To determine the effect of COVID 19 on the National TB Elimination Program(NTEP) and to determine programmatic factors associated with Case Notification, Diagnosis, and Management under the NTEP. Also, to explore perceptions of Program Managers on the Effect of COVID 19 on NTEP in Uttarakhand.

Intervention or response: The research is being carried out in Uttarakhand's tuberculosis units.

Ten TU's were chosen by simple random sampling. Quantitative data of two years was collected and qualitative data were collected through in-depth interviews. For numeric variables, mean and standard deviation are used, while ratios and proportions are used for categorical variables. The major themes in the qualitative section are described in the transcript. The content analysis is performed manually by the analyst, and the unit of analysis is themed in the transcript.

Results/Impact: Within 2 years, i.e., one year before the onset of pandemic and one year during a pandemic, a total of 14898 participants were enrolled through the NIKSHAY portal.

- TB registration was 7 % less in the Public sector during COVID 19.
- Overall, a reduction of 49% is seen in those cases that have completed their treatment and outcome has been assigned. Moreover, the cure rate has dropped by 6%, and a slight increase in attrition rate was observed(0.6%).
- An increase in MDR and XDR from 0.2% to 0.4% has been observed.
- A total of 2% decrease is seen in New case type during COVID 19, and an increase in re-treatment and presumptive cases have been observed.
- A total of 53% rise is seen in Missing cases who were diagnosed with TB and are not on treatment.

Conclusions: COVID 19 has impacted Tuberculosis program services due to the long imposed Lockdown and diversion of health facilities and human resources to fight the pandemic. TB services should be maintained in the face of the COVID-19 response.

EP-01-106 Impact of the Covid-19 pandemic on the diagnosis and treatment of patients with multidrug-resistant TB in Cameroon in 2020: a mixed-methods study

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Background: The COVID-19 pandemic continues to overwhelm health systems. While tuberculosis (TB) health personnel are confronted to deal with the COVID-19 pandemic, the continuum of TB care is affected by restriction of mobility and fear to contract Covid-19 in health facilities.

We assessed the impact of the COVID-19 pandemic in the care of multidrug-resistant TB (MDR-TB) care through health-system, clinical and socioeconomic factors.

Design/Methods: A mixed-method study was conducted in the 11 MDR-TB clinics in Cameroon from January to April 2021 All MDR-TB patients diagnosed were enrolled, clinical and socioeconomic data were collected. Also, a structured questionnaire assessed perceptions of the impact of Covid-19 in MDR-TB patients. In-depth interviews were conducted with 14 health personnel in the MDR-TB clinics and Laboratories to understand their perspectives.

Results: We enrolled 105 patients. The mean age (years) was 37±12, the majority (66.3%) were males and 44.2 % had attended high school. 21.1% were HIV positive, 28% had a history of smoking and 30% initiated treatment >14 days following diagnosis. Up to 21.2% of ambulatory patients reported not going to the clinic for their refill at least once due to COVID-19. Being HIV positive was marginally associated with non-attendance (aOR3.07,95% CI:0.94-9.92,p=0.053).

The main barriers for non-attendance were fear of exposure to COVID-19 in the hospital (83%) and COVID-19 stigma (50%). Prioritizing GeneXpert machines for COVID-19 testing, redeployment of TB staff to COVID-19 clinics and fewer patients showing up for MDR-TB testing were additional barriers reported by MDR-TB staff.

Conclusions: COVID-19 hindered the treatment of 2 in every 10 ambulatory MDR-TB patients. Prioritizing COVID-19 and the overwhelming of TB personnel

manpower constituted health system barriers. Enforced patients' counselling, provision of personal protective equipment, and increasing TB clinic staff manpower could mitigate the negative impact of COVID-19 on MDR-TB care.

EP-01-107 The impact of Covid-19 on routine TB services in South Africa: a cross-sectional survey of patients and healthcare workers

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Background and challenges to implementation: The impact of COVID-19 on tuberculosis (TB) care in South Africa is of concern given its high TB burden. We investigated the impact of COVID-19 on TB services from the perspective of TB patients and TB healthcare workers (HCWs) in three high-TB burden districts.

Intervention or response: TB patients and HCWs (nurses, community health workers (CHWs)) were recruited through TB clinics and hospitals in uMgungundlovu, eThekweni, and Cape Town Districts for standardised interviews, from October 2020 to March 2021. Researchers facilitated telephonic surveys with patients and CHWs, while nurses responded online. Questions included COVID-19 knowledge, and experience of healthcare services.

Results/Impact: Fifty-eight patients (43% female, age range=20-67 years) and 21 HCWs (86% female, 81% ≥5 years practice) participated. Patient knowledge of COVID-19 preventive measures was most frequent for mask use (95%) and regular hand washing (84%) and was low for avoiding handshakes (41%) and hugs (40%). Just over half of the patients reported fear of accessing TB care during the pandemic, and 59% of CHWs expressed concern that people with suspected TB could also have COVID-19. Both TB patients and HCWs reported staff shortages (at TB clinics and for contact tracing), and 16% of patients were turned away from care at least once. However, most patients (78%) knew where to get urgent help. While 48% of HCWs reported an increase in TB treatment interruption.

Conclusions: Key COVID-19 prevention measures about avoiding person-to-person contact were not well known by TB patients, potentially due to confusion between TB and COVID-19 transmission pathways. HCWs were concerned about occupational exposure to COVID-19 from TB patients. Although TB services appeared nega-

tively impacted by staff shortages and patient fears, the dispensing of multi-month treatment and apparent access to emergency care may mitigate some of the impact.

EP-01-108 The impact of anti-epidemic measures against Covid-19 in the prison TB hospitals in Ukraine

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Background and challenges to implementation: The first case of COVID-19 in Ukraine was detected on March 3, 2020. Following this on March 11, 2020, the Cabinet of Ministers provided national-level quarantine measures. On March 12, 2020, the Ministry of Justice (MOJ) of Ukraine introduced quarantine measures within the penal settings, such as prohibition of short-term/long-term visits, as well as visits by representatives of the media, religious and charitable organizations, except for law enforcement officers and representatives of the court.

Intervention or response: The anti-epidemic measures launched by MOJ were primarily aimed to prevent the spread of SARS-CoV-2 virus in the penal settings in Ukraine, including localization and elimination of the disease. Special attention was given to the 7 prison TB hospitals. PATH-led, USAID Serving Life project contributed to expanding MOJ's policy for utilizing telemedicine for HIV treatment initiation/re-initiation of treatment and adherence services for incarcerated PL-HIV. To strengthen infection control measures additional Ultra Violet lamps were procured and installed. While strict infection control measures were implemented in the prison TB hospitals, the inmates were allowed to use internet-protocol telephony and video communication to maintain social connection during the quarantine.

Results/Impact: In 2020, 93 cases of COVID-19 infection were registered in the prison TB hospitals, of whom 60 were prison staff and 33 prison healthcare workers. There were no detainees or prisoners among the infected cases, and no mortalities were reported. During the same period MOJ's Center of Health Care reported 11,125 cases within the all penal settings, of whom 31 were detainees, 36 prisoners, 924 prison staff, 132 prison health workers and four COVID-19-related deaths were reported.

Conclusions: The low incidence rate in prison TB hospitals could be attributed to timely implementation of infection control measures, along with additional COVID-19 control measures put in place during the quarantine, that proved to be effective in preventing TB/COVID-19 co-infection cases.

EP-01-109 Effect of the Covid-19 pandemic, response, and social protection on the social, economic and health situation of TB patients and their households

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Background: The COVID-19 pandemic and its subsequent response has had severe consequences on TB services, with lockdowns and limitations on diagnosis and treatment services. In response to the socio-economic consequences of the pandemic, the South African government expanded social assistance programmes by topping up existing grants and created the Social Relief of Distress grant (SRD grant). This qualitative study explored how the COVID-19 epidemic and response affected the social, economic, and health situation of TB patients, and explored access to the SRD grant.

Design/Methods: This is a cross-sectional exploratory qualitative study that focused on the lived experiences and perceptions of TB patients and healthcare workers. We interviewed 15 TB patients and 5 healthcare workers at a health facility in Cape Town and analysed data thematically.

Results: Results suggest that participants associated COVID-19 with TB and this affected their health-seeking behaviour. Some participants delayed care for fear of catching COVID-19 at the health facility (majority), while others confused their symptoms with COVID-19. Once they arrived at the clinic, however, they were given priority. Several participants reported that household members, on whom they depended, lost income which significantly affected the household budget and therefore the food availability. Participants reported that the household ran out of money for food before the end of the month. Coping strategies included skipping meals and/or meal rationing. Despite considerable pressure on the household budget and food supply due to COVID-19, few participants received the SRD grant.

Conclusions: Our study found that the pandemic increased pressure on TB patients' households due to loss of income leading to increased food insecurity. Despite this increased pressure, few participants received the SRD grant. Further research is needed on the impact of COVID-19 on TB patients and their households, and on the role of social protection for TB patients.

Prevention of TB in children

EP-05-140 Integration of TB symptom screening among children under five at child healthcare posts (posyandu) in Kulon Progo District, Yogyakarta Province, Indonesia

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Background and challenges to implementation: Children under 5 years of age are a vulnerable, underdiagnosed population for tuberculosis (TB). Integrating TB services into child healthcare services, including community based healthcare, is recommended to improve TB case finding. Posyandu is a monthly community-based child healthcare activity, including weighing of children under 5 in Indonesia. We assessed the feasibility of integrating TB symptom screening into Posyandu to identify presumptive TB cases among children under 5.

Intervention or response: This was a pilot project conducted in 20 selected posyandu in Kulon Progo district, Yogyakarta, Indonesia from November 2020 to April 2021. Key activities included development of a simplified protocol, training for posyandu cadres and on the job training and supervision. Children under 5 who visited posyandus were screened for TB symptoms and history of contact with a TB case. Presumptive TB children were referred to primary health care or mobile active case finding for evaluation. Data was collected using paper forms with subsequent entry into REDCap. Monitoring and support was carried out through a social media group.

Results/Impact: Twenty community cadres were trained. During the study period, 379 children under 5 were screened for TB in the selected Posyandu. Of them, 28 (7%) were identified with TB symptoms and 21 presented to the referral services for diagnosis. Of 21 children, 7 (33%) were agreed by doctor in health facilities to have TB symptoms. Three (0.8%) children were diagnosed with TB. Despite a modest yield of active TB, TB symptom screening can be integrated into posyandu activities at relatively low cost. This results in additional work for the posyandu cadre, particularly in recording and reporting.

Conclusions: Integrating TB screening in the posyandu is a feasible approach with potential to increase coverage of TB case finding among children under 5 relative easily and cost effectively.

EP-05-141 Effect of isoniazid prevention therapy on child contacts of TB patients

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Background and challenges to implementation: Preventive therapy (PT) is recommended for people with latent tuberculosis infection (LTBI) whereas combination chemotherapy (CC) is used for active disease. It can be difficult to distinguish between infection and active disease in children who are unable to produce sputum for microbiological diagnosis and clinicians can find it challenging to know whether to offer children PT or CC.

Here we evaluate the efficacy of preventive therapy among TB-exposed contacts with different levels of TB symptoms at enrollment.

Intervention or response: In a prospective cohort study conducted between 2009 and 2012 in Lima, Peru, we enrolled 14,044 household contacts (HHCs) of tuberculosis patients and followed them for incident tuberculosis. We retrospectively assessed baseline TB relevant symptoms (cough, fever, weight loss, shortness of breath, and sweating at night) and reviewed chest X-rays of 4,408 child contacts (age ≤ 15) and classified them into three categories: those that did not report any - symptoms, those who reported ≥ one symptom, and those who had an abnormal chest-x-ray. We used a modified Poisson regression to evaluate the efficacy of IPT among the three groups.

Results/Impact: Among child contacts, 3,432 reported no symptom, 799 ≥ one symptom, and 69 had an abnormal chest X-ray. After multivariable adjustment, the protective effects of IPT (risk ratio [95% CI] of children were 0.15 [0.07-0.32] among children with no symptoms; 0.29 [0.12-0.73] among those with ≥ one symptom, and 0.16 [0.05-0.52] among children abnormal chest films.

Conclusions: The efficacy of isoniazid preventive therapy against TB did not vary among TB-exposed children with levels of risk for undiagnosed TB. Our findings suggest that broadly implementation of preventive therapy may be effective against incipient or subclinical TB.

EP-05-142 Continuum of care in paediatric close contacts of TB cases in Peru, 2016–2018

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Background: Children <5 years old who are close contacts of tuberculosis (TB) patients are at high risk of developing active TB. There is an implementation gap in the continuum of care of TB contacts. We describe the continuum of care for <5 years old from the Peruvian national electronic TB register (Sistema Gerencial TB-SIGTB) for 2016-2018.

Design/Methods: The SIGTB has reached nationwide coverage since its implementation in 2016. We report contacts <5 years old eligible for isoniazid preventive therapy (IPT) (defined as those exposed to a drug-susceptible pulmonary TB index case, and who did not have clinical or radiological criteria of active TB), those with an IPT prescription, those starting IPT and those completing the six-months course of IPT. We also report those with active TB at baseline or during follow up.

Results: There were 18,814/211,383 (24.3%) contacts <5 years old registered in the 2016-2018 period. The number eligible for IPT were 4123, 4388 and 4851 in 2016-2018, respectively. The figure shows the continuum of care for the study period.

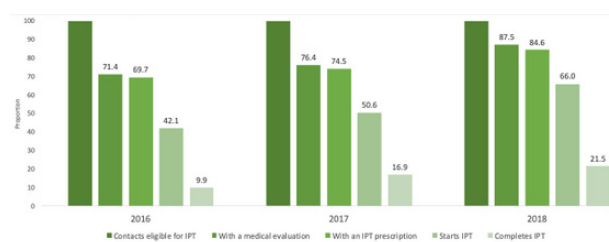


Figure. Continuum of care of close contacts <5 years old registered in the Peruvian tuberculosis electronic register, 2016-2018.

Out of all contacts <5 years old, active TB was detected at baseline or during follow-up among 1.7% (68/4123), 2.0% (86/4302) and 2.8% (137/4892) for 2016- 2018, respectively.

The proportion with active TB among those that started IPT was 0.5% (8/1735), 0.4% (9/2212) and 0.5% (16/3195) in 2016- 2018, respectively. While the proportion with active TB among those that did not start IPT was 2.5% (60/2388), 3.5% (77/2176) and 7.3% (121/1656) in 2016- 2018, respectively.

Conclusions: Data from TB routine surveillance provides valuable information to monitor TB interventions. Coverage of IPT among TB contacts under five years old in Peru is increasing steadily, though large gaps still exist in all steps, especially IPT completion. Shorter regimens and stronger counseling could address this gap.

EP-05-144 Programmatic roll out of 3HP, a new TB preventive option in Mozambique

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Background and challenges to implementation: 3HP is a combination of rifapentine and isoniazid administered weekly for three months. 3HP is a shorter regimen, associated with less adverse events than the isoniazid-based regimen, leading to better adherence and completion rates.

Fundação Aurum leads the IMPAACT4TB initiative funded by UNITAID in Mozambique, promoting the use of 3HP in partnership with the Ministry of Health. In Mozambique, the National TB Program published the National Policy for Latent TB Treatment at the end of 2020, and 3HP is recommended as the first option for people living with HIV and children between 2 and 15 years of age who are contacts of a confirmed case of TB.

Intervention or response: IMPAACT4TB aims to catalyze the roll out of 3HP within the TB and HIV national programs in Mozambique. Launched on March 24th 2021, administration started immediately in health facilities of Maputo City, Chokwe and Mandlakazi districts in the province of Gaza. In parallel with delivery at sites, IMPAACT4TB will conduct a prospective, multicentric and observational evaluation to describe implementation challenges and successes in order to guide 3HP scale up. Mozambique is the first country in the world to use 3HP in fixed-dose combination in routine care.

Results/Impact: 414 patients have started 3HP in 44 health facilities so far, out of which 74 are children. No side effects have been reported, while it is too soon to report on treatment completion rates.

As of end of April 2021, main health partners as Global Fund and PEPFAR are committing funds to purchase and import 3HP into Mozambique.

Conclusions: Prevention of TB through treatment of latent TB is an important part of the global fight against TB. The adoption of therapies facilitating treatment adherence and completion will be essential to achieve the objectives of the End TB Strategy.

EP-05-145 Impact of contact investigation on isoniazid preventive therapy in children under five in Afghanistan

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Background and challenges to implementation: The National TB program (NTP) of Afghanistan implemented the strategy of active household contact screening of all bacteriologically confirmed TB index cases since 2014. The aim of this abstract is to share the experience of contact screening in a routine program set up.

Intervention or response: NTP implement the active contact screening National wide, which included screening of TB index case contacts through home visiting. Those with sign and symptoms of TB were referred to TB centers for diagnosis. Children under five years of age without sign and symptoms of TB were started Isoniazid Preventive Therapy (IPT).

Results/Impact: From the total of 741,967 contacts screened for TB between 2014 and 2020, 141,327 (19%) were children under five years of age and 127821 (89%) were able to started on IPT. The contact screening volume increased progressively and the IPT coverage was also increased parallel (Table1). The average IPT completion rate was 78%.

Conclusions: Conclusions and key recommendations: The IPT coverage is very high for children and the completion rate is also high as compared to the global report. The active contact screening is good approach for IPT and IPT adherence.

EP-05-146 Acceptability and feasibility of TB screening in household child contacts and preventive therapy management in Cameroon and Uganda

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Background: In high-burden countries, the uptake of tuberculosis (TB) child contact screening and tuberculosis preventive therapy (TPT) is limited by the necessity to bring children to the facility. In preparation of a study evaluating a community-based intervention in Cameroon and Uganda, we conducted a qualitative assessment of the acceptability and feasibility of household child contact TB screening and TPT management.

Design/Methods: Twenty-four healthcare providers and community leaders were interviewed and 74 TB patients participated to 11 male and female focus group discussions in Cameroon and Uganda. The main topics of the discussions were TB knowledge, stigma, barriers to facility screening, acceptability and feasibility of a community-based intervention. Transcripts were coded and analyzed using ATLAS.ti 9.

Results: Transport cost and waiting time were the main barriers to facility screening reported by both patients and providers. Patients perceived household child contact screening by community health workers (CHW) to be convenient and helpful in ensuring their children access screening and TPT and in providing the opportunity to address other family health problems. Patients were worried about unintended disclosure by CHW and suggested use of unlabeled cars and no uniforms. They had no preference for the gender of the team, provided they are polite and clearly explain the purpose of the visit. Some participants were reluctant to screening beyond family members. From the providers' perspective, a community intervention is coherent with TB screening and TPT management and trusted CHW can perform the activities with proper training. Providers also highlighted the benefits of integrated community care. Both patients and providers insisted on the importance of visit preparation, including initial index case counseling.

Conclusions: Community-based child contact TB screening and TPT management is acceptable by patients and providers. The CONTACT cluster randomized trial is currently evaluating the impact of a community-based approach in the two countries.

Improving the care of TB contacts

EP-08-167 A comparative analysis of TB yield among contacts of drug-susceptible vs. drug-resistant TB patients in Nigeria

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Background: Oftentimes, contact tracing in Nigeria is focused on Index drug-sensitive TB (DS-TB) patients. Identifying and tracing close Contacts of patients with DR-TB could be a feasible strategy to achieve the goal of finding the missing TB cases. This study compared the yield of TB among Contacts of DR-TB with that of DS-TB Index cases in a routine program implementation setting.

Design/Methods: A comparative analysis of the TB yield among bacteriologically confirmed index DS-TB and DR-TB patients diagnosed in the preceding 2 years, whose Contacts were traced between December 2020 and March 2021 across 4 USAID TB-LON 3 supported States in South West Nigeria. GeneXpert was largely utilized for the diagnosis of TB among these Contacts.

Results: 3,348 index TB patients were included in this study. 3,323 (99.6%) were DS-TB and 25 (0.7%) were DR-TB index Cases. 13,717 and 110 Contacts were identified among the DS-TB and DR-TB patients respectively. 99.5% (13,648) of Contacts of DS-TB patients and 100% (110) of Contacts of DR-TB patients were screened for TB symptoms.

Presumptive TB yield from Contacts of DS-TB and DR-TB patients were 12% (1598/13717) and 27% (30/110) respectively. TB yield among DR-TB Presumptive TB Cases tested was 10% (3/30 - 2 DSTB and 1 DRTB) and among DS-TB Presumptive TB Cases tested was 7.6% (122/1598) while the overall TB yield (all forms) was 7.7%.

Type of TB	Index TB patients whose Contacts were traced	Contacts Identified	Index: Contact ratio	Screening coverage	Pre-sumptive TB Yield	Evaluation Rate	TB Yield
DS-TB	3,323	13,717	4:1	99.5%	12%	99.5%	7.6%
DR-TB	25	110	4:1	100%	27%	100%	10%
All forms of TB	3,348	13,827	4:1	99.5%	12%	99.5%	7.7%

Conclusions: The study has demonstrated a higher yield of presumptive TB and confirmed TB cases from Index DR-TB patients when compared with Index DS-TB patients. Although only 0.7% of total Index cases traced from this study were DR-TB patients, the high yield along the cascade highlights missed opportunities for finding both DS-TB and DR-TB among Index DR-TB Cases. There is therefore a need to scale up contact investigation among DR-TB patients in Nigeria and roll out strategies to address implementation bottlenecks.

EP-08-168 Tele-contact investigation and TB preventive treatment among household contacts of bacteriologically confirmed TB cases during the Covid-19 pandemic in the Philippines

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Background and challenges to implementation: When community transmission of COVID-19 was reported in March 2020 in the Philippines, enhanced community quarantine was imposed with most tertiary hospitals restructured as COVID-19 referral centers resulting in limited services for non-emergency care, including tuberculosis (TB). Jose B Lingad Memorial General Hospital (JBLMGH) became a COVID-19 referral hospital and discontinued intensified TB case-finding. Prior to COVID-19, JBLMGH did not conduct tele-contact investigation (tele-CI) for TB preventive treatment (TPT).

Intervention or response: To minimize COVID-19 impact on TB case finding, tele-CI and TPT were introduced in April 2020. Staff conducted tele-contacting, educating, and TB screening of household-members (HHM) of bacteriologically confirmed TB (BC-TB) cases and referred to JBLMGH to complete CI and TPT initiation. Virtual meetings with rural health units including orientation on tele-CI and TPT led to formation of a referral network with local government units (LGUs).

Results/Impact: From April 2020 to March 2021, households of 98 BC-TB index cases from JBLMGH were tele-traced, resulting in screening of 176 household members in 57 (58.2%) households. Among those screened, only 73.9% (130) underwent chest x-ray and were linked to Xpert MTB/Rif testing. Among them, 20.8% (95% CI: 14.2%, 28.8%) were diagnosed with active TB disease and 71.5% (95% CI: 63.0%, 79.1%, $p < 0.001$) had TB infection (TBI). Almost all with TB disease and TBI, 96.3% (95% CI: 81.0%, 99.9%) and 95.7% (95% CI: 89.4%, 98.8%) started TB treatment and TPT, respectively ($p = 1.0$). A dedicated TB team, robust tele-CI and collaborative and supportive LGUs facilitated the establishment of tele-CI and TPT services in JBLMGH. Tele-CI has been adopted in the country TPT roadmap (2021-2023) developed to improve contact investigation and increase TPT coverage.

Total number of BC-TB cases diagnosed who were tele-traced	98
Total number of households of BC-TB index cases accepted tele-contact screening in JBLMGH	57 (58.2%)
Total number of household members accepted tele-contact screening in JBLMGH	176
Total number of household members completed contact investigation (underwent symptom screening, CXR and Xpert testing)	130 (73.9%)
Total number of diagnosed as TB (all forms)	27 (20.8%)
Total number diagnosed as TB infection	93 (71.5%)
Total number started on TB treatment	26 (96.3%)
Total number started on TB preventive treatment	89 (95.7%)

Conclusions: These results prove that tele-CI can play a significant role in transforming TB services to adapt to challenging circumstances.

EP-08-169 Uptake of the 4-month rifampicin regimen among isoniazid-resistant contacts of index cases and their treatment outcomes

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Background and challenges to implementation: 4-month rifampin (4R) has been recommended as an alternative regimen for latent TB infection (LTBI). In Taiwan, 4R was provided only to the LTBI contacts who had isoniazid resistant index.

Intervention or response: 35,487 contacts with LTBI were enrolled from April, 2016 to December, 2019 and followed-up on until September, 2020. The demographics of index patients and contacts, treatment regimens

and outcomes were collected from the National TB Case Management System. Rates of completion and permanent discontinuation of treatment due to adverse event (AE) were stratified by regimens (4R; once-weekly rifapentine and isoniazid, 3HP; 9-month isoniazid, 9H). Hepatotoxicity was defined as glutamate-pyruvate transaminase level higher than 5 times of upper normal limit.

Results/Impact: Individuals received 4R comprised 5% of LTBI contacts in all age strata. The overall completion rate of 4R, 3HP and 9H were 88.6%, 85.6% and 79.6% ($p<0.001$). The rates of permanent discontinuation due to AE were lower among those received 4R than 3HP (6.8% vs. 10.1%, $p<0.001$). Hepatotoxicity was lower among contacts receiving 4R than 9H (0.3% vs. 2.4%, $p<0.001$) and no statistical difference was seen compared to 3HP (0.3% vs. 0.4%, $p=0.530$). A total of 3,011 LTBI contacts had isoniazid resistant index, but only 59.5% of them received 4R as the first regimen, while 4.5% received 3HP, 2.6% received 9H and 33.4% received no treatment at all. The uptake rate of 4R was higher among those aged younger than 65 years than 65 years and older (66.9% vs. 55.8%, $p<0.001$). After isoniazid resistance was diagnosed, 43.8% and 56.4% of those who took 3HP and 9H discontinued, respectively.

Conclusions: Although the completion rates and safety of 4R were acceptable, the uptake of 4R for LTBI contacts who had isoniazid resistant index was lower than 60%. Further analysis for the reasons of non-commencement of proper treatment is needed.

Design/Methods: Data of index TB patients registered between 1st January 2019 and 31st March 2019, and their contacts, were collected from TB and Contact registry in Lilongwe. A separate list of TB patients registered between 1st April 2019 and 31st March 2020 was compiled. Contacts were then searched from this list, to determine if any had developed TB after the 6 months follow-up.

Results: A total of 554 index cases were registered between the first quarter of 2019, with 1,118 contacts. Of the 1,118 contacts, 83 (7.4%) had developed TB within the study period. Among the 83, 16 (19.3%) had been diagnosed either upon immediate investigation or at 6 months follow-up, and 67 (80.7%) were diagnosed after 6 months – in other words, outside the CI. Furthermore, our results revealed that 6 months follow-up was not conducted for approximately half of the contacts (554/1,118). Yet, the proportions of those developing TB among those who did not receive the follow-up and those who declared not TB at the follow-up were similar (6.0%, 33/554 vs 6.3%, 34/544).

Conclusions: Overall, 7.4 % had developed TB among the household contacts, yet among them, only 19.3% were captured within the current contact investigation program. Innovative interventions are required to increase the participation rate of 6 months follow-up. Furthermore, more than simple symptom screening is required, to improve the case detection yield at the follow-up.

EP-08-170 Yield and effectiveness of TB household contact investigation in Malawi

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Background: Contact investigation is one of the key tools for early case detection of tuberculosis (TB). In Malawi, household contact investigation (CI) is conducted for all pulmonary TB cases. Follow-up symptom screening is further conducted after six months. However, to date, a detailed evaluation has not been conducted. We thus conducted a retrospective review of TB and Contact registry to determine the effectiveness and the yield of household CI in Lilongwe, Malawi.

EP-08-171 "They were very happy to find that I do not have TB...": home-based TB testing decreases health insecurities among household contacts in South Africa

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Background: Home-based TB testing advances identification of missed cases among household contacts (HHCs), in response to the high TB epidemic in South Africa. We sought to qualitatively understand acceptability and feasibility of home-based TB testing from the perspective and experiences of HHCs of TB index patients.

Design/Methods: As a qualitative sub-study embedded in a larger randomized study, a semi-structured interview guide was developed covering domains: TB educational content, GeneXpert machine, TB testing process, disclosure, confidentiality, household members, willingness to refer others, and home- versus clinic-based testing. Participants were tested using the GeneXpert machine (N=23) and household members who observed the testing (N=7). All interviews were conducted in their preferred language, and then audio-recorded, translated and transcribed into English for analysis. A constant comparison method was used to analyse the data to include developing causal pathways and matrices for review by research team members in order to confirm findings.

Results: Despite the novelty of home-based TB testing, many HHCs trusted the machine and believed the results by observing the testing process. Most participants felt that their confidentiality was maintained, ensuring comfort and the willingness to recommend home-based testing to others. HHCs expressed concern regarding their own health, health of household members and the community, acknowledging the gravity of the TB epi-

demic. Home-based testing was perceived as a tool to assist those who were "hiding the disease" or show reluctance to seek care; demonstrating how home-based TB testing using GeneXpert can alleviate household health insecurities.

Conclusions: Home-based TB testing is feasible and acceptable with HHCs demonstrating an understanding of TB exposure risks and community need. More research is needed to develop interventions to support linkage to care after home-based testing.

EP-08-172 The importance of tracing contacts of clinically diagnosed TB cases in high TB burden countries

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Background and challenges to implementation: Undertaking contact tracing around clinically diagnosed tuberculosis (TB) cases (smear negative) could assist with tracing initial infectious TB cases in households. In children with clinically diagnosed TB cases, reverse contact investigation could assist with tracing the infectious TB cases or index cases. We evaluated the yield of contact tracing in both bacteriologically and clinically diagnosed TB cases.

Intervention or response: Routine program data was collated from 250 health facilities from July-December 2020. Contacts of bacteriologically confirmed TB cases and clinically diagnosed pulmonary TB (PTB) cases were traced, documented, and screened; contacts were screened clinically for TB. Presumptive TB cases were evaluated for TB and the contacts of PTB cases were offered TB preventive therapy. The proportion of presumptive TB cases identified, screened, and evaluated to be TB cases among contacts were computed and compared (for bacteriologically confirmed and clinically diagnosed TB index cases) using the 95% confidence interval (CI).

Results/Impact: There were 1,946 bacteriologically confirmed PTB index cases and 1,347 clinically diagnosed index cases. The respective 4,888 and 2,606 contacts were traced around these index cases. About 5.3% (260/4,888) and 6.3% (163/2,606) presumptive TB cases were identified from screened contacts of bacteriologically confirmed and clinically diagnosed index cases, respectively. Around 2.0% (98/4,888, 95% CI: 1.96-2.05%) and 0.3% (7/2606, 95% CI: 0.26-0.34%) TB cases were

identified from contacts of bacteriologically confirmed and clinically diagnosed TB cases, respectively. The seven TB cases among clinically diagnosed contacts translate to 269/100,000 people.

Conclusions: Our findings show that TB cases that could have been missed were detected among contacts of clinically diagnosed TB cases.

While the focus of contact investigation should be around bacteriologically confirmed TB index cases; where feasible, contact investigation for contacts of clinically diagnosed index TB cases could be considered in high TB burden settings.

EP-08-173 The latent TB infection cascade of care at 86 treatment centres in Cambodia, 2020

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Background and challenges to implementation: Cambodia is one of the 33 high burden tuberculosis (TB) countries. While the TB incidence rate has declined significantly over the years, it was projected that 60% of Cambodians are infected with latent TB. The efforts to reach and treat persons with latent tuberculosis infection (LTBI) remain low.

We documented a community-based program to accelerate LTBI treatment in Cambodia.

Intervention or response: Community Mobilization Initiatives to End Tuberculosis (COMMIT) is a five-year USAID-funded project to improve access to TB services and reduce TB transmission. We described the LTBI cascade of care using COMMIT program data from 86 treatment centers between January and December 2020.

Results/Impact: In total, 499 persons diagnosed with pulmonary TB were identified, and their close contacts, including household members and neighbors (n=3378), were evaluated. Of which, 2589 (76.6%) were eligible for TB preventive treatment (TPT). Approximately half (55%) of those who were eligible for TPT initiated treatment.

The treatment regimens prescribed were 3HP: 12 weeks once-weekly isoniazid-rifapentine (n=218), 3RH: 12 weeks once-daily isoniazid-rifampicin (n=500), and 6H: 24 weeks isoniazid (n=713). To date, 401 persons have completed treatment, and 69 (15%) were lost to follow-up during treatment.

Conclusions: Community-based programs could increase TPT retention and treatment success. Nevertheless, the TPT uptake rate could be further improved. Hence, it is critical to understand the barriers and facilitators to TPT uptake, adherence, and the reasons for drop-outs at each step of the care cascade in refining and developing effective interventions.

EP-08-174 Programmatic management of TB preventive treatment among household contacts of TB patients in India: a pilot project supported by The Global Fund

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Background and challenges to implementation: India contributes about 26% of global tuberculosis (TB) cases annually. An estimated 40% of Indian population has latent TB infection (LTBI). World Health Organization recommends use of TB Preventive Treatment (TPT) in children (aged <6 years) and those with LTBI among household contacts (HHCs) of bacteriologically confirmed TB patients.

However, in India till 2019, the TPT implementation among child contacts was only about 40%. The NTEP envisages expansion of TPT to all HHCs with LTBI.

Intervention or response: Project Axshya, supported by The Global Fund undertook a pilot on programmatic management of TPT among HHCs in three districts of the state Maharashtra. Field staff visited houses of TB patients for line-listing HHCs. HHCs <6years, were initiated on TPT after excluding TB. The HHCs (aged ≥6 years) were screened for TB symptoms and those without symptoms were deemed eligible for IGRA testing using Quantiferon kits. Those positive for LTBI were initiated on TPT after excluding active TB. The demographic, clinical, and TPT care-cascade details were recorded by the field staff on EpiCollect5 with frequent quality assessments.

Results/Impact: The implementation was initiated in June 2020, and was affected by COVID19. During the period June 2020-March 2021, 1337 index TB patients were contacted, of which, 1284 were visited. Of the 5044 HHCs line-listed, 5041 were screened for TB symptoms (496 were <6years). About 2657 HHCs were tested for LTBI, 516 (19%) were IGRA positive. A total of 926 were initiated on TPT (including 491 <6years) of which 292 completed TPT till March 2021 (Table 1). Procuring IGRA testing services on field was one of the prominent challenges that hindered the implementation.

S.No	Care cascade indicator	June 2020 - March 2021
1	Number of index cases visited	1284
3	Number of contacts screened	5041
5	Number of IGRA tests done	2657
6	Number of IGRA positive	516
7	Number of IGRA positive put on TPT	468
8	Total child contacts eligible for TPT	491
9	Child contacts put on TPT	458
10	No. of chest X-rays	496
11	No. of those with abnormal chest X-ray	30
12	No. sent for TB confirmation (CBNAAT)	27
13	Number diagnosed with TB (clinical diagnosis 18+CBNAAT confirmed 1)	19
14	Total contact eligible for TPT (child contacts and adult contact)	964
15	Total contacts put on TPT as advised by the medical officer	926
16	TPT outcomes	TPT completion - 292 Loss to follow up - 5 Death - 1 Developed TB - 1 Discontinues TPT - 14

Table 1. LTBI care cascade indicators among household contacts of TB patients under Project Axshya, 2020

Conclusions: It is feasible to expand TPT for household contacts with adequate allocation of resources. Though there were no major challenges in identifying and symptom screening of contacts, the issues with IGRA testing need to be addressed.

EP-08-175 Operational research evaluation of an intervention for the diagnosis of TB (MIND-TB) in Kono District, Sierra Leone

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Background and challenges to implementation: Sierra Leone (SL) is one of the poorest countries globally. With an incidence of 298 per 100,000, is one of the 30 high-burden countries for tuberculosis with an estimation of 30% of cases undetected. Among those 40% are women. In Kono District, with a population of over 500,000, 11 facilities offer TB services and are connected through no or poor road infrastructure.

Most patients seek informal providers, easily accessible in their communities, as first points of care.

Intervention or response: Partners in Health in collaboration with the National TB program and CISMAT has developed a program to increase TB case detection in the district through Community TB screening engaging informal providers, household contact-tracing and screening through Community based program and facility-based TB case detection. The results were compared with case notifications in the control district Kailahun.

Results/Impact: From June 2020 to March 2021, 105,209 people were screened, 81,888 in the community, 21,382 in the facilities and 1939 through contact tracing. More than 50% were women. Among those 1948 were presumptive cases, 1640 from the community, 261 from facilities and 47 from contact tracing.

The number of tests done directly related to the intervention was 819 (42% of presumptive cases), 633 from the community, 159 from facilities and 27 from contact tracing. A total of 3681 tests were performed in the district.

Tuberculosis was diagnosed in 612 patients, 174 more than last year (40% increase). 99.5% started treatment. Kailahun as the control district found 503 cases in the same period of time, 132 less compared with last year.

Conclusions: The active case finding is a basic intervention to control tuberculosis in countries with a high burden of disease. The engagement of different health and non-health sectors in the community and facilities provides a multifocal approach and successful results.

EP-08-176 Determining the cut-off value of the tuberculin skin test for prophylactic treatment of TB infection in Eastern China

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Background: Students with induration diameter of Tuberculin skin testing (TST) ≥ 15 mm or blister who have contacted with active tuberculosis patient are recommended to have prophylactic medication. To confirm the cutoff of induration TST to increase the accuracy of TST of discovering students who needing to have prophylactic medication in school tuberculosis outbreak.

Design/Methods: TST and QuantiFERON-TB (QFT) Gold In-Tube test were administered to students who contacted with the confirmed tuberculosis cases in school. Using the QFT as the gold standard to determine the cutoff of the TST test.

Results: Overall, 1265 participants were screened of whom 136 (10.8%) were QFT positive and 827(63.4%) had an induration of TST ≥ 10 mm. Among 1265 students without adjusting of age and sex, the diagnostic value reached the highest when the induration diameter of TST was 11.25mm with a sensitivity and specificity 0.654 and 0.711, respectively. After adjusting for age and sex by Logistic regression, the diagnostic value reached a

peak with the sensitivity and specificity 0.793 and 0.630 using the induration diameter of 10.00 mm. Area under the curve was 0.742(95% CI: 0.699-0.784, $P < 0.001$).

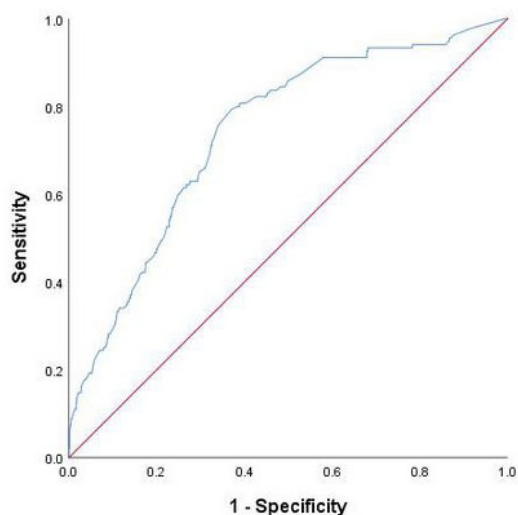


Figure 1. Receiver operator characteristic curve of Tuberculin skin testing.

Conclusions: This study revealed students who had contacted with active tuberculosis case in a school tuberculosis outbreak needed to have more examination like interferon- γ release assays to confirm whether they need to have prophylactic medication.

Towards better TB service delivery

EP-10-186 Comprehensive TB preventive treatment using multiple regimen options

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Background: Tuberculosis preventive treatment (TPT) is a pillar of tuberculosis elimination. In Vladimir City, Russian Federation, we implemented a program to provide TPT to all persons at high risk for TB, including persons exposed to MDR-TB and XDR-TB.

Design/Methods: Between January 2019 and December 2020, we identified three groups known to be at high-risk for TB: (1) close contacts of TB patients, (2) homeless individuals, and (2) people living with HIV. All underwent clinical examination, TB skin test, and chest X-ray. Those diagnosed with TB disease initiated treatment. Those in whom TB disease was ruled out were offered TPT with 3-month weekly isoniazid-rifampentine (3HP), alternative regimens: 6-month isoniazid (6H), 3-month isoniazid-rifabutin (3HRb), 4-month rifampicin (4R), unless they were exposed to either MDR-TB or XDR-TB. Those exposed to XDR-TB were offered bedaquiline, while those exposed to other forms of MDR-TB were offered moxifloxacin. We assessed the proportion of individuals completing each step: TB evaluation, TPT eligibility, TPT prescribed, TPT initiated, TPT outcome, and TB-free after one year.

Results: Of 3,861 individuals identified, 3,830 (99.2%) completed a TB evaluation; 24 (0.6%) had TB disease. 603 (15.7%) were eligible for TPT, of which 413 (68.2%) were prescribed TPT and 406 (98.3%) initiated TPT. 296 (73.8%) individuals completed at least 85% of prescribed doses. One-year after evaluation, 655/657 (99.7%) of individuals remained free of TB disease (Table 1).

Number of individuals	3HP	3HRb	4R	6H	4Mxf	3Bdq	Total
Initiated treatment	256	22	22	55	30	21	406
Completed treatment*	194 (75.8%)	12 (54.5%) P=0.03	15 (68.2%) P=0.43	37 (67.3%) P=0.19	21 (70.0%) P=0.49	20 (95.2%) P=0.04	299 (73.6%)
Developed TB disease	0	0	0	0	0	0	0
Had TB drugs discontinued for any reason	61 (23.8%)	10 (45.5%) P=0.03	7 (31.8%) P=0.40	18 (32.7%) P=0.17	3 (10.0%) P=0.09	1 (4.8%) P=0.04	100 (24.6%)
Had TB drugs discontinued due to adverse events (lab findings, clinical decision)	27 (10.5%)	6 (27.3%) P=0.02	0 (0.0%) P=0.34	6 (10.9%) P=0.94	2 (6.7%) P=0.51	1 (4.8%) P=0.40	42 (10.3%)
Had TB drugs discontinued due to patient decision	34 (13.3%)	4 (18.2%) P=0.52	7 (31.8%) P=0.02	12 (21.8%) P=0.11	1 (3.3%) P=0.12	0 (0.0%) P=0.24	58 (14.3%)

* Seven individuals remain on treatment

P-values reported are all in comparison to the 3HP group using chi-squared tests.

Table 1. TB infection treatment outcomes in 406 individuals receiving one of six regimens

Conclusions: Completion of a TB evaluation and TPT initiation were high. Gaps were identified in the other steps. This is the first use of bedaquiline for TPT in a program setting. Safe and effective TPT regimens can be designed for all known contacts, regardless of the drug-

susceptibility profile of the purported infecting strain. Results will support the development of national guidelines for TPT in Russia and beyond.

EP-10-187 Impact of implementing universal drug susceptibility testing in the private sector in rural Bihar, India

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Background and challenges to implementation: Private practitioners are the preferred primary point of care for people with tuberculosis (TB) symptoms. In rural India, patients travel long distances to access private care providers located in the urban hubs. Physicians depend mostly on chest X-rays and interferon-gamma release assay tests to complete TB diagnosis in a single visit and they request seldom microbiological tests. This jeopardizes the quality of the TB diagnosis and knowledge of potential drug resistance.

Intervention or response: As part of a TB REACH wave 7 project we engaged 37 private practitioners from two urban hubs in Samastipur, Bihar to notify TB patients. The project focused on improving diagnostic practices by ensuring universal drug sensitivity testing (UDST) for all the notified TB patients. We organized continual medical education sessions to orient the doctors about national diagnostic protocols and offered support for microbiological diagnosis. Two sputum transporters transferred on-spot collected samples from private clinics to the centrally located CBNAAT laboratory. The laboratory ensured testing and reporting results within two days of sample collection.

Results/Impact: A total of 1673 TB cases were notified by 28 provider's clinics from January 2020 to March 2021. In the 1st quarter of the intervention period, only 11% of TB patients had a CBNAAT test of which 34% tested positive. This increased to 67% coverage a year later with a positivity rate of 66%. The project was also able to identify 27 Rifampicin-resistant cases in this period. Physician's interest and reliance on microbiological tests to reach a final diagnosis improved significantly.

Conclusions: Regular engagement with providers, provision of a sputum transport and referral network, and prompt testing and reporting can improve the diagnostic practices in the private sector TB care.

EP-10-188 Perceptions about community pharmacists-led interventions for TB care in Malaysia

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Background: Pharmacist is a highly trusted profession and plays a key role in management of health diseases. However, the role of community pharmacist in tuberculosis (TB) control and prevention is unknown, as this is primarily managed in government-run clinics. This study aims to explore community pharmacists' perception and readiness to support and contribute to TB management in Malaysia.

Design/Methods: This was a mixed-method study conducted in Malaysia. A set of 31-item self-administered questionnaire was developed according to the Consolidated Framework for Implementation Study. The questionnaire was validated for content and face validity, before being distributed to community pharmacists. Semi-structured interview was conducted to supplement quantitative data for congruency. Data collection and coding process continued until saturation was reached. Chi-square test and binary logistic regression were conducted to analyze quantitative data. Thematic analysis was used to organize qualitative data.

Results: A total of 127 participants completed the questionnaire, with another 15 respondents participating in the interview. Findings showed 68.5% of the pharmacists were willing to offer directly observed therapies (DOTs) at community pharmacies if possible. Pharmacists felt that providing TB DOTs at community pharmacies had multiple benefits as there was better patient-provider relationship, which may lead to better treatment adherence and outcomes. Nevertheless, they felt the need for a structured referral pathway for presumptive TB, educational reinforcement, multidisciplinary collaboration and public-private partnership, given these were currently non-existent in Malaysia. Some potential barriers identified include concerns over potential risk of infection at the premise and perceived stigma from customers that might affect revenue and profits.

Conclusions: Community pharmacists in Malaysia were enthusiastic in contributing to TB care, particularly in offering TB DOTs, acting as a referral point, and offering public education. To ensure successful implementation, support and trainings are needed, in order to fortify their qualification and confidence in TB control and prevention.

EP-10-189 Scaling-up of latent TB infection diagnosis and treatment among PLHIV in Taiwan from zero

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Background and challenges to implementation: Tuberculosis preventive therapy (TPT) has been recommended for decades for PLHIV but was not a routine care in Taiwan except TB contacts. An initiative of latent tuberculosis infection (LTBI) diagnosis and treatment was launched since 2019, engaging HIV care teams to provide patient-centered service of Directly observed preventive therapy (DOPT). A total of 33699 PLHIV survived in Taiwan at the end of 2020.

Intervention or response: The initiative was a Pay-for-performance (P4P) pilot program including incentives for PLHIV who received TPT and 33% (26/79) of HIV designated hospitals nationwide participated in this initiative with the LTBI testing coverage of 31% of PLHIV. The demographics, LTBI results, regimens and outcomes were collected from the HIV LTBI System. Rates of completion and permanent discontinuation of treatment due to adverse event (AE) were stratified by regimens (once-weekly rifapentine and isoniazid, 3HP; daily rifapentine and isoniazid, 1HP; daily 9-month isoniazid, 9H; daily 3-month isoniazid and rifampin, 3HR; daily 4-month rifampin, 4R).

Results/Impact: Among 10563 PLHIV enrolled, 594 (5.6%) were tested LTBI positive (0.8% with indeterminate results) from October, 2019 to December, 2020. There are 373 (63%) of aforementioned LTBI candidates started TPT and followed-up until March, 2021. Among those who started treatment, 204 (55%), 138 (37%), 27 (7%), 2, and 2 individuals received 3HP, 1HP, 9H, 3HR and 4R, respectively. The overall completion rates were 91%, 92%, 22%, 100% and 0% and the rates of permanent discontinuation due to AE were 1.1%, 1.3%, 0%, 0% and 0.3%, respectively. Before the treatment started, 5 patients were diagnosed as TB with the rate of 47/100,000.

Conclusions: LTBI testing and treatment for PLHIV with incentives made the P4P program scale-up smoothly. In 2021, we extend the initiative to another 16 HIV designated hospitals to cover 51% (42/83) of PLHIV under the achievement of 90-93-95.

EP-10-190 Reducing initial loss to follow-up among people with TB in Cape Town, South Africa

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Background: In 2019, only 58% of people who developed tuberculosis (TB) in South Africa were recorded in the routine TB reporting systems. In the Western Cape Province, South Africa, following a diagnosis of TB, patients are required to attend a primary health care facility (PHC) for TB registration, and for their TB treatment to be continued. Initial loss to follow-up (ILTFU) refers to patients who do not link to these facilities within 30 days of their diagnosis.

We aimed to estimate the impact of a health system intervention to reduce ILTFU amongst individuals with TB.

Design/Methods: We implemented a quasi-experimental study using an integrated Provincial Health Data Centre (PHDC). We identified all newly diagnosed TB patients in 2 sub-districts of Cape Town. In Khayelitsha we implemented an escalating approach to support the linkage of ILTFU TB patients using SMS reminders, phone calls and community care worker tracing. In Tygerberg we observed patient linkage to care following the standard of care. We compared ILTFU prior to (October 2018-December 2018) and during (January 2019-December 2020) the intervention period across both sub-districts.

Results: During the intervention period 16,636 people were diagnosed with TB in the two sub-districts. ILTFU decreased from 24.5% in the pre-intervention period to 20.4% in the intervention period. The observed relative reduction in ILTFU was greater in Khayelitsha (20.6%) than in Tygerberg (13.8%).

	Pre-intervention Diagnosed	Pre-intervention ILTFU	Intervention Diagnosed	Intervention ILTFU	Reduction in ILTFU
Khayelitsha sub-district	1222	235 (19.2%)	7972	1217 (15.3%)	20.6%
Tygerberg sub-district	1361	397 (29.2%)	8664	2178 (25.1%)	13.8%
Total	2583	632 (24.5%)	16636	3395 (20.4)	16.6%

Table.

Conclusions: Over a 2-year period ILTFU reduced by 17% using a PHDC data platform. With the additional support for linking patients to care, Khayelitsha sub-district had a 1.5 times greater reduction in ILTFU. The use of the PHDC by routine health services for the identification of all diagnosed TB patients should be scaled-up and existing efforts to support linkage to ongoing care could benefit from the efficient use of SMS, phone calls and community care worker tracing.

EP-10-191 Improving TB treatment coverage in Nigeria – is public–private mix (PPM) the missing link?

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Background and challenges to implementation: The World Health Organization's report of 2020 showed Nigeria is among the seven countries that account for more than 60% of the global gap between estimated incidence and the number of people diagnosed with TB and reported. Although Nigeria achieved 27% TB treatment coverage there is still an estimated 323,000 persons with TB not identified and not diagnosed. This paper aimed to demonstrate the potential and contribution of PPM to improving TB case finding.

Intervention or response: In July 2020, the USAID TB LON 1 & 2 project across 14 states engaged private for profit (Pfp) facilities, patent medicine vendors (PMVs) and community pharmacists (CPs) in a 'hub and spoke cluster model' to provide different levels of TB services from referral of presumptive TB clients to TB case management. The project embarked on improving capacity of health care providers, providing national recording and reporting tools and strengthened sputum specimen transport mechanisms. Data on TB screening cascade was collected and reported using a mobile CommCare App. A performance based incentive was established for all TB clients diagnosed, initiated and completed treated.

Results/Impact: A total of 302 Pfps and 1,834 PMVs/CPs were engaged. In the reporting period, a total of 546,569 clients were screened, of which 46,703 presumptive TB were identified and 35,829 successfully evaluated. Amongst those evaluated, 1,750 were diagnosed with TB and 1,602 were placed on treatment.

Figures 1 & 2: Contribution TB case finding by PPM across 14 states from April to December 2020:

Conclusions: Engaging care providers in public and private sectors should be an integral component of national TB strategies, to ensure everyone with TB is detected and appropriately treated. PPM initiatives should also ensure quality of TB care across all private providers meet international standards.

EP-10-192 Latent TB and active TB risk factors among socially marginalised citizens and social workers in Denmark

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Background: Denmark has a low tuberculosis (TB) incidence but studies among socially marginalized citizens in recent years found a TB prevalence of more than 2000/100.000 at population screenings suggesting a high degree of transmission in this group. Social workers are not routinely screened for TB although workplace exposure must be considered a risk.

The objective of this study was to compare the groups of employees at public facilities with socially marginalized citizens with regard to latent tuberculosis infection (LTBI) and other risk factors for developing TB.

Design/Methods: The study was designed as a cross sectional study. Study participation including interferon gamma release assay (IGRA) blood testing and a short interview covering TB risk factors (country of origin, smoking, homelessness and drug abuse) was offered to socially marginalized citizens undergoing screening for active tuberculosis and employees at the institutions visited for screening from May 2017 to November 2020. Prevalence of LTBI and TB risk factors in the two groups was compared using the chi-square test.

Results: In the study period 364 socially marginalized citizens and 89 employees were interviewed and screened with IGRA testing. In the groups of socially marginalized citizens and employees 68/364 (18.7%) and 3/89 (3.4%) respectively had a positive IGRA-test.

The risk ratio for LTBI in the employee group compared with the high-risk group was 0.18 (95% CI: 0.06-0.56). Among socially marginalized citizens 297/364 (81.6%) had one or more TB risk factors, while this was the case for 13/89 (14.6%) employees. See table 1 for detailed results.

	Socially marginalized citizens (n=364)	Employees (N=89)	Risk Ratio, (95% CI)	p-value
Country burden > 10/100,000/year*	187 (51.4%)	11 (12.4%)	0.24 (0.137-0.422)	0.0000
Homelessness	98 (26.9%)	0 (0%)	-	0.0000
Alcohol abuse	111 (30.5%)	0 (0%)	-	0.0000
Drug use	137 (37.6%)	1 (1.1%)	0.03 (0.004-0.21)	0.0000
Latent TB infection	68 (18.7%)	3 (3.4%)	0.18 (0.058-0.56)	0.0004
One or more risk factors**	297 (81.6%)	13 (14.6%)	0.18 (0.108-0.30)	0.0000

*TB burden in country of origin, **Participants with at least one of: country burden > 10/100,000/year, homelessness, alcohol abuse, drug use, or latent TB infection

Table. Tuberculosis risk factors.

Conclusions: The socially marginalized population had a high prevalence of LTBI and other TB risk factors and the prevalence was significantly lower among employees at public facilities serving the group of socially marginalized citizens. The prevalence of LTBI found among the employees was similar to the level in the general Danish population.

EP-10-193 Options for delivering isoniazid-rifapentine (3HP) for TB prevention in people living with HIV: interim analysis of the 3HP Options Trial

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Background: Scale-up of 12 weeks of Isoniazid-Rifapentine (3HP) as TB preventive therapy is imminent in many high-burden countries, including Uganda. There are few data on acceptance and completion of 3HP in the context of routine HIV/AIDS care in sub-Saharan Africa.

Design/Methods: The 3HP Options Trial is an ongoing pragmatic, randomized parallel trial comparing three optimized strategies for delivering 3HP (facilitated directly observed therapy, facilitated self-administered therapy, or an informed choice between the two using

a shared decision-making tool) to PLHIV receiving care at a large urban clinic in Kampala, Uganda. Here we report an interim analysis of the primary outcome, the proportion of patients who accept and complete 3HP treatment (≥ 11 of 12 doses within 16 weeks), aggregated across study arms.

We use Bayesian inference analysis to estimate the posterior probability that this proportion exceeds 80% in at least one study arm, which is a co-primary hypothesis of the trial.

Results: By April 1, 2021, 600 (36%) out of 1,656 planned participants were enrolled. 420 (25%) had exited the treatment period. Of these, 390 (92.9%, 95% Confidence Interval (CI): [90.0-95.1]) had completed treatment within 16 weeks. There was no variation by age, sex, or time on ART (Figure 1).

The probability that treatment acceptance and completion exceeds 80% in at least one study arm is 99.9%.

Secondary aggregated outcome proportions were high, with treatment acceptance at 99.8% (95% CI: [98.3-100.0]; n=419/420) and completion at 93.1%, (95% CI: [90.2-95.2]; n=390/419).

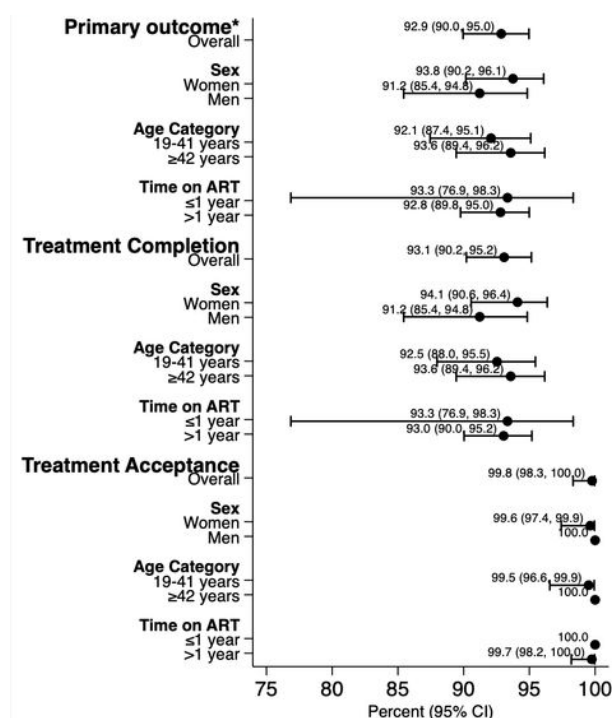


Figure 1. Outcome proportions, by sub-group. The forest plot shows the proportions and 95% confidence intervals of patients accepting and completing treatment (took at least 11 of 12 doses within 16 weeks of enrollment among those randomized; primary outcome), completing treatment (took at least 11 of 12 doses within 16 weeks of enrollment among those accepting treatment), and accepting treatment (took at least one dose of 3HP among those randomized), overall and by age, sex and time on ART.

*Accepting and completing treatment (≥ 11 of 12 doses within 16 weeks)

Conclusions: 3HP was highly acceptable to PLHIV in a high HIV/TB prevalence setting and can be delivered as part of routine HIV/AIDS care in manner that results in high levels of treatment completion. Data indicating 93% treatment completion and over a 99% probability of >80% completion in at least one study arm supports scale-up of 3HP as TB preventive therapy for PLHIV.

EP-10-194 Development and validation of a shared decision-making aid for choosing how to receive 3HP-based TB preventive therapy

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Background: Three months of weekly isoniazid-rifampentine (3HP) reduces TB incidence and mortality for people living with HIV (PLHIV). Shared decision making (SDM) may help PLHIV prioritize their values surrounding treatment preferences and make an informed choice between directly observed therapy (DOT) and self-administered therapy (SAT).

Design/Methods: We used human-centered design to identify treatment preferences and co-developed an 8-item decision aid tool. We administered the tool to PLHIV engaged in care at the Mulago AIDS clinic (Kampala, Uganda). Participants were asked to assign a weight (1-3) to each item (time, health worker interactions, side effects, travel time, stigma, work considerations, cost, and autonomy) and indicate their preference for SAT vs. DOT. We assessed item internal consistency using Cronbach's alpha (α), calculated the overall SAT-DOT difference score for each item per participant, associations between each item and final choice of SAT vs. DOT, and performed multivariate modeling to identify the subset of items most predictive of final choice. We performed ROC analysis to determine optimal cut-points for predicting final choice using full and abbreviated tools.

Results: The 8-item decision aid tool was administered to 158 PLHIV, of whom 39 (25%) chose SAT. The tool had good internal consistency ($\alpha=0.87$). For each unit increase in the weighted overall score, the odds of choos-

ing SAT increased by 44% (Odds Ratio: 1.44, 95% CI: 1.26-1.64, $p<0.001$). The model that best predicted participants' final choice included: time preference, side effects, and cost (c-statistic=0.97). Optimal cut points for weighted scores predicted SAT final choice with both high sensitivity and specificity for the 8-item (sensitivity 97.4%; specificity 92.4%) and abbreviated 3-item (sensitivity 94.9%; specificity 88.2%) tools (Figure).

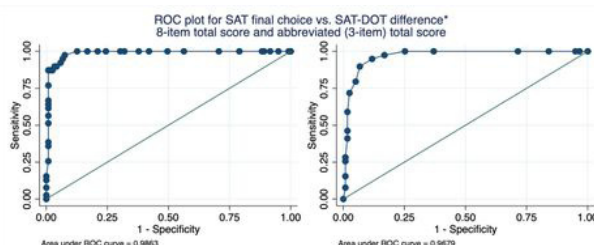


Figure. The left panel shows the ROC curve of the full 8-item decision aid tool. The right panel shows the ROC curve of the abbreviated 3-item decision aid tool, which included time preference, side effects, and cost.

*For each survey item, we calculated weighted preference scores for SAT and DOT by multiplying the importance weight (range: 1-3) by preference (DOT (1=yes/0=no) or SAT (1=yes/0=no)). Each item's weighted SAT and DOT scores can each range from 0-3. We then calculated the difference between each item's weighted SAT and DOT scores (SAT-DOT difference=SAT weighted score - DOT weighted score) and can range in value from -3 to +3. Negative difference values indicate preference toward DOT, and positive difference values indicate preference toward SAT.

Conclusions: A SDM tool can help PLHIV make a choice between SAT and DOT that aligns with their values and preferences around 3HP treatment.

EP-10-195 Risks associated with TB recurrence among former TB patients in five provinces of Vietnam

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Background: Recurrent TB episodes among former patients (FPs) is a serious challenge for eliminating TB in Vietnam. A better understanding of the risks of recurrent TB is required for Vietnam to benefit from early detection and treatment of FPs to contribute towards the goal of ending TB by 2030.

Design/Methods: Data were collected from mobile chest X-ray screening events in 5 provinces of Vietnam between June 2020 - March 2021. Out of the 3,633 people tested at these events, 990 (27.3%) self-reported previous treatment for TB. We excluded 102 FPs who reported taking anti-TB medication in 2020 or 2021, due to high potential risk of false-positive Xpert results. 888 FPs were included in the analysis. Data from the screening questionnaire were utilized for recurrent TB risk factors analysis, using a logistic mixed effect model.

Results: Among 888 FPs, 92 (10.36%) had a positive Xpert result. The odds of a positive Xpert result among FPs were 1.24 times (95% CI [0.96,1.60]) higher than that of the treatment naïve population tested. A multivariate model indicated that the factors associated with increased odds of having recurrent TB were: male (aOR = 2.34 [1.12, 4.90]), weight loss (aOR = 3.48 [1.85, 6.55]), fever (aOR = 2.32 [1.08, 5.01]), and last TB treatment 1-2 years ago (aOR = 4.31 [2.52, 7.36]).

Factors		Xpert(+)	Xpert(-)	aOR (95% CI)	p-value
Sex	Male	83 (11.9%)	614 (88.1%)	2.34 (1.12-4.90)	<0.05
	Female	9 (4.7%)	182 (95.3%)	Ref	
Weight loss	Yes	20 (26.0%)	57 (74.0%)	3.48 (1.85-6.55)	<0.001
	No	72 (8.9%)	739 (91.1%)	Ref	
Fever	Yes	13 (27.1%)	35 (72.9%)	2.32 (1.08-5.01)	<0.05
	No	79 (9.4%)	761 (90.6%)	Ref	
Years since last TX	1-2 years	44 (22.3%)	153 (77.7%)	4.31 (2.52-7.36)	<0.001
	2-5 years	18 (9.8%)	165 (90.2%)	1.43 (0.76-2.71)	0.27
	≥ 5 years	30 (12.8%)	478 (204.3%)	Ref	

Conclusions: As FPs are at higher risk of recurrent TB, they need to be prioritized for screening by Vietnam's National TB Control Program to reach the goal of ending TB by 2030.

This analysis can be utilized to target FPs for retesting, to prevent decline in their health, and to reduce community transmission of TB.

EP-10-196 Quantifying patient retention in the TB diagnostic cascade: the Diagnostic Cascade Evaluation (DiCE) toolkit

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Background: In 2019, the WHO estimated 73% of 440,000 incident TB cases in Nigeria went unreported. Patient loss along each step in the TB diagnostic cascade is difficult to quantify. The Excel-based Diagnostic Cascade Evaluation (DiCE) toolkit provides a straightforward approach to target cascade gaps for improved patient retention.

Design/Methods: DiCE was piloted at five high TB/HIV-burden sites in Benue, Nigeria, as the baseline and follow-up assessment tool for the Clinic-Laboratory Interface Continuous Quality Improvement (CLICQ!) program. DiCE assessments abstracted data along the TB diagnostic pathway from presumptive TB registers (point of entry), lab registers (TB lab), and TB treatment registers (TB clinic), including demographic and TB preventive treatment data. Aggregate-level sums were taken for the three months prior to each assessment and a random sample of patient-level data were collected for quality checks and various turnaround time calculations.

Results: DiCE assessments occurred in June and September of 2019. At baseline, the toolkit identified and measured cross-cutting gaps in specimen collection and referral across facilities which informed CLICQ! implementation. Through follow-up assessments, DiCE quantified a 40% increase (807 to 1,129) in the number of individuals with presumptive TB compared to baseline. The tool detected overall increases from 91% to 98% in the proportion of individuals with sputum collected and 80% to 98% in the proportion receiving Xpert MTB/RIF testing. Additionally, the number of individuals diagnosed with TB via laboratory testing and initiated on TB treatment increased by 20% (66 to 79) and 24% (80 to 99), respectively. DiCE also quantified drops in average time to treatment from 10.9 to 4 days.

Conclusions: The DiCE Toolkit measures discrete diagnostic cascade gaps for prioritization and targeted continuous quality improvement. The approach was incorporated into routine Ministry of Health monitoring and evaluation activities in Nigeria. DiCE offers a simple, adaptable approach for quantifying gaps in patient pathways.

TB hotspots

EP-12-207 Geographic distribution and predictors of delays in care-seeking among patients with presumed TB in Uganda

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Background: Delays to Tuberculosis (TB) care are associated to patient and health system untimely response. We sought to determine the geographic distribution and predictors of presumed TB patient and health system delays to diagnostic evaluation at referral hospitals of Uganda

Design/Methods: We conducted a secondary analysis of data from five referral hospitals in Uganda participating in a GeneXpert MTB/RIF implementation project. We described geographical distribution at sub-county level of presumed TB patients, care-seeking delays (≥ 21 days from onset of cough symptom to referral hospital presentation) and health-system delays (≥ 15 days from referral hospital presentation to acquiring results) in completing diagnostic evaluation, using Global Information System (Getis-Ord GI* statistic). We performed bivariate and multivariate logistic regression adjusting by referral hospital to identify predictors for both types of delays.

Results: Of 1602 adult pulmonary TB patients (median age 36; IQR 20), 719 (45%) experienced care-seeking delays and 1017 (63%) health-system delays. There were sub-counties of high concentration of presumed TB patients seen in sub-counties close to referral hospitals. However, there was no statistically significant clusters of care-seeking and health system delays across all five referral hospitals. Being married (OR 0.8, 95% CI; 0.68-0.92, $P=0.003$), living with HIV (OR 0.7, 95% CI; 0.56-0.97, $P=0.03$) and having noticeable weight loss (OR 0.7, 95% CI; 0.48-0.97, $P=0.04$) all reduced care-seeking delays. Seeking initial care at lower-level facilities (OR 6.5, 95% CI; 2.95-14.54; $P<0.0001$), illiteracy (OR 1.6,

95% CI; 1.17-2.04, $P<0.0001$), and having hemoptysis (OR 1.7, 95% CI; 1.18-2.58; $P=0.005$) increased health-system delays

Conclusions: Care-seeking and health-system delays were scattered geographically. Illiteracy and lower level facilities introduced further delays and interventions should focus on including all patients at all levels of health systems to reduce delays

EP-12-208 Identification of vulnerable areas for TB control in Ribeirão Preto, São Paulo, Brazil

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Background: Tuberculosis is one of the 10 leading causes of death worldwide, it is estimated that approximately one third of the world population is infected with *Mycobacterium tuberculosis*.

Design/Methods: Ecological study carried out in Ribeirão Preto, São Paulo, Brazil. The study population was composed of all TB cases notified TBWeb in the period from 2006 to 2017. Subsequently, the point density analysis was performed using the Kernel intensity estimator, generating a point density surface for the identification of areas vulnerable areas and classifying areas as “hotspots” or “coldspots”.

Results: The highest density of pulmonary tuberculosis cases was identified in the South and West districts, varying between 36 and 63.73 cases/Km² as well as for TB-HIV co-infection, with a variation between 10.42 to 17.24 cases/km². Regarding extrapulmonary tuberculosis, the South, West, North and Central districts varied from 9.39 - 14.95 cases/km², being classified as very high density, as well as tuberculosis in children, with a range from 3.11 to 5.54 cases / Km². Finally, resistant tuberculosis showed a higher density of cases in the Central, West and North districts, ranging from 1.15 to 1.87 cases/km² (Figure 1).

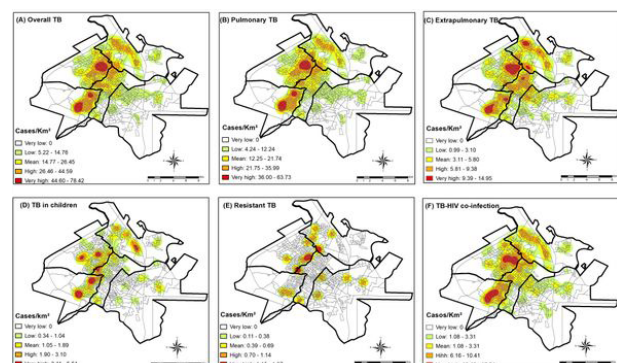


Figure 1.

Conclusions: It was possible to identify that there was no homogeneous distribution of TB cases in the municipality, with the highest densities of cases found in the North, South, West and Central districts.

Thus, this work sought to contribute to the identification of areas with a higher concentration of TB cases to support discussions and actions aimed at controlling and eliminating the disease, in addition to trying to assess changes that may have occurred over the period and that impacted growth or incidence decline.

EP-12-209 The contribution of hospital service delivery points to high TB yield: the TB-LON experience

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Background and challenges to implementation: Timeliness in case finding and proper case management plays a key role in halting the transmission of Tuberculosis (TB) infection, preventing disease complications and death.

The hospital based active TB case finding targeting hospital service delivery points to increase TB case finding has aided the search for missing TB cases and improved proper patient management.

Intervention or response: We initiated a hospital-based training of identified Ad-hoc staff and facility staff. Among Ad-hoc staff, a maximum of 5 to 6 Ad-hoc staff were appointed as data entry officers based on the number of monthly attendees recorded in a facility.

Data officers were further trained on the use of a mobile app called COMMCARE where patients screened, presumed, evaluated, and placed on treatment were uploaded and analysed.

Monthly meetings and weekly data submission aided the timeliness in data collection from all engaged sites. Follow-up Data Quality Assessment (DQA) visits were routinely done to ensure quality and improvement of data entry across all facilities.

We reviewed the contribution of hospital service delivery points to the total TB cases generated from October 2020 to March 2021.

Results/Impact: Results from a six months implementation showed that a total of 9,531,52 TB clients were screened of which 53,937 clients were presumed to have TB. Those successfully evaluated were 40,830(76%) resulting to 4,813 (12%) diagnosed TB cases. TB patients successfully enrolled on treatment were (4,310) revealing an enrolment gap of 10.5%. The cumulative TB yield among the total screened was 4.5% while TB yield among patients evaluated was 11%.

Conclusions: The institution of a targeted active TB case finding across hospital services delivery points has proven to be effective in finding missing TB cases within hospital settings. Scaleup of this initiative to all facilities both tertiary, private, and primary sites will address issues around low TB case-finding in Nigeria.

EP-12-210 Predictive modelling and spatial analysis of chest camp data for real-time location planning

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Background: With an estimated TB treatment coverage rate of 58% and ambitious notification targets to meet End TB goals, active case-finding (ACF) requires strategically selecting chest camp sites. Mercy Corps and Pakistan's National Tuberculosis Control Program (NTP) have partnered to conduct mobile TB ACF, and in recent years have collaborated with KIT Royal Tropical Institute and EPCON to optimize collection and use of data to increase case finding efficiency.

Design/Methods: While navigating COVID-19 lockdowns, Mercy Corps conducted mobile ACF using vans equipped with digital chest x-rays and CAD4TB software and sent sputum samples of individuals with presumptive TB for bacteriological examination. With KIT, EPCON and NTP support, in 2019 Mercy Corps digitized its chest camp data collection and fed these results into a Bayesian algorithm to predict local hotspots of missing people with TB. KIT complemented the predictions by spatially analyzing chest camp data to search for geographic patterns in TB positivity rates. Chest camp staff were interviewed regarding user acceptability and efficiency of the digital data collection process.

Results: Individual-level data were digitized for 253 chest camps conducted between April 2020 and March 2021, among which 258 bacteriologically positive and 653 all forms TB patients were identified. All chest camps were geolocated and mapped on an online visualization platform and analyzed for presence of spatial TB clusters ('hot-spots' and 'cold-spots') and outliers. Early results of the spatial analysis substantiated the predictions of the Bayesian model. These results and those of the focus group discussions will be presented.

Background and challenges to implementation: With one of the highest per capita estimated tuberculosis (TB) burdens globally and a large population with TB risk factors, achievement of adequate treatment coverage in Pakistan requires coordinated active case-finding (ACF) efforts.

Intervention or response: Mercy Corps conducted mobile TB ACF in close coordination with Pakistan's National TB Program (NTP) using vans equipped with digital chest x-rays and CAD software, collected sputum samples from individuals presumptive for TB on either verbal symptoms or radiographic abnormalities, and sent samples for bacteriological examination.

Together with support from KIT Royal Tropical Institute, EPCON and the NTP, starting in 2019 Mercy Corps digitized its data collection process and used predictive Bayesian modelling and spatial analysis to identify local hotspots of missing people with TB.

When and where possible amidst COVID-19 lockdowns, Mercy Corps staff visited or revisited these predicted hotspots with the objective of maximizing TB B+ yield.

Results/Impact: Data were collected electronically for 253 chest camps attended by 15,709 individuals, among which 258 bacteriologically positive (B+) and 653 all forms TB patients were identified.

All chest camps were geolocated and mapped on an online visualization platform and analyzed for presence of spatial TB clusters ('hot spots' and 'cold spots') and outliers. Recommended screening locations to increase case-finding yield were routinely shared with Mercy Corps staff.

Results will be presented on key aspects to the development of this novel method to monitor, evaluate, and steer case-finding in real-time.

Conclusions: A range of technological and operational specifications are necessary to implement this M&E and planning approach: digital tools must be fit-for-purpose; the Bayesian algorithm must be programmed with locally disaggregated and epidemiologically relevant indicators; results should be available promptly; and stakeholders should consider re-steering chest camp locations when evidence supports doing so.

EP-12-211 Where are the missed TB cases in Bangladesh? Addressing gaps in routine surveillance activities by linking prevalence survey and case notification data

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Background: Tuberculosis (TB) was the leading cause of death globally from a single infectious pathogen in 2019. To reduce this burden, the drivers that prevent people from accessing care each year, such as gaps in diagnosis and treatment initiation, must be better resolved. Fine-scale estimates of TB prevalence and case

notifications can be combined to identify priority-settings for strengthening routine surveillance activities in high-burden countries.

Design/Methods: We used a Bayesian spatial framework and data from the 2015-2016 national TB prevalence survey in Bangladesh to estimate prevalence at the second administrative unit (district). TB case notifications were used to calculate district-level prevalence-to-notification ratio, a key metric of under-diagnosis and under-reporting. We conducted a counterfactual analysis to estimate the number of additional TB cases that could be notified if each district reached at least the national prevalence-to-notification ratio.

Results: TB prevalence rates were highest in the north-eastern districts and ranged from 160 cases per 100,000 (95% Uncertainty Interval 80-310) in Jessore to 840 (690-1020) in Sunamganj. Despite moderate prevalence rates, the divisions of Rajshahi and Dhaka presented the highest prevalence-to-notification ratios, due to low case notification rates. Finally, the subnational counterfactual analysis showed that an additional 26,500 (8,500-79,400) people living with TB could be notified every year by reducing the prevalence-to-notification ratio in all districts to at least the national standard.

Conclusions: To our knowledge, this study is the first to produce subnational estimates of TB prevalence and prevalence-to-notification ratios in a high-burden setting. In the absence of reliable local indicators on TB incidence, subnational TB prevalence estimates are essential to target prevention and treatment efforts, while prevalence-to-notification ratios can support subnational need assessments for routine surveillance. Reaching people living with TB currently missing from care will be key to end the TB epidemic.

EP-12-212 Determining spatial heterogeneity of TB in a population with internal migration in China

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Background: The massive internal migration has been challenging the tuberculosis control progress in China in the past decades. Roughly 11 million (44%) of Shanghai's 24 million residents are internal migrants. We aimed to produce high-resolution spatial maps of tuberculosis risk and burden among migrants and residents in this setting.

Design/Methods: We collected routine surveillance data for all reported pulmonary tuberculosis (TB) cases in Shanghai between Jan. 1st, 2007 and Dec. 31st, 2016, and the national census data of each county in Shanghai. We used Kulldorff's scan statistical analysis to de-

tect temporal clusters of tuberculosis. The Moran' I and Getis-Ord G_i^* statistics were used to characterize TB overall and local aggregations.

Results: During the study period, the routine surveillance system reported 76,378 TB cases in Shanghai, among which 43% were among migrants, and 67% were male patients. Migrant TB patients were significantly younger than the urban residents (median age, 28 vs. 53). The temporal trends of TB notification rate in the population were consistent with that among internal migrants. The Moran's I analysis indicates a positive spatial autocorrelation of overall and migrant TB notification. Counties with high incidence also had a high population migration rate, and those counties with TB hotspots were overlapped with the residential aggregation of internal migrants--particularly the migrant labors.

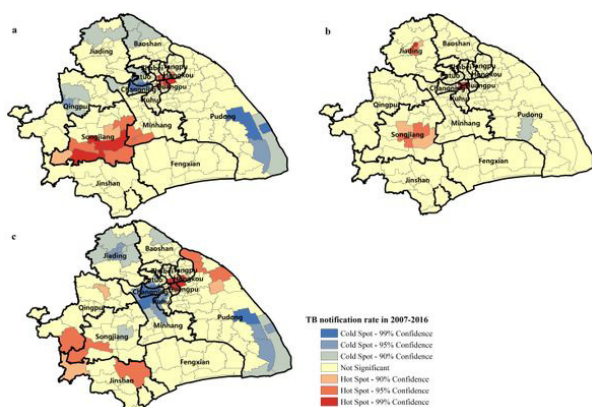


Figure 3. Getis-Ord G_i^* of TB notification rate at county level in Shanghai, 2007-2016. a, b and c illustrate the notification rate of annual average TB, migrant TB and resident TB, respectively.

Conclusions: Spatial analysis revealed striking geographic heterogeneity of TB in this mixed population. The spatial hotspots and aggregation of TB risk were consistent with the residential patterns of rural-to-urban migrants. Local transmission of TB could occur among the young migrant population and their Residential area. More aggressive and targeted interventions were needed to reduce the disease burden among migrants and residents in mega cities in China.

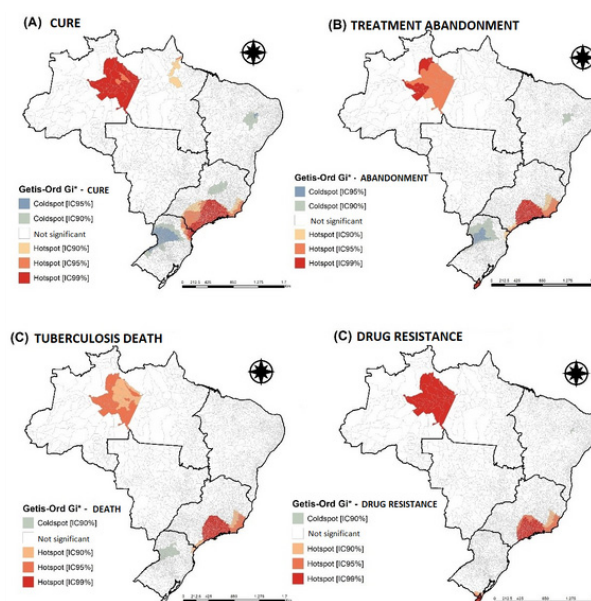
EP-12-213 Spatial analysis of TB treatment outputs, Brazil

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Background: Tuberculosis is an infectious disease, caused by the bacillus *Mycobacterium tuberculosis*. The objective of the study was to classify the temporal trend of tuberculosis cases whose outcome was cure, treatment abandonment, death and resistance and to identify areas with spatial association for these outcomes.

Design/Methods: Ecological study that used the cases of tuberculosis reported in Brazil between 2010 and 2018 and their outcomes: cure, abandonment of treatment, death from tuberculosis or drug resistance. To verify the spatial association of the outcomes, the Getis-Ord G_i^* technique was used considering the Brazilian municipalities as the unit of analysis.

Results: 785,988 new cases of tuberculosis were reported in Brazil in the period. In the analysis of the spatial association of the outcomes, it was possible to identify a similar pattern between the regions of the country, and the hotspots identified are mostly found in municipalities in the North and Southeast regions, indicating two regions of epidemiological importance for the control of the disease.



Conclusions: The results of this study contribute to the planning of actions for TB control programs at the local, regional and national levels. Monitoring areas with unfavorable outcomes in the treatment of tuberculosis becomes extremely relevant when the objective is to reduce the rates of the disease.

EP-12-214 Mapping national, sub-national and local prevalence of TB in Ethiopia: a geospatial meta-analysis

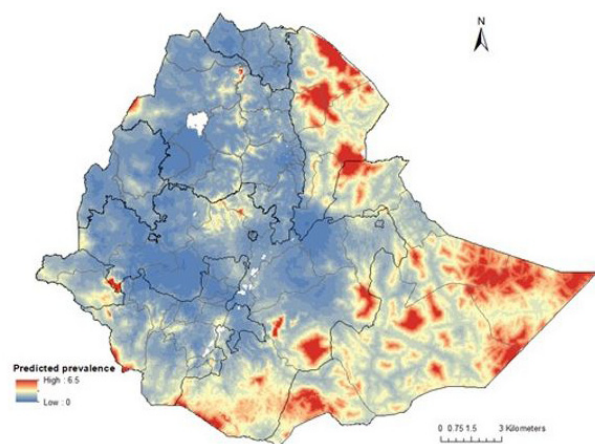
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Background: Reliable data on the prevalence of tuberculosis (TB) with sub-national estimates are scarce in Ethiopia. We address this knowledge gap by spatially predicting the national, sub-national, and local prevalence of TB, and identify drivers of TB prevalence across the country.

Design/Methods: TB prevalence data were obtained from the Ethiopia national TB prevalence survey and from a comprehensive review of published reports. Geospatial covariates were obtained from publicly available sources. A random effects meta-analysis was used to estimate a pooled prevalence of TB at the national level, and model-based geostatistics was used to identify geographical clustering of TB prevalence at sub-national and local levels.



Results: The overall prevalence of TB in Ethiopia was 0.19% (95% CI: 0.12%–0.28%). There was a high degree of heterogeneity in the prevalence of TB, which varied significantly by geographical locations, data collection periods, and diagnostic methods. The highest prevalence of TB was observed in Dire Dawa (0.96%), Gambela (0.88%), Somalia (0.42%), Addis Ababa (0.28%) and Afar (0.24%) regions. Nationally, there was a decline in TB prevalence from 0.18% in 2001 to 0.04% in 2009. However, prevalence increased back to 0.29% in 2014. Substantial spatial clustering of TB prevalence was observed at a regional level, with a higher prevalence observed in the border regions, and at a local level within regions.

The spatial clustering of TB prevalence was significantly associated with demographic and climatic factors such as long travel time to cities and low mean precipitation.

Conclusions: The results of this study showed a high prevalence of TB in Ethiopia, with significant spatial clustering observed at sub-national and local levels. Spatial patterns were associated with climatic conditions and demographic factors. These results suggest that targeted interventions in high-risk areas may reduce the burden of TB in Ethiopia.

EP-12-215 Using interactive voice response calls for improving TB self-referrals and identifying TB hotspots in selected districts of Pakistan

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Background and challenges to implementation: Pakistan is a high TB burden country, with an estimated 300,000 missing TB cases each year. The 2011 national prevalence survey shows that TB prevalence is higher in rural populations. There is limited knowledge about TB and limited or no access to TB care services among these communities.

Intervention or response: In order to create awareness about TB in general population, improve self-referral from the communities and to identify areas with potentially high numbers of presumptive TB cases, Mercy Corps (MC) disseminated key TB messages in native languages using IVR calls through a local telecom partner. The intervention reached to 300,000 users in rural areas of eight selected districts across Pakistan (October-December 2020).

Collectively there were three informative calls and two response calls, each followed by text messages. Each wave was of 30 seconds duration and were sent 3 days apart aiming towards the same user every time. In case the same users were unable to reach new users were added to bring a significant impact in the same community. The messages were disseminated to equal numbers of males and females, having high call concentration in central quintiles (age 20 - 40 years) and taper at both ends.

Results/Impact: The users who listened to the call farther than 30 seconds and recorded their opinion by pressing the options were considered as an informed impact of this intervention. 51,916 respondents identify knowing someone with TB symptoms. 119,415 respondents reported self-referrals or referring someone having TB related symptoms to the health facility.

Conclusions: The IVR calls followed by text messages can help in raising awareness, improving self-referrals and identifying hot spots to reach missing TB cases.

EP-12-216 Improving the effectiveness of hotspot analytics using the Early Warning Outbreak Recognition System (EWORS): a community-level approach

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Background and challenges to implementation: Community screening is one of the interventions implemented by KNCV Tuberculosis Foundation Nigeria. A major challenge of this intervention is selecting community(ies) where the missing TB cases significantly reside. To unravel this, InStrat uses ward-level information entered on electronic reporting system (Commcare) to map wards with potential epidemic outbreak (hot-spots). Though, these ward-level analyses seem helpful, they are not community specific. Finding significant missing TB cases would inevitably require a community-level approach.

Intervention or response: Five wards from 5 LGAs alerted as potential wards for epidemic outbreak were selected. In the first scenario, 3 of the 5 wards had 3 communities randomly selected, one from each ward. Screening was conducted in these three randomly selected communities. In a second scenario, 2 communities from 2 of the EWORS alerted wards were selected, guided by local data sourced from Program registers to determine communities with the highest frequency of TB cases, which were then prioritized for Community screening.

Results/Impact: Screening conducted in the first 3 randomly selected communities generated a presumptive TB yield of 12% and TB yield of 2%. In the second scenario of 2 communities that were selected using Program registers as guide generated presumptive TB yield of 47% and TB yield of 23%.

Conclusions: The yields for presumptive TB and TB cases for community screening guided by use of Program registers were 4 times and 12 times more than communities that were randomly selected respectively. For similar results replication, EWORS (hot-spots analyses) alerts should be subjected to filtering using local Program registers, and communities with the highest frequency of TB cases selected and prioritized for screening. Moreover, Commcare should be upgraded to capture communities, with scale-up for use in spoke sites. This will provide broader data for strategic decision making, using innovation demonstrated to be an effective strategy in finding the missing TB cases.

Global patterns in TB epidemiology

EP-13-217 Reasons for post-treatment TB disease recurrence and mortality in India: a systematic review

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Background: About 14% of patients who complete tuberculosis (TB) therapy in India may experience disease recurrence or death within 12–24 months of treatment completion. We conducted a systematic review to identify factors associated with TB recurrence or death after treatment completion in India.

Design/Methods: We searched PubMed, Embase, and Web of Science and queried experts to find studies published between January 1, 2000 and January 31, 2020 using search terms for TB, India, and recurrence. Two independent reviewers identified and extracted data from cohort studies that followed TB patients to identify factors associated with post-treatment disease recurrence or death. Studies assessing recurrence generally followed patients who had achieved treatment completion. Studies assessing mortality followed patients starting TB treatment into the post-treatment period. We report variables with statistically significant adjusted effect estimates (hazard, relative risk, or odds ratios) in association with these outcomes.

Results: Of 849 studies screened by systematic search, 13 met inclusion criteria. Factors significantly associated with higher adjusted risk of disease recurrence included: male sex, irregular medication adherence, drug resistance, current or past smoking, and worsening score on the St. George's Respiratory Questionnaire (SGRQ, a respiratory quality of life instrument). Factors significantly associated with higher adjusted risk of post-treatment mortality included: male sex, being ≥ 60 years old (vs. 15–44 years old), baseline weight ≤ 40 kg (vs. >40 kg), previous TB treatment history, smear-negative disease, loss to follow-up or failure during treatment (vs. cure or treatment success), higher baseline and time-updated SGRQ scores, smoking and alcohol use (vs. non-use of both), and being unemployed.

Conclusions: Post-treatment recurrence and mortality could potentially be reduced by addressing drug resistance, medication non-adherence, undernutrition, and smoking and alcohol use during TB therapy. Patients who are male, older, and have a previous TB treatment history may merit closer longitudinal follow-up during the post-treatment period.

EP-13-218 TB seasonality pattern in Ethiopia reversed during the initial Covid-19 report

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Background and challenges to implementation: Ethiopia reported the first COVID-19 case in early of March 2020. COVID-19 related restrictions in movement have a great potential to affect patient flow to health facilities that in turn may impact tuberculosis (TB) case notification and the seasonality in Ethiopia. The TB case notification has a seasonality pattern where April to June quarter is a peak period. We assessed TB case notification and change in seasonality immediately after COVID-19 in Ethiopia.

Intervention or response: From the national DHIS2 routine TB reporting system, we calculated the TB case notification from October 2018 to December 2020. The TB case notification was compared by quarter before and after COVID-19 and evaluated the effect on seasonality of TB observed in previous years.

Results/Impact: The proportion of decline of TB case notification during April-June of 2019 and 2020 was 24.5% (30,444 versus 22987). The quarter difference was 14.3% (29939 versus 25661) during July-September, and 8.0% (29049 versus 27288) during the October-December quarters of 2019 and 2020. The respective changes in notification pattern by sex and age in the quarter of April-June in 2019 versus 2020 were 0.9% (males=24.1% versus females=25%, p-value=0.19) and 0.5% (>14 year=24.5%, <14 year=25% p-value=0.23).

Conclusions: The expected peak in the TB case notification during April-June 2020 was dropped, indicating the noticeable change in the seasonality pattern of TB in Ethiopia. There was a one-fourth in the decline of TB cases during the peak quarter for TB notifications in Ethiopia immediately after COVID-19 report which might be due to decline in the patient flow to health facilities, TB service interruption or limited laboratory logistic supply due to the pandemic.

EP-13-219 TB mortality data from vital registration systems in Peru, 2017–2020

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Background: We describe tuberculosis (TB) mortality in Peru from 2017-20 as registered in the Peruvian vital registration system (SINADEF, acronym in Spanish), an electronic system using ICD-10 codes with open data. Coverage of the system is very high in Lima, the capital where a third of the population lives, and lower in other regions.

Design/Methods: We identified vital registers for deaths including TB as one of the six causes of death as text or as ICD-10. We excluded registers describing TB as a sequel. We also identified HIV diagnosis in death registers. To calculate TB mortality rates we used population projections from the national census. We analyzed mortality by year, sex, geographical location and standardized it by age.

Results: National mortality rates and characteristics are described in Table 1. In Lima in 2020, TB crude mortality rates in HIV-negative patients was 7.96/100,000, and 1.59/100,000 among HIV/TB; TB (all) age-standardized mortality rate was 9.22/100,000 and TB mortality rates per age group in years were 0.37/100,000 (<5), 1.48/100,000 (5-14), 5.70/100,000 (15-24), 8.96/100,000 (25-34), 7.80/100,000 (35-44), 9.05/100,000 (45-54), 15.89/100,000 (55-64) and 38.49/100,000 (65+); 734 (72.5%) TB deaths were among men and mean age was 52.5 (SD 22.7) years old. TB (all) age-standardized mortality rates per 100,000 population in Lima for 2017, 2018 and 2019 were 8.96, 9.54 and 9.39.

Indicator	2017	2018	2019	2020
N° of deaths	2061	2300	2363	2151
Men n (%)	1460 (70.8%)	1644 (71.5%)	1627 (68.9%)	1527 (71%)
Women n (%)	601 (29.2%)	656 (28.5%)	736 (31.1%)	624 (29%)
Age mean (SD)	53.4 (22.5)	54.0 (22.5)	53.7 (23.0)	52.2 (22.6)
HIV/TB crude mortality*	1.04	1.06	1.04	1.13
TB non HIV crude mortality*	5.44	6.09	6.23	5.42
Standardized TB mortality* (all)	6.99	7.65	7.65	6.77

*Mortality rates are per 100,000 population. TB= tuberculosis

Table 1: Tuberculosis mortality in Peru 2017-2020 from the vital registration system

Conclusions: TB mortality trends in Peru between 2017-19 need to account for expanding coverage of vital registration, while this does not affect TB mortality rates in Lima. Rates are within upper bounds of World Health Organization mortality estimates.

EP-13-220 The epidemiology of TB in Quebec, Canada, 1993–2018: tackling different epidemics

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Background: Canada has a low incidence of TB, estimated at 4.9/100,000 population in 2017. However, Indigenous and foreign-born persons were disproportionately affected, with TB rates 3-4 fold higher (21.5 and 14.7/100,000 respectively). Understanding TB epidemiology among key risk groups will enable better targeting of TB elimination efforts.

Design/Methods: We analysed all new TB cases reported in Quebec between 1993-2018. Persons with TB were stratified by ethnicity and country of birth [foreign-born (FB), Canadian-born non-Indigenous (CBNI), Canadian-born Inuit, and other Canadian-born Indigenous (CBI)]. Characteristics among FB, CBNI, and Inuit persons were compared.

Results: 6,941 new TB diagnoses were analysed [FB=4,082 (59%), CBNI=2,318 (33%), Inuit=389 (6%), CBI=111 (2%), unclassifiable=41 (0.6%)]. There were significant sex differences between FB, CBNI, and Inuit persons (male 54.0%, 62.0%, 59.9%, n=6,788, p<0.0001). Median age was also significantly different (median 38, 63, 18 years, p<0.0001). The proportion of extrapulmonary TB was highest for FB (29.2%, 16.4%, 1.8%, n=6,786, p<0.0001). Of those with culture-positive pulmonary/concurrent disease, Inuit persons were more likely to have smear-negative disease (45.6%, 36.6%, 66.4%, n=4,178, p<0.0001). Among culture-positive patients, FB and CBNI were more likely to have any drug resistance (13%, 12%, 2%, n=5,895, p<0.0001), however 46% of CBNI drug resistance was pyrazinamide mono-resistance. More than 80% of Inuit patients had a TB contact (2012-2018 data). Analyses of stratified annual rates are ongoing and will be presented.

Conclusions: TB epidemiology in Quebec over 25 years reflects three distinct patterns. FB persons were predominantly young adults, more likely to have extrapulmonary disease and drug resistance; CBNI persons were older, more likely to have pulmonary disease, with pyrazinamide resistance related to a known founder effect.

Inuit persons were younger with smear-negative pulmonary disease and known TB contact, suggesting ongoing community transmission.

These differences present specific challenges for TB prevention and care which need to be considered by health practitioners and policy-makers.

EP-13-221 Genetic composition and evolution of the prevalent M. tuberculosis lineages 2 and 4 in Chinese and Zhejiang Province populations

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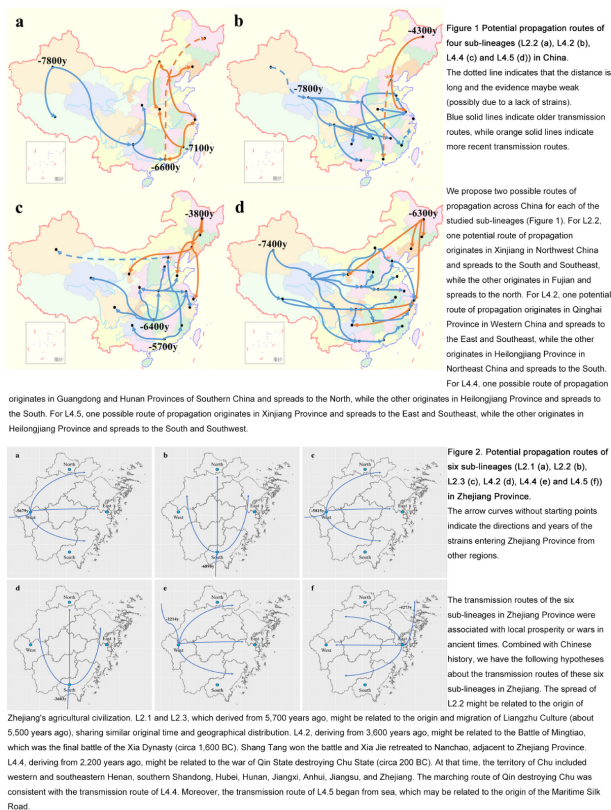
Background: There are seven human-adaptation lineages of Mycobacterium tuberculosis (Mtb). Tuberculosis (TB) dissemination is strongly influenced by human movements and host genetics. The detailed lineage distribution evolution of Mtb in Zhejiang Province is unknown.

We aim to determine how different sub-lineages are transmitted and distributed within China and Zhejiang Province.

Design/Methods: We analyzed whole-genome sequencing data for a worldwide collection of 1154 isolates and a provincial collection of 1296 isolates, constructed the best-scoring maximum likelihood phylogenetic tree. Bayesian evolutionary analysis was used to calculate the latest common ancestor of lineages 2 and 4. The antigenic diversity of human T cell epitopes was evaluated by calculating the pairwise dN/dS ratios.

Results: Of the Zhejiang isolates, 964 (74.38%) belonged to lineage 2 and 332 (25.62%) belonged to lineage 4. The distributions of the sub-lineages varied across the geographic regions of Zhejiang Province. L2.2 is the most ancient sub-lineage in Zhejiang, first appearing approximately 6897 years ago (95% highest posterior density interval (HDI): 6513-7298). L4.4 is the most modern sub-lineage, first appearing approximately 2217 years ago (95% HDI: 1864-2581).

The dN/dS ratios showed that the epitope and non-epitope regions of lineage 2 strains were significantly (P<0.001) more conserved than those of lineage 4.



Conclusions: An increase in the frequency of lineage 4 may reflect its successful transmission over the last 20 years. The recent common ancestors of the sub-lineages and their transmission routes are relevant to the entry of humans into China and Zhejiang Province. Diversity in T cell epitopes may prevent Mycobacterium tuberculosis from being recognized by the immune system.

EP-13-222 The yield of drug-resistant TB contact screening in three regions of Ethiopia

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Background and challenges to implementation: Tracing and screening the contacts of index tuberculosis (TB) cases is one of the globally recommended strategy for reaching the unreached TB cases and putting them on treatment. National TB program included contact screening around drug-resistant TB (DR-TB) index cases as one of the high impact interventions. We assessed the yield of TB among contacts of DR-TB in three regions of Ethiopia.

Intervention or response: To ensure roll-out of TB contact screening, the National Tuberculosis and Leprosy Program of Ethiopia led the training of health workers and the availing of recording and reporting materials to health facilities, with the support of partners. Using program level data collected via routine supportive supervision, we analyzed data from 20 DR-TB treatment initiation centers on contact screening covering July 2018-December 2020.

Results/Impact: A total of 203 DR-TB cases and 669 contacts were registered, and 92% (615/669) of registered contacts were screened for TB. Of those evaluated, 4.6% (28/615) were presumed DR-TB, and 89% (25/28) were tested using Xpert mycobacterium tuberculosis (MTB) complex/resistance to rifampin (RIF). The yield of DR-TB cases was 1% (5/615) among all screened while the positivity rate among presumptive TB tested for TB was 20% (5/25).

Indicators	#(%)
# of index DR TB cases whose contacts were screened for TB	203
# of contacts registered	669
# of contacts screened	615(92%)
# of presumptive TB cases identified	28
# of presumptive TB cases tested for TB	25(89%)
# of TB patients identified	6(5 DR TB)

Table: DR TB contact screening and its yield, July 2018-December 2020

Conclusions: DR-TB contact screening remains as a high-yield intervention that should be instituted to find missing TB cases.

EP-13-223 Epidemiology of isoniazid-resistant TB in Haiti

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Background: Isoniazid (INH)-resistant tuberculosis (TB) is the most common form of drug-resistant TB globally, yet little is known about its epidemiology. We retrospectively examined the epidemiology of INH-resistant, rifampin-susceptible TB in Haiti.

Design/Methods: GHESKIO, in Port-au-Prince, Haiti, is the largest TB treatment center in the Caribbean. Patients are diagnosed with TB based on clinical presentation, chest radiography and molecular testing (Xpert, Cepheid, Sunnyvale, USA). All Xpert-positive diagnostic sputum samples undergo culture with liquid media. *M. tuberculosis* (Mtb) culture isolates are archived per GHESKIO protocol.

Archived diagnostic Mtb isolates from patients with Xpert-positive TB between January 1 – June 30, 2017 were re-grown and tested for INH resistance with the Genotype *MTBDRplus* assay (Hain Lifescience, Nehren, Germany). Phenotypic drug susceptibility testing (DST) was performed on all isolates with molecular INH resistance and an equal number of randomly selected drug-susceptible isolates. DNA was extracted from all INH-resistant isolates and the subset of drug-susceptible isolates and shipped to the New York State Department of Health Mycobacteriology Laboratory for whole genome sequencing. Clinical and demographic information was extracted from the electronic medical record. Multivariate logistic regression was performed to identify risk factors for resistance.

Results: Between January 1 – June 30, 2017, 845 individuals were diagnosed with rifampin-susceptible culture-positive TB (Table 1). Prevalence of INH-resistant TB was 7.7% (n=65). In multivariate analysis, individuals < 20 years old had 2.4 times the odds of having INH-resistant TB compared to adults (p=0.014).

Sensitivity and specificity of the Genotype *MTBDRplus* assay in this population was 100% and 98.4% respectively. Of INH-resistant Mtb isolates, 69% had *katG*

Ser315Thr mutation and 28% had *inhA* C-15T mutation in the *mabA-inhA* promoter region. The most common spoligotypes identified among INH-resistant Mtb isolates were SIT 20 and SIT 53.

Patient cohort n=845 (%)	
Age	93 (11.0)
0 – 19	546 (64.6)
20 – 39	206 (24.4)
40+	
Sex	368 (43.6)
Female	477 (56.5)
Male	
HIV	111 (13.1)
Positive	734 (86.9)
Negative	
Antiretroviral regimen (if HIV positive)*	80 (94.1)
3TC+EFV+TDF	2 (2.4)
3TC+LPV/R+TDF	1 (1.2)
3TC+NVP+TDF	2 (2.4)
AZT+3TC+NVP	
AFB smear**	92 (10.9)
3+	374 (44.3)
2+	29 (3.4)
1+	333 (39.4)
Scant/negative	
Xpert semi-quantitative level	260 (30.8)
High	375 (44.4)
Medium	147 (17.4)
Low	63 (7.5)
Very low	
Episode of TB	746 (88.3)
First case of TB	99 (11.7)
Subsequent case of TB [^]	
INH resistance, by Genotype <i>MTBDRplus</i>	65 (7.7)
Resistant	780 (92.3)
Sensitive	

3TC: lamivudine; EFV: efavirenz; TDF: tenofovir disoproxil fumarate; LPV/R: lopinavir and ritonavir; NVP: nevirapine; AZT: zidovudine; AFB: acid-fast bacilli

* regimen unknown for n=26 patients

** missing=17

[^] includes relapse, reinfection, re-initiation of treatment due to LTFU

Table 1. Demographic and clinical characteristics

Conclusions: Prevalence of INH-resistant, rifampin-susceptible TB in Haiti is 7.7%. Adolescents are at high risk for INH-resistant TB.

EP-13-224 Molecular characteristics of Beijing genotype *Mycobacterium tuberculosis* strains isolated from patients with HIV-associated TB in the North-West of Russia

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Background: We aimed to study strains of *Mycobacterium tuberculosis* of the Beijing genotype in patients with HIV-associated tuberculosis, to compare the proportion of the Beijing genotype ancient sublineage in groups of tuberculosis patients with and without HIV infection in the North-West of Russia.

Design/Methods: We analyzed 105 strains of *M. tuberculosis* obtained from patients with HIV-associated tuberculosis living in St. Petersburg and the Leningrad region. All strains were genotyped at 24 MIRU-VNTR loci. Strains were assigned to the Beijing genotype and its clusters Beijing 94-32 and Beijing B0/W148 based on the analysis of specific markers: dnaA-dnaN :: IS6110, Rv2664-Rv2665 :: IS6110, and sigE98 SNP, respectively. MIRU-VNTR profiles were compared with the MIRU-VNTRplus database. The comparison group of HIV-negative TB patients included 403 previously studied strains from St. Petersburg and the Leningrad region in 1996-2020.

Results: Of the 105 strains isolated from patients with HIV-associated tuberculosis, 88 strains (83.8%) belonged to the Beijing genotype; 47 strains (44.8%) belonged to the cluster 94-32, 33 (31.4%) - to B0/W148, 8 (8.5%) - to the ancient Beijing sublineage. Genotyping of strains obtained from patients without HIV infection revealed 221 strains (54.8%) belonging to the Beijing genotype, of which 5 strains belonged to the ancient sublineage (1.2%).

Conclusions: Among the *M. tuberculosis* strains obtained from patients with HIV-associated tuberculosis, strains of the Beijing genotype prevailed, with almost half of all strains belonging to the Beijing 94-32 cluster, one third to B0, and others to the ancient Beijing sublineage. The proportion of ancient Beijing strains in the group of patients with HIV-associated tuberculosis significantly exceeded the proportion of ancient Beijing in the group of patients without HIV infection ($P = 0.0004$). This association is unexpected and warrants further pathogenomic study.

EP-13-225 Identifying TB “resistors” among case contacts in a prospective cohort study in Lima, Peru

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Background: A proportion of people are “TB infection resistors” as they remain uninfected despite ample exposure to *Mycobacterium tuberculosis* (MTB). We developed a prediction model to identify TB resistors using sociodemographic and clinical data from a cohort of TB patients and their household contacts.

Design/Methods: Between 2009 and 2012, we recruited 4,500 pulmonary TB patients and their 14,044 household contacts in Lima, Peru. We assessed twenty-nine variables that are potential predictors of TB infection based on *a priori* knowledge using a logistic regression model and a backward stepwise model selection algorithm. We then assessed the predictive probability of the model to identify household contacts who remained TST negative 12 months after a significant household exposure.

Results: After excluding household contacts with a previous history of TB disease or self-reported TST positivity in the past, we analyzed data on 8,635 household contacts of 2694 microbiologically confirmed index TB patients by developing a model to predict TST positivity by 12 months of follow-up. The final model included 13 statistically significant predictors with a C-statistic of 0.919. We then used this model to identify 71 household contacts who had predictive probability of 0.85 of becoming infected but who remained TST negative at 12-month follow-up.

Conclusions: Using a prediction model, we were able to identify TB-exposed individuals who were likely to become MTB infected but who escaped that fate. In future work, we plan to conduct a genome wide association study to identify potential genetic determinants of TB “resistor” status.

EP-13-226 A 30-year retrospective study of TB in New Brunswick, Canada

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Background: In 2017, 1,796 cases of active tuberculosis (TB) were reported in Canada, representing a 2.6% increase from the previous year. Although most cases occurred among foreign-born individuals, the importance of management and control of TB in Canada cannot be understated. According to the 2018 census data, New Brunswick (NB) had a population of 770,921. The Level 3 Laboratory at the Saint John Regional Hospital has maintained complete provincial records dating back to 1988.

This study focused on TB in NB to assess if more pertinent information that may not have been captured in previous national studies could be identified and leveraged to enhance the TB control program.

Design/Methods: This retrospective chart review examined the distribution of TB cases and *M. tuberculosis* (MTB) drug resistance patterns associated with cases among the seven health regions in NB from 1988 to 2018.

The study also appraised the provincial TB incidence rates of new or recurrent active TB cases to better understand the epidemiology of the disease in the province. Demographic data reviewed included the number of cases and mean age per year by region, recurrence rates, infection sites, and drug resistance patterns.

Results: A total of 311 cases of TB, including 118 males and 192 females (1 unknown), were identified during the study period, and mapped to each health region. The mean age of disease onset of the cases was 60.1 years old, with the majority (79.7%) having a respiratory infection site. The most common antibiotic resistance was to Isoniazid. Overall, the incidence rates of TB in NB during the study period closely matched national data trends.

Conclusions: Continuous monitoring of TB helps understand the incidence, prevalence, and spread of drug-resistance patterns of MTB and can facilitate the effective management, updating clinical guidelines, and evaluation of the TB program in NB.

EP-13-227 Spatial analysis and TB incidence in the Brazilian Eastern Amazon Region

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Background: TB is considered an old disease. Being a worldwide public health problem, and a major cause of death from *Mycobacterium tuberculosis*.

Design/Methods: Ecological study of spatial analysis and scanning statistics, carried out in Macapá-AP, with cases notified in the Notifiable Diseases Information System between 2001 and 2017. In order to identify vulnerable areas, classifying the areas in “hotspots” or “coldspots” and identify areas of risk.

Results: 1,730 cases were reported in the period. The highest densities of cases in the central region, in the neighborhoods: Perpétuo Socorro, Cidade Nova and adjacent areas, with a range from 70.67 to 88.33 cases per km². In this region are concentrated areas with low HDI. In the south central region, the Buritizal neighborhood and adjacent areas, with a range from 53.01 to 70.66 cases per km², where bridge areas are concentrated.

The other regions present cases, but with less density, ranging from 17.66 to 35.36 records per km². In the scanning statistics it was possible to identify three protection clusters, the AE1 (RR: 0.07; 95% CI: 0.01-0.48) in the South district; AE2 (RR: 0.23; 95% CI: 0.10 - 0.52) in the southern district of Macapá and AE3 (RR: 0.36; 95% CI: 0.20-0.59) located in the western district of the municipality.

A cluster of risk was identified - AE4 (RR: 1.47; 95% CI: 1.39–1.72) involving census sectors in the North, South and Center districts.

Conclusions: The identification of critical areas in the perspective of coping with the disease. Heterogeneous distribution, concentration in vulnerable territories, with a pattern of disease inequality in the territory. In the locations of the risk cluster, protection areas have been identified.

It must be analyzed by health surveillance teams, adopting strategies such as income transfer and / or compensatory policies, aiming to alleviate social inequality and its deleterious effects on the vulnerable population.

Take a deep breath 01

EP-23-318 Novel targeted cyclic voltammetric detection of TB-associated biomarkers in breath

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Background: Methyl nicotinate (MN) has been identified as a promising *Mycobacterium tuberculosis*-derived breath biomarker. To advance point-of-care detection of MN in complex breath samples, we designed a novel, point-of-care sensor device for gas phase cyclic voltammetry (CV) analysis.

Design/Methods: We enrolled patients with presumed TB at three health centers in Kampala, Uganda. Patient breath was collected in Tedlar® breath bags and introduced to a 1L chamber containing a cobalt functionalized TiO₂ nanotube (Co-TNA) sensor. A CV scanning from 0 to -2 V was collected from each patient. All patients underwent routine TB testing with sputum Xpert Ultra, and solid and liquid mycobacterial culture if Xpert Ultra-negative.

We compared the CV profile to positive and negative reference CV profiles of healthy breath spiked with and without.

Results: A total of 20 adult patients were included in the study, 9 with confirmed TB. Seventeen patients had breath results collected from two sensors, resulting in a total of 37 sensor results (21 from TB negative patients, 16 from TB positive patients). 11/16 (68.8%) patients with TB matched the positive CV profile, and 18/21 (85.7%) patients without TB matched the negative CV profile. There was concordance in 14[JD1] [SM2] [CW3] /17 (82.3%) of patients with two sensor results.

Conclusions: Gas-phase CV testing of MN using a point-of-care sensor could discriminate TB status, and has the potential to be used as a diagnostic tool. Ongoing breath collection can reveal unique CV profiles specific to MN to facilitate automated detection at the point-of-care.

Improvement in breath collection protocol, sample processing, and electrochemical methods are currently being explored to improve sensitivity and specificity.

EP-23-319 Algorithm modelling and detection of active pulmonary TB using a breath test via a real-time spectrometry

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Background: TB diagnostics are usually either inaccurate or too expensive and complicated for use. Exhaled breath test may diagnose tuberculosis through detecting volatile organic compounds (VOCs) produced by *Mycobacterium tuberculosis* and the infected host, which is an attractive option due to its non-invasive nature.

Design/Methods: In this cross-sectional study during 1 March 2020 to 30 September 2020 in a dedicated tuberculosis hospital in Shenzhen, China, we prospectively and consecutively collected breath samples from participants, stored them in customized bags and then directly detected by a real-time high-pressure photon ionization time-of-flight mass spectrometry (HPPI-TOFMS), which has a resolution >5000 and gives a result in a few minutes. Mass spectrum peaks with m/z <500 detected by HPPI-TOFMS and 31666 features were extracted. A dataset of confirmed pulmonary tuberculosis and healthy controls was extracted from the participants. Through a 7:3 randomization, the dataset was divided into a training set and a blind validation set. For the training set, a machine learning algorithm was used to build a diagnosis model of active PTB after 100 times of five-fold cross validation. Then we applied the model in the validation set to observe the performance. We repeated the randomization for 100 times and iteratively selected the optimal model.

Detailed Description

Inclusion criteria	Case group: (1) willing to participate in the study and sign informed consent; (2) 18 to 65 years old; (3) confirmed PTB by GeneXpert and/or culture, with suggestive clinical and radiological findings; (4) without initiation of anti-TB treatment before breath sampling. Control group: (1) willing to participate in the study and sign informed consent; (2) 18 to 65 years old; (3) without respiratory symptoms: cough, sputum, hemoptysis, shortness of breath, dyspnea or chest pain; (4) no pulmonary lesions by chest radiology, like chest X-ray or computed tomography (CT).
Exclusion criteria	(1) invalid results of VOCs; (2) history of TB; (3) extrapulmonary TB (EPTB); (4) concurrent NTM infection or other airway infection; (5) non-infectious chronic pulmonary disease, including chronic obstructive pulmonary disease, asthma, bronchiectasis, lung cancer, etc.; (6) if comorbidities (diabetes mellitus, liver diseases, kidney diseases, cardiovascular diseases, etc.) existed, hospitalized due to acute exacerbation of comorbidities in one month before breath sampling.

Table.

Results: Of 1398 participants, there were 338 confirmed PTB patients and 634 healthy controls, which were used to build the data set, from which we obtained an algorithm model with a $98.4 \pm 0.6\%$ sensitivity and a $98.4 \pm 0.5\%$ specificity.

Conclusions: Breath test via HPPI-TOFMS is simple, fast, non-invasive, inexpensive and accurate in differentiating active PTB from healthy controls, with a high sensitivity and specificity. Breath test with the algorithm model would be revolutionary for TB diagnostics. Further researches are ongoing.

EP-23-320 Diagnostic performance of the breath test for pulmonary TB when applied to clinical practice in China

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Background: TB diagnostics are usually either inaccurate or too expensive and complicated for use. Breath test may diagnose tuberculosis through detecting volatile organic compounds (VOCs) produced by *Mycobacterium tuberculosis* and host, which is an attractive option due to its non-invasive nature. We aim to validate a VOC model for diagnosing active PTB in the clinic setting.

Design/Methods: In this prospective cohort study during 1 October 2020 to 31 December 2020 in Shenzhen, China, we prospectively and consecutively collected breath samples from participants. Patients with active PTB, either confirmed PTB or unconfirmed PTB, and healthy controls were enrolled. Those with unconfirmed PTB were followed up for at least two months to confirm the treatment response. Exhaled breath samples were collected and then directly detected by a real-time spectrometry described before. We measured the diagnostic performance against a microbiological reference standard (MRS, including confirmed tuberculosis) and a composite reference standard (CRS, including confirmed and unconfirmed tuberculosis), respectively.

Results: Of 518 participants, there were 295 healthy controls and 323 patients with active PTB, including 119 confirmed 204 unconfirmed PTB cases. Using the microbiological reference standard, the sensitivity of VOC model was 92.1% (95% CI 83.9-96.5%; positive in 82 of 89 confirmed PTB), and the specificity was 87.6% (95% CI 84.0-90.5%; negative in 376 of 429 unconfirmed PTB and healthy controls). Against the CRS, the sensitivity of VOC model was 96.9% (95% CI 93.4-98.6%; positive in 216 of 223 confirmed PTB and unconfirmed PTB), and the specificity was 93.6% (95% CI 90.0-96.0%; negative in 276 of 295 healthy controls).

Conclusions: Breath test was accurate in differentiating active PTB patients from healthy controls. When using the CRS where microbiological methods became

less powerful, the performance was even better, with a higher sensitivity and specificity. These findings met the WHO target product profiles for diagnostic tests. Further researches are ongoing.

EP-23-321 Identification of breath volatile organic compounds in childhood TB

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Background: Non-invasive biomarkers for pulmonary TB have been identified through breath collection and analysis. There is limited understanding of the volatile organic compounds (VOCs) found in childhood TB.

Design/Methods: We prospectively enrolled children under 15 years old being evaluated for pulmonary TB in Kampala, Uganda. Children completed a standard TB evaluation with respiratory specimens tested for Xpert MTB/RIF Ultra and mycobacterial culture, and were followed for two months and classified as Confirmed, Unconfirmed, or Unlikely TB per NIH consensus definitions. Children provided 5-10 L of exhaled breath by blowing into a Tedlar bag with one-way valve or via a face mask connected to the bag. VOCs were concentrated with a Tenax tube, and gas chromatography-mass spectrometry (GC-MS) was performed.

Compounds were identified using the NIST library, and we evaluated the VOCs that were found in children with Confirmed or Unconfirmed TB, but not present in Unlikely TB.

Results: We collected breath from 62 enrolled children (6 with Confirmed TB, 22 with Unconfirmed TB, and 33 with Unlikely TB), with median age 3 years (IQR 1-6), and 7 (11.3%) were HIV positive. On average, 757 compounds (SD 186) were found per patient.

The most common compounds found in the collected breath among only children with Confirmed TB included 2-Norbornyl acetate (2/6, 33.3%), n-Pentadecanol (2/6, 33.3%), and Chloroacetic acid, nonyl ester (2/6, 33.3%).

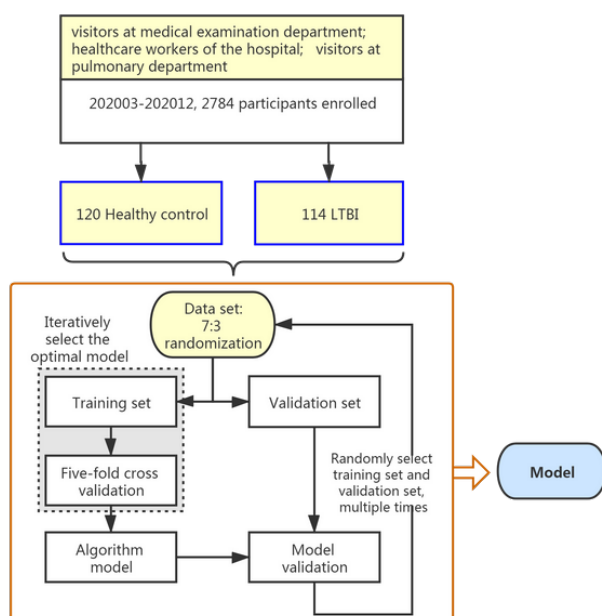
The most common compounds found in the collected breath among only children with Confirmed TB or Unconfirmed TB include Acetic acid ethenyl ester (6/28, 21.4%), 1-Hexadecanesulfonyl chloride (5/28, 17.9%), and 1,2-dimethylbutyl-Cyclohexane (5/28, 17.9%).

Conclusions: There were unique VOCs that are produced in children with Confirmed or Unconfirmed TB that were not found in children with Unlikely TB. Ongoing breath collection will investigate if these compounds can be used as non-sputum biomarkers for TB in children.

EP-23-322 Algorithm modelling and detection of active pulmonary TB with a breath test using real-time spectrometry

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Background: Approximately 33% of the world's population has latent tuberculosis infection (LTBI). Due to the paucibacillary characteristic of LTBI, there is no gold standard test now. Traditionally, either a tuberculin skin test (TST) or an interferon gamma release assay (IGRA) can be the detecting tool, but the application of them in large populations was usually hampered due to their repeat-visiting procedure or high cost.



Design/Methods: In this cross-sectional study during 1 March 2020 to 31 December 2020 in Shenzhen, China, we prospectively and consecutively collected breath samples from participants, stored them in customized bags and then directly detected by a real-time high-pressure photon ionization time-of-flight mass spectrometry (HPPI-TOFMS), which has a resolution >5000 and gives a result in a few minutes. Mass spectrum peaks with $m/z < 500$ detected by HPPI-TOFMS and 31666 features were extracted. A dataset of people with LTBI and healthy controls was extracted. Through a 7:3 randomization, the dataset was divided into a training set and a blind

validation set. For the training set, a machine learning algorithm was used to build a diagnosis model of LTBI after 100 times of five-fold cross validation. Then we applied the model in the validation set to observe the performance. We repeated the randomization for 100 times and iteratively selected the optimal model.

Results: Of 2784 participants, there were 114 LTBI cases and 120 healthy controls were matched, from whom we obtained an algorithm model to detect LTBI with a $98.0 \pm 1.6\%$ sensitivity and a $99.0 \pm 0.8\%$ specificity.

Conclusions: First in the field, we provide a biomarker other than TST and IGRA to distinguish people with LTBI and the non-infection, with a high sensitivity and specificity. The low metabolism of MTB during LTBI can be detected and breath test may contribute to the screening in large-scale populations. Further researches are ongoing.

EP-23-323 A trial of face mask sampling for TB in Conakry, Guinea, shows lower diagnostic sensitivity than sputum sampling for TB

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Background: The tuberculosis (TB) incidence rate in Guinea is estimated at 176/100.000 persons. About 28% of the estimated TB cases are not diagnosed. HIV-prevalence among TB patients is 25%. TB diagnosis mainly relies on sputum microscopy and GeneXpert MTB/RIF (Xpert) testing. We aimed to assess the added value of face mask sampling (FMS) for TB-diagnosis

Design/Methods: In a prospective study in adults with presumptive TB attending the TB reference centre in Conakry, supported by Damien Foundation, enrolled participants wore a surgical mask for 30 minutes during which they could breath, talk, cough or sneeze. Masks had a gelatine-like polymer membrane attached inside which was moistened with molecular grade water before sampling to facilitate aerosols capture. A direct sputum

sample was also collected. Paired samples were transported to the National Reference Laboratory. A trained technician performed acid-fast-bacilli staining on sputa and Xpert testing on mask and sputum samples

Results: From April 2019 to December 2020, 150/159 (94.3%) of presumptive TB patients accepted FMS, of whom 148/150 (98.7%) were included in the analysis while two (1.3%) patients with an error result on Xpert mask were excluded.

91.2% (135/148) of included participants were newly registered patients. Ninety (60.8%) patients were negative for both Xpert sputum and Xpert mask, 26 (17.6%) were positive for Xpert sputum and mask, while 28 (18.9%) were positive on Xpert sputum but negative on mask and only four (2.7%) were positive on mask while Xpert sputum was negative.

Conclusions: Although there is evidence that FMS may offer advantages for TB active case finding in South Africa, in our setting, this approach did not provide added value over the existing TB diagnostics strategies. However, there is a need to continue to explore how TB diagnostics could be improved in Guinea, especially for patients unable to produce sputum

EP-23-324 Infant Rhesus macaque model of TB and the presence of indoleamine 2, 3-dioxygenase

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Background: Tuberculosis (TB) is a disease caused by the bacteria *Mycobacterium tuberculosis* (*Mtb*) and is the cause of more deaths per year than any other infectious agent. Adult macaque models of TB have demonstrated that the suppression of indoleamine 2, 3-dioxygenase (IDO) reduced the bacterial burden and pathology in primary TB and increased host survival, but the role of IDO in the disease process in *Mtb* infected infants remains unknown.

Design/Methods: We recently completed our first attempt for aerosol-mediated *Mtb* infection in infant non-human primates (NHPs). These infant NHPs were followed using CBCs, blood chemistries, and flow cytometry to monitor the immune response during infection and after meeting end-point criteria, the infants were necropsied and tissue was collected for histology and immunohistochemistries.

Results: Our current data strongly support clinical findings in TB cases that young children are at increased risk of disease progression following primary infection.

We showed that TB symptoms in all 4 *Mtb*-exposed infants were more acute in onset, and they all had concurrent pulmonary and exclusively extrapulmonary TB (EPTB), which is distinct from adult NHPs infected with the same dose and the same strain of *Mtb* that had asymptomatic TB infection only.

More importantly, we also observed that, similar to adult TB NHPs, these TB infants presented with high levels of IDO expression in pulmonary granulomas colocalized within the band of epithelioid macrophages in the granuloma, suggesting inhibition of tryptophan metabolism via IDO blockade may enhance immune-mediated control of TB diseases.

Conclusions: Combined, we successfully established an aerosol infant model in NHPs that mimics clinical and bacteriological characteristics of *Mtb* infection as seen in human newborns/infants, which can be used to determine whether treatment with an IDO inhibitor will induce better formation of lymphoid tissues and increase the killing ability of macrophages leading to improvement of TB disease in pediatric host.

EP-23-325 Prevention of Mycobacterium tuberculosis-induced neutrophil necrosis restricts bacterial proliferation and could be used for host-directed therapy

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Background: Rising cases of multi drug-resistant tuberculosis require novel approaches to tackle the global tuberculosis epidemic including host-directed strategies. Neutrophils represent the main infected cell population in lungs of tuberculosis patients and are thought to drive pathology. We have shown before that clinical isolates of *M. tuberculosis* from different lineages of the *M. tuberculosis* complex induce necrosis of human neutrophils, a prerequisite for subsequent growth in other phagocytes like macrophages and dendritic cells leading, again, to host cell necrosis and release of a multiplicity of mycobacteria ready to infect new host cells. This scenario likely takes place in lungs of chronic active tuberculosis patients resulting in tissue damage and transmission of contagious aerosol particles.

Design/Methods: Primary human neutrophils, macrophages, and co-cultures thereof were infected with *M. tuberculosis*. We screened multiple inhibitors in their ability to reduce neutrophil necrosis and bacterial growth and examined cell morphology.

Results: We were able to interrupt this vicious circle of necrosis by pharmacological inhibition of myeloperoxidase (MPO) or scavenging of reactive oxygen species (ROS) by N-acetylcysteine thereby reducing neutrophil ROS production as well as necrosis and mycobacterial numbers in infected neutrophils, neutrophil-macrophage co-cultures, and whole blood assays.

Interestingly, ESAT-6-dependent *M. tuberculosis*-induced neutrophil necrosis could not be prevented by inhibitors of autophagy, necroptosis, ferroptosis, pyroptosis, and compounds that have been described to avert NETosis, such as inhibitors of neutrophil elastase (NE), histone deacetylases, peptide arginine imidases (PAD), and specifically PAD4 that citrullinates histone H3, the only known mechanistic premise to drive NETosis. However, *M. tuberculosis*-infected, dead neutrophils resemble the morphology of NETotic ones e.g., extracellular NET-like DNA associated with MPO, NE, and the pro-cathelicidin CAP-18.

Conclusions: Revealing the exact mechanism of neutrophil necrotic cell death is important to identify putative targets for host-directed therapies for tuberculosis as well as diagnostic markers for bed-side point-of-care testing to monitor therapy outcome.

EP-23-326 A clinical trial of oral N-acetylcysteine to replenish glutathione in TB

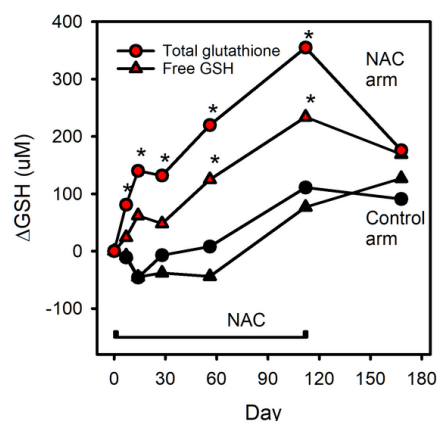
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Background: Sustained oxidative stress due to reactive oxygen species (ROS) predisposes to lung injury in TB. The oxidation/dimerization of glutathione (2GSH+O₂→GSSG+H₂O) consumes ROS but depletes GSH. Cysteine is required for GSH synthesis. This open-label randomized-controlled sub-study of the TB-SEQUEL trial examined if oral N-acetylcysteine (NAC) restores GSH and prevents lung injury (NCT03702738). This interim analysis examined effects on GSH.

Design/Methods: Patients were adults willing to provide written informed consent, with first episodes of pulmonary TB, sputum Xpert showing RIF-S and Ct≤27, chest X-ray showing moderate or far-advanced disease, lab safety parameters within specified limits, and, if HIV+, ≥100 CD4+ T cells/μL. Patients received standard TB therapy or that plus NAC 1200mg BID (NOW Foods) for days 1-112. The dose provides 5 times usual dietary cysteine intake. HIV+ patients not receiving ART began ART while on study. Oxidized glutathione (GSSG) and total glutathione (GSH+GSSG) were measured in whole blood samples using colorimetric kits (Arbor Assays). Free GSH was calculated as the difference between the measured values. Significance was determined by Mann-Whitney U test.

Results: An interim analysis included the first 88 patients. The average age was 34 yrs, 25% female, 29% HIV+, 51% far-advanced disease. GSH at baseline was

markedly low (217±148 μM). Baseline levels did not differ by HIV status, disease extent, or treatment. Levels remained low in controls, increasing only 127 μM by day 168. In contrast, significant increases in NAC recipients vs controls occurred by day 7 for total glutathione, and by day 56 for free GSH (stars). The maximal increase in GSH in NAC recipients (234 μM) occurred on day 112. GSH levels declined to levels similar to controls after day 112.



Conclusions: Oral NAC can help restore GSH in TB patients. The decline in GSH after stopping NAC may indicate sustained oxidative stress despite apparently successful treatment.

EP-23-327 BCG regulates the macrophage response to SARS-CoV-2 spike glycoproteins

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Background: Bacillus Calmette–Guerin (BCG) is an attenuated form of *Mycobacterium bovis*, used as a vaccine against non-pulmonary forms of tuberculosis (TB). The coronavirus disease 19 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, is a multisystem inflammatory disease elicited by dysregulation of the immune response leading to a cytokine storm. Severe COVID-19 patients have higher levels of pro-inflammatory cytokines.

Increasing evidence suggests that BCG vaccination may provide partial immunity against SARS-CoV-2 infection in TB-endemic areas. We aimed to study the effect of BCG on the inflammatory response of human macrophages for SARS-CoV-2 Spike glycoproteins.

Design/Methods: Human monocytic THP-1 cells were differentiated into macrophages with with phorbol-diester for 72 hours, and then exposed to BCG for 24 hours. Cells were then stimulated with various forms of the S protein. Activation of main inflammatory transcription factors *Nuclear factor kappa B* (NF-κB), and Interferon regulatory factors (IRFs) were assessed.

Results: We observed an increase in the activation of NF- κ B and IRF upon stimulation with all S proteins in cells pre-treated with BCG compared to untreated ones. This increase was evident after 24 hours of S protein stimulation, but it occurred earlier in the case of stimulation with an stabilized trimer of the S protein.

Conclusions: Our findings show that BCG can increase the activation of IRF in human macrophages. IRF activation leads to Type I IFN production, and an impaired Type I IFN activity is associated with worse clinical outcomes in COVID-19 patients. SARS-CoV-2 inhibits Type I IFN responses in infected cells, allowing an unchecked replication and triggering an exaggerated immune response which leads to major tissue damage. Further research is needed to elucidate the mechanisms of the immunotherapeutic effects against SARS-CoV-2 by BCG, so it could be as an adjuvant therapy for COVID-19.

No one size fits all - reaching out to key affected populations

EP-31-401 The "Ek Pahal" online TB awareness campaign among school children in India during the pandemic lockdown

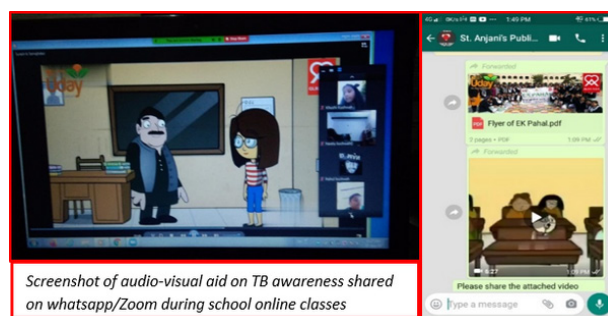
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Background and challenges to implementation: In 2020, with the entire world in the grasp of COVID-19, the project "Ek Pahal's" offline activities in Delhi and 4 districts of Uttar Pradesh in India halted. With a strict mandate to not undertake any physical interactive activities, schools across the nation started online classes for their students. Thus, the project's activities switched to the online mode to create awareness amongst students about TB.

Intervention or response: GLRA implemented diverse TB awareness activities in both offline and online modes during the lockdown to raise awareness amongst students about TB in coordination with schools of north India (Delhi and Uttar Pradesh). The GLRA team created IEC materials in digital format for the online dissemination of information. An in-house animation video was developed to educate students. It was shared with teachers who then circulated it amongst students during their online classes for enhancing awareness on TB,

WASH & COVID-19. The learning material was shared with students via WhatsApp groups and other online platforms employed by different schools. The teachers shared the relevant screenshots of WhatsApp and online platforms such as Zoom displaying successful dissemination of TB information to students. Online painting and essay competitions were also conducted.

Results/Impact: Under the Ek Pahal project from February 2020 to March 2021, a total of 1,34,046 students were sensitized by online mode for creating awareness about TB, WASH, and COVID 19 in schools of north India (Delhi and 4 districts of Uttar Pradesh). 80% (n=1,06,991) were sensitized through animation videos, online learning materials and 20% (n=27,055) through offline IEC activities.



Screenshot of audio-visual aid on TB awareness shared on whatsapp/Zoom during school online classes

Conclusions: During the pandemic when the lockdown came into effect, running an online campaign held greater importance for disseminating information about TB and continuing the awareness drive. The feedback from schools and children stated the effectiveness of the initiative and the scope of further scaling it up.

EP-31-402 Food insecurity and access to social protection for TB patients and their households in Cape Town, South Africa

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Background: Tuberculosis (TB) is a major health concern in South Africa. The disease predominantly affects those from lower socioeconomic strata but also puts patients and their families at risk of deepening poverty. The WHO End TB targets have an explicit goal of zero families affected by catastrophic costs as a consequence of TB. Social protection programmes have the potential to strengthen TB patients' and affected families' resilience and protect them from catastrophic costs. Such programmes have also been shown to improve treatment adherence and outcomes.

This study aimed to get a better understanding of the role of social protection and other forms of support in relation to the burden of TB on patients and their households in South Africa.

Design/Methods: This is a cross-sectional exploratory qualitative study using a phenomenological approach to focus on the lived experiences and perceptions of TB patients and healthcare workers. We interviewed 16 patients and six healthcare workers and analysed data thematically.

Results: The study found that TB patients' situation was inextricably linked with their households' situation. Participants reported a heavy physical burden, aggravated by a lack of nutritious food and that households could not provide the food they needed. Most patients received support from family, but their illness placed considerable strain on already stretched households. Those without family support had to regularly rely on charity to access food. While social protection is available to TB patients in South Africa through a Disability Grant, few participants accessed it and many reported challenges and high costs were incurred while trying to access it.

Conclusions: While TB patients and their households need support, few access state provided social protection. Alternatives to the disability grant, improvements in the assessment procedures, and considering entire households' situation when deciding grant eligibility, are recommended.

EP-31-403 A comparative analysis of TB policies and programmes in Tibetan refugee settlements in India and indigenous communities in Canada

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Background and challenges to implementation: Tibetan refugees in India and Indigenous persons in Canada are disproportionately impacted by TB. A comparative analysis of TB policies and programs in the two communities, which share similarities in historicities, may provide novel insight into tackling TB in the respective communities. Addressing the overlapping similarities in circumstances in these two communities will deepen the understanding of unique social and structural determinants of TB used to inform public health programmes. Furthermore, TB-related literature on these respective communities through a critical, social lens is lacking.

Intervention or response: To overcome the lack of socially critical literature on TB, a comparative analysis of TB policies and programs was taken on using an intersectionality approach. An intersectionality approach considers overlapping social categories that intersect to create and maintain social inequalities. Policies and programs were assessed in their capacity and dedication in integrating the social and structural determinants of TB.

Results/Impact: Policies and programs rarely integrate the social and structural determinants of TB in preventative measures. For both Tibetan refugees in India and Indigenous persons in Canada, forced displacement from traditional land, cultural discontinuity, consequent social and physical disconnection, and precarious (legal or Indigenous) status are major contributors to the prevalence of TB.

Conclusions: The results indicate that, in order for policies and programs to be effective in the respective communities, they must address structural and social determinants of TB. It is recommended that public health practitioners and programmes cultivate an in-depth understanding of the unique social determinants of TB in these communities. Social science inquiry into the parallels of their historicity and distinct approaches to reconciliation may lead to new and transferable approaches to tackle the structural determinants of TB in each community and other communities in similar circumstances.

EP-31-404 New distinctive integrated and sustainable health action to end TB among truckers and allied populations: an innovative approach in trans-shipment locations, India

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Background and challenges to implementation: WHO estimates 193 (132-266) new TB patients per 100,000 people amongst Indian population (*WHO TB burden 2019*) and about 12,000-18,000 TB patients may occur annually in 5-6 million Indian truckers. High mobility of truckers is a serious obstacle in the diagnosis of TB and initiation and continuation of treatment, increasing the risk of DR-TB (*Indian Journal of TB 2018, NACO India*). This was one of the key findings of GLRA's pilot project done in collaboration with Apollo Tyres Foundation at Delhi's trans-shipment locations (TSL).

Intervention or response: In May 2019, Nai DISHA (New Distinctive Integrated & Sustainable Health Action) project commenced under the slogan "On the road to end TB" for truckers, helpers, and allied populations in the three TSLs of Lucknow, Agra, and Jaipur. Various communication activities including one-to-one interaction between truckers/allied and counselors, canopy exhibitions, public announcements, group meetings, and awareness videos, were employed for creating awareness and identifying presumptive patients for screening, diagnosing, and initiating their treatment.

Results/Impact: During the period July 2019 - March 2021, the project reached 83,515 target populations, of which 81% (n=67924) were truckers and 18% (n=15591) allied population. A majority of the target population, 50,100 (43943 truckers, 6157 allied populations), were reached through interpersonal communication (IPC). 1624 presumptive were identified, of which 1048 (64%) were tested, 239 (15%) were provided symptomatic treatment and 337(21%) were pre-diagnostic loss to follow-up (PDLFU).

Out of 164 confirmed TB patients diagnosed, 161(98%) were initiated on DOTS treatment, and 49(83%) successfully completed their treatment amongst 59 patients whose outcome has been declared.

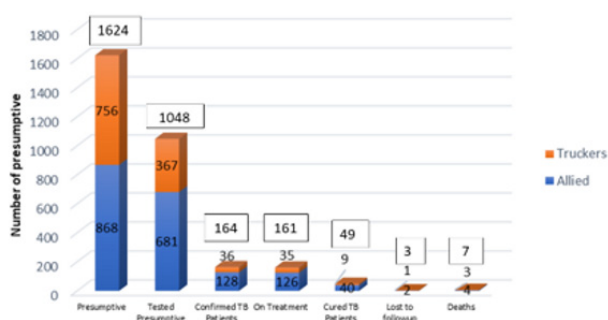


Figure. Treatment cascade: Truckers and allied population (July 2019 - Mar 2021)

Conclusions: Truck drivers are always on the move; hence, their diagnosis and treatment initiation gets delayed. Communication & screening activities amongst truckers and allied can help in early diagnosis of TB and treatment initiation who could have been undiagnosed and under-reported. Thus, the possibility of replicating this innovative intervention is being explored.

EP-31-405 Understanding TB care-seeking behaviour among employed men in Chennai, India: a qualitative research study

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Background: Delayed care-seeking for TB can enhance disease transmission and risk of death. Our 2018-2019 quantitative study in Chennai, India identified middle-aged, low-SEC, employed men who smoke and/or drink have the lowest TB care seeking rates and were most at-risk despite awareness of TB. To better understand specific enablers, barriers, and influencers of this target

group (TG), we conducted a follow-up qualitative study on their health attitudes, values, barriers in seeking care and preferred source of health information.

Design/Methods: Respondents were enrolled from 6 slums across Chennai based on the following criteria: men, age 30-50 years, employed with income upto INR 12000/month. 42 participants were interviewed via mini focus group discussions conducted on Zoom and digital ethnography interviews conducted on WhatsApp.

Results: Barriers for TB care-seeking included low risk perception for TB symptoms, stigma and inability to take time-off from work, while provision of convenient services was an enabler for early care-seeking. Low risk perception is likely driven by inability to connect early symptoms to TB and the normalization of symptoms due to unhygienic living conditions, occupational exposure and smoking. Despite a reported reduction in community-level stigmatization due to TB diagnosis, familial and self-stigma is still perpetuated by fears of disease spreading to vulnerable family members, particularly children. Using the Hofstede model, respect was found to be the central value for the TG. In addition to widespread use of traditional media, there was significant social media penetration among the TG that ranged from passive usage among older respondents to active engagement by younger respondents.

Conclusions: These results indicate a need for recalibration of TG's mental image of TB. Innovative, omni-channel communication strategy tailored for the TG with nuanced messaging to emphasize convenient services, build risk perception for early symptoms, address TB stigma in the current context and embed cultural values can achieve this.

EP-31-406 Barriers to accessing TB services in the Karamoja sub region, North Eastern Uganda: a gender, youth and social inclusion analysis

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Background and challenges to implementation: The Karamoja sub-region in North Eastern Uganda is a remote pastoralist region with a high TB burden which faces unique challenges in the delivery of and access to TB care services. We carried out a gender, youth and social inclusion (GYSI) survey to assess barriers to accessing TB care services.

Intervention or response: From 1st to 30th June 2020, we abstracted data from 24 high burden health facilities (HFs) across the nine districts of Karamoja sub-region.

In addition, we administered semi-structured interviews to nine district health officers and 24 health facility managers and carried out focus group discussions with 55 members of the community. Quantitative data was analyzed using Microsoft Excel and presented using counts and proportions. Qualitative data was coded and analyzed using nvivo software and presented according to emerging themes.

Results/Impact: The TB screening rate was 65% among men, 61% among women and 59% among children. TB care services were tailored to adults with minimal focus on adolescents and youth. Only 6 (25.0%) of the HFs surveyed had a workplan and budget for activities targeting gender and youth while 13 (54.2%) HFs integrated TB screening into adolescent and youth-friendly services. Main barriers to accessing TB care services included; low TB knowledge, preference for traditional medication, high TB stigma and high cost of accessing TB services due to long distances to HFs.

Barriers specific to women and youth included; having to seek for permission for hospital visits from men, inability to pay for transport fares to hospital and limited time for hospital visits due to home and childcare responsibilities.

Conclusions: Access to TB services in the Karamoja sub-region was influenced by various gender and socioeconomic barriers. Improving access to TB services across the region requires adopting programs to reach vulnerable segments of the population and mitigating the influence of TB stigma and cultural norms.

EP-31-407 Factors contributing to the spread of TB in rural areas, Ukraine

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Background and challenges to implementation: The burden of tuberculosis (TB) in Ukraine is unevenly distributed, and relatively prevalent among rural settlers. The aim of our study was to explore the experiences of TB patients with and health care providers pertaining factors that most influence the spread of TB in rural areas.

Intervention or response: Qualitative approach using phenomenology was employed to explore participants' experiences. In-depth Interviews were conducted in selected facilities - twelve (12) with regional TB doctors and primary health care specialists and sixteen (16) – with TB patients who are rural residents. We used questionnaire with list of possible factors that people in rural areas may encounter during TB diagnosis process. Respondents selected 5 main factors and ranked them in order of importance (Table 1).

Results/Impact: For patients, the most contribute factors to the spread of TB in rural areas were: inability to undergo all necessary procedures at the place of residence, remote location of medical facility. Health workers considered social factors to be the main ones: lack of funds, poverty, employment problems, irregular nutrition, poor living conditions.

The second most important factors among patients included: fears of prejudice, disclosure and loss job, breach of confidentiality, discrimination, lack of knowledge about TB, poor transportation, lack of funds to pay for some medical procedures. Medical workers to second rank included low level of patients' education and health literacy, alcohol abuse, labor migration.

	District TB doctors, paramedics, family doctors (N=12)	Patients (N=16)
* Healthcare workers and national experts selected 5 main factors and ranked them from 1 to 5 in order of importance, where 5 is the main factor. Patients chose 5 key factors and did not rank. The numbers indicate the fraction of the maximum possible score; "1" - if all participants have chosen this factor and set the maximum possible score; "0" - if none of the participants chose this factor. Color means the ranks of factors: "green" - 33.3% of the highest coefficients or the most important factors, "yellow" - 33.3% of the coefficients, the second most common, or mediocre factors; "red" - 33.3% of the lowest coefficients or the least important factors.		
1. Lack of opportunity to be examined (go through all the necessary procedures) at the place of residence	0.12	0.75
2. Remote location of the medical institution (you need to travel far to get tested)	0.05	0.63
3. Lack or lack of funds to pay for travel to a medical institution/ The need to pay for certain diagnostic procedures during the examination	0.17/ 0.12	0.31 /0.31
4. Unsatisfactory transport connections in the villages and between the village and the district center	0.05	0.25
5. Discrimination (restriction of rights, such as employment, access to certain services) of patients or persons suspected of having TB	0.00	0.25
6. Fear of biased negative attitude/ losing a job/ disclosure of the diagnosis, violation of confidentiality	0.07 /0.05/ 0.13	0.44 /0.25/ 0.25
7. Low level of education and sanitary literacy of the population, (lack of knowledge of how and where to seek medical help) / lack of general knowledge about tuberculosis (how to be examined, treated)	0.27/ 0.03	0.06 /0.25
8. Lack of funds, poverty (employment problems, irregular and poor nutrition, poor living conditions)	0.78	0.00
9. Alcohol use and other bad habits/ the need to go to other settlements for work - labor migration	0.48/ 0.37	0.13 /0.13

Table 1.

Conclusions: Perceptions of the problems affecting the burden of TB epidemic in rural areas differ between TB patients and health workers. Identified gaps - no factor chosen by patients as key were considered such by healthcare professionals, none of the health workers believed that discrimination or stigma has an impact on spread of TB. NTP will take into account results during developing of a national information campaign on improving early detection of TB in Ukraine.

EP-31-408 TB stigma and disclosure in three South African provinces

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Background: South Africa has one of the largest burdens of tuberculosis worldwide. Stigma against people with tuberculosis is driven by its perceived infectiousness, association with poor living conditions, and association with HIV. Fear of stigma can lead to poor adherence to treatment. We report the prevalence of tuberculosis-related stigma and disclosure of tuberculosis diagnosis among people receiving tuberculosis treatment in South Africa.

Design/Methods: These data are from an ongoing tuberculosis adherence trial conducted in South Africa (Gauteng, KwaZulu-Natal, Western Cape provinces). Participants are enrolled within 14 days of starting treatment, assessed monthly during their 6-month treatment and followed-up for a further year. For participants ≥ 16 years we administered a validated 10-point stigma questionnaire at enrolment and end of treatment. Analyses used chi-square test for unpaired data and conditional logistic regression for paired data.

Results: Data are from 2590 participants at enrolment and 1844 participants at both time points. Overall, median age was 36 years, 62% male, 72% single and 53% were people living with HIV (PLWH). At enrolment, 42% of participants had disclosed their tuberculosis diagnosis to someone outside their household. Disclosure was lower in PLWH versus those without HIV (37% versus 48%; $p < 0.001$); there was no difference by sex.

Excluding the disclosure question, 5% (134) had experienced at least some stigma; which was more among females ($P = 0.02$), higher levels of education ($P = 0.04$), PLWH ($P = 0.006$), and provinces other than Western Cape ($P < 0.001$). Stigma increased over time (odds ratio for end of treatment versus enrolment 2.04, 95% confidence interval 1.48-2.79; Table).

Conclusions: Excluding non-disclosure, the prevalence of any form of tuberculosis-related stigma was low in this population, especially in Western Cape, where tuberculosis incidence is highest. The burden of stigma was higher in PLWH, raising the issue of double-stigma. Although low overall, stigma increased over time highlighting the ongoing need for community tuberculosis stigma interventions.

	Stratified by:	No change in stigma status at enrolment and end of treatment	Stigma: at enrolment, not at end of treatment	Stigma: at end of treatment, not at enrolment	OR (95% CI) (end of treatment vs enrolment)	P-value	P-value for interaction
Overall	-	1671	57	116	2.04 (1.48-2.79)	<0.001	-
Sex	Male	1046	32	57	1.78 (1.16-2.75)	0.009	0.39
	Female	625	25	59	2.36 (1.48-3.77)	<0.001	
Province	Gauteng	500	13	55	4.23 (2.31-7.74)	<0.001	0.004
	KwaZulu-Natal	516	22	37	1.68 (0.99-2.85)	0.05	
	Western Cape	655	22	24	1.09 (0.61-1.95)	0.77	
Age group (years)	<30	467	13	31	2.38 (1.25-4.56)	0.009	0.50
	30-39	528	17	41	2.41 (1.37-4.25)	0.002	
	≥ 40	676	27	44	1.63 (1.01-2.63)	0.05	

EP-31-409 Burden and pattern of spirometry abnormalities in individuals working in small-scale mining in Northern Tanzania

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Background: Individuals working in small scale mining are exposed to hazardous free crystalline silica which gradually destroy their airways and alveoli. These people have high prevalence of tuberculosis and cigarette smoking. We aimed to describe the lung function of artisan miners using Spirometry and correlated with other exposures.

Design/Methods: A cross sectional design at the Occupation Health Center - Kibong'oto, where individuals working in mining were consecutively enrolled for pulmonary assessment after excluding active TB. Spirometry was collected using the EasyOne® Spirometer (nidd, Switzerland) according to the American Thoracic Society and European Respiratory Society standards. The best value of FVC and the best value of FEV₁ were reported. Normal lung function was regarded if the FEV₁/FVC > LLN; FEV₁ and FVC > LLN; obstructive lung disease was defined as FEV₁/FVC < LLN (fixed obstruction post-bronchodilator); restrictive lung disease as

FVC < LLN with a FEV₁/FVC > LLN, and mixed lung disease was when the FEV₁, FVC and FEV₁/FVC < LLN. Univariable and multivariable logistic regression models were used to estimate associations between potential risk factors and spirometry abnormalities.

Results: From 2018 – 2020, a total of 4127 attended the OHC for TB assessment and 687 individuals confirmed TB negative tested for lung function with Spirometry. Male contributed ,637 (93%) and the mean age (SD) was 41 ±10 years. The mean duration (SD) of underground dust exposure was 11±8 years. Cigarette smoking and previous TB disease was 117 (17%) and 91 (13%) respectively. Abnormal spirometry results were 218 (32%) – obstructive impairment 25 (3.6%), restrictive lung impairment 3 (<1%) and mixed impairment 190 (28%). History of TB treatment associated with mixed pattern 2.43 (1.96 – 3.03) (p=0.000). Cigarette smoking and HIV co-infection did not influence the spirometry pattern.

Conclusions: Considerable number of small-scale miners have impaired lung function requiring medical attention.

EP-31-410 Alcohol use disorder among patients diagnosed with TB in an urban TB case-finding project in central Uganda: an exploratory study

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Background: Heavy consumption of alcohol increases risk to tuberculosis (TB) disease contributes to delayed diagnosis and may affect adherence leading to undesirable outcomes among patients diagnosed with TB. We describe the prevalence of and the lived experiences with AUD in a large urban cohort of TB patients.

Design/Methods: We carried out a mixed methods study nested within an active TB case-finding project in two large urban districts in Uganda. We collected quantitative data on the prevalence of alcohol use disorder using the Cut, Annoyed, Guilty, Eye opener (CAGE) tool. Trained project staff conducted two focus group discussions (FGDs); one for men and the other for women to examine lived experiences of patients with AUD with linking and adhering to TB treatment. Interviews were transcribed and data was analyzed inductively and coded into themes.

Results: Out of 362 TB patients, 16.02% (58/362) had AUD. Majority 84.5% (49/58) were men, 87.9% (51/58) had successfully completed treatment and 19% (11/58) were HIV positive. Fourteen(eight men and six women) patients with AUD attended the FGDs. Patients with AUD did not report any difficulties linking or adher-

ing to TB treatment but reported experiencing adverse drug reactions while on TB treatment. Although they reported these ADRs to healthcare workers, many did not disclose alcohol use. Coping mechanisms included adjusting their drinking time, quitting or reducing alcohol intake in order not to interfere with medicines. Patients with AUD reported sometimes missing clinic refill appointments due to lack of money to pay the transport fare to the clinic. They also reported that lack of food coupled with the long treatment duration were challenges to TB treatment completion.

Conclusions: A large proportion of TB patients have undisclosed AUD and experience several challenges while on TB treatment. TB care programs need to design interventions in order to address AUD.

Lung health after and beyond TB

EP-32-411 TB and subsequent lung cancer risk: a systematic review and meta-analysis

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Background: Chronic inflammation in the lung could promote carcinogenesis. Increasing numbers of observational studies suggests a relationship between tuberculosis and subsequent lung cancer. We conducted a systematic review and meta-analysis of lung cancer risk after a tuberculosis episode.

Design/Methods: We searched Pubmed, Scopus, Cochrane, Lilacs and Scielo for cohort, case-control and cross-sectional studies published in English, French or Spanish between 01/01/1980 and 31/01/2021. We included studies that reported an effect estimate for the association between tuberculosis and subsequent lung cancer diagnosis.

With random-effects meta-analysis we pooled unadjusted effect estimates (model 1), estimates adjusted for at least age and any assessment of smoking (model 2), and estimates adjusted for age and smoking quantified by intensity, duration or cumulative amount but excluding studies that controlled only for qualitative (never/former/current) smoking status (model 3).

Heterogeneity was quantified by the I² statistic. Risk of bias was assessed using a modified Newcastle-Ottawa Scale. The protocol followed PRISMA guidelines and was registered in PROSPERO (CRD42020178362).

Results: Of 4840 retrieved abstracts we withheld 18 cohort and 42 case-control studies. Thirty-eight were from Asia, predominantly from China and Taiwan. The remainder came from Europe and North America. Ten, 24 and 26 studies had low, moderate and high risk of bias, respectively. To ascertain exposure, 14 cohorts linked records from large databases and 37 case controls used interviews. The pooled risk estimates for cohort and case-control studies are shown in the table. Of the 60 studies, 53 were eligible for at least one model. Adjusted estimates ranged from 1.43 to 1.83 and were all significant. Between-study heterogeneity was substantial.

	Modeled study estimates	Number of studies ^a	Pooled estimate (95% CI)	Heterogeneity
Cohort studies	Unadjusted (model 1)	11	HR = 3.26 (2.43 – 4.37)	I ² = 97%
	Adjusted for smoking ^b and age (model 2)	5	HR = 1.83 (1.13 – 2.96)	I ² = 94%
	Adjusted for smoking ^c and age (model 3)	3	HR = 1.43 (1.08 – 1.91)	I ² = 74%
Case-control studies	Unadjusted (model 1)	40	OR = 1.94 (1.61 – 2.33)	I ² = 87%
	Adjusted for smoking ^b and age (model 2)	23	OR = 1.76 (1.41 – 2.19)	I ² = 79%
	Adjusted for smoking ^c and age (model 3)	19	OR = 1.74 (1.42 – 2.13)	I ² = 59%

^astudies reporting the modeled estimate or for which it could be derived. ^bany adjustment for smoking. ^c adjustment for quantitatively assessed smoking.

Table. Pooled effect estimates for the association between tuberculosis and subsequent lung cancer.

Conclusions: We found a significant moderately increased risk of lung cancer after an episode of tuberculosis. We recommend conducting multisite large prospective studies controlling for other potential confounders beyond smoking and age, along with basic research to understand the mechanisms behind this association.

EP-32-412 Post-TB lung function impairment in Gambian children

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Background: Lung function impairment following treatment of pulmonary tuberculosis (PTB) is increasingly being recognised as an important debilitating outcome in adults. However, data on prevalence and pattern of this complication are sparse among children who suffered from PTB. We present lung function data of children at least six months after completing PTB treatment in The Gambia.

Design/Methods: We used portable spirometry to measure the lung function (FEV₁, FVC and FEV₁/FVC ratio) in children (aged 5 to 15 years) who were diagnosed with PTB between 2014 and 2019 and had completed anti-tuberculous treatment at least six-months before enrolment.

A comparison group of children, who lived in the same compound as the post-TB cases but with no history of TB disease, were also enrolled. We defined lung function impairment as FEV₁, FVC or FEV₁/FVC below the lower limit of normal using the Global Lung Initiative African reference values.

Results: We enrolled 68 post-TB cases (47% females) and 91 children in the comparison group (37% females). There was a statistically significant difference in the median (IQR) age of post-TB cases compared to the comparison group (8.9 years [IQR 7.1-11.2] vs 11.5 years [IQR 8.0-13.7], p-value 0.001).

The post-TB cases had significantly lower age- and sex-standardised Z-scores for FEV₁, FVC and FEV₁/FVC ratio compared to the comparison group (Table).

Variable	Post-TB cases (n=52)	Comparison group (n=86)	P-value
FEV ₁ Z-score, mean (SD)	-1.57 (1.02)	-0.85 (0.84)	<0.001
FVC Z-score, mean (SD)	-1.35 (1.02)	-0.89 (0.91)	0.007
FEV ₁ /FVC Z-score, mean (SD)	-0.60 (0.97)	-0.02 (0.81)	<0.001

Table: Z-scores of lung function volumes in post-TB cases compared to comparison group

Lung function impairment was seen in 22/52 (42%) post-TB cases compared to 18/86 (21%) of the children in the comparison group (p -value 0.042). The majority of children with lung function impairment had a restrictive pattern (20/22 [91%] among the post-TB cases and 16/18 [89%] among the comparison group).

Conclusions: There is significant lung function impairment in children post-TB treatment. Prospective cohort studies are needed to better understand the evolution and risk factors of lung function impairment in children after completing treatment for PTB.

EP-32-413 TB Sequel: lung outcomes at Month 6 after TB treatment initiation in patients across four African countries

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Background: Tuberculosis (TB) is a global health emergency with little known about the long-term sequelae. TB Sequel is a prospective and multi-country cohort study, which aims to advance the understanding of the evolution and characteristics of long-term pulmonary impairment after TB.

Design/Methods: Participants were enrolled at the time of TB diagnosis and followed up for at least two years. The following data were collected at baseline/day 14, month four and month six: clinical (ECG, spirometry, chest x-ray, etc.) and microbiological data (strain type, drug-resistance etc.), data on risk behaviour and comorbidities, demographic and socio-economic variables, as well as biological samples (sputum, urine and blood). The study is ongoing, and the preliminary results provide an overview of the lung function and associated risks at month six using GLI and ATS/ERS guidelines and reference standards.

Results: A total of 1,446 patients were enrolled into the study; 850 (59%) had valid spirometry results at month six. Among them 26,8% had normal lung function, 6,5% showed obstructive, 47,7% restrictive and 19% mixed ventilation patterns on spirometry.

The severity was distributed almost equally between categories: 26,8% normal, 28,2% mild, 23,2% moderate and 21,8% severe. From baseline to month six, 49,1% of participants maintained a stable lung function, in 36,1% of participants the lung function has improved, and in 14,3% - deteriorated.

Conclusions: Preliminary data suggests that following completion of TB treatment, a large proportion of participants suffer from lung impairment. There is a clear need for early identification of lung impairment including strategies for maintaining follow-up of TB survivors to improve health and well-being after TB.

EP-32-414 Burden of COPD attributable to TB: a microsimulation study

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Background: Tuberculosis (TB) is a risk factor for chronic obstructive pulmonary disease (COPD) and COPD is a predictor of TB. A portion of lost life-years attributable to COPD caused by TB potentially can be saved by screening for and treating latent TB. We aimed to determine the number of life-years saved by preventing TB and consequent TB-attributable COPD.

Design/Methods: A probabilistic microsimulation model of individual subjects was constructed using transition probabilities, stratified by age group, sex, and foreign-born status, based on observed rates in the Danish National Patient Registry (covering all Danish hospitals) between 1995 and 2014.

To determine the number of life-years saved by preventing TB in four TB and COPD incident disease groups, we compared the number of life-years accrued over a 100-year period under 'no intervention' and 'intervention' scenarios.

Results: Overall, 27,339 persons (0.5%) developed TB according to the model. Of these, 12,950 (47.4%) developed TB without COPD and 14,389 (52.6%) developed TB with COPD. Preventing TB saved 186,469 life-years. Table 1 shows mean life-years saved for the different incident disease groups.

Overall, mean life-years saved per person with TB was 6.7 years. We also found that an additional 4.9 life-years lost per person was attributable to COPD caused by TB, in addition to 7.1 years lost due to TB alone.

Conclusions: Life-years lost to TB-related COPD are substantial, even in regions where TB is likely to be identified and treated promptly. While the majority of COPD cases could not be attributed directly to lung

morbidity caused by TB, 73% of the life-years lost in patients with TB and COPD occurred in the group without COPD prior to TB. Prevention of TB could avert a substantial amount of COPD-related morbidity, and the benefit of latent TB screening and treatment is likely underestimated when TB is considered alone.

Population	Incident disease pathway	Number of persons	95% SI	LY saved	95% SI	Mean LY saved per person
Individuals without COPD or TB at baseline (n = 5,206,922)	Developed TB, no COPD	13,345	10,321 -15,321	94,319	95,551 -88,997	7.07
	Developed TB, subsequent COPD	5,604	3,652 -8,012	66,871	64,646 -73,413	11.93
	Developed COPD, subsequent TB	7,939	6,521 -9,216	20,953	13,000 -31,505	2.64
Individuals with COPD (COPD, no prior TB) at baseline (n = 110,663)	Developed TB	895	851 - 870	4,326	3,120 -5,811	4.83
Total	All TB	27,783	N/A	186,469	N/A	6.71

Table 1. Life-years saved in each incident disease group via TB prevention

EP-32-415 Risk of active TB in patients with chronic airway disease: a systematic review and meta-analysis

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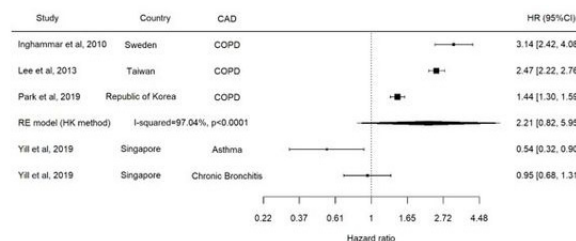
Background: Tuberculosis (TB) and chronic airway disease cause a significant number of deaths and illness, particularly in low and middle income countries. A few studies suggest an increased risk of TB in people with chronic obstructive pulmonary disease (COPD). We conducted a systematic review to inform the need for TB preventive treatment.

Design/Methods: We searched Medline and Embase for studies published from 1 January 1993 to 15 January 2021 that reported the association between the incident risk of TB in people with chronic airway diseases (asthma, COPD and bronchiectasis).

We also searched abstracts of relevant conferences. Two reviewers independently performed screening of papers, data extraction, and quality assessment of individual studies using the Newcastle-Ottawa Scale. Random effects meta-analysis was conducted using the

Hartung-Knapp adjustment. The protocol is registered on PROSPERO (www.crd.york.ac.uk/prospero/; CRD42019136065).

Results: Nine studies included; three from low-income high TB burden countries. Three cohort studies reported a statistically significant independent association between COPD and risk of TB in high-income countries (N=711,389) (Figure).



CAD: chronic airway disease; COPD: Chronic obstructive pulmonary disease; HR: hazard ratio; RE: random effects; HK: Hartung-Knapp; CI: confidence interval

Ruzangi et al was not included in the plot because of lack of an adjusted estimate.

Figure. Forest plot including cohort studies.

Hazard ratios (HR) for incident TB ranged from 1.44 to 3.14, adjusted for multiple confounders including age, sex, and co-morbidity. The pooled estimate was imprecise (HR 2.21, 95% CI 0.82- 6.0) given the small number of studies with large between-study heterogeneity ($I^2 = 97.0\%$).

The direction of effect on the TB risk from asthma was inconsistent across three case control studies and one cohort study. Chronic bronchitis or bronchiectasis studies were limited.

Conclusions: The small number of available studies demonstrated an increased risk of TB in people with COPD; however, the magnitude of the increase would vary by setting and population. Systematic testing and treatment of TB infection in people with COPD needs exploration. Data in high TB burden countries and on other chronic airway diseases are limited.

EP-32-416 TB recurrence and case fatality in India: post-treatment follow-up to ensure recurrence-free survival

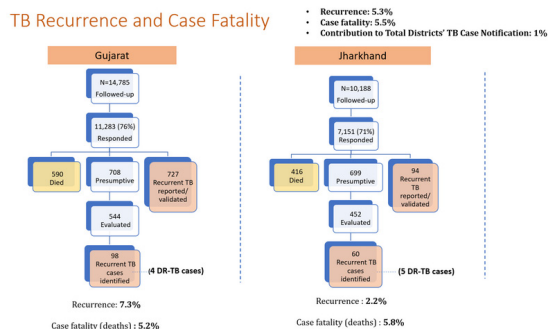
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Background and challenges to implementation: Patients who complete TB treatment remain at risk of TB recurrence and case fatality, reflecting the quality of care patients received. Undiagnosed drug resistance or medication non-adherence are examples of factors associated with increased risk. Although post-treatment follow-up is part of national program guidelines, it is not currently practiced.

Intervention or response: The intervention was implemented across 7 districts in two states of Gujarat and Jharkhand over the period of October 2020 - March 2021. A total of 24,973 successfully treated patients from 2018 to 2021 were followed-up telephonically at intervals of 6, 12, 18, and 24 months post-treatment completion. Home visits were conducted for patients who were unreachable by call. Any subsequent TB episodes experienced or death post-treatment was documented. Reported recurrent cases were validated in the national TB platform (Nikshay). Patients were also screened for TB symptoms and referred for diagnostic testing. Recurrence rate was defined as the proportion of observed patients who experienced another episode of TB. Case fatality was defined as the proportion of observed patients who died due to any cause post-treatment.

Results/Impact: Overall response rate was 74%. Average follow-up time post-treatment was 14.7 months in Gujarat and 16.8 months in Jharkhand. Overall recurrence rate was 5.3% (7.3% and 2.2% in Gujarat and Jharkhand respectively). Overall post-treatment case fatality was 5.5% (5.2% and 5.8% in Gujarat and Jharkhand respectively). 1,407 symptomatic cases were identified; 71% (996) of these cases were evaluated, out of which 16% (158) recurrent TB episodes were identified, including 9 DR-TB cases. Cases identified through symptomatic screening contributed to 1% of total districts' notified cases in the reporting period.



Conclusions: Findings indicate that post-treatment follow-up can be routinely implemented for early detection of TB recurrence, high-yield case-finding, and as a metric for quality of care. The intervention continued during COVID-19, demonstrating feasibility in difficult circumstances.

EP-32-417 Epidemiological characteristics and spatial analysis of infections by non-tuberculous mycobacteria in Rio de Janeiro, Brazil

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Background: This study aimed to investigate clinical-epidemiological characteristics and spatial distribution patterns of nontuberculous mycobacteria (NTM) cases in the city of Rio de Janeiro, Brazil.

Design/Methods: This is an ecologic study that used data reported in the Special Tuberculosis Treatment Information System (SITETB), from January 1, 2010, to December 31, 2018. The home address information of patients notified with NTM was georeferenced for the construction of dot density thematic maps, showing the geographic distribution of NTM cases within the district perimeters of the city.

Results: During the study period, a total of 368 NTM patients were reported. The most frequent species reported were *M. kansasii* (121; 32.9%), followed by *M. avium* (57; 15.5%), *M. abscessus* (53; 14.4%), and *M. intracellulare/M. chimaera* (35; 9.5%). When analyzing the distribution cases by species, it can be observed that *M. kansasii* and *M. abscessus* are more concentrated in the neighborhoods of the Southern zone. In contrast, *M. avium* and *M. intracellulare/chimaera* cases are most common in neighborhoods in the Western and Northern regions.

Conclusions: The detailed clinical data collection, through the SITETB, is an important tool to help understand the NTM epidemiology and to evaluate the real impact on human health. Furthermore, identification of illness vulnerable areas is necessary for the knowledge of the disease spatial distribution and its risk factors.

EP-32-418 Prevalence of silicosis and silicoTB among respiratory admissions: a hospital-based, cross-sectional study in Northern Tanzania

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Background: Despite employing an estimated 40.5 million people, there is little evidence describing respiratory disease amongst small-scale miners. Mererani in

the Manyara region, Northern Tanzania is the only source of Tanzanite worldwide, the majority of which is mined in small scale and artisanal mines. We describe the prevalence, clinical characteristics and management of silicosis and silicotuberculosis amongst adult respiratory inpatients in a tertiary hospital Northern Tanzania serving the Manyara region.

Design/Methods: In this retrospective, cross-sectional study, patient files were selected at random from all available notes, aiming for a sample size of 250, and included if a respiratory diagnosis was made on discharge. Demographic, clinical characteristics and primary diagnosis on discharge were electronically entered into pre-prepared electronic forms and subsequently reviewed and cleaned before analysis.

Results: Of 223 patients with respiratory conditions included in the study 32 (14.3%, 95% CI 10.0-19.6%) were diagnosed with silicosis and a further 17 (7.6%, 95% CI 4.5-11.9%) with silicotuberculosis. As observed in Figure 1, Mining was the most frequent occupation in those with both silicosis (15/32, 46.9%) and silicotuberculosis (15/17, 88.2%). Amongst those with silicosis or silicotuberculosis, 23/49 (46.9%) were aged under 45 years while women represented 13/49 (26.5%) of patients. Silicosis and silicotuberculosis patients commonly presented with features of right heart failure and respiratory failure, and were managed with the administration of multiple therapies, often concurrently.

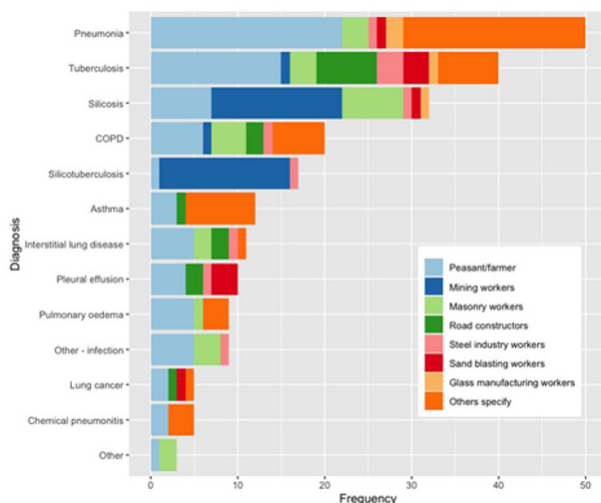


Figure 1. Bar chart of adult respiratory inpatient condition by occupation ($n = 223$)

Conclusions: Despite limitations, our study has found a high prevalence of silicosis and silicotuberculosis amongst men and women with occupational exposure. In addition, patients have features associated with significant morbidity at a relatively young age. These findings are consistent with previous evidence of high levels of silica exposure and support the need for community prevalence studies linked to sustainable interventions.

EP-32-419 Aetiology of non-Covid community-acquired pneumonia during the Covid-19 pandemic

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Background: The emergence of SARS CoV-2 may have modified epidemiological patterns in community-acquired pneumonia (CAP). The aim of this work is to describe the aetiology of CAP during the COVID-19 pandemic in a metropolitan University-affiliated hospital.

Design/Methods: Retrospective case-series of hospitalized patients with CAP and negative PCR for SARS CoV-2 between January 6, 2020 and February 15, 2021. All patients met ERS/ATS criteria for the diagnosis. An Excel template was created to register and analyze the demographic, clinical and laboratory data, once the Hospital Ethical Committee approved the study.

Results: During the study period, 229 patients (143 men, 86 women) with negative PCR for SARS CoV-2 were hospitalized for CAP. Mean age was 66.4 for men and 71.08 for women ($P=0.6$). The causative pathogen was identified in 77 cases (34%), and in 25 of those (32%) it was *S pneumoniae*. Other bacteria isolated from patients' respiratory samples and/or blood cultures or pleural fluid were other streptococci (4), *Pseudomonas aeruginosa* (5), *Klebsiella pneumoniae* (4), *E coli* (3), *Haemophilus influenzae* (2), other gramnegative bacilli (2), *Moraxella catarrhalis* (2) and *S aureus* (1). Serological test for atypical pathogens and respiratory viruses arrays were performed in 32 (14%) and 48 (21%) cases, respectively. Positive results were found in 18/32 serologies (56%), *Chlamydomphila pneumoniae* (8), *Mycoplasma pneumoniae* (6), *Chlamydomphila psittaci* (4), *Legionella pneumophila* (3) and *C burnetti* (1); whereas respiratory viruses (Syncytial Respiratory Virus-SRV, Influenza A/B, Adenovirus and Rhinovirus) were found in 11/48 patients (23%), one of which had *Chlamydomphila pneumoniae*-IgM plus SRV+ in virus array.

Conclusions: These results indicate that serologies and virus arrays may help to identify the causative pathogen in patients with SARS CoV-2 negative PCRs, who are admitted with CAP whose clinical and radiological pictures are indistinguishable from COVID-19's.

EP-32-420 Characteristics of adults with chronic respiratory symptoms attending hospital outpatient departments in Ethiopia, Kenya and the Sudan

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Background: The greatest burden of chronic respiratory diseases is in low- and middle-income countries. Recent population-based studies have reported substantial levels of obstructive and restrictive patterns of lung function. This study aimed to characterise the common chronic respiratory diseases in symptomatic patients attending clinics in three African countries.

Design/Methods: A cross-sectional study of consecutive adult patients with chronic respiratory symptoms (>8 weeks) attending hospital outpatient departments in Addis Ababa, Ethiopia, Nairobi, Kenya and Khartoum, Sudan. Tuberculosis (TB) was excluded on clinical grounds and negative GeneXpert testing. Patients were assessed by respiratory focused questionnaire, spirometry, allergen skin prick tests, 6-minute walk test and chest radiography.

Results: 519 patients (209 Kenya, 170 Ethiopia, 140 Sudan) were recruited. The group mean (SD) age was 45.2 (16.2) years and 53% were women. In addition, 83% were never smokers, 34% reported a prior asthma diagnosis, 4% a COPD diagnosis and 18% had been treated for TB. Wheeze was the most common symptom (71%). Mean (95% CI) FEV₁ and FVC: 74% (72-77%) and 82% (80-84%) predicted, respectively. 33% had normal spirometry, 18% had purely obstructive, 17% purely restrictive and 23% had a mixed obstruction/restriction pattern. 49% of those with obstruction were categorized as severe/very severe. About 25% of patients diagnosed with asthma had lung function consistent with asthma

and 22% had lung function consistent with COPD. Of those without diagnosed asthma 20-25% fulfilled lung function criteria for asthma. Numerically, symptomatic patients without diagnosed COPD (n=147) exceeded those with diagnosed COPD (n=23). The lung function of patients in Ethiopia and Sudan was similar, but lower than Kenya.

Conclusions: Patients with chronic respiratory symptoms, TB has been excluded, there is an unmet clinical need to diagnose and manage asthma and COPD in Ethiopia, Kenya and Sudan. Further studies are required to identify the burden of chronic respiratory disease in other African countries.

EP-32-421 The size of lung parenchyma as a function of age: a study of 250,000 normal chest radiographs from Southern China using deep learning and radiomics

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Background: This study is to establish a normal mean value in size of lung parenchyma (SLP) of the population in Southern China using chest radiography to serve as baseline for different ages and genders such that this can be used as a screening tool for the healthiness of teenager, tuberculosis, cardilomegy, etc.

Design/Methods: Standard radiographs including 250,000 cases were collected from six sources in southern China from 2012 to 2018 in this study. All of these cases were confirmed by at least one radiologist with radiology reports or other diagnostic report with no findings of that will reduced the size of lung at the time.

An adapted histogram equalization was applied to normalize image. A deep learning-based image segmentation algorithm was applied to automatically segment lung area. The lung size for each lung was calculated based on number of pixel and pixel distance. The lung size for each age and for each gender are calculated. Performances of the trained deep learning algorithm and the regression model were further validated by an independent test, where 53,938 normal CXR images were involved.

Results: Model accuracy was expressed as the correlation between chronological age and predicted age (Pearson's r, mean absolute error [MAE] and root mean squared error [RMSE]). The developed algorithm performed a high segmentation accuracy (DICE =0.983). Mean SLPs of the study population were 399, 368, and 435 cm², for

the general, female, and male population, respectively. The model accurately predicted chronological age using LPS ($r=0.930$, $MAE=5.368$, $RMSE= 6.403$). Moreover, the age trend predicted from this model corresponds to that of spirometry model based on FEV1.

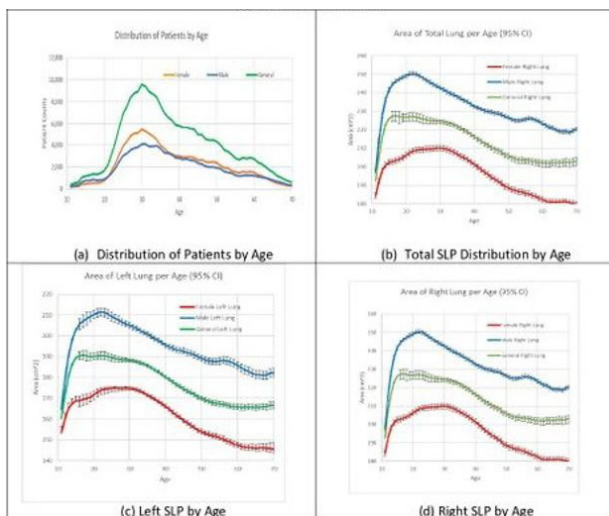


Figure 1. Distribution of patients in training set by age (a) used to generate SLP; Total SLP distribution by age (b); Left SLP distribution by age (c); and Right SLP distribution by age (d). The mean SLP increased gradually from age 12 till age 24, within females having less values than males. The right SLP is greater than the left SLP.

Conclusions: This is the first large-scale investigation about size of lung parenchyma as a function of age. It has shown the relationship between age and patient's lung volume and lung functions which compares favourably with many findings of studies.

TB and diabetes: current issues

EP-36-451 Diabetes mellitus and its predictors among patients with active TB in Addis Ababa, Ethiopia

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Background: Diabetes mellitus (DM) is a common co-morbidity among TB patients. When the two diseases co-exist, they worsen treatment outcomes in each other. Routine bidirectional screening is recommended but implementation has been slow. Our objective was to determine the yield of routine DM screening among patients with active tuberculosis.

Design/Methods: Between September 2020 and March 2021, we conducted routine screening for DM among patients with tuberculosis in 17 public health facilities in Addis Ababa, Ethiopia. All consenting adult patients were included. We asked each patient about current diagnosis of DM, risk factors for DM, and any symptom suggestive of DM or its complications. We used finger-prick blood tests to confirm DM diagnosis. Random blood sugar (RBS) ≥ 200 gm/dl or Fasting Blood Sugar (FBS) ≥ 126 gm/dl on two separate occasions or previous diagnosis as confirmed by medical records, was considered confirmatory. We used logistic regression analyses with adjusted Odds Ratio (aOR) to identify predictors of DM.

Results: We screened 732 TB patients, nearly all (728) were receiving treatment for drug-sensitive TB. Extra-pulmonary tuberculosis accounted for 38.7% of the cases followed by bacteriologically confirmed pulmonary TB in 35.4%, and clinically diagnosed pulmonary TB in 25.4%. HIV co-infection rate was 12.8%. We detected 60 (8.2%) DM patients which is 2.5 times higher than the prevalence of 3.2% in the general population. Twenty five (42%) of these were newly diagnosed. A family history of DM (aOR=9.4; $p<0.001$), age 45+ (aOR=5.9; $p<0.001$) and fatigue (aOR=3.4; $p<0.001$) predicted DM diagnosis. However, DM diagnosis did not differ by sex, HIV status, or type of TB.

Background and challenges to implementation: Diabetes mellitus (DM) is a common co-morbidity among TB patients. When the two diseases co-exist, they worsen treatment outcomes in each other. Routine bidirection-

al screening is recommended but implementation has been slow. Our objective was to determine the yield of routine DM screening among patients with active tuberculosis.

Intervention or response: Between September 2020 and March 2021, we conducted routine screening for DM in 17 public health facilities in Addis Ababa, Ethiopia. All consenting adult patients were included. We asked each patient about current diagnosis of DM, risk factors for DM, and any symptom suggestive of DM or its complications. We used finger-prick blood tests to confirm DM diagnosis. Random blood sugar (RBS) ≥ 200 gm/dl or Fasting Blood Sugar (FBS) ≥ 126 gm/dl on two separate occasions or previous diagnosis as confirmed by medical records, was considered confirmatory. We used logistic regression analyses with adjusted Odds Ratio (aOR) to identify predictors of DM.

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Conclusions: The rate of diabetes co-morbidity was 2.5 higher than the prevalence estimate in the general population, and a significant share of this was due to undiagnosed DM, justifying the need for routine screening. The impact of the routine screening on treatment outcomes of both diseases should be evaluated.

EP-36-452 Persistent dysglycaemia is associated with unfavourable treatment outcomes in patients with TB in North Lima, Peru

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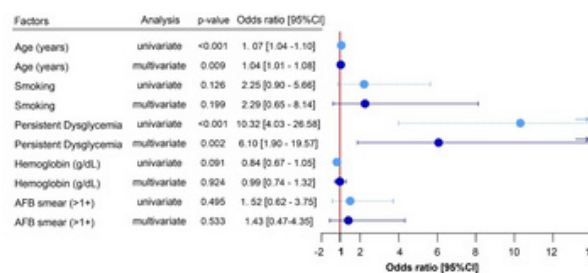
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Background: Association between tuberculosis (TB) and dysglycemia (diabetes mellitus-DM and prediabetes-preDM) is increasingly reported. The evidence suggests that dysglycemia persists during TB treatment and presents distinct clinical profiles potentially related

to unfavorable outcomes. We examined the association between persistent dysglycemia (PD) and TB treatment outcome among people with TB from North Lima, Peru.

Design/Methods: We evaluated and followed-up for 24 months a cohort of adults with TB from health centers of North Lima between February and November 2017. We screened dysglycemia by fasting glucose (FG) and HbA1c at baseline and at follow-up visits at two and six months after initiation of tuberculosis treatment. PD was defined as dysglycemia that did not change or became normoglycemic and returned as dysglycemic in any of the visits. Independent associations between PD and unfavorable outcome were evaluated by logistic regression adjusted for age, anemia, smoking and smear grade.

Results: Among 125 TB patients included, the prevalence of DM, preDM and PD were 14% (95% CI:9.3–21.6%); 32% (95% CI:24.5–40.6%) and 29.6% (95% CI:22.3–38.1), respectively. Non persistent dysglycemia was observed in twenty-three preDM-TB patients. Medians of FG and HbA1c levels were higher among patients with unfavorable TB treatment outcome. Twenty-nine patients (23%; 95% CI:16.7%–31.3%) had unfavorable outcome, were older (median age: 51.3 vs. 27.9 years $p < 0.001$), had higher BMI values, more lung lesion types ($p < 0.001$) and persistent dysglycemia ($p < 0.001$). The logistic regression showed that PD was independent associated with unfavorable TB treatment outcome (aOR: 6.1; 95% CI:1.9–19.6) adjusted by age, smoking, smear grade and hemoglobin level.



Multivariable logistic regression analysis was conducted to analyze the association between indicated variables and odds of persistent dysglycemia in univariate model, each variable was tested individually. The adjusted model included all the variables shown in the graphs in addition to age, smoking, $\geq 1+$ AFB smear and hemoglobin level. Unfavorable TB outcome was defined as treatment failure or modification, recurrence or death, whereas favorable outcome was cure or treatment completion.

Figure. Logistic regression analysis of persistent dysglycemia on TB treatment outcomes.

Conclusions: Persistent dysglycemia was frequent among patients with TB and significantly associated with unfavorable TB treatment outcomes in people from North Lima. Dysglycemia screening at TB diagnosis and trough treatment can potentially help the clinician guide care to improve outcomes and ensure the good performance of TB control.

EP-36-453 Systematic TB screening among patients with diabetes: a multicentre programme experience in Ogun State, Nigeria

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Background: Individuals with Diabetes Mellitus (DM) are at increased risk of developing TB compared to the general population. Diabetes comorbidity increases the risk of death and other adverse treatment outcomes when compared with TB patients without diabetes. Despite its effectiveness in reducing TB transmission and preventing diabetes complications, a policy guiding bidirectional TB-DM management is yet to be institutionalized in Nigeria. We assessed the yield of systematic screening for TB among DM patients attending two public secondary and tertiary hospitals supported by the USAID funded TB-LON 3 Project in Ogun State, Nigeria.

Design/Methods: Between July 2020 and February 2021, the Project trained and stationed TB screening volunteers at entry points in the DM clinics of two hospitals, to verbally screen DM patients for TB symptoms - cough of two weeks, weight loss, fever and night sweat ask questions about symptoms of TB among diabetes patients attending the clinics. Screening outcomes were documented in the screening register and other reporting and recording tools. Identified presumptive were referred for diagnosis. We then carried out a cross-sectional retrospective analysis on 1,889 patients that attended these diabetic clinics over the 8 months' period.

Results: 100% (1,889) DM patients were screened out of which 148 (7.8%) were presumptive TB cases and 100% of them received diagnostic evaluation for TB. 16 (11%) of those evaluated were bacteriologically diagnosed with TB. The Number Needed to Screen and Number Needed to Test to identify one TB case among the screened diabetes population were 118 and 9 respectively.

Conclusions: The prevalence of TB among diabetes patients in Nigeria is higher than the general population. Screening for tuberculosis among DM patients is an effective strategy in finding the missing TB cases. There is a need for urgent scale up of chest X-ray services among diabetes patients who may be asymptomatic in this setting.

EP-36-454 Glycosylated haemoglobin dynamics: pre- and post-TB treatment, diabetes-range glycaemia in Dhaka, Bangladesh

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Background: In recent non-pandemic periods, tuberculosis (TB) has been the leading killer worldwide from a single infectious disease. Patients with DM are three times more likely to develop active TB and have poor treatment outcomes. Data are limited regarding glycaemic dynamics from TB diagnosis through treatment and single glycaemic measurements at treatment initiation may inaccurately diagnose DM or DM severity.

Design/Methods: A prospective study of glycemia dynamics in response to TB treatment measured point-of-care glycosylated hemoglobin (HbA1c) in patients presenting to TB screening centers in Dhaka, Bangladesh, to determine the prevalence and risk factors of new DM prior to and at completion of TB treatment.

Results: 429 adults with active TB infection enrolled from October '18-July '19 were divided into three groups based on initial HbA1c range: normoglycemic, prediabetes and DM group. DM was diagnosed in 158(37%): 14% were newly diagnosed DM by HbA1c despite normal random blood sugar testing. At end of treatment, 14(6%) additional patients from the normoglycemia and prediabetes groups had HbA1c level >6.5%, thus increasing the prevalence to 39%. The number needed to screen to diagnose one new case of DM pre-TB treatment was 5.7 and 16 when repeating at the end of treatment in the subgroup without DM at enrollment. Weight gain >5% at end of treatment significantly increased the risk of diabetic range glycemia in patients who had normoglycemia or prediabetes at TB treatment initiation (OR 5.66, 95% CI 1.23-26.04, p<0.05).

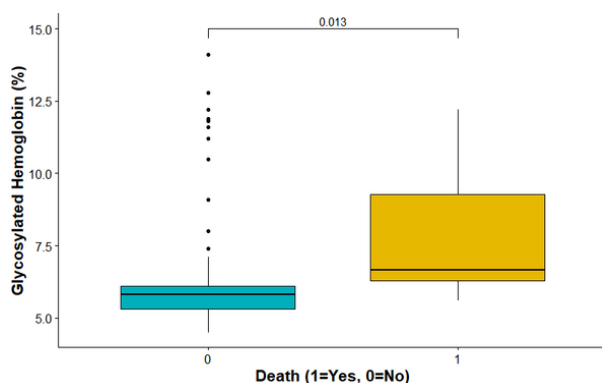
Conclusions: HbA1c testing for undiagnosed DM pre and at completion of TB treatment found a high prevalence of prediabetes and DM, including a proportion that was found only at the end of treatment and more commonly in people with higher percentage of weight gain. Further longitudinal research is needed to understand the effects of TB disease and treatment on insulin resistance, impacted immune pathways, and long-term DM complications.

EP-36-455 Clinical aspects and treatment outcomes in patients with pulmonary TB and dysglycaemia in Rio de Janeiro, Brazil

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Background: Dysglycemic patients with pulmonary tuberculosis (PTB) may have more severe clinical presentation and higher risk of unfavorable treatment outcome. To analyze the association between dysglycemia and clinical/laboratory aspects and treatment outcome of patients with PTB at a basic health unit.

Design/Methods: A longitudinal study was carried out in Rio de Janeiro, Brazil, between 2016 and 2020. 140 adult patients with proven PTB (positive culture for Mycobacterium tuberculosis or Xpert MTB RIF in sputum) were included. Patients with PTB were classified as normoglycemic (TBNG; HbA1c < 5.7%), dysglycemic/pre-diabetic (TBPD; HbA1c 5.7- 6.4%) and dysglycemic/diabetic (TBDM; HbA1c > 6.5%). TB treatment outcomes were evaluated at Months 2 and 6 (M2, M6), and classified as favorable (cure/treatment completed) and unfavorable (death, treatment default or failure).



Results: Dysglycemia was detected in 61.3% (86/140); 14.2% were TBDM. Median age (44.0 vs. 33.5; $p=0.01$) and body mass index (23.1 vs. 19.6; $p<0.005$) were higher in TBDM than in TBNG. Sputum smear positivity (94.2% vs. 75.9%; $p=0.005$) was more frequent among

dysglycemic patients at baseline (M0). Dysglycemic patients presented cavities (80.2% vs. 63.0%; $p=0.03$) and bilateral lesions (67.4% vs. 46.0%; $p=0.02$) more frequently than TBNG, as well as a higher median number of pulmonary areas affected (3.0 vs. 4.0; $p=0.03$). TBPD percentage decreased from 47% at M0 to 14% at M2. There were no differences in TB treatment outcome between the groups, but TB mortality was higher among TBDM (20% vs. 2.2% in pre-DM and TBNG).

Conclusions: Dysglycemic patients with PTB presented clinical manifestations indicative of more advanced disease and in TBDM the risk of death was higher.

EP-36-456 Routine chest X-ray-based TB screening and its yield among patients with diabetes mellitus in public health facilities in Addis Ababa, Ethiopia

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Background: People with diabetes mellitus (DM) are at increased risk of developing tuberculosis (TB). As a result, routine screening for TB is recommended but implementation has been slow. The commonly used symptom-based screening has a low yield in this group of patients.

Our objective was to determine if combining chest x-ray with symptom-screening could have a better yield compared with symptom-based screening alone.

Design/Methods: We conducted routine TB screening for DM patients in Addis Ababa, Ethiopia between September-December 2020. All DM patients were screened for TB symptoms (≥ 2 weeks of cough, weight loss, fever and loss of appetite) using nationally approved symptom screening checklists. Patients were offered chest x-ray screening irrespective of their symptom status.

Results: Of 843 patients screened, 408 (48%) were screened by chest x-ray, 55% (464) were female, median age was 53 years, 93.6% had type 2 DM, and 429 (50.9%) were on a combination of oral hypoglycemic agents and metformin. Fifteen patients (1.8%) reported a past history of TB of which 9 were clinically diagnosed. Two were on treatment for bacteriologically confirmed TB. Symptom and x-ray based screening identified 29 (3.4%) and 7 (1.7%) presumptive TB patients respectively.

On subsequent evaluation, one rifampicin resistant and three clinically diagnosed pulmonary TB cases were detected. The overall yield was 474 per 100,000 (4/841)

which is more than 3-times the national incidence estimate for the general population (140 per 100,000). When combined with the two patients under treatment, the yield increased to 711 per 100,000 (6/843) which is 5-times the estimate in the general population.

Conclusions: Routine TB screening led to identification of two additional TB cases for every active TB case under treatment. Chest x-ray based screening accounted for three-quarters of all the newly detected active TB cases. Routine x-ray based screening could be considered for larger scale screening programmes.

EP-36-457 Accuracy of a new risk scoring tool to identify diabetes mellitus in TB patients in Addis Ababa, Ethiopia

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Background: Current global guidelines recommend routine blood testing to DM in patients with active TB. However, such tests are not yet readily available in resource constrained settings.

Our objective was to identify the most sensitive combination of risk factors and symptoms to identify TB patients at high risk of DM.

Design/Methods: In a cross-sectional health facility-based study in Addis Ababa between September 2020 and March 2021, we recorded risk factors for and symptoms of DM in a standardized questionnaire before performing blood tests. The risk factors included: family history of DM, age, waist circumference, smoking history, and alcohol use. We administered a checklist of nine common symptoms associated with acute and chronic complications of DM. Patients were categorized as “symptomatic” or “asymptomatic” depending on the presence or absence of any ≥ 1 of the 9 symptoms.

We used logistic regression analyses, then analyzed the accuracy of the risk factors and symptoms against blood test results, and presented as receiver characteristic curves (ROC), with areas under the curve (AUC).

Results: Sixty patients had DM out of 732 (50.2% men) enrolled in the study. Of these, 30% (18/60) reported family history of DM, 61.7% (37/60) were aged ≥ 45 years, and 78.3% (47/60) had a cumulative risk factor score of ≥ 2 .

One or more of the DM symptoms were reported in 68.3% (41/60). A risk factor score ≥ 2 predicted DM diagnosis with moderate accuracy (AUC=0.74, 95%

CI=0.64-0.84), sensitivity of 80% and specificity of 67%. When combined with symptom score, sensitivity increased to 92%, but the AUC was slightly lower. Symptom alone had low accuracy (Figure).

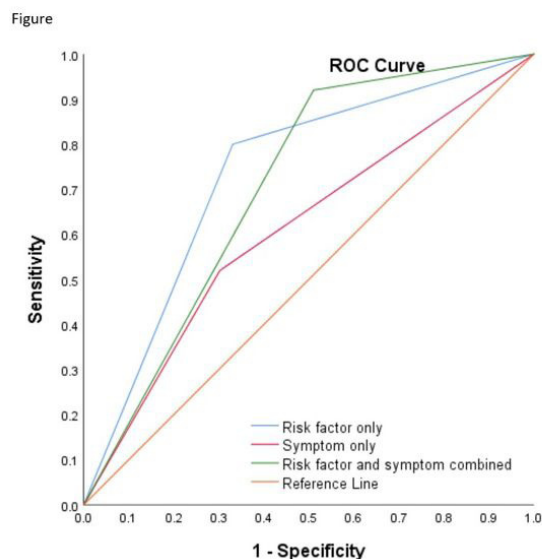


Figure.

Conclusions: Combining risk factors with symptoms can be used as a sensitive tool to identify adult TB patients at high risk of developing DM in Ethiopia. Its utility should be further validated in other settings and as a digital self-screening tool.

EP-36-458 The effect of diabetes and pre-diabetes on anti-TB treatment outcomes: a multicentric prospective cohort study

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Background: The increase in the number of people with DM may further complicate care and control of tuberculosis (TB), especially in many areas with a high burden of both diseases. There is also evidence that people with TB (PWTB) and DM have an increased risk of unfavorable anti-tuberculosis treatment outcome such as failure, recurrence and death compared to normoglycemic patients. However, the findings have not been consistent.

Design/Methods: 756 culture-confirmed PWTB, enrolled in the Regional Prospective Observational Research in Tuberculosis (RePORT)-Brazil cohort between 2015 and 2019 were stratified based on baseline glycated hemoglobin levels. Glycemic status was reported to SINAN as diagnosis of diabetes (yes or no), not exclusively based on HbA1c level. Unfavorable TB outcome was defined as treatment failure or modification, recurrence or death, whereas favorable outcome was cure or treatment completion.

Our findings were validated using data from PWTB reported to the Brazilian National System of Diseases Notification (SINAN) during 2015-2019 (n=20,989). Associations between glycated hemoglobin status and unfavorable outcomes were evaluated stepwise by binary multivariable regression analysis models.

Results: In both cohorts, the univariate analysis showed that unfavorable outcomes were more frequently associated with drug resistance and HIV infection. In RePORT cohort PWTB who experienced failure, recurrence or died exhibited a median HbA1c of 6g/dL (IQR:5.4-6.8). Prediabetic condition was not associated with an unfavorable TB treatment outcome and death.

However, diabetes was associated with unfavorable outcomes in the RePORT (aOR: 2.85, p=0.001) and in SINAN (aOR: 1.56, p=0.040) cohorts (Figure 1A).

Furthermore, diabetes was associated with higher risk of death in both, RePORT-Brazil (aOR: 3.23, p=0.006) and in the SINAN (aOR: 2.75, p=0.047) cohorts (Figure 1B).

Conclusions: Diabetes was associated with an increased risk of unfavorable outcomes and mortality in Brazilian PWTB. Interventions to improve tuberculosis treatment outcomes in persons with diabetes are needed.

EP-36-459 Educational counselling of patients with combined TB and diabetes mellitus: a randomised trial in Indonesia

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Background: A patient's own understanding and knowledge of tuberculosis (TB) and diabetes mellitus (DM) is thought to be crucial for good management and clinical outcomes, but little is known about the knowledge of

patients who have both DM and TB disease. We aimed to describe the effect of educational counselling on patients' knowledge about their combined TB and DM in an urban setting in Indonesia.

Design/Methods: All patients received counselling at the time of enrolment, and were then randomized to either structured education on TB-DM at 6 time points, combined with more frequent glucose monitoring and standardized adjustment of DM medication (intervention arm), or no further structured education (as per routine practice). Patients' knowledge of TB-DM and adherence to medication were assessed by questionnaire.

Results: Baseline and 6-month questionnaires were available for 108/150 patients. Patients knew much less about DM than about TB, even though 72% had previously diagnosed DM. There was no significant difference proportion of patients who showed knowledge improvement at 6 months, both for TB (difference of differences 14%; p=0.20) and DM (10%; p=0.39). Higher education level was associated with good knowledge at baseline. Patients in the intervention arm were more likely to adhere to taking DM medications.

Conclusions: Structured education did not clearly improve patients' knowledge. It was associated with better adherence to DM medication, but this could not be attributed to education alone.

Global lessons learnt in tobacco control

EP-38-470 How immune is the South Asian Region against tobacco industry interference?

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Background and challenges to implementation: All South Asian countries (Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka) are parties to the Framework Convention on Tobacco Control (FCTC). FCTC Article 5.3 helps Parties to protect their tobacco control and public health policies from commercial interests of the tobacco industry. Our study aimed to describe the implementation status of the WHO FCTC Article 5.3 in the South Asian countries.

Intervention or response: This study is based on content analysis of identified government documents and websites.

Results/Impact: In relation to the policy status, none have national level policies on FCTC Article 5.3. However, 12 states and 18 districts of India have developed a Policy for Article 5.3. Nepal's Tobacco Control 2030 Strategy includes Article 5.3 (2018), Pakistan has an Action Plan (2018), and Sri Lanka a Policy Guideline (2019).

A Code of Conduct is present in India (2020) and is still in the process of development in Maldives.

Sponsorships from the Tobacco Industry is prohibited in all South Asian countries and Nepal Tobacco Control Act specifically prohibits government officers taking any sponsorships from Tobacco Industry.

The Tobacco Control Act of Maldives and Nepal, prohibits tobacco industry representatives being appointed to the controlling entity and Maldives prescribes the board members to be transparent.

There are civil society organisations monitoring tobacco industry interference in all countries except in Bhutan. The region hosts one of the three WHO-FCTC tobacco observatories, Centre for Combating Tobacco (CCT) in Sri Lanka since 2016. South Asian Regional Consortium Centre for Combating Tobacco (SARC-CCT), the regional observatory incorporating all South Asian countries, was initiated in 2019.

Conclusions: All South Asian countries have started initial steps on implementation of FCTC Article 5.3, even though most of these are yet to be fully implemented. The current policy context related to FCTC Article 5.3 is deficient and needs significant reinforcement.

EP-38-471 Areca nut consumption among the adult population in India

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Background: Areca nut is one of the most widely consumed substances globally, after nicotine, ethanol and caffeine and classified as carcinogenic to humans. This study examines the disparity and determinants of areca nut consumption with and without tobacco in India.

Design/Methods: We utilized the nationally representative Global Adult Tobacco Survey (GATS) 2016-17. The analytical sample size was 74,037 individuals aged 15 years and above. We estimated the current use of areca nut without tobacco and with tobacco. We examined determinants of areca nut consumption using multinomial logistic regression, accounting for complex survey design.

Results: About 23.9% (95%CI 23.1-24.8) of the adult population consume areca nut, i.e. approximately 223.79 million people in India; majority of users (14.2% 95%CI 13.5-14.9) consumed areca nut with tobacco. When compared to females, males were more likely to consume areca nut (with tobacco RR=2.02; 95%CI 1.85-2.21 and without tobacco RR=1.13; 95%CI 1.07-1.20). Age, marital status, education, occupation, caste, religion and region were significantly associated with areca nut consumption. However, the direction and magnitude of association differs with respect to the areca nut consumption with and without tobacco.

Conclusions: The on-going tobacco control efforts would not address the majority of areca nut users until greater attention to areca nut consumption with and without tobacco is reflected in health policies in India.

EP-38-472 Smoking cessation support in TB and HIV treatment in low- and middle-income countries: a systematic review

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Background: Smoking is the single most significant preventable risk factor for morbidity and mortality, especially among people living with Human Immunodeficiency Virus (PLHIV) and tuberculosis (TB) patients. Although the incorporation of smoking cessation (SC) is recommended by the World Health Organization and the International Union Against Tuberculosis and Lung Disease, research to inform smoking cessation interventions among PLHIV and TB patients is limited, especially in low- and middle-income countries (LMICs).

Design/Methods: Systematic searches of SCOPUS, Web of Science, PubMed, MEDLINE (Ovid), and Embase from 2007 to 2019 were conducted. Included studies examined the feasibility, applicability, efficacy, and effectiveness of the integration of smoking cessation programs in existing TB and HIV programs of developing countries.

Results: Eighteen studies from nine developing countries met the inclusion criteria. Types of interventions included brief advice, behavioural counselling, medication, and community-based care. Almost all studies recommended applying for SC programmes in existing TB and HIV health care settings. Although all interventions increased SC between 15% and 82%, many studies had

a high risk for bias, including six studies without a control group. The type of personnel delivering the interventions did not produce a significant difference in cessation rates, suggesting that national TB and HIV programmes may be customized according to their needs and limitations.

Conclusions: The integration of SC interventions in existing TB and HIV settings is feasible and appears to be an efficient strategy to tackle the demand for support, but there are comparatively far fewer studies of SC *effectiveness* in TB and HIV patients than in the general population or in developed countries. More intervention-oriented research among LMICs on smoking cessation for HIV and TB settings is required. Policymakers in low-resource settings should encourage greater collaboration between tobacco and TB/HIV initiatives and develop appropriate and consistent measures to monitor and optimize outcomes.

EP-38-473 Implementing the “Yellow Line Campaign” for tobacco-free educational and government establishments in Uttar Pradesh, India

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Background and challenges to implementation: Uttar Pradesh has a higher incidence of tobacco use (about 35.5%) than the national average. The state also has the highest prevalence of throat and mouth cancer cases - about 20% of the national burden. Government of UP has targeted to declare all educational institutions and government establishments under “Yellow Line Campaign”.

Intervention or response: The objective of “Yellow line campaign” is to save young generation from ill effect of tobacco, through demarcation yellow line to stop tobacco sale and use within 100 yards of school, to develop greater awareness in community and ownership in school tobacco control committee and students to develop and sustain tobacco free educational institution, sensitize enforcement officers to penalise violations under smokefree rules (-section 4) and protection of youth and minors (Section 6b) and thus enable making Educational Institutions Tobacco Free zones. On other hand also and making Government Establishments Tobacco Free zones and insure compliance of sections 4 of COTPA.

Results/Impact: The Yellow Line Campaign run in all 75 districts meetings organized on the theme Freedom from Tobacco with District administration ownership participation of hundreds of NGOs and media support. More than 135 circulars from district administration to all govt. establishments including education, Panchyati-raj and Health department. Almost 16550 educational

institutions and 3500 other government institutions were declared tobacco free through campaign. District administration in 7 districts declared all government institutions tobacco free.

Conclusions: Yellow line campaign was incorporated in school programme guidelines, civil societies actively participated and supported the programme. District administration across state encourage all departments to declare their offices tobacco free through yellow line campaign and enforcement of section 4. Media plays very positive role and big media coverage gained. So far 16550 numbers of educational institutions have been declared tobacco-free. It is anticipated that by 2025 all educational institutions in the state would achieve this goal.

EP-38-474 Tobacco-Free Generation, Karnataka 2025: strategies, progress, learnings and challenges

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Background and challenges to implementation: In India more than 55% tobacco users reported initiating tobacco use before the age of 20 years. Prevalence of tobacco use in Karnataka is 22.8% and average age of initiation is 19.8 years. Indian Tobacco Control Law i.e. COTPA 2003 section 6a and 6b restrict the sale of tobacco products to minors. However, compliance with these provisions is not satisfactory and require greater effort to protect the minors. Tobacco Free Generation – 2025 (TFG) campaign by the State Tobacco Control Cell a step towards that end.

Intervention or response: Department of Health and Family Welfare, Government of Karnataka (GoK), India has initiated TFG in FY 2018-19. As per this initiative, no one born in or after the year 2007 can ever be sold tobacco products in Karnataka after 2025.

This proposal has been positively accepted by GoK to review for its adoption in the State. It has organized state level consultation with multi stakeholders to lay out the roadmap, developed and released IEC materials on TFG.

Results/Impact: TFG 2025 concept has given new dimension to over all implementation of Tobacco Control program in the State. In FY 2017-18, District Tobacco Control Cells have done 2355 school programs and sensitized 3.54 lakhs children whereas in FY 2020-21, conducted 3032 school programs and reached 4.67 lakhs children. COTPA section 6 Compliance has increased

from 61.81 % (2018-19) to 75.46 % (2020-21). COTPA state amendment is in process which includes increasing the legal age for sale to 21 years also.

Conclusions: TFG initiative has set the clear vision for implementation of NTCP in the state. While the state is moving forward to achieve this mile stone the tobacco control coalition members are also supporting positively to achieve this vision. TFG is only possible with collective responsibility, sustained and focused efforts by all stakeholders.

EP-38-475 Smokefree expansion in rural Uttarakhand, India: an early experience

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Background: GATS – 2 indicates that the tobacco burden in rural Uttarakhand is significantly high compared to the urban areas. wherein adults who are exposed to tobacco smoke at home, workplace and any place is 62.2%, 24.5% and 33.4% respectively. The Indian government enacted the Cigarettes and Other Tobacco Products Act in 2003 and it prohibits smoking in public places. This study documents the smoke free village efforts undertaken in the rural areas of Uttarakhand.

Design/Methods: A quick and dirty compliance assessment [AY1] [RS2] [AY3] was undertaken by observing 4 criteria i.e. availability of No Smoking Signages, active smoking, specification of signages as per COTPA section 4, evidence of recent smoking (smell and/or cigarette and bidi stubs) to check the compliance level during May and August 2020. Number of strategies were implemented to help villagers become Smokefree wherein Gram Panchayats officials, Pradhans (Head of Village level constitutional body), Police and Self-help group women of 21-gram panchayats were sensitised on COTPA 2003 provisions, enforcement mechanism was established, smokefree signages and signboards were pasted and displayed at public places such as community centre, Panchayat offices; Primary Health centres banks, Anganwadi Kendra, schools, tea/grocery shops etc.

Results: 21-gram panchayats nearly 82 villages achieved Smokefree status according to 4 assessment criteria of section 4 of COTPA and declared as Smokefree villages by the head of Gram Panchayat. More than 50 thousand population is protected from tobacco smoke. Each village has passed the resolution to adopt Smokefree criteria.

Background and challenges to implementation: GATS – 2 indicates that the tobacco burden in rural Uttarakhand is significantly high compared to the urban areas wherein adults who are exposed to tobacco smoke at home, workplace and any place is 62.2%, 24.5% and 33.4% respectively. The Indian government enacted the

Cigarettes and Other Tobacco Products Act (COTPA) in 2003 which prohibits smoking in public places. This study documents the smoke free village efforts undertaken in the rural areas of Uttarakhand.

Intervention or response: A convenient compliance assessment was undertaken in each village by observing 4 criteria i.e. availability of No Smoking Signages, active smoking, smoking aids, and evidence of recent smoking to check the compliance level during May and August 2020. Before the compliance, implementation was initiated to help villagers become smokefree wherein local body officials, Pradhans (Elected head of village), Police and Self-help groups of 21 gram panchayats were sensitised on smokefree policies, enforcement mechanism was established, smokefree signages and signboards were displayed at public places such as community centre, Panchayat offices; Primary Health centre, banks, Anganwadi Kendra, schools, tea and grocery shops etc.

Results/Impact: 21 Gram Panchayats covering nearly 82 villages had achieved the Smokefree status based on compliance assessment criteria of Section 4 of COTPA and declared as Smokefree villages by the respective Head of Gram Panchayat. This has protected more than 50 thousand people from second-hand smoke. Each village has passed the resolution to adopt Smokefree criteria.

Conclusions: Tobacco-free village campaign demonstrates exposure to tobacco smoke can be controlled and prevented through continuous engagement with village-level stakeholders, motivated local-leaders and community-workers establish new social norms in villages. This low-cost, community-driven program holds promise for helping public-health practitioners and governments implement and achieve the goals of tobacco control policies.

EP-38-476 The filter fraud: banning the sale of filtered cigarettes as a new key strategy for tobacco control

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Background and challenges to implementation: Deceptive cigarette descriptors such as “low tar” and “lights” were banned by Congress in 2010. Yet the biggest deception remains unchallenged: the filter. Although present on 99% of cigarettes, with the implication of reduced harm, filters do not reduce lung cancer or heart disease. Can new evidence of the filter’s environmental harm change public perception?

Intervention or response: As with flavorings, filters facilitate nicotine addiction by making smoking less harsh and easier to initiate. This false security diminishes the urgency to quit. Lung cancer mortality risk among smokers doubled for men and increased by almost 10-

fold for women from 1960-1980; relative risks for lung adenocarcinoma increased from 4.6 to 19.0 in men and from 1.5 to 8.1 in women. These increases are linked to the adoption of filtered brands. The tobacco industry and public health community alike have known for decades that the filter does not provide any health protection. Meanwhile, as filtered cigarette sales increased, the filters on discarded butts became the most common trash item collected on beach and urban cleanups. Made of cellulose acetate, a non-biodegradable plastic, cigarette filters have become a significant environmental problem and a hazard to wildlife and humans.

Results/Impact: The health community's failure to heed warnings by researchers since the 1970s about the filter deception contributed to public ignorance and regulatory complacency. The filter should have been banned along with the descriptors "low tar" and "lights." Now that plastic filters comprise the bulk of tobacco waste, leaching toxic chemicals into water and soil, they should be subject to hazardous waste and clean water regulations and banned as an upstream environmental intervention.

Conclusions: Tobacco control agencies can engage with environmental groups to challenge state and local jurisdictions to ban sales of filtered cigarettes and reeducate consumers about the harmfulness of filters to health and the environment.

EP-38-477 "Tobacco endgame" in India: critical analysis of the existing tobacco control policies and the way forward

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Background: The broad aim of tobacco endgame is to reduce the prevalence of tobacco use by less than 5% by 2030 in India. Reducing availability of tobacco products to younger age groups are the key policy recommendations for tobacco endgame. GATS, 2017 shows significant reduction in tobacco use from 34.6% (2010) to 28.6% in India. There is remarkable decline of 54% and 33% in the tobacco use in the age group of 15-17 and 15-24 years respectively. The age of initiation has increased from 17.9 to 18.9 years also. Youth (15-29 age groups) comprises 27.5% of Indian population and they are the potential target of tobacco industry also. The objectives of this study is to explore the possibilities to protect youth from Tobacco use to achieve tobacco endgame.

Design/Methods: The rationalist model by Carl V. Patton has been used for the policy analysis. The MPOWER policies, Indian Tobacco control laws (COTPA), National Tobacco control Program (NTCP), Consumer protection act, Food safety act (FSSAI), Juvenile justice act, Tobacco Vendors Licensing act, Municipalities act, Poison act and Central Board of Secondary Education (CBSE) guidelines have been analyzed to explore the

possibilities for protecting youth from tobacco use.

Results: The MPOWER policies and COTPA provides restrictions on sale of tobacco to and by the minor. NTCP have awareness component for youth protection. Food safety act regulates the sale and manufacture of smokeless tobacco. Consumer protection act and Juvenile justice act have very stringent provisions for tobacco control. The CBSE has also issued guidelines for tobacco control at school levels. But the implementation of these policies is quite low.

Background and challenges to implementation: The broad aim of tobacco endgame is to reduce the prevalence of tobacco use by less than 5% by 2030 in India. Reducing availability of tobacco products to younger age groups are the key policy recommendations for tobacco endgame. GATS, 2017 shows significant reduction in tobacco use from 34.6% (2010) to 28.6% in India. There is remarkable decline of 54% and 33% in the tobacco use in the age group of 15-17 and 15-24 years respectively. The age of initiation has increased from 17.9 to 18.9 years also. Youth (15-29 age groups) comprises 27.5% of Indian population and they are the potential target of tobacco industry also. The objectives of this study is to explore the possibilities to protect youth from Tobacco use to achieve tobacco endgame

Intervention or response: The rationalist model by Carl V. Patton has been used for the policy analysis. The MPOWER policies, Indian Tobacco control laws (COTPA), National Tobacco control Program (NTCP), Consumer protection act, Food safety act (FSSAI), Juvenile justice act, Tobacco Vendors Licensing act, Municipalities act, Poison act and Central Board of Secondary Education (CBSE) guidelines have been analyzed to explore the possibilities for protecting youth from tobacco use

Conclusions: GATS - 2017 results are motivating in terms of huge reduction in tobacco use among youth despite low attention. A targeted intervention is required for youth protection to achieve tobacco endgame in India

EP-38-478 Tobacco retailer landscape in India: a multi-state survey

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Background: The Indian tobacco market is known for its diverse tobacco products, with smokeless tobacco (SLT) being the most prevalent, followed by bidis. There are currently no estimates on the numbers of tobacco points-of-sale (PoS) that exist in India and compliance

has been consistently low for PoS restrictions (advertisement size, content restrictions, sale to minors etc.). Tobacco retailers are not licensed and are permitted to sell tobacco products along with other consumer goods.

The objective of this study was to determine the tobacco retailer density in 11 Indian states, covering wide geography with high burden of tobacco use.

Design/Methods: Between November 2019-January 2020, we collected data from the three most populous cities from 11 Indian states (Bihar, Gujarat, Haryana, Jharkhand, Karnataka, Kerala, Maharashtra, Punjab, Tamil Nadu, Uttar Pradesh, West Bengal). Within each city, markets were classified as high/medium/low based on the socioeconomic status (SES); three markets were identified, resulting in a total of 99 sampled market sites. A customized mobile-based data collection application was used for geo-tagging each tobacco retailer identified within each surveyed 3 km market transect.

Results: We mapped 2198 tobacco retailers along all the surveyed market transects. Four states (West Bengal, Jharkhand, Kerala and Karnataka) accounted for more than half (55.25%) of the retailers; we found more than 8 times the number of retailers in West Bengal (19.1 PoS/km) that sell tobacco than in the state of Punjab (2.4 PoS/km).

Conclusions: This study found wide variation in tobacco retailer density across states. Because there were no reliable data (city-wide housing or office rental data), our findings are based on market estimates/SES in the selected cities, the absolute count of tobacco retailers might differ. Tobacco retailer licensing could ensure stronger compliance with tobacco control and civic laws while raising revenues for city administration and individual retailers.

LATE BREAKER PRESENTATIONS WEDNESDAY 20 OCTOBER 2021

OA-16 The Union late-breaker session on COVID-19

LB-1879-20 Covid-19 among TB patients in Peru: an operational report from the national registry

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Background: Peru faced one of the highest burdens of COVID-19, with the higher number of deaths reported worldwide. Amongst American countries, Peru reports a high tuberculosis (TB) burden, with more than 80% persons with TB living in urban areas, same areas where also COVID-19 pandemic hits. This is an operational report of characteristics of people with TB and COVID-19 in Peru.

Methods: TB electronic records from the Peruvian National TB Program operational database (SIGTB) were reviewed. Adult persons who started drug-sensitive TB between 2020-2021 in Peru were included. We evaluated socio-demographic and clinical characteristics and operational variables on TB and COVID-19.

Results: 32755 persons diagnosed with drug-sensitive TB were identified, among them 6.9% (n=2246) were diagnosed with COVID-19. People who had TB and COVID-19 co-infection had a higher probability of death compared to those who did not have TB and COVID-19 co-infection (7.3% vs 4.6%, p<0.05). In addition, people with TB and COVID-19 had a slightly higher median age (37 years vs. 33 years, p<0.05), higher proportion of previous diabetes diagnosis (13.2% vs. 9.4%, p<0.05) compared to people with TB who did not have COVID-19. In relation to severity, we found that among those who had COVID-19 and TB, 20.4% (n=457) had moderate disease (12.0% of those who had moderate disease died) and 3.5% (n=78) had severe disease (69.2% of those who had severe disease died). Three of the 5 departments with the highest frequency of TB (Lima 53.8%; Ica 4.4% and La Libertad 4.2%) were also the areas with the highest frequency of TB and COVID-19 (Lima 33.4%; La Libertad 9.4% and Ica 4.3%).

Conclusions: Based on the available evidence and preliminary results, TB patients are a vulnerable population for COVID-19, not only because of socio-economic conditions (overcrowding, informal work) but also because of their pulmonary pathology, which can complicate both diseases.

LB-1858-20 An automated deep learning-based approach for a two-for-one screening of TB and Covid-19

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Background: Tuberculosis (TB) is one of the top 10 causes of death worldwide, while COVID-19 is an ongoing pandemic. Both TB and COVID-19 are respiratory illnesses that primarily affect the lungs and have overlapping symptoms such as cough and fever. Since the advent of COVID-19, TB screening programs have come to a stall, having a massive impact on the vulnerable population affected by TB.

Our work proposes an automated deep learning-based framework with rapid report generation for predicting the likelihood of COVID-19 and TB from a chest X-ray scan in two different settings (hospital and mobile diagnostic vans).

Methods: The Genki solution developed by DeepTek, Inc. was deployed in an Indian hospital (for COVID-19 screening) and in mobile diagnostic vans (for TB screening). Genki AI models have been trained on 1.5 million chest X-ray scans manually annotated by expert board-certified radiologists.

The solution provides an efficient radiology workflow with quick prescreening and rapid report generation by experts.

Results: For diagnosis of COVID-19, the AI model matched the radiologist's performance and obtained a sensitivity of 0.87 at a specificity of 0.60 from 9098 chest radiographs belonging to 3180 patients.

The model had a sensitivity of 0.91, a specificity of 0.82, and an accuracy of 0.82 for diagnosing tuberculosis in a TB population screening program involving over 80,000 subjects. Performance of the model was measured with Area Under the Curve (AUC) of 0.87 for COVID-19 and 0.96 for TB.

Conclusions: These results indicate that the model matched human expert-level performance in detecting tuberculosis and COVID-19 from chest radiographs. This model could be useful for identifying two chest conditions at the same time and providing immediate triage, especially in low-resource situations. Furthermore, the tool can also be optimized for the screening, quantification, and follow-up assessments of lung cancer and lung nodules.

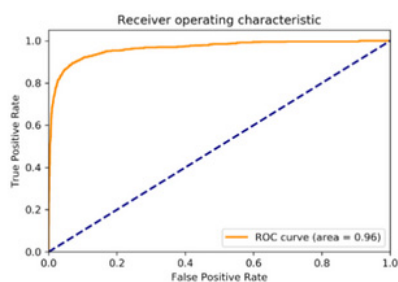


Fig (a) : ROC curve for Tuberculosis with AUC = 0.96.

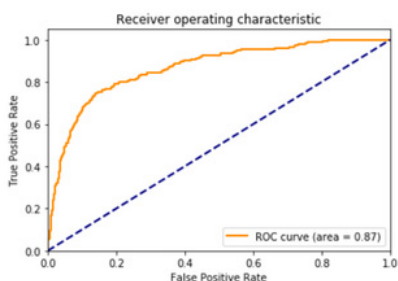


Fig (b) : ROC curve for COVID-19 with AUC = 0.87.

Figure. Receiver Operating Characteristic (ROC) curves of the model. (a) ROC curve with an area under the ROC curve (AUC) of 0.96 for tuberculosis. (b) ROC curve with an area under the ROC curve (AUC) of 0.87 for COVID-19.

LB-1868-20 Validation of rapid molecular testing for Covid-19 and integration with tuberculosis TB diagnostics in Lima, Peru

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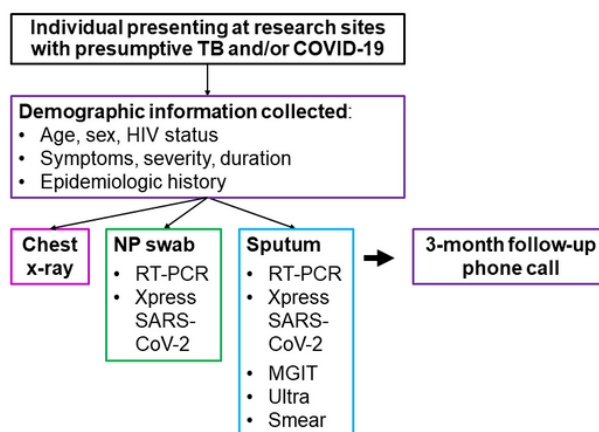
Background: Integrating tuberculosis (TB) and COVID-19 testing is an opportunity to provide care for both diseases. Many high TB burden countries already have existing GeneXpert networks for TB detection, and now a COVID-19 assay, Xpert Xpress SARS-CoV-2 (Xpress), for GeneXpert is available.

We are evaluating the diagnostic accuracy of Xpress for COVID-19, and assessing the feasibility of concurrently testing for TB with Xpert MTB/RIF Ultra (Ultra) in Lima, Peru.

Methods: We are conducting a multisite, prospective diagnostic accuracy study in Lima. We are recruiting 500 adults presenting with clinical symptoms suggestive of TB and/or COVID-19. See Figure 1 for diagnostic work-ups. Xpress diagnostic accuracy was determined using

a composite reference standard approach. Diagnostic yield of each GeneXpert test on a single sputum sample was also calculated to assess testing integration.

Results: At the time of reporting, data were available from 452 participants. Compared to RT-PCR on nasopharyngeal swab (NPS), Xpress sensitivity was 90% (95%CI: 84-95) on NPS and 84% (95%CI: 77-90) on sputum, while specificities were 81% (95%CI: 76-85) and 93% (95%CI: 89-96), respectively. Using a definition of RT-PCR positivity on NPS, COVID-19 prevalence was 30% (137/452), while Ultra-positive TB prevalence was 9.5% (43/452). Of these 43 participants, 3 were RT-PCR positive on NPS, 9 were Xpress positive on NPS, and 3 were Xpress positive on sputum, suggesting about 20% of TB patients may have COVID-19. Diagnostic yield using one sputum sample was high, as Ultra detected 97% of culture-positive TB cases, and Xpress detected 84% of COVID-19 cases defined by a positive RT-PCR on NPS.



Conclusions: Capitalizing on available technologies like GeneXpert to concurrently test for TB and COVID-19 may simplify and improve access to healthcare in high TB burden settings with high COVID-19 levels. Sputum may be an appropriate specimen for COVID-19 testing using Xpress, especially during times of supply chain issues.

LATE BREAKER PRESENTATIONS THURSDAY 21 OCTOBER 2021

OA-22 The Union student late-breaker session on lung health

LB-1886-21 The use of acute phase proteins as biomarkers of response to pulmonary TB treatment among children and adolescents

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Background: Pulmonary tuberculosis (PTB) in young children is paucibacillary and a challenge in monitoring response of anti-TB treatment. The use of biomarkers as point-of-care tests has become a useful alternative to this challenge. Vascular endothelial growth factor (VEGF), Interleukin-6 (IL-6), Matrix metalloproteinase-1 (MMP-1) and Procalcitonin (PCT) are acute phase proteins (PFA) that have been studied as biomarkers in TB treatment. Our aim is to verify whether these biomarkers have serum levels capable of monitoring TB treatment among children and adolescents.

Methods: A prospective study was carried out with samples collected from patients aged 0 to 19 years, from September / 2014 to February / 2018, with PTB considered confirmed if the patient had a Gene Xpert molecular test and / or a positive culture for *M. tuberculosis*. Blood samples were collected at diagnosis (T0), and in the first (T1), second (T2) and sixth (T6) month following treatment. Serum levels of the four biomarkers were measured by multiplex microsphere tests. Data were analyzed using the Wilcoxon test using the GraphPad Prism v.8.0 program (GraphPad Inc., San Diego, CA). Statistical significance was $p < 0.05$.

Results: Twenty-eight patients were included, 17 females; the median age was 12 years. Serum levels of biomarkers decreased during treatment, between T0 and T6, for VEGF the medians were $1787.50 > 936.50$ ($p < 0.0001$); for IL-6 $423.50 > 262.00$ ($p = 0.02$); MMP-1 $3203.00 > 1978.00$ ($p < 0.0001$) and PCT $0.60 > 0.48$ ($p < 0.0001$). The greatest drop in levels of each biomarker occurred between diagnosis and T1, with statistical significance for all biomarkers studied.

Conclusions: The four AFPs evaluated proved to be promising biomarkers to differentiate anti-TB treatment times in pediatric patients, especially in the first month of treatment.

LB-1880-21 Healthcare worker experiences of implementing TB infection control: a qualitative evidence synthesis to inform implementation recommendations

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Background: Implementation of TB infection prevention and control (IPC) measures in health facilities are frequently inadequate, despite nosocomial TB transmission to patients and health workers causing harm. We undertook a qualitative evidence synthesis to explore TB IPC implementation in health facilities and develop implementation recommendations.

Methods: We searched Pubmed, Web of Science, Embase and Global Health by Ovid, Global Index Medicus and CINAHL in February 2020, complemented by citation tracking in August 2020, for studies that used qualitative methods to explore the experiences of health workers implementing TB IPC in health facilities. Two reviewers independently screened titles and abstracts and reviewed full texts of potentially eligible papers.

We used the Critical Appraisals Skills Programme checklist for quality appraisal, thematic synthesis to identify key findings and the GRADE-CERQual method to appraise the certainty of review findings.

Results: We screened 1799 titles and abstracts and reviewed 93 full texts. 34 studies were included in the synthesis.

Key findings include:

1. TB IPC training is often offered to health workers managing TB patients, rather than all frontline workers who are exposed to TB;
2. health workers attach greater importance to TB IPC when hearing about occupational TB in others
3. weak TB IPC relates to health workers feeling undervalued and unsafe at work;
4. health workers may compromise clinical care of patients (avoiding contact, blocking referrals) when concerned about their own TB exposure;
5. access to particulate filter respirators and ventilation infrastructure for TB are reportedly poor,
6. TB IPC tools are directed towards areas where patients with confirmed TB receive care.

Conclusions: TB IPC resources should be directed to high-risk areas for TB transmission in health facilities instead of predominantly focusing on patients known with TB. Implementation plans should link IPC with occupational health. Further research about local solutions to TB IPC implementation challenges are needed.

LB-1850-21 Smoking cessation and advice given to TB patients at hospital-based TB-DOTS clinics in North Sumatera, Indonesia

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Background: TB patients are recommended to receive smoking cessation support to potentially reduce disease severity and outcomes. However, the coverage of advice given and its adequacy for smoking cessation among TB patients have been rarely reported. The study aimed was to assess its coverage and adequacy with smoking cessation among TB patients in North Sumatera, Indonesia.

Methods: A cross-sectional study was conducted at four hospitals in Medan from December 2019 to February 2020. ABC (Ask, Brief advice, Cessation support) for TB approach by the International Union Against Tuberculosis and Lung Disease was used. TB patients with at least one month treatment with prior consent were face-to-face interviewed using a structured questionnaire. Patients who received brief advice from healthcare workers and did not smoke at all after diagnosis considered as quitters. Data were analysed using multivariate logistic regression with adjustment for potential confounders.

Results: Of 131 ever-smokers, 118 reported for being asked (90.1%) regarding their smoking status. Among those being asked, 62.7% been advised (B=brief advice) at one point during their TB-related clinic visits (for diagnosis or treatment). For the "C" component, 8 patients (10.8%) outlined once received it. Among current smokers who received brief advice from healthcare workers compared to those without given advice was not statistically significant with becoming quitters (52.4% vs. 36.8%, AOR 1.64; CI = 0.33 – 8.27) after adjustment for nicotine dependence level and DOTS providers smoking messages.

Conclusions: Support for smoking cessation was seriously lacking, which may explain ineffectiveness of the intervention program for these TB patients.

LB-1782-21 Allergic rhinitis of adults in industrial city

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Background: Severe wind white dust storms during spring in Orkhon province.¹ Asian dust storm aggravated lower respiratory symptoms in adult patients with asthma.^{2,3} The aim of the study was to investigate the association between proximity to mine dumps and prevalence of asthma, allergic rhinitis of adults.

Methods: A cross-sectional, population based study including 1125 subjects from 30 to 81 years selected by probabilistic sampling techniques in industrial city was conducted. The questionnaire performed on the basis of WHO Protocol for Assessment of Prevalence of Major Respiratory Diseases. The respiratory symptoms were defined as follows: Allergic rhinitis is defined as presence to all of its 3 symptoms including sneezing, running nose and nasal congestion. Allergic rhinoconjunctivitis is defined as allergic rhinitis accompanied with itchy eye and redness. Logistic regression was used for exploring risk factors.

Results: A total of 1125 subjects were included. Mean was a gender; age 48.35 ± 10.5 years and BMI 27.7 ± 4.97 kg/m² were no difference three groups but a significantly decreasing pulmonary function defined in industrial areas than other 2 groups. Rhiniconjunctivitis defined 26.8% (301), which had the highest subjects living near the industry in March, Apr, and May. Male OR 1.6 (CI 1.1- 2.2), Heating coal and wood OR 1.3 (CI 0.9-1.8), Second smoking OR 1.1 (CI 0.8-1.5), Current smoking OR 0.9 (CI 0.6-1.3), Occupation industry OR 1.6 (1.0-2.2), Occupation unspecified OR 1.4 (CI 0.9-2.2)

Conclusions: We described the epidemiologic situation of allergic rhinoconjunctivitis in adults 30 years an industrial city of Mongolia.

LATE BREAKER PRESENTATIONS FRIDAY 22 OCTOBER 2021

OA-32 The Union/CDC late-breaker session on TB

LB-1836-22 First evaluation of the performance of the portable IGRA, QIAreach® QuantiFERON®, and its potential use in low-resource settings

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Background: The QIAreach® QFT is a novel portable immunoassay that uses the same TB2 tube of QFT-Plus to detect IFN- γ in plasma released from both CD4 and CD8 T cells. Assay utilizes a highly sensitive digital lateral flow technology on a portable battery-operated platform (eHub) eliminating the need to perform enzyme-linked immunosorbent assay (ELISA). It's capable of analyzing up to eight tests in 20 minutes time, providing a qualitative result (positive or negative). This study aims to evaluate QIAreach® QFT diagnostic performance in resource-constrained setting using QuantiFERON®-TB GoldPlus ELISA (QFT-Plus) as a reference standard.

Methods: QIAreach® QFT and QFT-Plus were performed in 196 patients referred for routine TB infection screening at the National Public Health Laboratory, Malaysia. Qualitative IFN- γ responses were compared between tests, and total concordance of the outcome was analyzed.

Results: The overall percentage of agreement was 94.4% (two-sided 95% CI 90.6-97.6%) with a Cohen's κ of 0,88. The positive percent agreement (sensitivity) was 96.5% (CI 87.9-99.6%) and a negative percent agreement (specificity) was 94.2% (CI 88.4% to 97.6%). QIAreach® QFT overall error rate was 5.6% (11/196) and the indeterminate rate of QFT-plus was 4.1% (8/196). Of nine (4,59%) samples with discordant results, 7 and 2 were positive by QIAreach® QFT alone and QFT-plus alone, respectively. In thirteen QFT-plus positive specimens, both TB1-Nil and TB2-Nil value were <1IU/ml and all returned a positive QIAreach® QFT.

Conclusions: This study demonstrated an excellent level of agreement as well as high sensitivity and specificity of QIAreach® QFT compared to QuantiFERON-TB

Gold Plus when implemented in high TB incidence settings. In addition, given its operational advantages, QIAreach® QFT is suitable to be implemented in remote areas where limited infrastructure has hampered the accessibility of IGRA technologies. Rapid turnaround time make this assay a valuable tool for the decentralization of TB infection diagnosis.

	Frequency	Agreement	Upper 95% CI	Lower 95% CI
OPA	169/178	94.4%	90.6%	97.6%
PPA	55/57	96.5%	87.9%	99.6%
NPA	114/121	94.2%	88.4%	97.6%
Cohen's κ score		0.88		

LB-1831-22 Crossing the last mile: effective government-NGO collaboration for TB care in rural Madagascar

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Background: Despite free TB care for all, provision of and access to TB care in rural Madagascar faces many challenges. Public care facilities are poorly staffed and suffer from supply chain interruptions. A reliable power supply or access to clean water are rare, working conditions low and many facilities closed. Extreme poverty, affecting 78% of the population, is concentrated in rural areas and precludes many from seeking care. Thus, TB in this rural population might be underdiagnosed. We hereby aim to describe an integrative approach in alleviating barriers to TB care in Ampanihy, a rural district with a population of 386,000 in Atsimo Andrefana region, Madagascar.

Methods: We involved all stakeholders in assessing barriers in TB care and defined two main interventional pillars:

1. Fostering community engagement and
2. Decentralizing service provision.

Starting from 08/2019, we equipped 4 health workers to perform bimonthly motorbike-based TB clinics in 14 remote villages. We trained 22 community health workers in active case finding. Supervision and evaluation were

ensured by the national TB program. Based on 2010-2020 notification data from the national TB office, we calculated trend-adjusted additional notifications during the intervention (2019 and 2020).

Results: Trend-expected notifications for 2019 and 2020 in the intervention district were 1,003. During this time, 2,724 cases were reported. Thus, our activities led to the detection of 1,721 additional TB cases (2.6-fold increase). The intervention district's TB incidence increased from 178/100,000 in 2018 to 424/100,000 in 2020. Regionally, an additional 610 cases were reported.

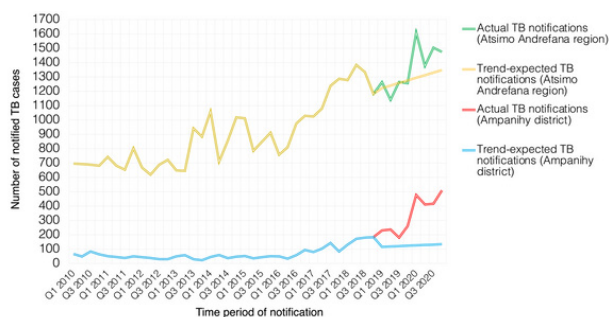


Figure. Trend-expected vs. actual TB notifications in Ampanihy district and Atsimo Andrefana region, Southern Madagascar, 2010-2020.

Conclusions: Our collaborative approach led to a stark increase of TB notifications and incidence in a rural district of Madagascar. Combining community engagement and motorbike-based mobile clinics offer a simple but effective solution for reaching vulnerable populations.

LB-1867-22 Acoustic analysis of cough as a novel technology for the screening and diagnosis of active pulmonary TB

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Background: Preliminary results for a portable technology to record cough and perform acoustic analyses utilizing machine learning to potentially provide low-cost diagnostic screening for TB.

Methods: This is a prospective observational study enrolling patients reporting cough at a primary health facility in a high TB burden setting. Cough recordings are

collected using a smartphone and a high-fidelity recording system at baseline and at defined intervals until the cough is resolved and diagnosed. At baseline, data were collected on spirometry, Xpert MTB/RIF assay, chest radiography, TB symptom screen, vital signs, medical history, and socio-demographics.

Results: 428 adults had been recruited, of whom 72 (16.82%) were healthy controls. Among the patients with cough 84 (19.63%) were diagnosed with TB, 246 (57.48%) with other respiratory conditions, and 26 (6.07%) with cardiac conditions. 122 (28.50%) patients were HIV positive, 65 (15.19%) had hypertension and 8 (1.87%) had diabetes. At baseline, 216 (60.67%) patients reported chest pain, 198 (55.62%) cough more than 2 weeks, 135 (37.92%) fever, 137 (38.48%) night sweats, and 186 (52.25%) had experienced weight loss. Mel-frequency cepstral coefficients (MFCC) features and derivatives (50 in total) extracted from the cough recordings were used in a support-vector classification (SVC) model with leave-one-patient-out cross-validation. The model positively identified 95.24% of TB patients at 90.12% specificity, with 91.12% accuracy. Using vital metrics alone resulted in a sensitivity of 70.24% and a specificity of 74.12%. With only symptoms as features, the model positively identified 79.76% of TB patients at a specificity of 78.49%. Combining acoustic, symptoms, and vital metrics features yielded a sensitivity of 96.43%, a specificity of 90.12%, and accuracy of 91.36%.

Conclusions: Preliminary results indicate that mobile cough analysis technology might be a feasible front-line triage tool for non-invasive screening of active pulmonary Tuberculosis from other respiratory conditions in a low resource setting.

LB-1835-22 A randomised Phase 2 trial of pretomanid-containing regimens for drug-susceptible TB: 12-week results

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Background: Pretomanid is a new nitroimidazole with demonstrated treatment-shortening efficacy in drug-resistant tuberculosis. In mice, regimens including pretomanid, rifamycins, and pyrazinamide are especially potent. In humans, rifampicin (but not rifabutin) reduces pretomanid concentrations. Pretomanid-rifamycin combinations have not previously been tested clinically.

Methods: In Assessing Pretomanid for Tuberculosis (APT, NCT02256696) a Phase 2 open-label randomized trial, South African adults with pulmonary

tuberculosis received isoniazid (H), pyrazinamide (Z), plus (a) pretomanid (Pa) and rifampicin (R) (2PaHRZ/1PaHR/3HR, Arm 1) (b) pretomanid and rifabutin (Rb) (2PaHRbZ/1PaHRb/3HR, Arm 2) or (c) rifampicin and ethambutol (E) (2HRZE/4HR, standard of care (SOC), Arm 3).

During Study Treatment (first 12 weeks), sputum for liquid and solid culture and safety labs were collected at Weeks 1, 2, 3, 4, 6, 8, 10, and 12. Time to culture conversion on liquid media in the modified intention-to-treat (mITT) population over 12 weeks was the primary outcome.

Results: Among 157 participants enrolled, 125 (80%) had cavitory disease. Median time to liquid culture negativity in the mITT population (n=150) was 41 days (Arm 1), 28 days (Arm 2), and 55 days (Arm 3) (p=0.01, Figure) (Hazard ratios of 1.62 (1.08 – 2.43, p=0.02, Arm 1 vs. Arm 3) and 1.77 (1.17-2.69, p=0.01, Arm 2 vs. Arm 3). 8-week culture conversion was 79%, 89%, and 69% on liquid culture and 98%, 100%, and 96% on solid culture (Arms 1, 2, and 3, respectively).

Grade ≥ 3 adverse events occurred in 3/56 (5%), 5/53 (9%), and 2/56 (4%) of participants, with elevated transaminases in 5 (1 in Arm 1, 4 in Arm 2). There were 3 SAEs (Arm 2) and no deaths during study treatment.

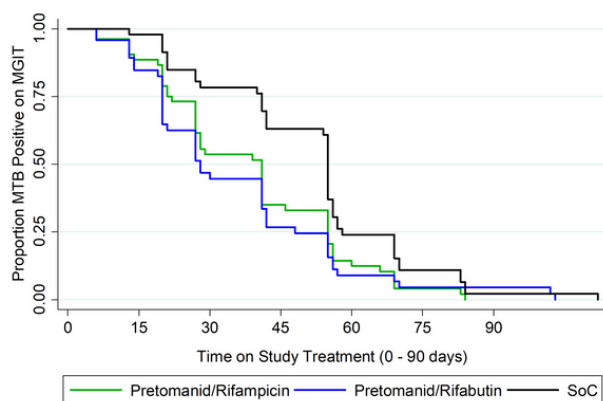


Figure. Kaplan-Meier estimate of time to culture conversion on liquid media (MGIT)

Conclusions: Pretomanid enhanced the microbiologic activity of rifamycin- and pyrazinamide-containing regimens. The pretomanid and rifabutin-containing regimen had the highest efficacy overall, but with more liver enzyme elevations. Whether this is due to higher pretomanid concentrations merits exploration.

LB-1825-22 A Phase 2 open-label, randomised-controlled trial of adjunctive N-acetylcysteine (NAC) in TB: interim findings of a TB-SEQUEL sub-study in Mbeya, Tanzania

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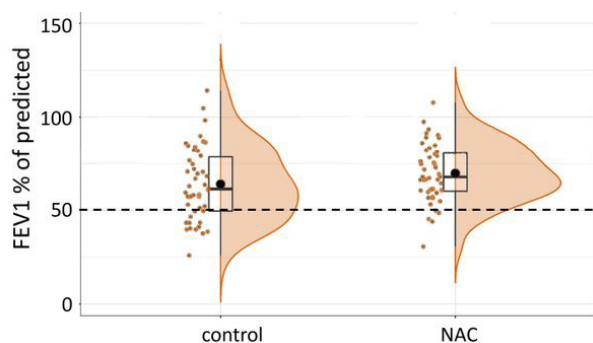
Background: Most TB patients are left with bronchiectasis and/or fibrosis, causing disability and shortening longevity despite cure. Oxidative stress contributes to lung damage. In preclinical TB models, NAC restores glutathione and reduces necrotic lung injury. NAC similarly increases glutathione in TB patients (abstract WCLH-2021-00289).

We here report an interim analysis of its clinical effects in TB patients through month-6.

Methods: Participants were adults providing written informed consent, with first TB episodes, sputum Xpert showing RIF-S and Ct ≤ 27 , chest X-ray showing moderate or far-advanced disease, lab safety parameters within specified limits, and, if HIV+, ≥ 100 CD4+T cells/ μ L.

Patients were randomly assigned to standard TB therapy with/without NAC 1200mg BID for days 1-112. HIV+ patients either started or continued ART. Spirometry was performed at baseline, 0.5, 2, and 6 months. Sputum was examined at specified intervals by liquid and solid culture.

Results: 93 patients with spirometry data at month-6 were included in this analysis. At baseline, the mean age=35.6yrs, BMI=19.7, and Xpert Ct=16.4. 75.3% were male, 53.8% had far-advanced disease and 26.9% were HIV+ (mean CD4=474). Arms were reasonably balanced, although 43 patients recruited under pre-2019 ATS/ERS guidelines did not have baseline spirometry. NAC was well-tolerated, with no discontinuations due to AEs or intolerability. At month-6, mean FEV1% = 69.8 \pm 15.6 in NAC recipients and 63.9 \pm 19.7 in controls (P=0.085). 5 NAC recipients (22.7%) vs 13 controls (46.4%) had FEV1 $\leq 50\%$ of predicted (P=0.038, see histogram below). There was no effect on FVC. FEV1/FVC was superior in NAC recipients (90.7% vs 86.8%, P=0.047). There was no effect on risks of death, failure, or discontinuation, or the HR for stable culture conversion. 30 additional subjects have not yet reached month-6.



Conclusions: Adjunctive NAC appears to promote recovery of lung function in TB, reducing the proportion of patients with severe FEV1 impairment and increasing FEV1/FVC, consistent with ameliorating bronchiectasis.

LB-1832-22 An economic evaluation of three novel stool processing methods for the diagnosis of paediatric TB

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Background: To close the pediatric TB diagnostic gap, stool is considered as a non-invasive alternative to sputum. Three new stool processing methods (SPM) were developed for use in combination with Xpert Ultra MTB/RIF: Stool Processing Kit (SPK), Simple One Step (SOS), and Optimised Sucrose Flotation (OSF). A recent diagnostic accuracy study (separate abstract AS-WCLH-2021-01252) showed the SPMs have similar sensitivity (SOS 52.1%; SPK 48.3%; OSF 46.8%) and specificity (all >97%). Because the SPMs vary substantially in consumables and processing time required, cost becomes a critical driver of decision-making for scale-up. This economic evaluation informed a recent WHO review.

Methods: We focused on children ≤ 5 , using a health system perspective and costs in 2020 USD. A micro-costing study estimated the average cost per test for each SPM/ Ultra in a referral hospital laboratory in Kampala, Uganda. The most cost-effective SPM/ Ultra was then

modelled for implementation at peripheral outpatient clinics. A decision tree model aligned with Ugandan pediatric TB guidelines compared diagnosis with SPM/ Ultra to standard of care (SOC), primarily clinical evaluation. The outcome was the incremental cost-effectiveness ratio (ICER) per life-year saved (LYS).

Results: The average cost per test was lowest for SOS/ Ultra (\$13.90), followed by OSF/ Ultra (\$19.89) and SPK/ Ultra (\$20.27). Having the highest sensitivity and lowest cost, SOS/ Ultra was modelled for implementation. At 3% TB prevalence, the ICER for SOS/ Ultra was \$611 per LYS, above the cost-effectiveness threshold (CET) of \$288 for Uganda. In sensitivity analyses, TB prevalence had the largest impact on the ICER. SOS/ Ultra became more cost-effective as prevalence increased and crossed the CET at 7% prevalence.

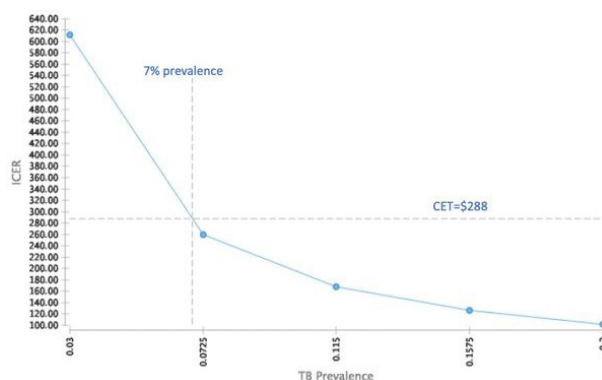


Figure. The sensitivity analysis varying the prevalence of TB disease from 3% to 20% impacts the incremental cost-effectiveness ratio (ICER). At a TB prevalence above 7%, SOS/ Ultra was below the cost-effectiveness threshold (CET) for Uganda of \$288.

Conclusions: In this first economic evaluation of these SPMs, we show SOS/ Ultra is more cost-effective than other SPMs and SOC. Further analyses need to identify screening algorithms for children that balance cost, accuracy, and access to identify the sub-populations that would benefit most from stool testing.

LB-1816-22 An all-oral 6-month regimen for multidrug-resistant TB (the NExT study)

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Background: Improving treatment outcomes, reducing drug toxicity, eliminating injectable agents, and shortening the treatment duration to 6-months (the same as rifampicin-susceptible tuberculosis) remains an aspirational goal for the treatment of multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB).

Methods: We conducted a multicentre randomised controlled trial in adults with MDR/RR-TB (i.e. without resistance to fluoroquinolones or aminoglycosides). Participants were randomly assigned (1:1 ratio) to a ~6-month all-oral regimen that included levofloxacin, bedaquiline and linezolid, or the standard-of-care ≥ 9-month WHO-approved injectable-based regimen. The primary endpoint was a favourable WHO-defined treatment outcome 24 months after treatment initiation.

Results: 93 of 111 participants randomised were included in the modified intention-to-treat analysis; 51 (55%) were HIV co-infected (median CD4 count 158 cells/mL). Participants in the intervention arm were 2.2 times more likely to experience a favourable 24-month outcome than participants in the standard-of-care arm [RR 2.2 (1.2-4.1); p=0.006]. Toxicity-related drug substitution occurred more frequently in the standard-of-care arm [(65.9% (29/44) versus 36.7% (18/49), p=0.001)]; 79.3% (23/29) due to kanamycin (mainly hearing loss; replaced by bedaquiline) in the standard-of-care arm, and 83.3% (15/18) due to linezolid (mainly anaemia) in the interventional arm. Culture conversion was significantly better in the intervention arm [HR 2.6 (1.4-4.9); p=0.003] after censoring those with bedaquiline replacement in the standard-of-care arm.

Conclusions: An all-oral 6-month levofloxacin, bedaquiline and linezolid-containing MDR/RR-TB regimen was associated with significantly improved 24-month treatment outcomes compared with traditional injectable-containing regimens. However, drug toxicity occurred frequently in both arms. These findings inform strategies to develop future regimens for MDR/RR-TB.

LB-1786-22 Diagnostic accuracy of the Cepheid 3 gene host-response fingerstick blood test in a prospective, multi-site study

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Background: The development of a fast and accurate, non-sputum-based point-of-care triage test for tuberculosis (TB) would have a major impact on combating the TB burden worldwide. A new fingerstick blood test has been developed by Cepheid (Xpert-MTB-Host Response (HR)-Prototype). Here we describe the first prospective findings of the MTB-HR prototype.

Methods: Fingerstick blood from adults presenting with symptoms compatible with TB in South Africa, The Gambia, Uganda and Vietnam was analysed using the Cepheid GeneXpert MTB-HR prototype. Accuracy of the Xpert MTB-HR cartridge was determined in relation to GeneXpert Ultra results and a composite microbiological score (GeneXpert Ultra and liquid culture) with patients classified as having TB or other respiratory diseases (ORD).

Results: When data from all sites (n=75 TB, 120 ORD) were analysed, TB score discriminated between TB and ORD with an AUC of 0.94 (CI, 0.91-0.97). When sensitivity was set at 90% for a triage test, specificity was 86% (CI, 75-97%) at a cut-off of 2.05. These results were not influenced by HIV status or geographical location. When evaluated against a composite microbiological score (n=80 TB, 111 ORD), the TB score was able to discriminate between TB and ORD with an AUC of 0.88 (CI, 0.83-0.94).

Conclusions: Our interim data indicate the Cepheid MTB-HR cartridge reaches the minimal target product profile for a point of care triage test for TB using fingerstick blood, regardless of geographic area or HIV infection status.

TBSCIENCE2021 ORAL ABSTRACTS

TBS-02 Tools to guide personalised therapy: what is achievable? Oral Abstracts

TBS-02-01 Bedaquiline in cerebrospinal fluid

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Background: Central nervous system tuberculosis (CNS-TB) is the most severe form of TB, disproportionately affecting children and the immunocompromised. Data are limited on the use of novel anti-TB agents bedaquiline, delamanid and pretomanid for CNS-TB. Bedaquiline is the first new agent developed for TB in decades. It is standard of care for drug-resistant pulmonary TB and is being investigated for treatment shortening in drug-sensitive TB. Bedaquiline penetrates into rodent brains, yet cerebrospinal fluid (CSF) concentrations were undetectable in one patient with CNS-TB. This remains the only evidence underpinning the current concern for its use in CNS-TB.

Methods: We conducted a nested pharmacokinetic study of bedaquiline and its M2 metabolite in CSF. Seven participants with rifampin-resistant pulmonary TB, without CNS-TB, received 14 days of oral bedaquiline 400 mg, followed by 200 mg three times per week for 22 weeks, and multi-drug background therapy. After 24 weeks plasma was collected pre-dose and 3, 5, 7, 10, and 22 hours post-dose; CSF was collected at either 5, 7, or 10 hours. BDQ and M2 concentrations in plasma and CSF were obtained using validated liquid chromatography tandem mass spectrometry assays.

Results: Plasma concentrations of bedaquiline and M2 were in the typical range. In CSF, both were detectable in all patients at all timepoints (Figure).

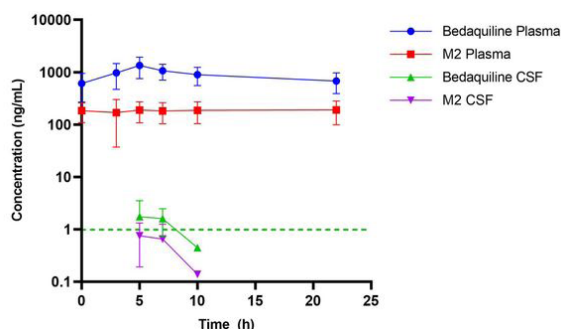


Figure. Bedaquiline and M2-metabolite plasma and CSF concentrations.

Bedaquiline and M2 protein binding are greater than 99.9% and 99.7% respectively. Therefore, the CSF concentrations for bedaquiline and M2 are in range of the expected unbound concentrations in plasma. The CSF to plasma ratio of 1 suggests free penetration of unbound drug into CSF.

Conclusions: Our results suggest bedaquiline may be useful for patients with CNS-TB. The potential role of bedaquiline in the treatment of CNS-TB deserves active investigation.

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TBS-02-02 The rabbit model of active TB predicts antibiotic penetration at the site of disease in patients

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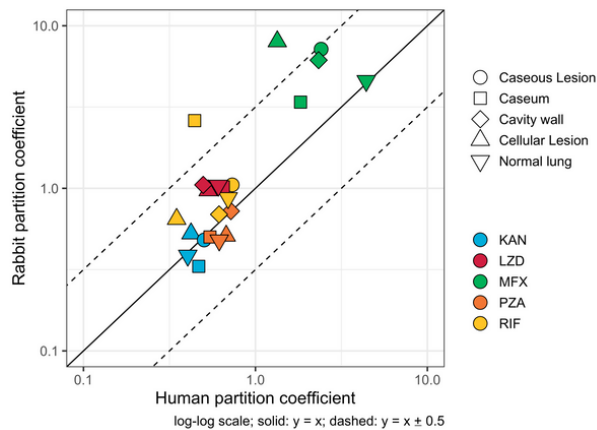
Anti-tuberculosis drugs must travel from plasma to bacterial lesions to be effective. Due to the lack of available clinical lesion samples and invasive nature of obtaining such samples, animal models are commonly used to understand drug distribution at the site of action. However, in the context of the diverse pathology of pulmonary tuberculosis, a nonclinical model has not yet been externally validated to be predictive of human lesion-centric pharmacokinetics.

We generated rabbit lesion pharmacokinetic profiles for rifampicin, pyrazinamide, linezolid, moxifloxacin, and kanamycin in five distinct lung compartments (normal lung, cellular lesion, caseous lesion, caseum, and cavity wall) and compared results to human lesion profiles from clinical lung resection studies. An aggregate of 1,030 plasma and 1,577 lesion samples from 141 rabbits were modeled. Physiological plasma-lesion pharmacokinetic models were developed for each drug using NONMEM v7.4.2. where the extent (partition coefficient) and rate were estimated for each lesion.

We found that partition coefficients obtained from the rabbit and clinical data are highly correlated (Pearson correlation: $r=0.816$, $p\text{-value}=3.5e-6$), indicating that extent of partitioning is similar between species. The high degree of correlation was consistent for all lesion types. Correlations deviated somewhat as values increased. For example, moxifloxacin had higher partitioning in rabbits overall compared to humans, however both models indicated excellent penetration in all lesion types. Drug ranking based on penetration were comparable between the two species.

Our results indicate that clinical lesion-centric drug penetration and pharmacokinetics in patients can be predicted and quantified using rabbit model of tubercu-

losis. Our work validates the use of rabbit experiments as a surrogate for costly and invasive clinical studies. Evaluating extent of penetration in rabbits can be used to evaluate new anti-tuberculosis drugs, predict clinical drug concentrations at the site of infection, and propose drug combinations and doses for clinical trials.



TBS-02-03 Genome-wide identification of *Mycobacterium tuberculosis* genetic markers associated with 2-month culture and smear positivity

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The genetic heterogeneity of *Mycobacterium tuberculosis* (MTB) characterized by drug-resistance-or-pathogen-virulence-associated variants, may contribute to the variability in treatment outcomes. Genome-wide association studies (GWAS) may identify novel genes and SNPs that could be associated with 2-month-culture-and/or-smear-positivity – implicating suboptimal treatment response.

We aimed to identify genes/regions/SNPs in the MTB genome that may be contributing to 2-month-smear-and/or-culture-positivity among TB patients receiving first-line treatment.

We enrolled a cohort of 4,500 adult patients with pulmonary TB in Lima, Peru between September 2009 and August 2012. Sputum samples were obtained at baseline and 2-months after treatment initiation.

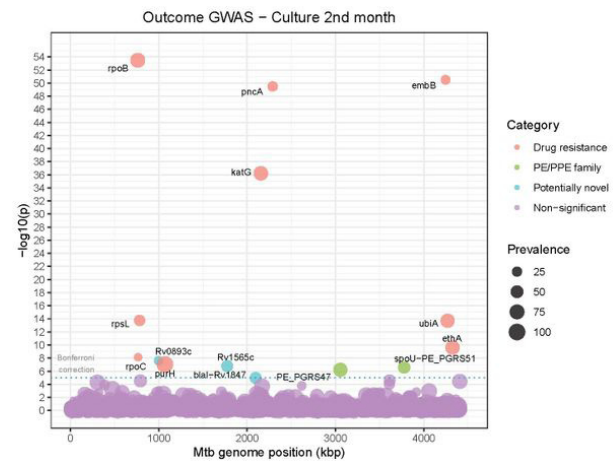
Among 3573 patients with positive cultures at treatment initiation, 495 (13.9%) remained culture-positive-at-2-months. Of these, we sequenced 2-month samples of 2445 (68.4%) patients.

We aligned the reads to the reference MTB_H37Rv NC_000962.3 and performed variant calling and annotation.

We conducted:

1. Gene-and-SNP-based GWAS for 2-month-smear-and-culture-positivity,
2. GWAS stratified on drug susceptibility testing phenotype i.e., GWAS conducted separately among drug-sensitive and resistant samples, and;
3. GWAS conditional on well-known drug-resistance genotypes.

We excluded any gene/region with a <0.01 minor allele frequency, computed a genetic relatedness matrix to correct for population structure, and set a <0.05 Bonferroni correction for multiple comparisons testing.



In addition to previously well-characterized drug-resistance mutations, we identified loci associated with 2-month-culture-positivity in genes *Rv1565c* and *purH* among drug-resistant isolates, and genes *Rv1976c*, *Rv1176c*, *esxI* and *espC* among drug-sensitive isolates. Among isolates without known *rpoB* mutations, we identified *Rv1976* and *Rv1532c*; among isolates without known *katG* mutations, we identified *nicT*, *mbtA*, *fadE5-Rv0245*; and among isolates without *embB* mutations, we identified *rpoC*, *nicT* as significant genes.

In addition to recognized drug-resistance variants, our study identified new loci which were predictors of 2-month-culture/smear-conversion. Our findings have diagnostic implications for early detection of suboptimal treatment response and may help advance our understanding of the genetic basis of culture and smear outcomes for tailored TB therapy.

TBS-02-04 PRACTECAL-VAMS: a successful novel approach to microsampling to determine TB drugs levels

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VAMS (volumetric absorptive microsampling) is a method used to collect, store and transport blood samples for measurement of drug levels. It is cheaper and easier to use, especially in resource constrained settings. The study was carried out in South Africa in a subgroup of participants enrolled in TB-PRACTECAL Clinical Trial's investigational arms containing bedaquiline (Bdq), pretomanid (Pa), linezolid (Lzd), moxifloxacin (Mfx) or clofazimine (Cfz).

We aimed to determine the accuracy of quantification of anti-TB drugs using VAMS dried blood (capillary and venous) compared to liquid whole blood in cryotubes. Intensive PK samples at day 1 and week 8, and sparse samples at week 12 and 16 were collected. Drugs were extracted from blood samples by protein precipitation using organic solvents. Blood samples were quantified by HPLC-MS/MS.

Data were analysed with STATA v.15 and Prism v.9.1.2. Preliminary data on Pa, Lzd and Mfx are presented.

Thirteen patients contributed 650 drug measurements for analysis. Correlation across all timepoints for Pa was 95.4% for VAMS capillary blood versus VAMS venous blood, 96.5% for VAMS capillary blood versus liquid venous blood and 96.3% for VAMS venous blood versus liquid venous blood. For Lzd it was 98%, 98.1% and 96.9%, respectively. For Mfx it was 96.5%, 95.8% and 99.3%, respectively. Figure 1 presents the Bland-Altman plots for Pa comparing the paired percentage difference of the three sampling techniques.

VAMS method results correlate highly with liquid blood. The results allow expanded access to blood level measurements for novel TB drugs. To our knowledge, this is the first time that data on Pa and Mfx sampled by VAMS are reported. We acknowledge the limited sample size, further analysis on Bdq and Cfz are pending and modelling for estimating exposure will be conducted.

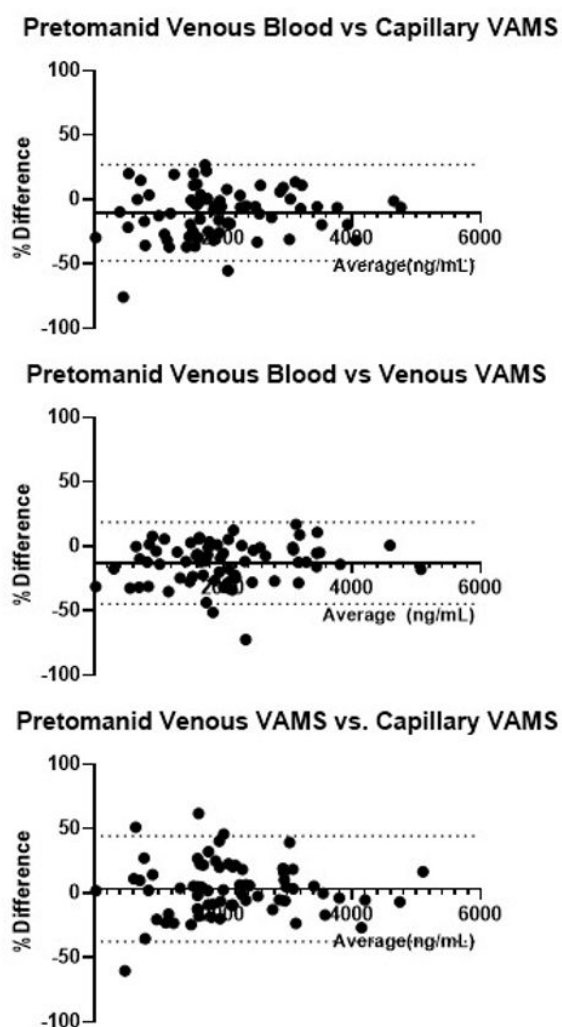


Figure 1 Bland-Altman plots of pretomanid sampling techniques' comparison

TBS-05 Recent innovations in trial design: where does TB 'treatment regimen shortening' go from here? Oral Abstracts

TBS-05-01 Increasing comparability of results from TB clinical therapeutic trials using the ICH E9 (R1) estimand framework

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Background: For the development of public health guidelines for TB treatment, it is essential to compare outcomes and pool data *across* clinical trials. This, however, appears to be extremely challenging, due to lack of standardization of trial outcomes. We conducted a systematic review of 31 TB phase III and phase IIC trial protocols and statistical analysis plans to understand similarities and differences in outcome definitions. The ICH E9 (R1) addendum introduces the "estimand" framework for defining outcomes and outlines strategies for dealing consistently with post-randomization events that affect or preclude their measurement, termed "intercurrent events" (ICEs).

Methods: To tailor this framework to TB trials, we derived standardized TB trial component and outcome definitions for use in future trials, adapting the estimand framework to provide detailed explanations of strategies for dealing with ICEs, dependent on different estimands. An iterative process is planned to involve TB trialists in the development of definitions and potential guidelines, based on our proposal.

Results: While there were many consistent definitions, trials included in the systematic review showed heterogeneity in outcomes and offered inconsistent strategies for dealing with ICEs. The estimand framework requires specification of five trial attributes: treatment being tested, population of patients, specific endpoint being measured, analytic plans for dealing with ICEs, and the population summary that will be used. We propose four estimands and outline attributes for each: a "TB-specific estimand," designed to address the treatment effect from the developer's perspective; a "composite estimand," similar to conventional outcome definitions, an "assessable estimand," which allows comparison to previous trials, and the "per-protocol estimand," which targets the treatment effect among participants who complete treatment.

Conclusions: Developing consensus guidelines for defining TB trial outcomes is critical to enable comparison of results across trials. Encouraging estimation of multiple estimands allows different stakeholders' interests to be specifically addressed.

TBS-05-02 Harmonised specification of estimands for TB treatment randomised controlled trials: an application in the REMoxTB study

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The International Conference on Harmonization recently adopted a framework for the specification of estimands in randomized controlled trials (ICH E9(R1) addendum). It will be both necessary and constructive to implement this idea framework in new randomized trial protocols for Tuberculosis treatments.

An estimand provides a "precise description of the treatment effect reflecting the clinical question posed by the trial objective" and has five attributes; treatment, population, endpoint, intercurrent events, and population-level summary. Intercurrent events address post-randomization occurrences all trials face which either preclude observation of the final endpoint or affect its interpretation.

Trials may pre-specify multiple estimands to address the respective objectives of different stakeholders. We have proposed a detailed specification of estimands for a composite efficacy endpoint regularly used in phase III Tuberculosis treatment trials.

We identified a common set of intercurrent events and defined four estimands distinguished by the application of a unique combination of handling strategies. To illustrate these TB estimands and to compare resulting population-level summaries, we re-analyzed data from REMoxTB study. Any new estimand should provide the same conclusion (ie not non-inferior); any estimand giving a different result is not fit for purpose.

We identified the occurrence of 18 intercurrent events from our proposed set and found similar distributions between the 3 treatment arms. We estimated our four estimands according to the difference in proportions and difference in cumulative probabilities.

When applying the hypothetical strategy for intercurrent events, we explored several estimation methods including binary multiple imputation, right censoring, inverse probability of censoring weighting (IPCW), and imputation of times to event to demonstrate the impact on each resulting estimand.

The specification of estimands is imperative in new randomized trial protocols and analysis plans. Harmonization of intercurrent events and estimation strategies from the start will benefit the advancement of the complex field of TB therapeutic research.

TBS-05-03 Treatment effect measures for culture conversion endpoints in Phase IIb TB treatment trials

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Phase IIb trials of tuberculosis therapy rely on early biomarkers of treatment effect to answer their primary efficacy objective. Despite limited predictive ability for clinical outcomes, culture conversion, the event in which an individual previously culture positive for *Mycobacterium tuberculosis* yields a negative culture after initiating treatment, is a commonly used endpoint.

Lack of consensus on how to define the outcome and corresponding measure of treatment effect complicates interpretation and limits between-trial comparisons. One common analytic approach is to compare the times to culture conversion between two treatment arms and use a hazard ratio as the measure of treatment effect. However, hazard ratios have limitations and are difficult to interpret.

We introduce the difference in restricted mean survival times (RMST) as an alternative measure to identify faster times to culture conversion and express the magnitude of effect on the time scale (ex. days). We illustrate the approach in the PanACEA MAMS-TB trial where we find the hazard ratio of 1.46 comparing highest dose rifampicin (R35HZE) to standard of care translates into an equivalent difference in RMST of 8 days over 12 weeks of treatment. That is, over 12 weeks of treatment, those in the R35HZE arm experienced culture conversion 8 days faster, on average, compared with those in the control arm (95% CI 1 to 15 days, $p=0.02$).

While an 8-day reduction in mean time to culture conversion over 12 weeks may ultimately predict treatment shortening with high dose rifampicin, this finding tempers enthusiasm compared with a large relative HR effect. It is plausible that large differences in RMST for time to culture conversion may be a better predictor of long-term clinical outcomes than relative measures like HR.

Future phase IIb/c TB treatment trials using a culture conversion endpoint should consider supplementing analysis reports with this attractive measure of effect.

TBS-05-04 EU-PEARL: design considerations on platform trials for TB

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The IMI project EU-PEARL has been launched in November 2019 to develop a generic framework for the design and implementation of integrated research platforms. This generic framework is supported by designing four platform trials in very different indications, namely Major Depressive Disorders, Tuberculosis, NASH and Neuro-Fibromatosis.

The objective of the proposed Tuberculosis platform trial is to develop novel regimens for DS TB, which are better tolerable and/or which may require shorter treatment duration while sustaining efficacy, resulting in potentially better compliance.

The platform study design shall limit allocation of patients to suboptimal treatment regimens via early futility stopping, while generating additional design efficiencies through sharing of a common control group and early interim analyses. Adaptive decision making on dropping suboptimal regimens early is particularly challenging in the setting of Tuberculosis, as the sub-optimality of candidate regimens may only be detected after sufficient follow-up of a sufficient number of patients.

The planned platform study will consist of multiple simultaneously enrolling Phase 2 substudies, which evaluate different regimen durations vs. standard of care. The primary endpoint for final decision making per substudy is the rate of favorable outcomes at 12 months post randomization, while interim analyses on short-term endpoints will be implemented to refocus resources on the most promising regimens through adaptive randomization and futility stopping.

Extensive simulation results indicate that the platform trial approach adds opportunities from the development duration and sample size perspective, while it may also add challenges to individual sub-study research objectives.

TBS-08 Bioaerosols: threats and opportunities. Oral Abstracts

TBS-08-01 Face mask sampling of patients with pulmonary TB predicts acquired *Mycobacterium tuberculosis* infection in household contacts

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Background: *Mycobacterium tuberculosis* (Mtb) relies on airborne transmission. We have previously shown the utility of mask sampling to capture exhaled Mtb as a non-invasive diagnostic tool in pulmonary TB (pTB). Here we evaluate whether mask sampling can additionally stratify transmission risk in household contacts of pTB.

Methods: Mask sampling was performed on forty-six microbiologically confirmed pTB patients prior to commencing TB treatment. Patients were stratified according to quantitative mask Mtb capture, into high ($\geq 20,000$ copies) and low/neg output ($<20,000$ copies) IS6110 output groups. Transmitted Mtb infection was determined in 181 of their household contacts with serial QuantiFERON (QFT) testing at baseline and 6 months, and defined by QFT seroconversion, or increase in interferon- γ of ≥ 1 IU/ml. Multilevel mixed-effects logistic regression was used to calculate adjusted odds ratios (AORs), correcting for household clustering and adjusted for significant co-founders ($p=0.1$).

Results: Mtb was detected in 91% (42/46) mask samples with high output in 19 (45%) individuals. Household contacts of high output patients had a threefold increased risk of transmitted Mtb infection compared to contacts of patients with low/neg output: QFT conversion 26% vs. 14%; AOR 3.20, 95% CI 1.26 - 8.12, $p=0.01$; and interferon- γ increase ≥ 1 IU/ml 34% vs. 15%; AOR 3.62, 95% CI 1.54 - 8.53, $p=0.003$. Neither conversion nor increase ≥ 1 IU/ml in QFT was associated with sputum bacillary burden, CXR score of disease extent/cavities or sleeping proximity.

Discussion: Mask sampling provides a novel non-invasive clinical tool for both diagnosis and stratification of infectivity risk in pTB patients, which can support and enhance TB control programmes for active case finding, stratified contact tracing and outbreak management. Similar to our previous work and published cough aerosol work, this study also highlights the superiority of aerosol sampling compared with traditional markers of infectivity, to better predict infection transmission risk in close contacts.

TBS-08-02 Effect of face masks, respiratory manoeuvres and detection methods on TB infectiousness readouts

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Tuberculosis (TB) predominantly spreads via cough aerosols. The potential effect of face masks (especially non-surgical forms) on TB's infectiousness requires clarification in the COVID-19 era. Furthermore, whether cough is essential for transmission is unclear and would have major infection control implications. We assessed if face masks (bandanas, cyclist buffs, paper masks, surgical masks) were associated with reduced infectiousness in pre-treatment patients. A Human Aerosol Chamber (HAC) was used to accumulate and capture aerosols across three phases:

1. Tidal breathing,
2. Spontaneous cough, and
3. Forced cough.

Patients did these three phases twice on consecutive days (one day no face mask and the other a randomly assigned face mask type). Aerosols were separately captured in each phase on solid medium using a six-stage Andersen Cascade Impactor and in liquid medium using SKC Biosamplers. Both media underwent culture and the liquid also Xpert MTB/RIF Ultra (Ultra). Aerosol particle size counts were collected, and the utility of novel culture methods explored.

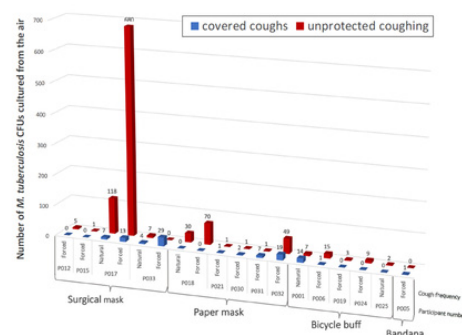


Figure. Number of M. tuberculosis colony forming units (CFUs) retrieved from the air of a 1000-liter tank in which select TB patients coughed during spontaneous and forced cough sessions on separate days. One set of sessions was with a face mask (blue columns) and the other session without a face mask (red columns). Wearing a face mask, including simple alternatives to surgical and paper masks, were associated with reduced CFUs. Not all patients are shown.

The figure shows patients (13/34) who grew CFU from aerosol from at least one phase. All face masks, including non-traditional alternatives, showed a trend towards reduced infectiousness proxies including: CFU [median

IQR 5 (1–49) for no mask vs. 1 (0–4.2) any mask], Ultra-positivity [18/34 vs. 15/34], and particle counts [81 (23–36200) vs. 46 (8–26700) ppm]. Without masks, CFU were still detected during breathing in phase 1 (3/27, not all patients underwent phase 1), however, these individuals all also had a spontaneous cough suppressed with a tissue. We also documented aerosolised *Mtb* with a dormancy-associated phenotype (culturable only after cell-free supernatant supplementation).

We demonstrate that non-surgical forms of masks may reduce infectiousness, that cough suppression during tidal breathing may still represent an infection risk, and that routine tools like Ultra can be used to partly quantify infectiousness on aerosol.

TBS-08-03 Differential lipid profiles among *Mycobacterium tuberculosis* isolates recovered from aerosol and sputum samples

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Background: *Mycobacterium tuberculosis* is transmitted almost exclusively by small particle aerosols. We explored the hypothesis that a more hydrophobic phenotype of the outer membrane lipids of mycobacteria may enhance *M. tuberculosis* aerosolization and therefore, augment transmission.

Methods: We conducted a proof-of-concept study of ten patients with culture-proven pulmonary tuberculosis (TB) in Kampala, Uganda. Five of them were defined as high transmitters based on the presence of culturable *M. tuberculosis* from cough aerosols, and five were low transmitters based on negative cough-generated aerosol cultures. We conducted lipidomic analyses of unprocessed sputum, standard and quantitative 7H11 cultures to evaluate host and *M. tuberculosis* lipid composition of aerosol-positive and aerosol-negative isolates. We also compared lipid profiles of *M. tuberculosis* isolates from aerosol and quantitative sputum cultures of aerosol-positive individuals.

Results: We found significant over expression of long, large chain components and phthiocerol dimycocerosates (PDIM) in quantitative sputum cultures from aerosol-positive subjects when compared to aerosol-negative individuals. Alpha-mycolic acid species with chain lengths of C75, C76, C78; methoxy-mycolic acid

species with chain lengths of C77, C82, C85, C87, C89 and C84, C86, C87, C88 keto-mycolic acids species were overexpressed in aerosol-positive isolates. Likewise, 14 of the 23 species of phthiocerol dimycocerosates (PDIM B) lipid species were significantly more abundant in aerosol-positive isolates (Figure 1).

In contrast, there were no differences in phthiocerol dimycocerosates (PDIM A) lipids between aerosol-positive and aerosol-negative isolates. There were no differences in lipid profiles among isolates obtained from standard sputum cultures, unprocessed sputum or from aerosol cultures.

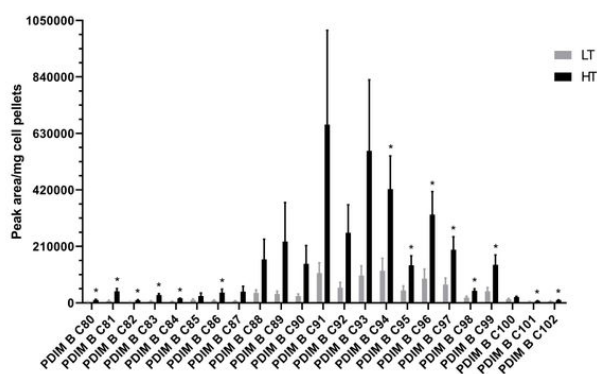


Figure 1

Conclusions: Differential lipid profile expressions from *M. tuberculosis* in quantitative sputum cultures were associated with *M. tuberculosis* viability in aerosol, suggesting a potential mechanism underlying bacillary survival in cough-generated aerosols and, increased infectiousness.

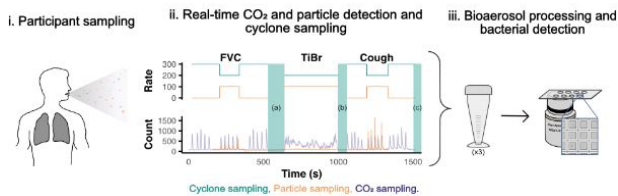
TBS-08-04 Cough-independent aerosolisation of *Mycobacterium tuberculosis* suggests a significant role for tidal breathing in asymptomatic TB transmission

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Disrupting *Mycobacterium tuberculosis* (*Mtb*) transmission remains an attractive anti-tuberculosis (TB) strategy, however our limited understanding of how particulate matter (including *Mtb*) is aerosolized in the peripheral lung during respiration undermines this approach. This study aimed to compare the aerosolization of *Mtb* and particulate matter from TB-positive patients during three respiratory manoeuvres: Tidal Breathing (TiBr), Forced Vital Capacity (FVC), and Coughing. GeneXpert-positive patients ($n = 39$) were recruited from TB clinics in Cape Town, South Africa. Bioaerosols were sampled within a Respiratory Aerosol Sampling Chamber (RASC), with real-time assessment of

CO₂ concentration and particle numbers stratified into 5 size categories. *Mtb* bacilli were detected using fluorescence microscopy.

On average, single TiBr manoeuvres produced 6-20 times fewer particles than either FVC or cough. No differences were observed across all manoeuvres in the proportions of particles detected in the size categories ranging from 0.5 to 5µm; however, cough produced proportionately fewer particles >5µm in diameter compared to FVC ($p = 0.026$). *Mtb* were detected consistently for all manoeuvres after the five-minute sampling, with 66%, 70%, and 61% of the samples positive for *Mtb* in TiBr, FVC, and cough respectively. Although a single TiBr manoeuvre produced approximately 1.6- and 2.2- times fewer *Mtb* than FVC and cough, respectively, TiBr and cough produced 64.5 and 3.8 *Mtb* bacilli per hour.



These findings suggest that coughing significantly increases particle aerosolization compared to TiBr, however, this increase in particle production does not appear to be associated with increased aerosolization of *Mtb*, with TiBr producing more *Mtb* per particle compared to coughing.

If the number of organisms detected reflects infectivity, this would suggest that TiBr might contribute to asymptomatic transmission in high-burden endemic settings.

TBS-11 TB vaccines: aspiring is not enough! Oral Abstracts

TBS-11-01 Cytomegalovirus acquisition in infancy and the risk of TB disease in childhood: a longitudinal birth cohort in Cape Town, South Africa

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Introduction: The risk of tuberculosis after recent exposure is greatest in the first few years of life, however the mechanisms responsible for this vulnerability are not well elucidated. Acquisition of viral infections, such as cytomegalovirus, in early life may modulate the immune system.

We studied the relationship between acquisition of cytomegalovirus in infancy and subsequent development of tuberculosis in children prospectively followed until 9 years of age.

Methods: We enrolled pregnant women between 20–28 weeks' gestation attending antenatal care in a peri-urban, poor South African setting in the Drakenstein Child Health study, a birth cohort. Nasopharyngeal swabs for cytomegalovirus detection using qPCR were done in infants at birth, three weeks, six weeks, three months, six months, 12 months, and 24 months. Children were followed prospectively for tuberculosis infection or disease using tuberculin skin testing done annually, and radiographic examinations with GeneXpert, culture, smear on induced sputum samples. We compared tuberculosis incidence in children with and without cytomegalovirus infection using Cox regression and hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: Among 963 children tested for cytomegalovirus infection ($N_{\text{tests}}=7,186$; median 6 tests per child, interquartile range, 2–11), 42% had cytomegalovirus infection by one year of age. Children who were breast-fed were at greatest risk (44% versus 14%, $P<0.0001$). Mother-child pairs were followed for tuberculosis for a median of 6.9 years (IQR, 6.0–7.8) and children with cytomegalovirus by one year of age had an increased hazard of subsequently developing tuberculosis (AHR, 3.2; 95% CI, 1.6–6.4) including microbiologically-confirmed disease (AHR, 4.4; 95% CI, 1.2–16.3). Infants with a high cytomegalovirus load were at consistently greatest risk of developing tuberculosis.

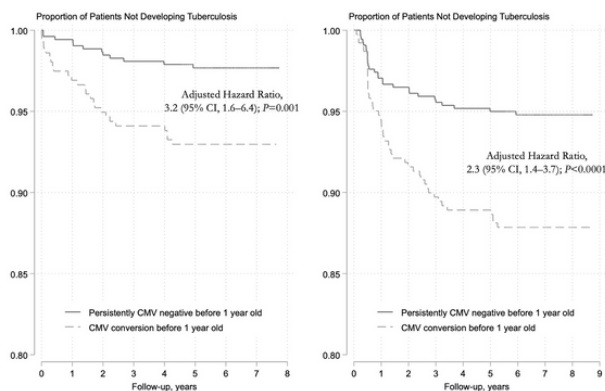


Figure. Acquisition of cytomegalovirus before 1 year of age and development of tuberculosis after 1 year of age (a) and throughout all of follow-up (b).

Discussion: Prevention of tuberculosis in childhood in high-burden countries may need to include strategies to deter or delay acquisition of cytomegalovirus prenatally or in the first months of life.

TBS-11-02 H107: a novel M. tuberculosis-specific subunit vaccine that provides synergistic immunity with BCG

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Recent phase II clinical trials investigating novel tuberculosis (TB) subunit vaccines as well as *Bacillus Calmette-Guérin* (BCG) revaccination have demonstrated encouraging efficacy results. These results are in support of combining BCG and subunit vaccines for increased efficacy. BCG and *Mycobacterium tuberculosis* (*Mtb*) share ~98% of their genome and current subunit vaccines are almost exclusively designed as BCG boosters. This might affect both T cell functionality as well as BCG colonization/take if the two vaccines are administered closely together in time.

The goal of our development efforts was to design a subunit vaccine that does not share antigens with BCG and explore the advantages of a BCG+subunit vaccine co-administration strategy, where the two vaccines do not cross-react. Eight individually protective antigens were selected to create H107, an *Mtb*-specific subunit vaccine.

Whereas subunit vaccines with BCG-shared antigens displayed cross-reactivity to BCG *in vivo* in both mice and humans, H107 showed no cross-reactivity and did not inhibit BCG colonization in mice.

Encouragingly, co-administering H107 with BCG led to increased adaptive immune responses, cellular and humoral, against both H107 and BCG. In contrast to a BCG-boosting vaccine that expands BCG-primed T cells, H107 broadened the overall vaccine repertoire with new T cell clones and introduced additional ‘adjuvant-

imprinted’ qualities to the vaccine response, including Th17 responses and less-differentiated Th1 cells. This phenotype was maintained after *Mtb* infection, and BCG+H107 provided significantly increased long-term protection compared to both BCG and H107 alone, as well as BCG combined with a traditional BCG boosting vaccine.

Overall, we identify several advantages of the *Mtb*-specific antigen design and introduce H107 as a ‘BCG-complementing’ vaccine with distinct properties compared to traditional BCG boosting vaccines. Based on the total pre-clinical data package, we have initiated GMP manufacturing in preparation of clinical testing.

TBS-11-03 Towards an efficacious single-visit TB subunit vaccine regimen by co-administering BCG

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The only licensed tuberculosis (TB) vaccine, *Bacillus Calmette Guerin* (BCG), fails to reliably protect adolescents and adults from pulmonary TB, resulting in approximately 1.5 million deaths annually. A variety of strategies towards an improved vaccine are currently under investigation, including adjuvanted protein subunit vaccines.

Unfortunately, subunit vaccines require multiple administrations for maximum efficacy, which leaves these vaccines vulnerable to loss of follow up and necessitates more complex and costly logistics.

Given the well-documented adjuvant effect of BCG, we hypothesized that a way to reduce the number of vaccine administrations without compromising immunogenicity would be to co-administer BCG together with the first dose of subunit vaccine. To explore this hypothesis, we took advantage of our H107 candidate vaccine, which does not cross-react with BCG due to selective inclusion of *Mtb*-specific antigens, ensuring that subunit-responses will not compromise BCG immunity and adjuvanticity.

When combining BCG with the first dose of a three-dose H107 regimen, H107 vaccine immunogenicity as well as protection after *Mtb* challenge was enhanced.

Further investigating the potency of BCG co-administration, we investigated whether this enhanced immunogenicity could compensate for a reduced number of subunit administrations. As observed for the three-dose regimen, we found that after a single administration of BCG+H107, H107 immunogenicity was increased.

Strikingly, this BCG+H107 single-dose regimen was as protective as a standard three-dose BCG+H107 regimen, both early and late after *Mtb* challenge. Contrarily, in the H107 regimens without BCG co-administration three doses remained more protective than one.

Interestingly, we also found that in a BCG revaccination setting a single-dose H107+BCG regimen was more protective than BCG or H107 alone.

Taken together, this data supports the combination of BCG and subunit vaccines for a more optimal TB vaccine regimen in a broad setting, by conferring protection through a minimal number of administrations.

TBS-11-04 Intranasal therapeutic immunisation targeting Rel Mtb and MIP-3 α /Rel Mtb induces immune signatures associated with better in vivo TB control

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Background: Tuberculosis (TB) is one of the leading causes of death from a single infectious agent worldwide. The lengthy treatment regimen reflects the unique ability of a subpopulation of “persister” bacteria to remain in a nonreplicating state in the infected host through various adaptive strategies, including induction of the stringent response. The key stringent response enzyme, Rel_{Mtb}, is essential for long-term *Mycobacterium tuberculosis* (Mtb) survival under physiologically relevant stresses *in vitro* and in animal lungs. Recently, our group has generated a therapeutic, parenteral, *rel*_{Mtb} DNA vaccine, which induces Rel_{Mtb}-specific cellular immunity and augments the activity of the first-line drug isoniazid against active TB in mice and guinea pigs. Our group also has applied a novel vaccination strategy involving the fusion of an antigen of interest with the immature dendritic cell (iDC)-targeting chemokine MIP-3 α /CCL20, which significantly enhances antigen-specific T-cell responses.

Objective: We sought to determine if this iDC-targeting strategy along with intranasal administration improves the immunogenicity of the therapeutic *rel*_{Mtb} DNA vaccine.

Design: We cloned the *rel*_{Mtb} DNA and chemokine MIP-3 α into the eukaryotic expression plasmid pSec-tag2b. We conducted an immunogenicity study using C57BL/6J mice, comparing the T-cell responses between the *rel*_{Mtb} vs. MIP-3 α /*rel*_{Mtb} DNA vaccination groups, as well as different administration routes (intramuscular vs. intranasal).

Results: Intranasal administration of the *rel*_{Mtb} and MIP-3 α /*rel*_{Mtb} vaccines induced increased production of various Mtb-protective cytokines (IL-17 α , IL-2, TNF- α ,

IFN- γ) in various mouse tissues, including spleen, lungs, draining lymph nodes and peripheral blood mononuclear cells, relative to the intramuscular route. Notably, intranasal administration of the MIP-3 α /*rel*_{Mtb} vaccine induced a higher percentage of antigen-specific CXCR3+KLRG1-cells compared to *rel*_{Mtb}, an immunologic signature which has been previously associated with enhanced control of Mtb infection.

Conclusions: Intranasal therapeutic immunization with DNA vaccines expressing *rel*_{Mtb} or MIP-3 α /*rel*_{Mtb} induces Mtb-protective immune signatures *in vivo*.

TBS-LB TBSscience late-breaker session

TBS-LB-02 Prospective validation of concise diagnostic and prognostic host transcriptomic TB signatures using PCR

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Background: Sensitive point-of-care screening tests are urgently needed to identify individuals at highest risk of tuberculosis for further microbiological testing and targeted preventive therapy. We prospectively tested diagnostic and prognostic performance of host-blood transcriptomic tuberculosis signatures for active case finding.

Methods: HIV-negative and HIV-positive adults without suspicion of tuberculosis were recruited from five endemic South African communities. Nine concise transcriptomic tuberculosis signatures were measured by microfluidic RT-qPCR on blood collected at enrolment. Upper respiratory swab specimens were tested with a multiplex bacterial-viral RT-qPCR panel in a subset of participants. Diagnostic and prognostic performance for microbiologically-confirmed prevalent and incident pulmonary tuberculosis was tested in all participants at baseline and during active surveillance through 15 months follow-up, respectively.

Results: Among 2,923 HIV-negative and 861 HIV-positive enrolled participants there were 61 and 10 baseline prevalent, and 24 and 9 incident, tuberculosis cases respectively. Signature scores were highly correlated (ρ 0.22-0.96). 1,000 HIV-negative participants were tested for respiratory microorganisms and 413 HIV-positive for HIV plasma viral load; 8/9 signature scores were higher ($p < 0.001$) in participants with viral respiratory infections or detectable HIV viraemia than those without.

Diagnostic AUCs for prevalent tuberculosis ranged from 0.63-0.79 in HIV-negative and 0.65-0.88 in HIV-positive cohorts. Diagnostic performance was superior among symptomatic HIV-negative participants (AUCs 0.85-0.98) and 7/9 signatures met minimum WHO triage test target product profile (TPP) criteria.

Among HIV-negative individuals, prognostic performance for incident tuberculosis occurring within 6-12 months was higher relative to 15 months. Over 6 months, 7/9 signatures met minimum WHO incipient test TPP criteria; one signature met these criteria over 12 months.

Signature	HIV-Negative Diagnostic AUC (95%CI)	HIV-Positive Diagnostic AUC (95%CI)	HIV-Negative Prognostic AUC over 6 months (95%CI)	HIV-Negative Prognostic AUC over 12 months (95%CI)	HIV-Negative Prognostic AUC over 15 months (95%CI)	HIV-Positive Prognostic AUC over 15 months (95%CI)
Darboe11 (RISK11)	0.77 (0.68-0.86)	0.88 (0.78-0.97)	0.95 (0.92-1.00)	0.80 (0.65-0.94)	0.63 (0.48-0.80)	0.80 (0.71-0.87)
Francisco2	0.66 (0.56-0.76)	0.69 (0.52-0.85)	0.82 (0.77-0.87)	0.67 (0.48-0.87)	0.52 (0.37-0.69)	0.62 (0.45-0.76)
Maertzdorf4	0.73 (0.63-0.83)	0.88 (0.77-0.95)	0.83 (0.73-0.97)	0.70 (0.47-0.93)	0.59 (0.43-0.77)	0.69 (0.57-0.80)
Penn-Nicholson6 (RISK6)	0.78 (0.69-0.87)	0.79 (0.69-0.90)	0.91 (0.86-0.97)	0.80 (0.65-0.95)	0.66 (0.51-0.82)	0.76 (0.60-0.86)
Roe1 (BATF2)	0.77 (0.67-0.87)	0.83 (0.71-0.93)	0.87 (0.73-0.97)	0.76 (0.50-0.94)	0.62 (0.45-0.80)	0.81 (0.76-0.88)
Roe3	0.79 (0.70-0.88)	0.87 (0.75-0.96)	0.87 (0.78-0.98)	0.76 (0.50-0.93)	0.63 (0.45-0.82)	0.80 (0.70-0.88)
Suliman4 (RISK4)	0.72 (0.61-0.85)	0.87 (0.71-0.99)	0.82 (0.49-0.98)	0.70 (0.46-0.91)	0.60 (0.43-0.78)	0.76 (0.59-0.87)
Sweeney3	0.63 (0.54-0.73)	0.65 (0.47-0.81)	0.80 (0.72-0.87)	0.63 (0.42-0.85)	0.49 (0.34-0.66)	0.54 (0.36-0.72)
Thompson5 (RESPONSE5)	0.68 (0.58-0.79)	0.66 (0.49-0.83)	0.84 (0.66-0.96)	0.70 (0.54-0.87)	0.62 (0.47-0.78)	0.62 (0.43-0.78)

Conclusions: Several concise signatures met incipient test targets, and triage test targets among symptomatic participants, and warrant translation to point-of-care devices. Tuberculosis signatures were highly correlated, and most were upregulated with viral infection, indicating that they essentially measure similar IFN-stimulated gene pathways.

TBS-LB-03 C-reactive protein as a triage tool for adults with presumptive pulmonary TB in South Africa: a prospective cohort study

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Background: Identification of an accurate, low-cost triage test for pulmonary TB is an urgent research priority. C-reactive protein (CRP)-based screening for TB among people with HIV was recently endorsed by the World Health Organization (WHO). We assessed the diagnostic accuracy and clinical utility of CRP for TB triage among symptomatic adult outpatients, irrespective of HIV status.

Methods: We prospectively enrolled adults reporting at least one (for people with HIV) or two (for people without HIV) symptoms of cough, fever, night sweats, or weight loss at two TB clinics in Cape Town, South Africa. Participants provided sputum, tested with culture and Xpert MTB/RIF Ultra. We evaluated the diagnostic accuracy of CRP (using a laboratory-based assay) against a TB-culture reference standard as the area under the receiver operating characteristic curve (AUROC) and sensitivity and specificity at pre-specified thresholds. We assessed clinical utility using decision curve analysis, benchmarked against WHO recommendations.

Results: Of 932 included individuals, 255 (27%) had culture-confirmed TB and 389 (42%) were living with HIV. CRP demonstrated an AUROC of 0.80 (95% confidence interval 0.77–0.83), with sensitivity 93% (89–95%) and specificity 54% (50–58%) using a primary threshold of $\geq 10\text{mg/L}$ (Table).

	Cases / N	% Triage positive	AUROC	Sensitivity	Specificity	PPV	NPV	NNT (CRP+)	NNT (CRP-)
Overall	255 / 932	59	0.80 (0.77-0.83)	0.93 (0.89-0.95)	0.54 (0.50-0.58)	0.43 (0.39-0.47)	0.95 (0.92-0.97)	2.3 (2.1-2.6)	20.3 (13.2-31.5)
HIV Positive	113 / 389	68	0.77 (0.73-0.82)	0.95 (0.89-0.98)	0.43 (0.37-0.49)	0.41 (0.35-0.47)	0.95 (0.90-0.98)	2.5 (2.1-2.9)	20.8 (9.9-45.1)
HIV Negative	142 / 535	52	0.82 (0.79-0.86)	0.91 (0.85-0.95)	0.62 (0.57-0.66)	0.46 (0.40-0.52)	0.95 (0.92-0.97)	2.2 (1.9-2.5)	19.7 (11.8-33.4)

Table. Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (NPV) and Number needed to test to detect one TB case (NNT) among CRP positive (CRP+) and CRP negative (CRP-) individuals reported at a CRP threshold of $\geq 10\text{mg/L}$. N: Number of included individuals; AUROC: area under the receiver operator characteristic curve.

Using a $\geq 5\text{mg/L}$ threshold, sensitivity was higher (97% [94–98%]) but specificity only 39% [35–42%]. Performance was similar among people with and without HIV.

In decision curve analysis, CRP-based triage offered greater clinical utility than confirmatory testing for all up to a number willing to test threshold of 20 confirmatory tests per true positive TB case diagnosed. Above this threshold, confirmatory testing for all was preferable.

Conclusion: CRP approached the WHO-defined minimum performance for a TB triage test and showed evidence of clinical utility among symptomatic outpatients, irrespective of HIV status. Urgent further evaluation of CRP-based triage in interventional trials and health economic studies is warranted.

TBS-LB-04 Genomic signatures of pre-resistance in *Mycobacterium tuberculosis*

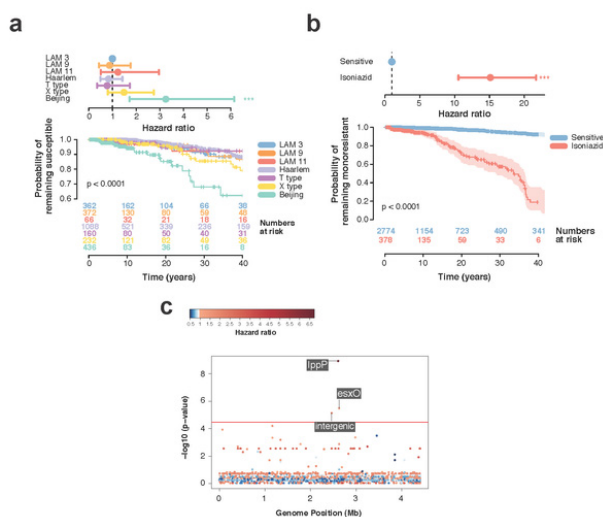
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Background: Recent advances in bacterial whole-genome sequencing have resulted in a comprehensive catalog of genomic signatures of antibiotic resistance in *Mycobacterium tuberculosis*. Despite this, post hoc approaches to diagnosis miss opportunities to implement preventive measures prior to the acquisition and spread of antibiotic resistant disease.

Methods: Whole-genome sequencing was performed in samples collected at the population level and over a time span of 17 years from patients presenting tuberculosis symptoms at health centers in Lima, Peru. A novel genome-wide survival analysis was applied to a time-calibrated phylogeny using the time between phylogenetic nodes in order to identify genomic determinants in inferred susceptible strains that led to drug resistance acquisition along the phylogenetic branch.

Results: A total of 3135 isolates were analyzed, of which 2807 were lineage 4 and 327 were lineage 2. Lineage 2 had a significantly higher incidence of drug resistance acquisition than lineage 4 (HR 3.36, 95% CI 2.10–5.38, p-value=4.25e-7). Similarly, the hazard of evolu-

ing multidrug-resistance following isoniazid resistance acquisition was 14 times that of genomes with a susceptible background (HR 14.45, 95% CI 8.46-15.50, p -value $<10e-15$). Moreover, a deletion in a gene coding for the cell surface protein lppP (HR 6.71, 95% CI 4.824-11.22, p -value $=1.17e-9$) also predisposed susceptible genotypes to the acquisition of drug resistance.



Discussion: Using a novel ancestral state genome-wide survival analysis to move in time through the phylogenetic tree, we show genomic signatures in *Mycobacterium tuberculosis* that increase the risk of acquiring drug resistance mutations at the lineage level, after mono-resistance, and at the level of nucleotide polymorphisms. Identifying pathogen genetic factors that predispose strains to evolve drug resistance could help prevent the acquisition and spread of resistance and treatment failure by expanding treatments to those strains most likely to become resistant in the future.

TBS-LB-05 Impact of systematic TB detection using Xpert Ultra on nasopharyngeal aspirates and stool samples on mortality in children with severe pneumonia

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Background: In children with severe pneumonia, TB is usually considered only in case of prolonged symptoms or antibiotic failure, leading to missed or delayed TB

diagnosis. Systematic screening with molecular assays could increase TB case detection and thus reduce child mortality.

Design/methods: From April 2019 to June 2021, we implemented a stepped-wedge cluster-randomized trial in 15 hospitals from 6 high TB incidence countries. Children aged <5 years with WHO-defined severe pneumonia received either the WHO standard of care (control) or SOC plus Xpert MTB/RIF Ultra (Ultra) on 1 nasopharyngeal aspirate (NPA) and 1 stool sample at hospital admission, followed by immediate treatment if positive (intervention). Hospitals were randomly selected to switch from the control to the intervention at 5-week intervals. We assessed the impact of the intervention on 12-week mortality using a generalized linear mixed effect model adjusted on severe acute malnutrition and baseline peripheral oxygen saturation (SpO₂).

Results: We enrolled 1401 and 1169 children in the control and the intervention groups, respectively (table). 71 (5.1%) and 87 (7.4%) children were initiated on TB treatment in the control and intervention groups, respectively ($p=0.012$). In the intervention arm, 1007 (97.4%) children had NPA collected, 850 (82.2%) had stool collected, and 24 (2.1%) had positive Ultra on either sample, contributing to 29% microbiological confirmation of TB (24/87). At 12 weeks, 110 (7.9%) and 90 (7.7%) had died ($p=0.868$) in the control and intervention groups, respectively, and 60 (30%) deaths occurred within 48 hours of admission. The intervention was not associated with decreased mortality [adjusted OR: 0.95 (95% CI 0.58 – 1.58)].

Conclusions: Screening with Ultra at the time of admission did not lead to reduced mortality in children with severe pneumonia. High TB treatment initiation and microbiological confirmation rate support the more systematic use of Ultra in this vulnerable group.

	Control group (N=1401)	Intervention group (N=1169)	P-Value (unadjusted)
Gender female – n (%)	610 (43.5)	492 (42.1)	0.449
Age (months) – median [IQR]	11 [5-20]	11 [6-20]	0.791
SpO ₂ (%) – median [IQR]	92 [87-96]	94 [88-97]	<0.001
HIV-infection – n (%)	73 (5.2)	59 (5.0)	0.775
Severe acute malnutrition – n (%)	240 (17.1)	302 (25.8)	<0.001
TB treatment initiated – n (%)	71 (5.1)	87 (7.4)	0.012
Lost to follow-up – n (%)	40 (2.9)	42 (3.6)	0.289
Deaths – n (%)	110 (7.9)	90 (7.7)	0.890

TBS-EP TBSscience - E-posters

TBS-EP-01 Cerebral tryptophan metabolism and mortality of 1119 HIV-infected and HIV-uninfected tuberculous meningitis patients in Vietnam and Indonesia

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Background: Immunopathology contributes to the high mortality of tuberculous meningitis (TBM). We have previously associated low cerebrospinal fluid (CSF) tryptophan levels with improved survival among HIV-uninfected TBM patients in Indonesia. This may be explained by accelerated *IDO1*-activity, the rate-limiting enzyme in tryptophan to kynurenine metabolism. We therefore now measured tryptophan and downstream metabolites in large cohorts of HIV-infected and uninfected TBM patients.

Methods: TBM patients were included prospectively in Bandung, Indonesia and Ho Chi Minh City, Vietnam. Metabolites were extracted from CSF at hospital admission, separated using hydrophilic interaction liquid chromatography and then measured using mass spectrometry in positive mode, targeted to detect tryptophan and downstream metabolites. Primary endpoint was 180-day mortality using Cox regression.

Findings: We included 389 Indonesian (8.7% HIV-infected) and 730 Vietnamese (36% HIV-infected) TBM patients. After quality control, 11 metabolites could be analysed. CSF tryptophan predicted mortality in HIV-uninfected Indonesian patients, both in Indonesia (hazard ratio for mortality 0.85, 95% CI = 0.79-0.93, per each halving), and Vietnam (hazard ratio 0.81, 95% CI = 0.73-0.89), and in 263 HIV-infected Vietnamese patients (hazard ratio 0.84, 95% CI = 0.77-0.92). Kynurenine, kynurenic acid and further downstream metabolites were not associated with mortality.

Interpretation: Low CSF tryptophan is associated with improved survival in TBM patients, regardless of HIV-status and this does not seem to reflect an upregulated *IDO1* (kynurenine pathway) effect. Further metabolomic and multi-omics studies within the ULTIMATE consortium (NIH 1R01AI145781-01) may help unravel underlying mechanisms and identify targets for host-directed therapy.

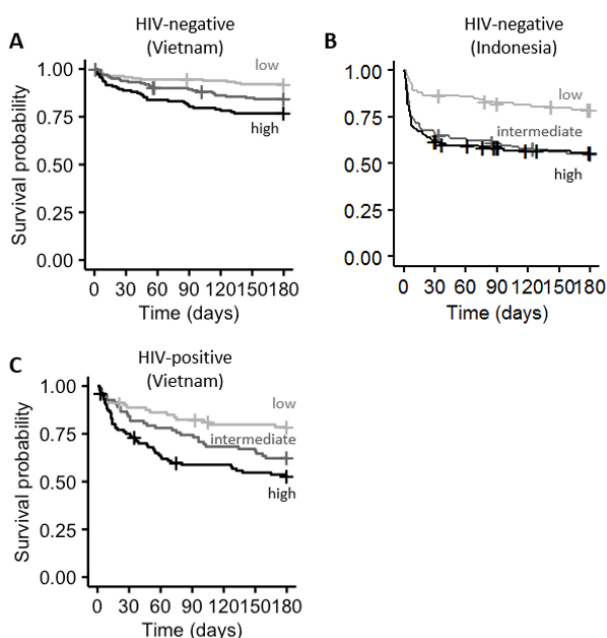


Figure: Kaplan-Meier graphs of HIV-uninfected tuberculous meningitis patients from Vietnam (A, n=467) and Indonesia (B, n=355) and HIV-infected patients from Vietnam (C, n=263) showing 180-day patient survival, based on strata of cerebrospinal fluid tryptophan levels in three equal groups. The small sample size of HIV-infected patients from Indonesia (n=34) precluded mortality analysis in this group.

TBS-EP-03 Quantitative measurement of antibiotic resistance in *Mycobacterium tuberculosis* reveals genetic determinants of resistance and susceptibility in a target gene approach

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The World Health Organization goal of universal drug susceptibility testing for patients with tuberculosis is most likely to be achieved through molecular diagnostics; however, to date these have focused largely on first-line drugs, and always on predicting binary susceptibilities.

Here, we used whole genome sequencing and a quantitative microtiter plate assay to relate genomic mutations to minimum inhibitory concentration (MIC) in 15,211 *Mycobacterium tuberculosis* patient isolates from 27 countries across five continents as a part of the Comprehensive Resistance Prediction for Tuberculosis: an International Consortium (CRyPTIC) project.

Using a linear mixed effect model of target genes controlling for site variation and phylogenetic lineage, we identified 449 unique MIC-elevating genetic determinants across thirteen drugs, as well as 91 mutations resulting in hypersensitivity for eleven drugs.

In addition, we also discovered interactions between mutations that result in greater-than-additive resistance to rifampicin and ethambutol, as well as mutations that overrode co-occurring resistance mutations for bedaquiline and the aminoglycosides to result in strains hyper-susceptible to these drugs.

Our results provide a guide for further implementation of personalized medicine for the treatment of tuberculosis using genetics-based diagnostics and can serve as a training set for novel approaches to predict drug resistance.

In addition, they can be a foundation for the design of trials investigating the potential of informed higher-dose drug therapy for strains with lower-level genetic resistance determinants, such as the “borderline” mutations in *rpoB*.

TBS-EP-04 Exploring the role of pathogen characteristics and host ancestry in tuberculosis transmission

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Introduction: Globally, *M. tuberculosis* lineages show distinct geographical patterns that parallel that of human subpopulations, suggesting co-adaptation (sympatry) between host and pathogen. Here, using epidemiological and whole genome sequencing (WGS) data from three major cosmopolitan cities, we measure the effect of *Mtb* lineage and host ancestry on tuberculosis (TB) infection among contacts of TB index cases.

Methods: We obtained socio-demographic, clinical, WGS, and contact tracing data for pulmonary TB cases in New York City, Amsterdam, and Hamburg. We inferred *Mtb* lineage from WGS data and defined sympatric occurrences between *Mtb* lineage and host ancestry based on published TB WGS literature (Figure 1A). We used multivariable generalized estimation equations to quantify the effect of host ancestry, *Mtb* lineage and other host risk factors on TB infection.

Results: We included 1,965 pulmonary TB index cases with 12,158 close contacts. A contact was more likely to be infected if age >45 years, born in a TB high-incidence country and if the contact's index case was smear positive (Figure 1B). Contacts exposed to *Mtb* lineage 1 strains were significantly less likely to have TB infection compared to lineage 4 strains (Figure 1B). In a multi-

variable model among 3,020 contacts exposed to geographically restricted lineages L1, L3, L5 and L6, contact sympatry, i.e., when the contact's ancestry matches the endemicity of the *Mtb* strain, was associated with TB infection (aOR 1.67 [95% CI 1.23, 2.26], $p < 0.001$) (Figure 1C).

Discussion: We explored the effect of *Mtb* lineage and host ancestry on TB infection in three cosmopolitan cohorts. Reduced infectivity by ancestral *Mtb* lineage 1 is consistent with emergence of modern *Mtb* (L2/L4) as drivers of the current global TB epidemic. The measured association between contact sympatry and TB infection provides the first controlled preliminary evidence for co-adaptation between *Mtb* and its human host.

TBS-EP-06 Biomarkers for active pulmonary tuberculosis treatment response: a systematic review

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Background: Current World Health Organization recommendations for monitoring treatment response in adult pulmonary tuberculosis (TB) are sputum smear microscopy and/or culture conversion at the end of the intensive phase of treatment. These methods either have sub-optimal accuracy or a long turn-around time. There is a need to identify alternative biomarkers to monitor TB treatment response.

Methods: We conducted a systematic review of active pulmonary TB treatment monitoring biomarkers. We screened 9,739 citations published between January 1st 2008 and December 31st 2020, of which 77 met the inclusion criteria. We included assays and biomarkers that are commercial, near commercial, or have commercial potential for TB treatment monitoring. When ≥ 5 studies quantitatively reported biomarker levels, we calculated the average fold-change in biomarkers from pre-treatment to week 8 of treatment. We also performed a meta-regression using a random intercept model to assess the average difference in fold change per week of treatment.

Results: A total of 81 biomarkers were identified. Of these, C-reactive protein (CRP), interleukin-6 (IL-6), interferon gamma-induced protein 10 (IP-10) and tumour necrosis factor alpha (TNF- α) had sufficient data to analyze fold-changes. All four biomarker levels decreased during the first 8 weeks of treatment relative to baseline. CRP had the greatest average 8-week fold decrease of -0.660 (95% CI: -0.842, -0.479).

Results of the meta-regression found that for each one week increase in treatment duration, there was a significant decrease in fold change of CRP, IL-6 and IP-10. CRP had the greatest weekly decrease in fold change of -0.041 (95% CI: -0.045, -0.038).

Bio-marker	Baseline to week 8 average fold-change			Average weekly difference in fold-change (meta-regression)		
	# studies	# participants	Average fold-change (95% CI)	# studies	# participants	Average weekly difference in fold-change (95% CI)
CRP	5	275	-0.660 (-0.842, -0.479)	8	447	-0.041 (-0.045, -0.038)
IL-6	4	522	-0.312 (-0.733, 0.110)	5	558	-0.009 (-0.009, -0.008)
IP-10	5	272	-0.379 (-0.726, -0.032)	9	430	-0.015 (-0.020, -0.009)
TNF- α	4	497	-0.186 (-0.350, -0.022)	6	517	-0.003 (-0.009, 0.004)

Conclusion: Based on limited data, CRP, IL-6, IP-10 and TNF- α seem promising for TB treatment monitoring, but further investigation is needed. Overall conclusions were limited by substantial heterogeneity in the reporting of data for treatment monitoring biomarkers. Guidance for designing and reporting treatment monitoring studies are urgently needed.

TBS-EP-07 Treatment interruptions as predictors of treatment outcome among drug-resistant TB patients in the Philippines

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Background: High levels of adherence are needed to achieve optimal TB treatment outcomes, especially for the treatment of drug-resistant TB. However, the impact of the frequency, distribution and duration of treatment interruptions is unknown.

Methods: We extracted daily six day a week adherence data from treatment cards for all pre-XDR and XDR TB and a 1:1 random sample of MDR TB patients initiated on treatment under the Philippines National TB Program between 2013 and 2016. We calculated the median duration of treatment interruptions (defined as non-adherence for at least two consecutive days) and median duration of gaps between interruptions. We used a generalized additive model to determine whether median interruption duration and median gap duration were associated with treatment outcome (cure/complete vs. failure/death/loss to follow-up), adjusting for patient demographics.

Results: Among 672 patients, the average age was 41 years, 30.1% were female and average adherence was 78.7%. 50.0% had MDR, 48.4% pre-XDR and 1.6% XDR TB. Seventy patients (70/672, 10.4%) did not have any treatment interruptions. Among those with at least one treatment interruption, the median number of interruptions was 11 (IQR 4-25). The median duration of interruption was 2 days (IQR 2-4) with a median gap of 4 days (IQR 2-14). Adherence above 78% was protective against unfavorable treatment outcomes, as was having fewer than 11 interruptions (Figure). The effect of the median duration of interruptions was not significant (OR 0.90 per day, 95% CI [0.80, 1.01]) but longer gaps between interruptions were protective (OR 0.98 per day, 95% CI [0.97,0.99]).

Conclusions: Monitoring patient treatment interruptions could be a useful programmatic indicator of high-risk patients. Further work is needed to explore the relative effects of treatment interruptions due to nonadherence vs. adverse events.

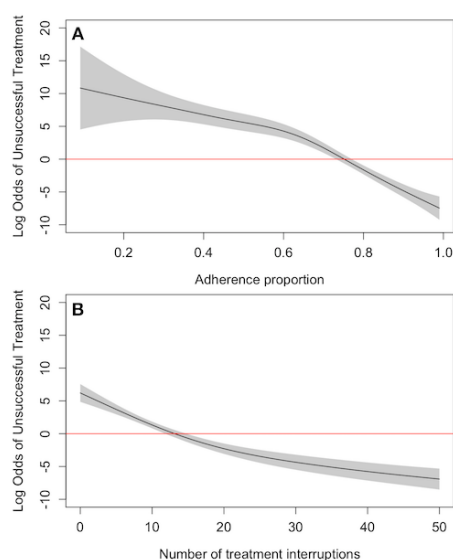


Figure. Generalized additive model spline terms for (A) adherence proportion and (B) number of treatment interruptions. The solid black line is the estimated log odds of unsuccessful treatment with all other variables in the model held constant. Shaded regions represent the confidence intervals. Red lines indicate the null log odds of zero.

TBS-EP-08 A treatment recommender clinical decision support system for individualized TB treatment

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Background: Tuberculosis (TB) is a public health problem with 10 million cases annually, of which 465 000 are rifampicin-resistant (RR). RR-TB patients should ideally initiate an individualized regimen upon receipt of drug susceptibility test (DST) results, but this is a lengthy and complex process.

Whole Genome Sequencing (WGS) could identify the complete resistance profile in a single step but translation of results into the most effective regimen requires expertise that is scarce, particularly in high burden countries.

Methods: We developed a treatment recommender Clinical Decision Support System (CDSS) for automated translation of WGS results into optimal individualized RR-TB regimens. Stakeholders identified and quantified the key features of drugs and regimens.

Using a dataset of 355 patients with 82 unique drug resistance profiles, feedback from experts was harvested and machine learning methods were applied to identify complex relations and patterns.

Model performance was assessed by the rank of the first accepted regimen for a resistance profile and the rank of regimens accepted by experts. A validation data set of 64 additional resistance profiles was used to assess model overfitting.

Results: Key features identified were cost, toxicity, QT prolongation, early bactericidal, bactericidal and sterilizing activity, mechanism of action, route of administration, propensity to acquire resistance, and drug-drug interactions. After three rounds of expert feedback, 95% of resistance profiles during training and 78% (93% when considering two highest ranked regimens) during validation had a highest ranked regimen considered appropriate by experts, indicating some overfitting of the model (Figure 1).

Additionally, 99% (training) and 87% (validation) of highest ranked regimens presented to the experts were considered appropriate.

Conclusion: The treatment recommender CDSS showed promise for automated individualized RR-TB treatment. While this could increase the feasibility of using WGS in high burden countries, research is needed to evaluate the treatment recommender in clinical settings.

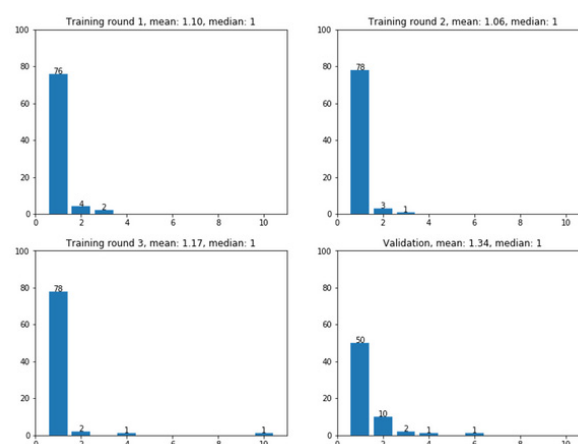


Figure 1. The rank of the first accepted regimen for each resistance profile.

TBS-EP-09 Phase variation as a major mechanism of adaptation in *Mycobacterium tuberculosis* complex

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Background: The tuberculosis bacillus, *Mycobacterium tuberculosis* complex (MTBC), has co-evolved with its obligate human host for millennia. Understanding the global genetic diversity of MTBC is essential for personalizing treatment and vaccine design.

Methods: We leverage a large sample of 31,428 genetically and geographically diverse clinical isolates to identify regions of the MTBC genome under positive selection. We used ancestral reconstructions and developed a new method (TopDis) to estimate the homoplasy score i.e. the rate of independent single nucleotide variant (SNV), and insertion/deletion (INDEL) arisals within the phylogeny suggestive of positive selection. We measured the rate of mycobacterial homopolymer expansion in a neutral setting by fusing a 7-base pair homopolymeric tract (HT) to an out-of-frame kanamycin resistance gene, where the addition of an eighth guanine within the homopolymer resulted in antibiotic resistance.

Results: Over 90,000 SNVs and INDELS emerged repeatedly across the MTBC phylogeny (10.57% of variants). Only 0.49% (n=4,098) of SNVs arose independently ≥ 5 times, occurred in known resistance markers and postulated transmission enhancing mutations (Figure 1A). Simulations of neutral point-mutations on our phylogenies indicate that SNVs arise independently ≥ 5 times with probability < 0.0002 . For INDELS, 15.6% represent phase variation/frameshifts in HTs (0.02% of the genome, 82% in coding regions and 18% in noncoding, Figure 1B). We measured the INDEL rate in the *glpK*

HT at $\approx 5.8 \times 10^{-4}$ INDELS/HT/year (endogenous *glpK* locus under investigation) and simulate the expected number of INDELS in HTs in the 31,428-isolate phylogeny.

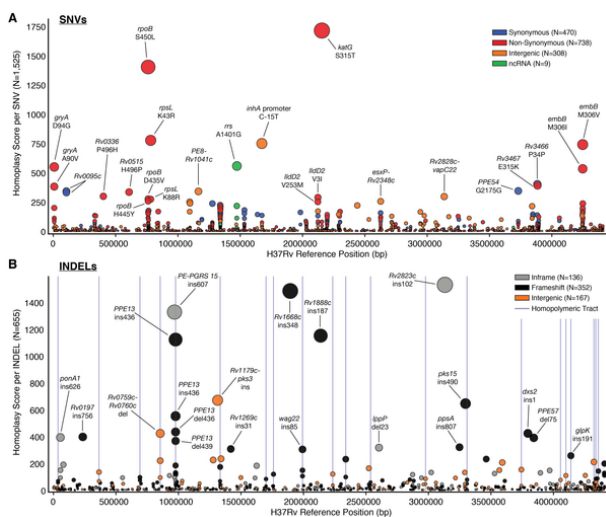


Figure 1. Parallel evolution of SNVs & INDELS.

(A) The number of independent arisals that occur for 1,525 SNVs with homoplasy score ≥ 5 and minor allele frequency $> 0.1\%$ among 31,428 isolates, plotted against position on the genome.

(B) The number of independent arisals that occur for 655 INDELS with homoplasy score ≥ 5 and alternate allele frequency $> 0.1\%$ among 31,428 isolates, plotted against position on the genome. Bubble size corresponds to homoplasy score.

Conclusions: Slipped-strand mispairing errors in HTs contribute substantially to genetic diversity, supporting the recent implication of these regions in drug-tolerance. In simulations, homoplasy at a frequency ≥ 5 times in the MTBC phylogeny is an unlikely event due to chance. We uncover evidence for pervasive positive selection in MTBC that may play a role in transmission or host-adaptation in addition to tolerance and resistance.

TBS-EP-10 Tracking autophagy progression in Mycobacterium tuberculosis-infected macrophages

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Autophagy is a cellular process that degrades unwanted proteins, organelles and pathogens. This pathway is involved in the host defence against Mycobacterium tuberculosis (M.tb), the pathogen that causes Tuberculosis (TB). The progression of autophagy during M.tb infection is, however, not fully elucidated. It is still not known

when cytosolic translocation of M. tb occurs which is crucial for autophagy research as bacterial translocation induces autophagy. We aimed to track the activity of the autophagic machinery using western blotting and immunofluorescence imaging of autophagic markers-LC3B and p62 in M. tb-infected THP-1 and RAW 264.7 macrophages. Turnover of intracellular bacteria was also enumerated in these M. tb-infected macrophages at 4, 24, 48 and 72 hours post-infection.

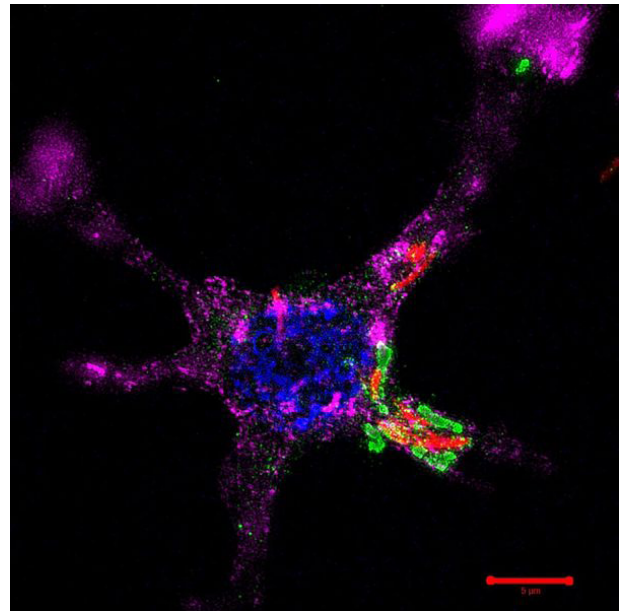


Figure 1: RAW 264.7 macrophage, with nucleus (blue), Beta-actin filaments (magenta) and LC3B (green), encapsulating M. tb bacilli (red). Scale bar= 5 μm .

We found that THP-1 and RAW 264.7 macrophages exhibit different patterns of autophagic turnover that were time and infection dependent. Immunofluorescence microscopy identified 48 hours as the time point of highest autophagic turnover in bacteria-containing macrophages. We further showed that LC3B and p62, and combined measurement of puncta counting and relative cell volume were more accurate measures of autophagy. Bacteria enumeration in both cell lines showed a steady increase in autophagic turnover of M. tb up until 48 hours.

We, thereafter, identified 48 hours as the time point with the highest intracellular M. tb turnover. This suggests cytosolic translocation occurs at this time point and should be considered when investigating autophagy in M.tb infection. Our study also highlights the potential use of LC3B and p62 as intracellular biomarkers for TB prognosis. With research investigating autophagy for personalized host-directed anti-tuberculosis therapy, our research provides more clarity on the involvement of autophagy in M. tb clearance and identifies potential avenues for personalized drug targeting.

TBS-EP-12 Adherence trajectory as an on-treatment risk indicator among drug-resistant TB patients in the Philippines

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Background: High adherence is needed to achieve optimal TB treatment outcomes, especially for drug-resistant TB. Identifying adherence patterns associated with unsuccessful treatment could serve as an on-treatment indicator for patients requiring additional adherence support or change in drug regimen.

Methods: We extracted daily dosing data from treatment cards for all pre-XDR and XDR TB and a 1:1 random sample of MDR TB patients treated by the Philippines National TB Program between 2013 and 2016. Patients were considered adherent if all expected medications for a given dosing day were recorded as taken.

We identified groups of similar weekly adherence trends in the first 12 weeks of treatment and estimated group mean trends using group-based trajectory modeling, considering models with two to five groups.

Group membership was used in logistic regression to predict final treatment outcome (favorable: cure/completed vs. unfavorable: failure/death/lost to follow-up).

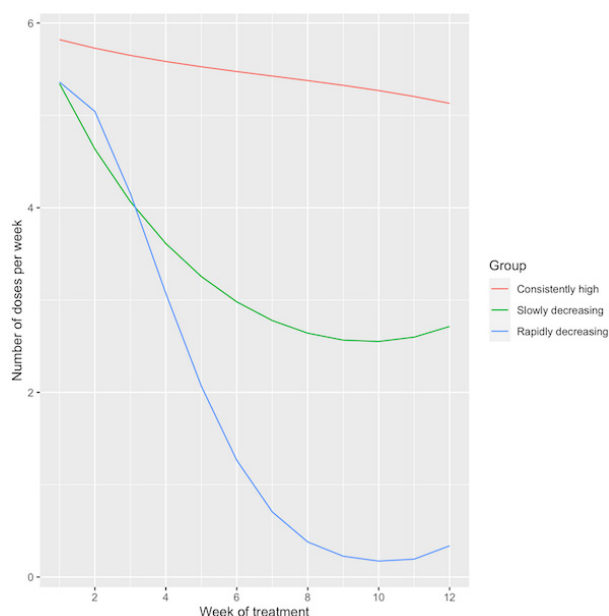


Figure. Predicted means of adherence trajectory groups estimated by group-based trajectory modelling.

Results: Among 596 patients, the average age was 40 years and 30.5% were female. 50.7% were treated for MDR, 47.5% pre-XDR and 1.8% XDR TB. The three-group model demonstrated the best fit, identifying consistently high (n=480), slowly decreasing (n=101), and rapidly decreasing (n=15) adherence groups (Figure). In the rapidly decreasing group, 100.0% (15/15) of patients experienced unfavorable outcomes, as did 52.5% (53/101) and 32.1% (154/480) of the slowly decreasing and consistently high groups, respectively. The slowly decreasing group was associated with unfavorable outcome (OR 2.34, 95% CI [1.51, 3.62]) compared to the consistently high group. Adding age and sex did not significantly improve model fit (likelihood ratio test p-value=0.46) suggesting that the adherence trajectory groups captured information not correlated to standard patient demographics.

Conclusions: Adherence trajectory early in drug-resistant TB treatment is predictive of final treatment outcome. Patients without consistently high adherence (adherent on >5 of 6 days) in the first 12 weeks require additional support or regimen change.

TBS-EP-13 NETosis-associated proteins in human TB immunopathogenesis

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Background: NETosis is a specific type of cell death unique to neutrophils that may contribute to pathological lung damage associated with granulomas in *Mycobacterium tuberculosis* infection. We therefore aim to identify the mechanisms of NETosis that may be associated with pathological tissue damage and thus serve as potential biomarkers of disease progression and targets for host-directed therapy (HDT).

Method: RNA was extracted from the blood of individuals with active tuberculosis (TB) lung disease (n=12), healthy (n=9) and latently infected individuals (LTBI) (n=10). Quantitative PCR was used to determine the gene expression of specific genes (n=11) associated with NETosis. Multiplex cytokine, GSDMD and MPO ELISA assays were done to quantify protein expression in all 3 groups.

Results: GSDMD, MPO and LCN2 were upregulated in the TB group compared to the healthy group (p<0.05). S100A8, AZU1, MMP8, NCF2 and CD117 were downregulated in the TB compared to the healthy group (p<0.05). MPO and GSDMD protein expression was higher in the TB group (p<0.05). In the TB

group, circulatory inflammatory markers such as IL-8, MIP-1beta and TNF-alpha ($p < 0.05$) had a direct, significant correlation with MPO protein expression in the blood. In the LTBI group, only IL-8 correlated with MPO ($p < 0.05$). We observed a significant correlation between GSDMD and IL-1RA and FGF-basic in the LTBI group ($p < 0.05$).

Conclusion: Our data suggest that NETosis specific genes and proteins are detectable in the blood of individuals with TB disease and may serve as potential markers for disease progression and targets for HDT.

TBS-EP-14 Serum human microRNAs in the differential diagnosis between active tuberculosis and tuberculosis infection

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Infection with *Mycobacterium tuberculosis* most commonly leads to a state of persistent immune response to stimulation by specific antigens, with no clinical evidence of active disease, referred as tuberculosis infection (TBI). If the host immune system becomes impaired, progression to active tuberculosis disease (ATB) may occur. Despite the importance of discriminating between TBI and ATB, biological markers currently available do not always allow an unambiguous definition. Circulating human small non-coding RNAs (sncRNAs) may have a role as biomarkers. In our work we aimed at identifying a sncRNA signature able to distinguish active TB disease from TB infection.

Serum from 93 individuals (34 with ATB, 39 with TBI and 20 healthy controls, CTRL) was collected for total RNA extraction. RNA-sequencing (RNAseq) was performed by Illumina technology using the small RNA kit from Clontech. Quality of the reads was assessed using FastQC software considering quality score per sequence and base above 30, absence of overrepresented sequences and the correct removal of adapter after trimming phase using Cutadapt. Trimmed reads were mapped (bowtie) on known Human sncRNA sequences (miRNAs, snRNAs, piRNAs, and snoRNAs) and on Human Genome. Quantification of reads was performed using samtools software, whereas differential sncRNA-level analysis was performed by DESeq2. Statistical significance was set at $p < 0.05$.

RNAseq analysis detected 8811 different transcripts: 68 were in common between TBI and CTRL group and absent in ATB; 18 were present only in ATB. Compari-

son of sncRNA levels between ATB and CTRL showed the presence of 134 differential transcripts (4 miRNAs, 4 piRNAs, 71 snoRNAs, and 55 snRNAs). ATB and TBI showed 168 differential transcripts (7 miRNAs, 46 piRNAs, 38 snoRNAs, and 77 snRNAs). No differences were detected between TBI and CTRL.

This results support the hypothesis that serum RNA profiling can enable discriminating between different TB infection outcomes in human adults.

TBS-EP-15 Diaskin and tuberculin skin test as tuberculosis diagnostics in Russian children: comparative observational study

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Background: The Diaskintest (DT) is an intradermal skin test using recombinant ESAT-6/CFP-10 for diagnosis of tuberculosis (TB) licenced in the Russian Federation (RF) since 2009. Both tuberculin skin test (TST) and DT are used in TB annual screening. The aim of this study was to describe the DT performance in paediatric routine clinical data.

Methods: Children aged <18 years referred to the TB dispensary in Archangelsk (RF) between 1 January 2018 and 31 December 2019 were included. TST cut-offs were defined as >5 mm and ≥ 10 mm induration and DT as an induration of any size. DT results were compared with TST in children with both tests performed within an interval of 91 days and conclusive results.

Results: A total of 2726 children were included in the final analysis. The median age was 9.0 (IQR 5.7 to 13) years and 53% were male. BCG vaccination status was as follows: 98% vaccinated, 1% not vaccinated and 1% unknown. TST and DT results were reported for 767(28%) and 2616(96%) children respectively; 657(24%) had results reported for both tests. Of those 18(2%) TST and 51(2%) DT results were inconclusive and excluded from analysis. Overall, 656/749 (88%) had a TST >5mm, 467/749 (62%) a TST at ≥ 10 mm and 296/2565 (12%) a positive DT. Test agreement between TST ≥ 10 mm and DT was evaluated for 551 children (agreement not evaluated if either test inconclusive or

interval > 91 days): TST+/DT+ in 50, TST-/DT- in 33 and TST+/DT- in 468 (Kappa 0.01). TST and DT size of induration increased with age (Pearson correlation coefficient 0.22 (95% CI 0.15-0.28) and 0.20 (95% CI 0.16-0.23, respectively)).

Conclusion: Our data indicate high prevalence of TST positivity in a setting with high proportions of annually screened and BCG-vaccinated children. Positivity was lower based on DT, likely due to its higher specificity.

TBS-EP-16 Estimation of country-specific tuberculosis antibiograms using a large genomic dataset

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Background: The World Health Organization reports multidrug-resistance (MDR) tuberculosis (TB) estimates, but other drug resistance (DR) estimates are more limited. Here, we leveraged public and surveillance *Mtb* whole genome sequencing (WGS) datasets, to generate country-level resistance prevalence estimates (antibiograms) using *in silico* phenotype prediction.

Methods: We curated and quality-controlled *Mtb* genomes including convenience samples and DR surveys. We used a validated random forest model to predict phenotypic resistance in *Mtb* to thirteen drugs and bias-corrected for imperfect model performance, outbreak sampling, and resistance oversampling. We validated our estimates using a national DR survey conducted in South Africa.

Results: *Mtb* isolates from 29 countries met criteria (n=20,245). WGS based marginal estimates for South Africa (n=3,134) overlapped with the national DR survey for all drugs but were underestimated for isoniazid and second-line injectables, while among MDR isolates, the estimates overlapped for pyrazinamide and the fluoroquinolones but were overestimated for other drugs. Estimated marginal resistance to pyrazinamide was highest in Moldova (31% [95% CI:23-39%, n=278]). Levofloxacin resistance among rifampin susceptible *Mtb* was highest in South Asia (Pakistan 3.4% [0.1-11%], n=111, India 2.8% [0.08-9.4%], n=114, **Figure-1**), while among MDR isolates, it was highest in Japan (48.72% [26.55-68.57%], n=135).

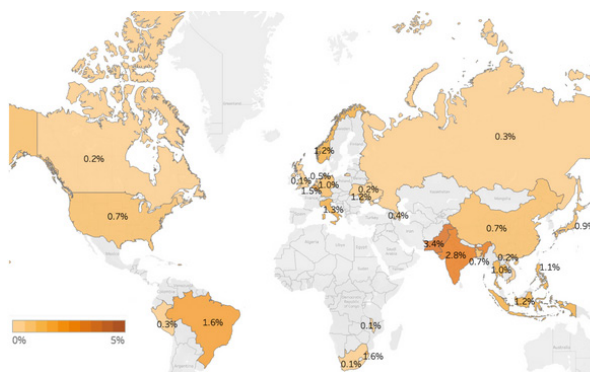


Figure 1. Bias-corrected estimates of levofloxacin mono-resistance in rifampin susceptible isolates. Only countries with at least 100 total isolates of which at least 50 were rifampin susceptible are shown.

Conclusions: The estimation of DR prevalence in MDR *Mtb* using public WGS and phenotypic resistance prediction is feasible for pyrazinamide and the fluoroquinolones. The measured rates of fluoroquinolone mono-resistance, pyrazinamide and fluoroquinolone resistance among MDR-TB can inform policy on optimal roll out of short-course regimens for drug susceptible and MDR-TB at the national level.

For other drugs, limited sampling and predictive performance of genotypic tests currently hinder accurate genomic surveillance but should be surmounted with the anticipated wider adoption of clinical *Mtb* sequencing.

TBS-EP-17 Evaluating new phenotypic and genotypic resistance in pulmonary TB index patients undergoing treatment

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Prior to the roll-out of rapid-diagnostic-tests for rifampicin-resistant-tuberculosis, drug susceptibility testing (DST) relied on culture-based-methods which can take weeks-to-months to process. Thus, many patients who were ultimately diagnosed with drug-resistant-TB were started on first-line-treatment pending the results of DST, which may have led to the amplification of resistance. We assessed the frequency of new phenotypic and genotypic resistance in patients undergoing TB treatment.

We enrolled a cohort of 4,500 patients initiating TB therapy in Lima, Peru. Patients provided sputum samples for DST prior to the initiation of therapy and at regular intervals thereafter. We used MIRU-VNTR and whole genome sequencing to exclude mixed and new infections among individuals with serially positive cultures and estimated the frequency of newly emergent genotypic and phenotypic drug resistance among the remainder.

Among 1151 patients with at least 2-positive-cultures, 59 (5.1 %) had serial DSTs suggesting acquisition of resistance during treatment. Of these, 28 (47.5%) samples had MIC testing, of which 20 (71.4%) were inconsistent with DST change i.e., resistance at treatment initiation was detected by MIC in 11(55%) samples due to 1-2-concentration-changes near the established threshold for resistance; 7 (35%) due to 3-6-concentration-changes; and 2 without change between baseline-and-2-month-MIC-values.

New phenotypic resistance was confirmed in 8 (28.6%) patients whose MICs changed, of whom 2 (25%) received optimal treatment i.e., effective treatment 0-6 days after enrollment, while the remaining 6 (75%) got sub-optimal therapy.

Among the patients with new phenotypic resistance, 3 (37.5%) who received sub-optimal therapy also had confirmed new genotypic resistance, of whom 1 had a known drug-resistant-SNP, and 2 had potentially novel SNPs.

We identified relatively few drug-resistance amplification events in patients undergoing TB treatment even among those receiving sub-optimal therapy. In future work, we will perform deep sequencing on samples with genotypic evidence of drug-resistance amplification to determine whether minority resistant variants had been present at baseline.

TBS-EP-18 First-line anti-tuberculosis drug exposure in newly diagnosed TB patients: Latvian perspective

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Background: Recent studies have shown that pharmacokinetic variability of first-line anti-tuberculosis (anti-TB) drugs (rifampicin, ethambutol, isoniazid, pyrazinamide) could result in insufficient drug exposure and, along with patient dependent factors (e.g. other health conditions), may account for acquired M. tuberculosis drug resistance and TB treatment failure.

Aim: This study aimed to evaluate first-line anti-TB drug exposure in newly diagnosed TB patients and assess implications of drug exposure on treatment response.

Methods: Plasma samples from TB patients (n=34) subjected to treatment with first-line anti-TB drugs were collected pre-dose, 2 h and 6 h post-dose on the 10th day of treatment. The plasma concentration of anti-TB drugs was measured using in-house liquid chromatography-tandem mass spectrometry method. Time to sputum culture conversion (tSCC) was used as a treatment

response marker and was extracted from patient's medical records (n=23). The data analysis was performed with GraphPad Prism 9.0.

Results: Among the 34 patients, the prevalence of lowered plasma concentration 2 h post-dose for ethambutol, isoniazid, and pyrazinamide was 29.4%, 61.8%, and 11.8%, respectively. Rifampicin plasma concentration was lowered in all cases; underexposure of rifampicin and one more drug was observed in 50% of patients. The median tSCC was 49 days (IQR: 40-84). Of all four drugs, only for ethambutol correlation between AUC_{0-6h} and tSCC was moderately strong ($r = -0.55$, $p < 0.01$). Weak but insignificant correlation was found for rifampicin ($r = -0.27$, $p = 0.21$).

Conclusions: The observed tendency of lowered anti-TB drug exposure in Latvian TB patients corresponds to findings reported globally. Although pharmacokinetic profiling might be a valuable approach to identify potential risks of delayed treatment response or treatment failure, in our study, pharmacokinetic data alone did not explain variability of patients' treatment response and, therefore, a more personalized approach should be considered.

Acknowledgements: This study was supported by Latvian Council of Science, project No. lzp-2020/1-0050.

TBS-EP-19 A Bayesian approach to personalized drug resistance treatment by estimating the probability of resistance to bedaquiline in the presence of specific genomic variant

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Background: Bedaquiline (BDQ) is a core drug for rifampicin-resistant tuberculosis. The interpretation and clinical use of sequencing data is limited as few genetic variants are statistically associated with BDQ resistance. Alternative approaches to determine the genotypic-phenotypic association for BDQ are needed.

Methods: We used a Bayesian approach to estimate the probability (and 95% credible interval) of BDQ resistance in the presence of a genomic variant. Expert opinions were collected to determine the prior probability distribution. Genotypic-phenotypic data of individual isolates from a systematic literature review was used for the data likelihood. After combining the prior and the data distributions, the posterior inference was made for different types of mutations (e.g. synonymous and missense mutations) in the genes of interest (*atpE*, *Rv0678*, *pepQ*, and *Rv1979c*) and for each unique variant reported in the systematic review.

Results: Experts agreed on the role of *atpE* and *Rv0678* in conferring BDQ resistance but were uncertain about the role of *pepQ* and *Rv1979c*. Most experts (79%,

Gene	Mutation class	n*	Prior probability	Data			Posterior probability	
				R	S	Total	P	95% CI
atpE	Synonymous mutation	32	2.9%	0	1	1	2.4%	~0 - 20.7%
	Missense mutation	30	57%	18	13	31	58%	41-74.2%
Rv0678	Synonymous mutation	32	19.8%	1	5	6	16.86%	0.64-51.3%
	Nonsense mutation	33	80%	4	2	6	70%	46-98.6%
	Frameshift mutation	32	76%	33	120	153	22.3%	15.6-28.6%
	Missense mutation	30	63.1%	52	103	155	34%	26.4-41.2%
pep Q	Frameshift mutation	33	45.2%	0	3	3	18.1%	0.4-59.4%
	Missense mutation	33	38.8%	0	31	31	3.5%	0.12-12.2%
Rv1979c	Synonymous mutation	32	42%	0	2	2	24.9%	0.8-71.3%
	Nonsense mutation	32	42%	3	119	122	3.3%	0.9-7.1%

TBS-EP-19 Table.

n=26) believed that resistance-conferring mutations occurring in isolation would also confer resistance when co-occurring with other variants. Only 67% of experts (n=22) believed that laboratory experiment results can be transferred to clinical isolates. Expert opinions on the probability of resistance of variant types differed substantially. Posterior probability of resistance was 2.4% (0-21%), 16.9% (1-51%), 18.1% (0-59%), and 24.9% (1-71%) for synonymous mutations in *atpE*, *Rv0678*, *pepQ*, and *Rv1979c* genes, respectively. The posterior probability of resistance was 58% (41-74%), 34% (26-41%), 3.5% (0-12%), and 3.2% (1-7%) for missense mutations in *atpE*, *Rv0678*, *pepQ*, and *Rv1979c*, respectively. Probabilities for specific mutations ranged from 2.3% (0-25%) for *Rv0678* 798T>G to 94.9% (78-99.9%) for *atpE* 187G>C.

Conclusion: Probabilistic Bayesian approaches can be useful to guide clinical decision-making. Future studies should investigate how physicians interpret and use Bayesian probabilities in practice.

TBS-EP-20 Identification of mycobacterial persisters by resuscitation promoting factors in sputum samples

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Sputum of pulmonary tuberculosis (TB) patients has mycobacterial mixture with different phenotypic properties. The sputum mycobacteria can harbor subpopulations known as persisters that are slowly replicating or non-replicating cells induced by multiple stresses. The persister has not genetic alteration of drug-resistance related genes, but it has temporary resistance to anti-tubercular agents, thus it is estimated to be the cause of long-term treatment, treatment failure or recurrent TB.

The goal of this study, through the establishment of resuscitation condition using the *in vitro* persistent model, was to determine the distribution rate of the persisters in the serial sputum samples according to the treatment duration. After two weeks culture under hypoxia and nutrient starvation condition, D-cycloserine treated for one week to remove the actively growing tuberculosis bacteria.

We tested for *in vitro* persister resuscitation in the media which containing *Mycobacterium tuberculosis* H37Rv culture filtrate (CF) and six recombinant resuscitation promoting factors proteins (rRpf; RpfA to RpfE, RipA). In the media with *M. tuberculosis* CF 20% of the total medium amount and final concentration 0.1 $\mu\text{g/ml}$ of each rRpf antigens showed the most appropriate resuscitation performance.

Also, similar reactivation results were showed in experiments using clinical serial sputum samples from Korea TB patients. The culture conversion test was performed at two-month after initial treatment to monitor the therapeutic effect. It is estimated that the accuracy of the treatment effect monitoring and determination can be promoted through facilitating the cultivation of TB persister cells in sputum.

TBS-EP-21 TB - COVID 19 co-infection - a deadly diagnosis

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Introduction: Both TB and COVID-19 are infectious diseases that primarily involve the lungs. It is possible that one infection increases the probability of contraction of the other; possibly due to a weakening of the host immune system. Most importantly, both TB and COVID-19 can be deadly.

Purpose: To analyze the demographic and clinical characteristics of TB patients diagnosed with COVID-19 from the beginning of the pandemic situation.

Methods: Screening by a real-time reverse transcriptase-polymerase chain reaction assay of patients with TB and COVID-19 symptoms.

Results: 107 cases with both co-infection (TB+COVID-19) have been reported. The demographic characteristics: gender ratio $\text{♀}/\text{♂}=1:5$; mean age=45.5years (range:0-79; 7 children), 82.2%(88/107) were new cases, urban/rural ratio=1.8. As diagnostic, 13 cases had pleural effusion, 69 cases with severe TB forms: cavitations and extensive cazeous pneumonia, 9 cases had extrapulmonary TB (renal and lymph nodes tuberculosis) and 4 cases had miliary tuberculosis. From those tested for HIV infection,

only 2 cases have been found positive. Social condition, comorbidities and severe form of TB have contributed to unfavorable prognosis and death in this case. Of 75 cases with positive culture, only 2 had MDR-TB. Overall outcome was unfavorable in 14 cases, who died shortly after diagnosis.

Conclusions: Pre-existing stigma around TB and the added stigma of COVID-19 might have discouraged people from getting tested, even after experiencing symptoms common to both diseases. For those diagnosed with tuberculosis, holistic, person-centred care and support has been difficult to maintain during the COVID-19 pandemic.

Impact: The symptom similarity between TB and COVID-19 probably resulted in a delay in suspecting TB, as most people could have attributed similar symptoms to COVID-19 and preferred to wait it out.

Finding and treating people with TB remain the fundamental pillars of TB prevention and care and those would require maintained attention.

TBS-EP-22 As simple as possible but not one bit simpler: modelling the effects of a simplified regimen for drug-resistant TB on clinical and drug resistance outcomes

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Emerging evidence suggests that shortened, simplified treatment regimens for drug-resistant tuberculosis (DR-TB) can achieve comparable end-of-treatment outcomes to WHO-recommended longer regimens. Treatment decisions should take account of clinical outcomes and the potential amplification of drug resistance.

We use a microsimulation model to compare diagnostic and treatment strategies for patients over 15 years with rifampicin-resistant TB diagnosed using GeneXpert:

- A simplified treatment strategy (6 months of bedaquiline, moxifloxacin, linezolid, and clofazimine) with no routine drug-susceptibility testing (DST) beyond GeneXpert,
- Individualized treatment regimens guided by routine genomic DST, and,
- The current WHO guidelines, where patients start with a WHO longer regimen, with modifications based on fluoroquinolone resistance and any drugs used in previous treatment.

Genomic and demographic data from a Moldovan patient cohort were used to parameterize a model simu-

lating long-term treatment outcomes for each of these strategies. In the model, individuals are followed over their lifetime, simulating the natural history of TB and associated treatment effects, as well as the process of acquired drug resistance.

Strategies are compared in terms of their impact on TB cure and death, changes in average survival, and the proportion of patients who develop further drug resistance. As the effectiveness of simplified regimens is still being studied in clinical trials, scenario analyses explore what happens if the effectiveness of the simplified regimen is varied, or if the regimen's duration is altered.

TBS-EP-23 Antimycobacterial, antioxidative, anti-inflammatory, cytotoxic, anti-biofilm and synergistic interaction effects of five medicinal plants species used for tuberculosis infections

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Tuberculosis (TB) is a life-threatening disease for both humans and animals caused by various *Mycobacterium* species and is a leading cause of human mortality in the developing world. This high incidence of infection and the increased rate of multi-drug resistant and extensively-drug resistant strains of the organism further complicated the problem of TB control with Covid-19 pandemic worsening matter, have called for an urgent need to develop new anti-TB drugs and possible corona from plants.

In this study, the in vitro activity of leaves of, *Eucalyptus camadulensis* and *Euphorbia tirucali*, *Aloe marlothii*, *Schotia brachypetala*(bark) and roots *Elephantorrhiza elephantina* were evaluated against *M. tuberculosis*, *M. smegmatis* and *M. bovis* strains.

Toxicity on African green monkey kidney (Vero) cells was evaluated using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. The antibacterial efficacies of the different combinations of *E. elephantina*, *A. marlothii*, *E. camaldulensis*, *E. tirucali* and *S. brachypetala* plants varied. They were investigated for in antimycobacterial activity against *M. tuberculosis*, *M. smegmatis* and *M. bovis* strains.

All the tested plant highest antimycobacterial activity compared to acetone with MIC values ranging from 0.02 to 2.50 mg/ml strains. All plants have IC50 above IC50 > 0.1 mg/ml which means they are non toxic and anti-inflammatory above Curcumin. All extracts are above 50% inhibition biofilm growth.

The results support the indigenous use of these plants in the treatment of TB and it is suggested that these plants may have curative value in the treatment of TB. The synergistic interaction observed indicates that combinational therapy may improve biological activity.

TBS-EP-24 Phase I/II, randomized, active-control, open-label trial evaluating activity, pharmacokinetics and safety of multiple oral doses of OPC-167832 in uncomplicated drug-susceptible pulmonary tuberculosis: interim results

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Background: OPC-167832, a novel decaprenylphosphoryl- β -D-ribose 2'-epimerase inhibitor, demonstrated potent anti-TB activity and a favorable tolerability profile in preclinical model systems.

Design/methods: We conducted the first stage of a two-stage, phase I/II study to assess bactericidal activity, pharmacokinetics and safety of multiple ascending doses of OPC-167832 in 4 cohorts of participants with rifampicin- and isoniazid-susceptible pulmonary TB. For each cohort, participants were randomized to either once-daily oral OPC-167832 (3mg, 10mg, 30mg or 90mg; n=14 per cohort) or local standard of care (Rifampin e-275 [RHEZ]; n=4 per cohort) for 14 days. Bactericidal activity was assessed by quantitative change in sputum colony-forming units (CFU) on 7H11 medium.

Results: In Stage 1, the most common adverse events in pooled OPC-167832-treated subjects were headache (12/59 [20.3%] vs. RHEZ 2/16 [12.5%]) and pruritus (11/59 [18.6%] vs. RHEZ 6/16 [37.5%]). One serious adverse event, hemoptysis in the 3 mg group, was considered a complication of the underlying disease and unrelated to study treatment. There were no abnormal ECG TEAEs. Following multiple once-daily doses, OPC-167832 plasma concentrations increased ~1.4- to 2.3-fold and steady state was reached after 10-14 days. Plasma exposure increased dose-proportionally from 3mg to 90mg. Inter-subject variability was moderate, with CV% typically <40%.

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Mean (SD) change from baseline in log₁₀CFU at 14 days was -1.10 (0.62), -1.93 (0.98), -2.23 (1.02) and -2.08 (0.75) for OPC-167832 3mg, 10mg, 30mg and 90mg, respectively, and -2.69 (0.95) for RHEZ (Figure 1). Time to detection of *M. tuberculosis* (MGIT system) and sputum lipoarabinomannan measurements were consistent with observed falls in log₁₀CFU.

Conclusions: Once-daily dosing of OPC-167832 for 14 days was well tolerated in patients with pulmonary TB. OPC-167832 exhibited early bactericidal activity at all tested doses, with significant bactericidal activity consistently observed at 10mg and higher doses. Stage 2 of the study is ongoing.

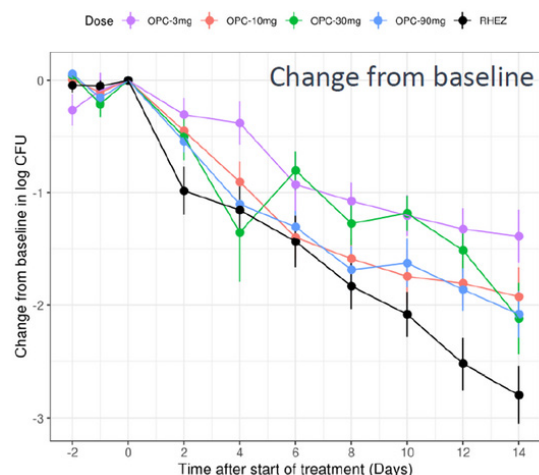


Figure 1. Mean (SD) change from treatment baseline in log₁₀CFU at 14 days (average of day -2 and -1).

TBS-EP-25 Phase I, double-blind, placebo-controlled trial in healthy subjects assessing tolerability, pharmacokinetics, and food effects of single ascending doses of OPC-167832, a novel anti-tuberculosis agent

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Background: OPC-167832, a novel oral inhibitor of decaprenylphosphoryl- β -D-ribose 2'-oxidase, demonstrated potent antimycobacterial activity as monotherapy and in combination with other anti-tuberculosis (TB) agents in in vitro and animal models and was safe in toxicology studies up to 2000mg. A first-in-human, two-part, randomized, placebo-controlled, single ascending dose study was conducted to assess safety, tolerability, and pharmacokinetics of OPC-167832 in healthy subjects after a standard meal.

Design/Methods: In Part 1, dosing was conducted in 6 sequential cohorts (OPC-167832 30mg, 60mg, 90mg, 120mg, 240mg, and 480mg), with 6 OPC-167832 and 2 placebo subjects randomized per cohort (pooled cohort [n=48]: male, 100%; mean age, 34.5 years; mean BMI, 25.1 kg/m²).

In Part 2, subjects received a single dose of 60mg OPC-167832 after a standard meal in a fasted state and after a high-fat meal.

Results: The most common AEs were headache (3/36 [8.3%]), constipation (2/36 [5.6%]) and back pain (2/36 [5.6%]) in Part 1, and mild increased ALT (2/12 [16.7%]) and pruritus (2/12 [16.7%]) in Part 2. There were no SAEs or AEs leading to discontinuation. Exposures were less than dose proportional and were inversely associated with QT interval. Median t_{max} ranged from 2.5–3.5

hours. C_{max} increased slowly up to and including the 60-mg dose (188 ng/mL) and dose proportionally thereafter (90–480mg, 182–634 ng/mL). AUC_{inf} increased dose proportionally up to 240mg (2340–9402 ngxh/mL), exceeding the EC_{80} AUC at all doses (2033 ngxh/mL; determined in the mouse model of chronic TB). $t_{1/2}$ ranged from 18–40 hours across cohorts. Minimal differences were observed in C_{max} and AUC_{inf} following standard or high-fat meals, compared to the fasted state.

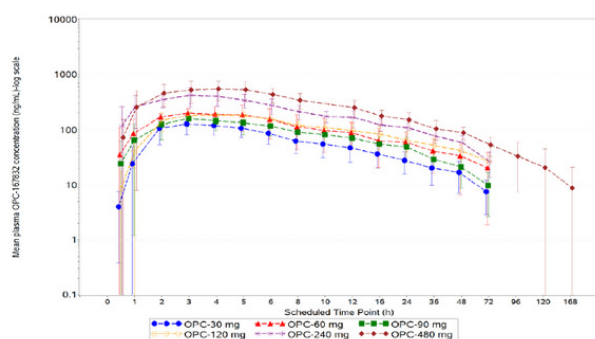


Figure 1. Mean (+/- SD) plasma concentration versus time curves - part one.

Conclusions: OPC-167832 was well-tolerated at all single doses up to 480mg. A multiple ascending dose study is ongoing in drug-susceptible TB patients.

TBS-EP-26 Efficacy and safety of high dose rifampicin containing regimen in treating pulmonary tuberculosis patients – a phase II B randomized controlled clinical trial

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Background: Limited data available in India on usage of higher daily doses of Rifampicin (RMP) in treating Tuberculosis (TB).

Methods: A Multicentric trial was conducted across India comparing the efficacy and safety of high dose RMP, 25 or 35 mg/kg/day, versus standard 10 mg/kg/day dose of RMP containing regimen in treating new smear positive pulmonary TB patients. The outcomes were early culture conversion in liquid media, relapse free cure and treatment emergent adverse events. Clinical and bacteriological progress were assessed weekly for 2 months and every month till 18 month. Time to sputum culture conversion were analysed using Kaplan-Meier method. Adverse events (AE) were graded as per DAIDS AE Grading Table Corrected Version 2.1-July 2017.

Results: Out of 295 taken for analysis, the mean age was 35 ± 12 years, and 70% were males. Sputum culture conversion was observed in 90/100 (90%), 92/101 (91%) and 77/94 (82%) in 35mg, 25mg and 10 mg/kg of RMP containing regimen respectively at week 8 in Liquid media {HR: 1.43, CI 1.051-1.968, P= 0.028}. Time to stable culture conversion in liquid media was significantly faster in high dose group versus control group (median 35 days vs 41days; p=0.03). 6/295 (4 in 10mg and 2 in 25mg regimen) had TB recurrence at 18 months. Out of 249 AEs which occurred during treatment, 61/79 clinical AEs and 119/170 lab AEs were of grade 1 severity. Grade 1 toxicities were 16 % in regimen with 10/25 mg/kg RMP and was 25% with 35mg/kg. No significant difference between regimens with respect to grade 3/4 AEs. 5/18 Serious Adverse events were related to High dose RMP needing treatment modification.

Conclusion: Faster sputum culture conversion and Relapse free cure with similar adverse events as compared to conventional dose, suggests 25mg/kg Rifampicin containing daily regimen can be successfully implemented in treating pulmonary TB patients.

TBS-EP-27 The risk-benefit trade-off and its role in confirmatory trial designs for TB regimens

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Non-inferiority trials are commonly used in confirmatory evaluations of novel TB regimens. The choice of the non-inferiority margin (NIM) has been a controversial aspect of such trials. The NIM implies that patients are willing to accept some loss in efficacy if the regimen is safer and/or more tolerable/acceptable.

I will introduce a novel concept called the “maximum acceptable decrease in efficacy” (MADE) to quantify the risk-benefit trade-off, and then show how MADE can be systematically elicited from stakeholders. MADE can be used as a tool to inform the NIM.

Alternatively, a superiority trial can be designed using a risk-benefit composite outcome.

TBS-EP-28 Innovating sample size calculations for a pragmatic RR-TB trial: a non-linear mixed effects model of longitudinal measures of mycobacterial load

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Background: The classic endpoint in rifampicin resistant (RR)-TB trials is time to sputum-culture-conversion (TSCC), a proxy for mycobacterial load (MBL). TSCC however disregards data from serial cultures.

Objectives: To improve the sample size (SS) efficiency by using serial data of Time To Positivity (TTP) in Mycobacterial Growth Indicator Tubes (MGIT) in the design of RR-TB trials.

Methods: We compared different strategies to determine the SS required to detect an effect of a novel strategy for management of DR-TB versus standard of care. Specifically, we compared the use of the Kaplan-Meier (KM) curve for TSCC to the use of serial TTP measurements. We fit a non-linear mixed effects model to simulated data. The model consists of three simultaneously fitted components: a longitudinal model for decline in MBL in function of time on treatment (TOT), a probabilistic component for presence of mycobacteria in sputum in function of TOT, and a time-to-event model for TTP. We calibrated the simulation model using data from a RR-TB cohort. This assumed 50% retreatment patients, 80% HIV positivity and a 50% hospitalization-rate at treatment initiation. All simulation results were based on 250 runs.

Results: To achieve 80% power to detect a meaningful difference in medium TSCC (8 vs 12 weeks), a total SS of 410 individuals is required when using the KM approach. Using the serial data model, a total SS of 173 individuals was required to achieve 90% power to detect a meaningful difference between the two arms (28% reduction in half-life of the MBL).

Conclusion: Use of serial TTP data outperforms standard SS calculation approaches of based on TTSC at a single timepoint, resulting in a smaller number of patients per treatment group to show the intervention's effect.

TBS-EP-29 Study to evaluate the safety and efficacy of four antibiotic drugs in fixed-dose for tuberculosis treatment

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Introduction: Tuberculosis (TB) is a multisystemic disease caused by *Mycobacterium tuberculosis*, which affects the respiratory, gastrointestinal, central nervous, and musculoskeletal systems, among others. TB is considered the leading cause of death from infectious disease worldwide, with its presence being most evident in developing countries.

Objective: To detect and describe the adverse events and efficacy presented during the administration of rifampicin, isoniazid, pyrazinamide, and ethambutol in patients with tuberculosis during the intensive and support phase of the Strictly Supervised Shorter Treatment (TAES) scheme, in Health Centers of the State of Colima, Mexico.

Methods: Through a questionnaire directed and applied via telephone, information related to the adverse events presented in patients with a diagnosis of pulmonary tuberculosis under treatment with doTBal® (rifampicin, isoniazid, ethambutol, pyrazinamide) and doTBal-S® (rifampicin, isoniazid) was collected and classified according to the severity, seriousness, outcome of the event, probable cause and whether they were an expected or unexpected adverse event.

Results: Of 62 screened patients, 47 patients were evaluated, mean age 37 years (range 12-69 years), 17% reported diabetes, 21% malnutrition; 270 adverse events identified in 45/47 patients evaluated (4 screen failure, 4 dropouts, 7 withdrawn). The nervous system was the mainly affected (21.5%), with headaches being the most frequent (9%), 12.6% of the adverse events were unexpected, classified as doubtful to the use of the drug.

There were no risks that generated any warning signal, whence the safety profile of the doTBal® and doTBal-S® are confirmed. At the end of the intensive and support phase of TAES with doTBal® and doTBal-S®, the efficacy observed was 85.37% and 97.56%, respectively.

Conclusion: The safety and efficacy profile of doTBal® and doTBal-S® keep with the benefit/risk balance described in its prescribing information since there was no new risk and maintained an efficacy close to 100%.

TBS-EP-30 SARS-CoV-2-pneumonia in patients with pulmonary tuberculosis: case series analysis

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The pathological process in pneumonia caused by SARS-CoV-2 virus determines severe hypoxic reactions with a decrease in saturation. This scenario is especially unfavorable for the patients with existing pulmonary diseases.

We've analyzed the cases of treatment and outcomes of coronavirus pneumonia in 135 patients with pulmonary tuberculosis. Pulmonary tuberculosis in the examined group was detected at least a year before COVID-19, occurred in all patients in the active phase and the majority of patients were discharging bacteria (84; 62,3%).

Moreover all patients had anti-tuberculosis therapy for at least 3 months. The body mass index in all patients didn't exceed 25 kg/m² and in 38.5% - less than 18.5 kg/m². Coronavirus infection complicated by pneumonia was confirmed in all cases: virus RNA was detected by PCR in the nasopharynx and chest CT.

In the absolute majority of observations the therapy was undoubtedly successful: on average, on 4-6 days from the beginning of the disease, 112 patients (82,6%) showed regression of clinical and radiological manifestations.

Only 9 (6,7%) patients with extremely severe coronavirus pneumonia, despite the treatment in the intensive care unit and the transfer to a ventilator, died. The cause of death was progressive tuberculosis inflammation and background diseases: diabetes mellitus and CHD.

Analyzing the data we noted that in the main cohort of patients with pulmonary tuberculosis receiving etiotropic treatment, as well as with the signs of subsiding of tuberculosis inflammation, coronavirus pneumonia can course, on average, as in the main population.

This is probably due to the adaptive mechanisms to hypoxia in patients with pulmonary tuberculosis, the absence of such a predictor of an unfavorable prognosis as obesity, as well as the weak activity of immune mechanisms and the absence of a pronounced cytokine reaction against the background of chronic bacterial infection and the treatment of immunosuppressive anti-tuberculosis medication.

TBS-EP-31 MPT51 and MPT64-based antigen detection assay for the diagnosis of extrapulmonary tuberculosis from urine samples

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Extrapulmonary tuberculosis (EPTB) is a diagnostic challenge and WHO-endorsed tests (Xpert MTB/RIF assay/culture) fall short of END-TB strategy targets. To meet this diagnostic challenge, we aimed to develop an adjunct urine-based assay as a quick screening platform for EPTB.

For the assay development we used urine samples (n=137) for the diagnosis of three forms of EPTB i.e., Pleural TB (pTB), Abdominal TB (ATB) and Tuberculous meningitis (TBM). This innovative assay assessed the presence of two *Mycobacterium tuberculosis* antigens namely MPT51 & MPT64 in the urine samples of the EPTB patients.

All patients were categorized as 'Definite' EPTB (n=10) who were Xpert MTB/RIF and/or culture positive & 'Probable' EPTB (n=77) and 'Non-EPTB' group (n=50) using defined composite reference standards. ROC-curves were generated using ELISA results of 'Definite' EPTB and 'Non-EPTB' groups for both antigens independently and cut-off values were selected to provide 86.2% specificity (95%CI:73.3-94.2) for MPT51 and 92% specificity (95%CI:80.8-97.8) for MPT64.

In 'Definite' EPTB group, the developed assay had a sensitivity of 70% (95%CI:34.7-93.3) for MPT51 and 80% (95%CI:44.4-97.5) for MPT64 antigen. Both antigens had a relatively lower sensitivity in the 'Probable EPTB' group i.e., 32.5% (95%CI:22.2-44.1) for MPT51 and 31.2% (95%CI:21.1-42.7) for MPT64.

On combining the results of both antigens, an increased sensitivity of 90% (95%CI:55.5-99.7) was observed both in the 'Definite' EPTB group (n=10) and 'Probable' EPTB category [41.6% (95%CI:30.4-53.4)]; although there was a slight decrease in specificity [80% (95%CI:66.3-89.9)] as compared to individual antigens. On comparing the results of the developed assay based on form of EPTB, the assay worked remarkably well for TBM diagnosis followed by ATB and pTB.

The developed urine-based diagnostic assay has a potential for EPTB diagnosis and shows promise to be evaluated in larger studies to accurately assess its utility for various forms of EPTB.

TBS-EP-33 Sensing of Interferon- γ by *Mycobacterium tuberculosis*

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Mycobacterium tuberculosis (Mtb) is one of the most successful human pathogens and remains a leading cause of death from infectious disease. A central regulator of the immune defense against Mtb is Interferon- γ (IFN- γ), which directly activates macrophages to kill phagocytosed Mtb in addition to other immunomodulatory effects.

However, cytokines have also been shown to increase virulence of several bacterial pathogens, leading us to investigate the potential direct effect of IFN- γ on Mtb.

Firstly, we observed binding of IFN- γ to Mtb (H37rv) by flow cytometry and confocal microscopy.

Secondly, we find that recombinant IFN- γ causes a significant increase in oxygen consumption rate (OCR) in Mtb, suggesting it induces increased bacterial respiration. This was a dose-dependent effect that was not observed in the attenuated strain Bacillus Calmette-Guérin.

This increase in OCR is specific to IFN- γ , as no increase was observed for IL-1 β , IL-4, IL-6, IL-10, GM-CSF, M-CSF and TNF- α . Importantly, the same effect was observed using supernatant from activated T-cells, and was abrogated when IFN- γ was depleted by antibody.

A discrete IFN- γ binding fragment was observed by Western blotting and subsequent mass spectrometry identified mycobacterial membrane protein large 10 (MmpL10) as a potential transmembrane binding partner.

Consistent with this, a *mmpL10* mutant strain does not exhibit an increase in OCR in response to IFN- γ , whereas this was restored in the complemented strain.

Finally, when IFN- γ is combined with isoniazid, Mtb cultures are sterilized compared to isoniazid treatment alone. Our data suggest a potential novel mechanism that allows Mtb to respond to host immune activation.

TBS-EP-34 Potential monoclonal antibody treatment against *Mycobacterium tuberculosis*

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The current TB vaccines focus on either improving the current BCG vaccine or boosting it with a second dose of a different TB vaccine. All these strategies target cell-mediated immunity only. The effective vaccines against most respiratory pathogens protect by generating neutralizing antibodies against the agent.

However, the humoral response against *Mycobacterium tuberculosis* (*M. tb*) has not been thoroughly studied, partly due to its variable response. *M. tb* does induce a humoral immune response to several mycobacterial antigens in humans. Thus, an additional, unexplored tool for disease prevention and treatment is the use of human monoclonal antibodies (MAbs) targeting conserved *M. tb* proteins.

In the present study, mAbs were purified from *M. bovis* BCG vaccinated individuals and tested for specificity against *M. tb* whole cell lysate (WCL), lipoarabinomannan (LAM) and lipoarabinogalactan (LAG), and *M. tb* cell wall proteins from BEI. Lysates from *E. coli* strain BL21, and human metapneumovirus F protein were used as controls.

Preliminary studies show that only one (LAM2) of five isolated mAbs binds with high specificity to *M. tb* LAM. Further characterization shows that LAM2 mAbs have high affinity to both BCG strain Danish 1551 and *M. tb* strain Erdman *in vitro*.

Design: Briefly, either fixed BCG or *M. tuberculosis* bacilli or *M. tb* proteins were used for ELISA. Absorbance at 405 nm was measured and plotted using GraphPad Prism 9.0.

Similarly, BCG and *M. tb* bacilli were stained with carboxyfluorescein succinimidyl ester (CFSE) followed by LAM2 mAb. After fixation, the cells were analyzed by FACS. All CFSE⁺ cells were further gated on cells stained with goat anti human APC.

Results: LAM2 mAb binds to BCG, *M. tb* bacilli and *M. tb* LAM as analyzed by both ELISA and FACS.

Future prophylactic studies in mouse model of tuberculosis are planned.

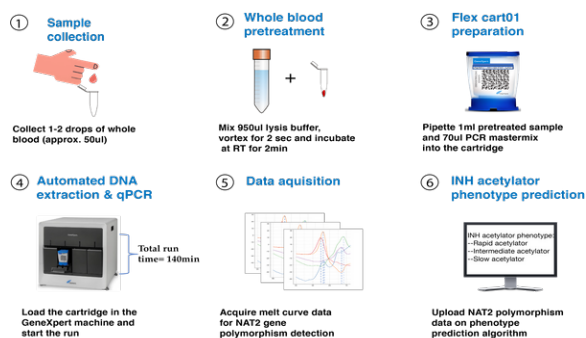
TBS-EP-35 A rapid pharmacogenomic assay to detect NAT2 polymorphisms and guide isoniazid dosing for tuberculosis treatment

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Background: Standardized dose of TB drugs contributes to a substantial incidence of toxicities, inadequate treatment response, and relapse, in part due to variable drug levels achieved. Single nucleotide polymorphisms (SNPs) in the N-acetyltransferase-2 (NAT2) gene explain the majority of interindividual pharmacokinetic variability of isoniazid (INH).

However, a major obstacle to implementing pharmacogenomic-guided dosing is the lack of a point-of-care assay. We developed a NAT2 classification algorithm to predict INH clearance, and a prototype pharmacogenomic assay on a GeneXpert to guide INH dosing.

Methods: We trained random forest classification models to predict NAT2 acetylation type (slow, intermediate, rapid) using unphased SNP data from a global collection of 8,561 phased genomes. We enrolled 48 pulmonary TB patients and estimated their INH clearance levels measured at 1 hour and 8 hours after the first dose and 1 hour after a dose on day 14. We tested the accuracy of our acetylator prediction algorithm (5-SNP model) against INH clearance rates from these participants. We then developed a cartridge-based 5-SNP qPCR assay on the GeneXpert platform and assessed its analytical sensitivity directly on 20 whole blood samples from healthy individuals.



Results: With a 5-SNP model trained on two thirds of the data (n=5,738), out-of-sample genotype prediction accuracy from unphased data on the remaining one third (n=2,823) was 100%. Among the 48 TB patients, predicted acetylator types were: 27 (56.2%) slow, 16

(33.3%) intermediate and 5 (10.4%) rapid. INH clearance rates were lowest in slow acetylators (median 19.3 L/hr) and highest in fast acetylators (median 46.7 L/hr). NAT2-PGx assay could accurately classify all allele patterns directly from as little as 25 ul of whole blood in 140min of total run time.

Conclusion: An automated assay on a platform widely used globally for tuberculosis diagnosis could enable improved dosing of isoniazid, averting toxicities and improving treatment outcomes.

TBS-EP-36 Adverse effects in linezolid treatment of MDR-TB - genetic patterns and solution approach

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Background: The World Health Organization estimates that 465.000 individuals fell ill with multidrug-resistant tuberculosis (MDR-TB) in the year 2019. Linezolid is a WHO group A drug for the treatment of MDR-TB. However, there is time- and dose-dependent toxicity leading to adverse events (AE) in a significant proportion of patients including myelosuppression and polyneuropathy.

Methods: Adult patients with pulmonary MDR-TB were enrolled in a German Center for Infection Research (DZIF) multi-center trial at 7 centers in Germany. Treatment and AE data were collected and whole blood RNA was analysed at baseline and during therapy. Whole blood transcriptomic analysis was performed from Paxgene tubes on Agilent 44k arrays (Agilent, Böblingen, Germany). Enrichment analysis was performed to identify genetic patterns and pathways for patients with and without linezolid-related AE.

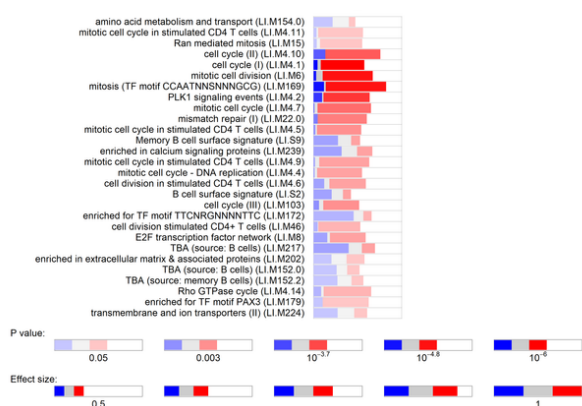


Figure 1: Transcriptional modules (tmod) enrichment Analysis for comparing MDR-TB patients under linezolid treatment with and without adverse event (AE) at baseline.

Results: Treatment and AE information was available from 79/82 MDR-TB patients with culture confirmed pulmonary TB. 53 Patients were treated with linezolid (67.1%). Of those, linezolid-associated AE occurred in 29 patients (54.7%). The enrichment analysis between patients with and without AE revealed pathways that represent very energy-rich processes such as the cell

cycle, even before the start of therapy. The downregulation of respiratory chain pathways also indicates a pre-therapeutic disturbance in the energy balance.

Conclusion: The majority of patients with MDR-TB undergoing a linezolid-containing treatment regimen experienced linezolid-attributed AEs. Our data suggests a vulnerability for linezolid-associated AEs in patients who have upregulated genes involved in energy-rich pathways and downregulated genes involved in the respiratory chain prior to the start of treatment.

TBS-EP-37 A nutraceutical polyherbal tea using *Kigelia africana*, *Senna singuena* and *Cassia abbreviata* for adjunct TB therapy

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Indigenous herbal products are used as prophylaxis, or treatment for various ailments such as TB and HIV in Zimbabwe. These have been taken mainly as crude plant parts and used to prepare teas, steam infusions or incorporated into porridge.

This study aims to evaluate the physico-chemical characteristics of some indigenous herbs commonly used in TB treatment, and prepare a range of polyherbal tea products for ease of administration and increased market appeal. The air-dried fruit of *Kigelia africana*, *Cassia abbreviata* leaves, root and bark, as well as *Senna singuena* fruit, root and bark were crushed into a powder; and passed through a mesh sieve.

A mixture of the herbs was obtained, and filled into 2.5g tea bags and sealed. Preliminary phytochemical studies showed the presence of flavonoids, saponins, tanins and alkaloids. The tea was free of heavy metal contamination as determined by ICP-OES. Lead and arsenic were not detected, whilst 0.01mg/g of Copper was detected, and this is well below the WHO permissible limit of 2mg/kg plant weight. An alkaloid content of 1.5mg/g was indicative of a low Caffeine content. This is lower than that of Oolong tea, and green tea.

The tea had a mineral ash content of 6.8%, indicating the presence of inorganic minerals, although some essential minerals such as Magnesium (0.14mg/kg), Zinc (0.19mg/kg, and Iron (1.13mg/kg) were detected in rather low quantities.

The hot water infusion also demonstrated moderate antimicrobial activity against Gram positive (*S. aureus*), Gram negative (*E. coli*) and non tuberculous mycobacterium (*M. aurum* and *M. smegmatis*). The tea produced therefore has some nutraceutical potential, and could find use as an adjunct treatment for TB.

TBS-EP-38 A preliminary study shows that an NGS and AI-based model can accurately predict antibiotic susceptibility in *Mycobacterium tuberculosis*

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According to the World Health organization Global TB report 2020, Tuberculosis (TB) accounted for more than 1.4 million deaths globally in 2019. The highest burden of the disease lies in India with over 2 million cases each year. A major factor that contributes to the high morbidity and mortality is the emergence of drug resistance in *Mycobacterium tuberculosis* (*M. tuberculosis*), the causative agent of TB. Due to its slow growth rate in culture medium, identifying drug resistance in *M. tuberculosis* is a time consuming process. Hence, even though still a reference standard, the phenotypic DST is slowly being replaced by alternate methods.

CBNAAT based assays were introduced in 2009 and were approved by WHO in 2010. For the prediction of RIF resistance, the test targets an 81 bp core region of the *rpoB* gene. Although the majority of the current resistance determining mutations lie in this region, it inherently misses out on 4% of the mutations that lie outside this region. Even though these mutations are currently rare, the absence of detection is introducing a selection bias enabling their continued spread. The XDR assay targets only 7 loci with 10 differently colored probes.

Thus, in case of ethionamide the assay can only target the *inhA* promoter region resulting in only 64% sensitivity compared to the phenotypic DST.

Whole genome sequencing based resistance detection has made remarkable advances in DR-TB diagnosis. With the development of the AarogyaAI® rapid susceptibility test for TB, we show that a hybrid of feature and artificial intelligence-based model can be a useful tool to detect resistance in *Mtb* aiding in effective treatment and positive outcomes.

Initial comparison studies on whole genome sequences have shown that the test can predict antibiotic susceptibility status with sensitivity in the range of 53-92% and specificity of 78-95% for 10 drugs.

TBS-EP-39 Can nonspecific immunological memory be a protection against COVID-19?

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BCG is able to induce not only a specific anti-tuberculosis effect, but also a nonspecific protective effect against a variety of viral and bacterial infections due to the formation in monocytes-macrophages (Mn-Mf) the phenotype of nonspecific immunological memory (aka “trained immunity”, TI). Increasing the intracellular pool of mevalonic acid was also shown to induce TI in Mf (Bekkering et al., 2018).

This study aimed to assess experimentally the ability of BCG- and mevalonate-induced TI of Mn-Mf to exert antiviral effect against SARS-CoV-2.

TI was induced by 24 h incubation of Mn-Mf of the U937 line with BCG vaccine strain, MOI 1:1, and/or with mevalonate lactone, 2 mM/L, and/or with zoledronate, 100 µM/L (a selective inhibitor of farnesyl-pyrophosphate synthase). Since the SARS-CoV-2 virus is unable to replicate in Mf, to evaluate the cytopathic effect (CPE) and replication of the virus, a culture of intestinal epithelial cells CaCo2 was infected, and then for 4 days 1. co-cultured with U937 preincubated with BCG, mevalonate, zoledronate, or their combinations, or 2. with the supernatants of these preincubated U937. Additionally, the effect of BCG, mevalonate pathway modulators (MevPM) and their combinations was evaluated directly in infected CaCo2. CPE was assessed by TCID50, and viral replication by Ct.

Both preincubated U937 and their supernatants, added to infected CaCo2, reduced TCID50 and suppressed viral replication tens and hundreds of times; the combinations of BCG with mevalonate and/or zoledronate significantly potentiated the effects of BCG. Interestingly, in CaCo2 cells cultured with BCG, and/or with MevPM (without U937 or their supernatants), CPE was suppressed as well, though less pronounced than with U937. Thus, we demonstrated that the BCG vaccine, due to its nonspecific action, has a pronounced antiviral effect against SARS-CoV-2; moreover, this effect can be potentiated by MevPM.

Study was supported by RFBR grant No. 20-515-80006 BRICS_COVID-19.

TBS-EP-40 Characterizing individual-level tuberculosis transmission dynamics in high-burden urban and rural settings: a model-based analysis

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Background: *Mycobacterium tuberculosis* transmission dynamics in high burden settings are poorly understood. Growing evidence indicates transmission may be characterized by a high degree of individual heterogeneity (i.e., “superspreading”), or variation in the number of secondary cases between index cases, yet the degree and influence of such heterogeneity is unknown and unmeasured in high burden settings.

Quantifying the propensity of this phenomenon will improve our understanding of its role in shaping tuberculosis (TB) epidemiology.

Methods: We fit two mechanistic (branching process) models of TB transmission using geospatial, social network, clinical, and genotypic data to identify transmission clusters in a prospective, population-based study from Botswana representing both urban and rural high-burden populations.

We inferred the effective reproductive number, R , and quantified individual heterogeneity using the negative binomial dispersion parameter, k , to model transmission; $k < 1.0$ implies increased heterogeneity and suggests large outbreaks are rarer but more extensive.

We further compared model likelihoods with six different parametric assumptions, ranging from completely distinct to uniformly identical parameters, to determine if transmission dynamics meaningfully differed between these urban and rural populations.

Results: We estimated $R=0.44$ (95% CI: 0.39-0.50) and $k=0.48$ (95% CI: 0.31-0.87) in the urban population and $R=0.75$ (95% CI: 0.48-1.46) and $k=0.08$ (95% CI: 0.04-0.14) in the rural population. Likelihood comparisons supported distinct underlying transmission dynamics between the populations; the rural population was characterized by more extensive heterogeneity and was markedly more likely to observe large outbreaks (Figure).

Ongoing transmission was attributed to an estimated 17.1% of cases in the rural population compared to 26.8% in the urban population.

Conclusion: Individual heterogeneity plays a critical role shaping the epidemiology of TB transmission in high-burden settings, particularly in rural populations. Intervention strategies aimed at interrupting transmis-

sion would benefit from considering the role and source of such heterogeneity. Importantly, country-level estimates may obscure informative differences in transmission dynamics within subpopulations.

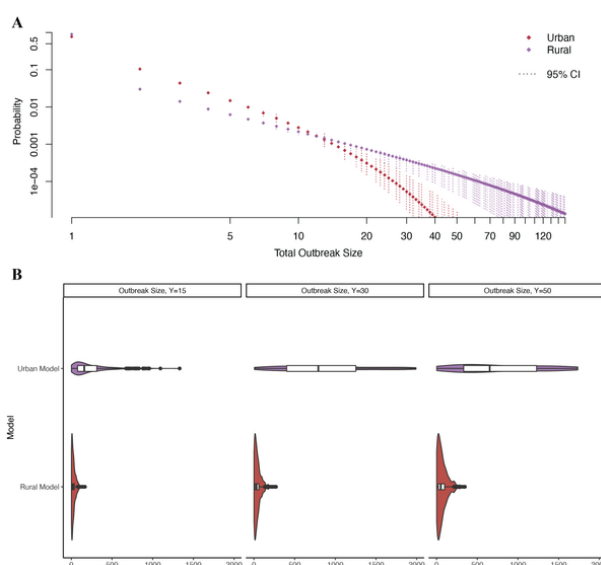


Figure. Number of incident cases until first large outbreak (results from 500 simulated surveillance systems).

TBS-EP-41 Complementary non-sputum detection of tuberculosis in HIV-coinfected patients

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Background: For diagnosis of tuberculosis (TB) in HIV-coinfected patients, tests for mycobacterial lipoarabinomannan (LAM) in urine are practical but relatively insensitive alternatives to microbiological testing of sputum. Here, we evaluated urine LAM testing alongside PCR-based tests for *Mycobacterium tuberculosis* DNA in tongue swabs, an emerging alternative non-sputum sample for TB testing. We hypothesized that the two non-sputum sample types would deliver complementary, not redundant, results.

Approach: The study included 131 South African patients of whom 64 (48.1%) were confirmed to have TB by GeneXpert MTB/RIF Ultra or culture analysis of sputum. 120 patients (91.6%) were co-infected with HIV and 130 yielded a valid urine LAM result (Alere DETERMINE™ LAM Ag). Tongue swab samples were tested by manual IS6110-targeted qPCR and, in some cases, GeneXpert MTB/RIF Ultra.

Results: Relative to the sputum microbiology reference standard, tongue swab qPCR using a Cq cutoff of 38 was significantly more sensitive than urine LAM (respectively, 42/64 [67%] vs. 22/63 [35%]), but less specific (respectively, 52/67 [78%] vs. 67/67 [100%]).

When a more stringent Cq cutoff of 32 was used, tongue swabs and urine testing performed similarly (respectively, 25/64 [39%] vs. 22/63 [35%] sensitive, and 65/67 [97%] vs. 67/67 [100%] specific). The two methods delivered complementary, not redundant, results.

When TB positivity was defined as either urine- or tongue swab-positive, sensitivity improved to 36/63 at Cq <32, significantly better than urine LAM alone (57% vs. 35%, p=0.006), with 97% specificity. A subset of tongue swabs (N=19) were also tested by using GeneXpert Ultra, which reproduced all true positive and true negative manual qPCR results, and resolved the two false-positive tongue swabs.

Conclusion: Tongue swabs and urine can serve as complementary non-sputum samples for improved diagnosis of TB in HIV-coinfected patients.

TBS-EP-42 COVID-19 Impact on US Tuberculosis Programs: National Tuberculosis Controller Association Survey

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Background: Early in the pandemic, efforts made to capture the effects of COVID-19 on tuberculosis (TB) elimination efforts in the US showed that resources were being diverted from central TB activities. The goal of this National Tuberculosis Control Association (NTCA) survey was to assess and detail the impact of COVID-19 on US TB programs, including early evidence of TB-COVID-19 Co-infections, identify strategies for addressing COVID-19 impact on TB programs, and to evaluate potential need for additional resources to TB programs.

Method: The survey was developed by the NTCA Survey Committee and launched between January-March 2021. The survey was distributed to all NTCA members representing Centers for Disease Control and Prevention Cooperative Agreement programs and other local health departments. The survey was also promoted by the National Association of County and City Health Officials via an e-announcement to members. One survey was requested per jurisdiction.

Findings: A total of 46 State/Territory/District programs and 96 local programs (county, city, and regional levels) responded. Changes in TB activities are shown in Figure 1: Decreases in TB program staffing, clinic

hours/appointments, as well as TB reporting, contact investigations and diagnostic work-ups were seen.; and an increased use of electronic directly observed therapy (eDOT) and telemedicine visits.

Conclusion: The survey revealed the need for increased qualified staff and/or time dedicated to TB including the need for flexible and sustained funding to expand TB program staff. The increase use of electronic platform have led to efforts to sustain and expand these programs and to improve reimbursement for these activities. Delayed and missed diagnosis required additional efforts to educate health care providers to “Think TB”. It is important to invest in TB program now so that we can respond to the depletion of resources and staffing and to build out a solid infrastructure and knowledge base.

	Reduced	No Change	Increased	n	
Staffing and service changes	TB program staff time devoted to TB activities	120	16	1	137
	TB clinic hours	76	31	4	111
	TB clinic appointments	92	22	2	116
	Proportion of B notifications known to have arrived being evaluated	64	37	0	101
	Proportion of close contacts being evaluated	42	70	3	115
Service delivery changes	LTBI treatment initiation	84	43	4	131
	Treatment via in-person DOT for patients with presumptive or confirmed TB	78	38	4	120
	The use of telemedicine for clinic visits	3	22	65	90
	The use of electronic DOT (eDOT)	6	26	80	112
Diagnosis and reporting change	Reporting of presumptive TB from providers	61	50	2	113
	Collection or receipt of sputum specimens to the public health laboratory for MTB testing	45	56	0	101

Figure 1. Changes in TB activities due to COVID-19

TBS-EP-43 Derivation of Scoring System for Multidrug Pulmonary Tuberculosis Subjects to Stratify the Risk Factors Based on Radiological Investigation

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Clinical prediction model was developed to estimate the probability of the presence of risk factors and clinical outcome from multidrug resistant pulmonary tuberculosis subjects. Radiological imaging technique used for grading the severity of the disease. To assess the performance of the prediction model and to enhance both the diagnostic and prognostic approaches we developed and validated clinical prediction model based on radiological presentation. This novel scoring system helps to screen the subjects who are on multidrug resistant anti-tubercular therapy and at risk of developing severity of the lung involvement.

We analyzed 271 subjects undergoing multidrug resistant tuberculosis treatment at the Government Chest and Tuberculosis hospital, Warangal, India. The changes in the immune cell characteristics were analyzed using ANOVA. The result extracted the changes in the clinical characteristics of lymphocytes, platelets, mean platelet volume and posed as a significant risk factors in the severity of lung infection in subjects.

Statistical methods and study design used to develop prediction model. We first performed the Univariate logistic regression using chest X-ray as a dependent variable and clinical investigations as independent variables.

The variables with $p < 0.2$ in univariate logistic regression analysis were chosen for the second step data analysis. Collinearity examined using Pearson correlation.

In the second step, a step-wise multivariate logistic regression analysis was used to select the independent variable prediction with a $p < 0.05$ to evaluate regression coefficient (β).

The constant used in developing this score was based on Framingham study. This study evaluated the performance of the scoring system in multidrug resistant tuberculosis subjects to distinguish between the patients with prognosis and the extent of lung involvement.

The subjective investigations revealed past history of tuberculosis, history of multidrug resistant tuberculosis and resistance towards anti-tubercular drugs established the progression of the disease. This investigation may serve as a practical methodological reference for researchers.

TBS-EP-44 Detection of pulmonary tuberculosis via exhaled volatile organic compounds by a breath test

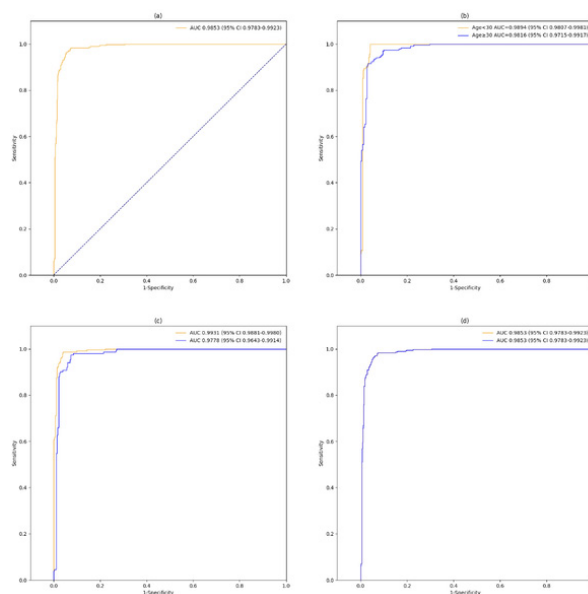
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Background: Tuberculosis diagnostics are usually either inaccurate, too expensive or complicated for use. Exhaled breath test, which detects volatile organic compounds (VOCs) by real-time high-pressure photon ionization time-of-flight mass spectrometry (HPPI-TOFMS), may be an attractive option for tuberculosis diagnosis. We aim to evaluate its performance in diagnosing pulmonary tuberculosis (PTB).

Methods: In this cross-sectional study, confirmed PTB patients and healthy controls were prospectively and consecutively recruited in a tuberculosis hospital in Shenzhen city, China. Exhaled breath samples were collected and stored in customized bags, and then detected by HPPI-TOFMS. The support vector machine (SVM) algorithm was employed for feature selection and model construction. Participants were randomly assigned in a 4:1 ratio to training and external validation data sets. We calculated sensitivity, specificity, accuracy and relative 95% confidence interval (CI) of VOC model overall and stratified by clinical characteristics.

Results: 812 healthy controls and 522 PTB patients were included in the final analysis. The VOCs model reached an accuracy of 95.6% (95% CI, 93.4-97.9), sensitivity of 93.7% (95% CI 89.4-97.9), and specificity of 96.9% (95% CI 94.5-99.3) in the training set (n=1064). In the external validation set (n=270), the VOC model had an accuracy of 97.4% (95% CI 95.5-99.3), sensitivity

of 95.2% (95% CI 91.2-99.3), and specificity of 98.8% (95% CI 97.1-100.0). Age, sex and treatment had no significant impact on diagnostic performance of the VOCs detection model.



Conclusions: Breath test via HPPI-TOFMS is simple, non-invasive, inexpensive, and fast for PTB diagnosis, with a high sensitivity and specificity. Its diagnostic performance, especially for PTB screening, should be further investigated.

TBS-EP-45 EU-PEARL: a systematic review on tuberculosis treatment response biomarkers

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The EU-PEARL project aims to develop an innovative, reusable, accessible, and sustainable integrated research platform (IRP), a novel concept for development of medical innovations to enhance efficiency to design and implementation complex clinical trials. A challenge in the clinical pathway development of new tuberculosis (TB) treatments is the lack of biomarkers or surrogate endpoints that are sensitive and specific enough to assess the efficacy of treatment and/or predict success or failure early in the course of treatment.

We performed a systematic review of the literature to analyse which biomarkers could act as surrogate endpoints, and which common gaps in their validation could be overcome by an IRP. We classified the outcomes estimated by the biomarkers in three groups:

- α) bacterial load estimates,
- β) early treatment outcomes and individual-level treatment outcomes, and
- γ) trial-level outcomes and post-treatment outcomes.

After screening 1691 citations, reviewing 245 articles, we identified 70 studies, and added another 16 through reverse citation. The 86 studies reported 1344 biomarker entries correlating a measure with clinical or microbiological outcomes during TB treatment. Of these, 189 entries were reported with performance data, with only 21 based on commercial tests with sensitivity and specificity of $\geq 75\%$, and most predictions were at the individual-level.

Importantly, we found many examples showing that isolated baseline values or changes during treatment are not always sufficient to predict clinical outcomes, and if even so, are not valid for different populations.

The heterogeneity of outcomes, designs, and statistical measurements made it not possible to quantitatively summarize our findings.

A platform trial implemented within an IRP could provide standardized data collection, inclusive population, and multiple intervention comparisons that, summarized with a meta-analytic approach, can ensure validation of biomarker as a surrogate endpoint.

TBS-EP-46 Evaluation of a targeted next-generation sequencing diagnostic assay for identification and characterization of drug-resistant M. tuberculosis isolates

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In 2019, an estimated 10 million people were infected with Mycobacterium tuberculosis (Mtb) and approximately 1.5 million people died as a result of Mtb infection. Resistance to one or more antibiotics was present in nearly 500,000 cases, reducing treatment success to an average of 57%.

It has become increasingly necessary for clinicians to not only identify Mtb in patients, but to also quickly provide an accurate drug-susceptibility profile during diagnostic testing. One tool that could fill this need is GenoScreen's Deeplex Myc-TB targeted, next-generation sequencing (NGS) panel. As marketed, the assay is capable of identifying both Mtb and non-Mtb mycobacterial species, determining drug-resistance profiles for 13 first- and second-line drugs, and generating spoligotyping and lineage information.

Here we show preliminary analysis of the Deeplex Myc-TB amplicon panel for drug-resistance determination, as well as mycobacterial species identification. Utilizing 14 previously characterized strains in the National Institutes of Health (NIH) Tuberculosis Quality Assessment Program (TBQA) Mtb isolate repository and an additional 16 non-tuberculosis (NTM) isolates obtained from the ATCC, we compare Deeplex Myc-TB performance to results from other diagnostic methods.

TBS-EP-47 Evaluation of Deeplex-MycTB with MDR-TB isolates in Japan

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Background: Antimicrobial Resistance (AMR) prediction using amplicon deep sequencing is expected as a culture-free rapid drug susceptibility testing (DST) of *Mycobacterium tuberculosis* (MTB). The accuracy of molecular DST depends on the accurate detection of mutations/indels, and the confidence of the database. AMR prediction test kit for 15 anti-TB drugs, Deeplex-MycTB (Genoscreen, Lille, France), was evaluated using MTB isolates in Japan.

Design/Methods: A total of 131 MTB isolates including 102 multidrug-resistant MTB (MDR-TB) and 19 pan-susceptible were collected through 2011–2014 over Japan, and phenotypic DST (minimum inhibitory concentrations, proportion on Löwenstein-Jensen, and MGIT-AST) and genotypic DST (Deeplex-MycTB and Illumina whole-genome sequencing) for 15 drugs were performed. Deeplex-MycTB results were compared and analysed with phenotypic DST and Illumina sequencing.

Results: A total of 300 mutations/indels were detected in 113 isolates by Deeplex-MycTB predicting the resistances of rifampicin (RIF), isoniazid (INH), fluoroquinolone (FQ) and pyrazinamide (PZA). Using phenotypic DST as reference, the sensitivities for RIF, INH, FQ and PZA were 100%, 92.6%, 91.2% and 98.2%, respectively (excluding insecure mutations). The specificities were 91.7%, 91.7%, 100% and 98.2%, respectively. Two isolates were predicted as bedaquiline (BDQ) resistant, but one was phenotypically susceptible. The proportions of insecure mutations detected in INH and ethionamide (ETH) were 12.4% (15/121) and 33.1% (40/121), respectively.

Conclusions: Deeplex-MycTB is a rapid diagnosis tool for the detection of drug resistant MTB. However, in our setting, it might be challenging to predict the drug susceptibilities of several drugs, i.e., INH, ETH and BDQ, because the mutations/indels are not surely confident. This study showed the usefulness of the kit, but further studies shall be warranted for accurate drug prediction of several specific drugs.

TBS-EP-48 Evaluation of the COVID-19 pandemic on tuberculosis investigations and tuberculosis treatment initiations in Tshwane, South Africa

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Introduction: It is estimated that lockdown measures to prevent the spread of COVID-19 infection could lead to an estimated 6.3 million cases of TB during 2020–2025 and an additional 1.4 million tuberculosis (TB) deaths globally unless additional measures are put in place. The South African Government announced a hard lockdown (level 5) from 26 March 2020 and varied the lockdown levels subsequently as the number of COVID-19 cases changed.

We aimed to evaluate the impact of the COVID-19 pandemic on the number of TB case investigations, drug-sensitive TB cases confirmed and drug-sensitive TB treatment initiations in a large district in South Africa.

Methods: Data on TB investigations performed, confirmed drug-sensitive TB cases and treatment started in ≥5-year-olds in Tshwane were obtained from the South African Department of Health. Outcomes following the announcement of the initial lockdown period (April 2020–September 2020), and subsequent COVID-19 period (October 2020–June 2021) was compared to the four quarters preceding the announcement using Poisson regression.

Results: TB investigations reduced significantly after the hard lockdown announcement (39% reduction, $p < 0.001$) in comparison to pre-COVID-19. The number of confirmed drug-sensitive TB cases per TB investigation increased significantly (26% increase, $p < 0.001$), as well as drug-sensitive treatment started per confirmed TB case (12% increase, $p < 0.001$).

Conclusion: The reduction in TB investigations indicates that the lockdown due to COVID-19 disrupted TB services significantly. The TB positivity rate appears to have increased post hard lockdown. This suggests that lockdown-related disruptions due to COVID-19 can cause long-lasting increases in TB burden and require targeted interventions to recoup gains made in reducing the TB burden in previous years.

TBS-EP-49 Evaluation of the performance of rapid, point-of care, antigen test for SARS-CoV-2 in Zambia

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Background: Point-of-care antigen rapid-diagnostic-tests (POC-Ag-RDTs) are a cheaper, quicker and simpler alternative to RT-PCR, but have lower sensitivity. WHO advises that POC-Ag-RDTs should be validated in different populations and epidemiological settings before they are implemented, but there have been very few field evaluations in 'real-life' community settings in low-income countries. We evaluated clinical performance of the PanBio™ POC-Ag-RDT for detecting SARS-CoV-2 infection compared to Xpert-Xpress™ in one peri-urban community in Zambia.

Methods: Study participants (≥15 years) attending community-based testing locations provided one nasal and one oropharyngeal swab, on the same day, tested with PanBio™ POC-Ag-RDT and Xpert-Xpress™ assay, respectively. Socio-demographic characteristics and symptoms suggestive of COVID-19 were recorded. The cycle threshold (Ct) values for N2 genes were obtained for the Xpert-Xpress™. We calculated sensitivity, specificity and positive and negative predictive values (PPV and NPV) of the Panbio™ POC-Ag-RDT compared to Xpert-Xpress™.

	Sensitivity		Specificity		Positive Predictive Value		Negative Predictive Value	
	n/N	95% CI	n/N	95% CI	n/N	95% CI	n/N	95% CI
All	148/368 (40.2%)	35.2-45.4	891/892 (99.9%)	99.4-100	148/149 (99.3%)	95.4-100	891/1111 (80.2%)	78.8-81.5
Symptomatic	123/225 (54.7%)	47.9-61.3	310/311 (99.7%)	98.2-99.0	123/124 (99.2%)	95.5-99.9	310/412 (75.2%)	72.5-77.8
Asymptomatic	25/143 (17.5%)	11.6-24.7	581/581 (100%)	99.4-100	25/25 (100%)	99.4-100	581/669 (83.1%)	82.0-84.2
N2 Ct values ≤30	136/183 (74.3%)	67.4-80.5	891/892 (99.9%)	99.4-100	136/137 (99.3%)	95.0-99.9	891/938 (95.0%)	93.7-96.0

Results: Between 1st of May and 31st August 2021, 1260 individuals were tested with both the Panbio™ POC-Ag-RDT and Xpert-Xpress™, 728 (58%) were males and median age was 30 years. Out of these 368 (29%) had a positive result on Xpert-Xpress™ and 149 (12%) on the Panbio™ POC-Ag-RDT. Overall the sensitivity and specificity of the Panbio™ POC-Ag-RDT were 40% (95% CI:35-45) and 100% (95% CI: 99-100) respectively. Sensitivity was higher in symptomatic (55%. 95% CI: 48-61) than in asymptomatic participants (18%.95% CI: 12-25) and increased as N2 Ct values decreased in the Xpert-Xpress™, rising to 74% (95% CI: 67-80) in individuals that had N2 Ct values ≤30.

Conclusions: In Zambia, the Panbio™ POC-Ag-RDT detected three-quarters of all individuals that tested positive on Xpert-Xpress™ with high viral loads (Ct≤30) and, thus, likely to be most infectious. This shows the usefulness of these simple, rapid, low-cost POC-Ag-RDTs for controlling transmission in settings where RT-PCR is not available.

TBS-EP-50 Expression of Mycobacterium Tuberculosis Induced SOCS3 and STAT3 and the Implications on Innate Immunity in TB patients vs healthy contacts in high TB/HIV Endemic Setting

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Background: Mycobacterium tuberculosis (TB) remains a disease of global health concern and a leading cause of mortality arising from an infectious agent. Protective immunity to TB remains unclear. Suppressor of cytokine signaling -3 (SOCS3) and signal transduction and activator of transcription-3 (STAT3) genes have the potential to influence innate immunity. We, therefore, explored the expression of SOCS3 and STAT3 and their implications on the innate immunity in TB patients and their healthy close contacts.

Methods: We recruited 72 TB patients and 62 healthy contacts from a high TB and HIV endemic setting (Lusaka, Zambia). We used RT-PCR and flow cytometry to quantify the expression of SOCS3, STAT3 and cytokines respectively. Data was analysed Stata version14.0 and figures were developed in GraphPad prism version 9.1.0 (2.2.1). Assessment for associations for categorical and continuous variables was analysed using the Chi-square test and Mann-Whitney test respectively. A *p*-value < 0.05 was considered statistically significant.

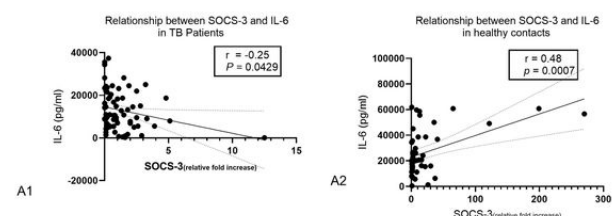


Figure. A1 shows an inverse relationship SOCS3 and IL-6 in TB patients and A2 shows a positive and significant correlation between SOCS3 and IL-6.

Results: Healthy contacts markedly expressed SOCS-3 in both unstimulated and stimulated whole blood in comparison to TB patients ($p < 0.0001$). STAT3-3 was elevated in TB patients in TB patients in stimulated blood only. IL-6 ($P = < 0.0001$), IL-10 ($P = < 0.0001$), IL-17 ($P = 0.0171$) were significantly expressed in Healthy contacts in comparison to TB patients. TNF- α ($p = 0.044$)

were markedly elevated in TB patients in comparison to healthy contacts. IL-6 and SOCS3 correlated significantly in healthy contacts only ($r = 0.429$, $p = 0.02$).

Conclusions: Both SOCS3 and STATS3 are genes of importance in mounting protective innate immunity against TB. We propose that SOCS-3 stimulation and inhibition of STATS-3 as possible approaches in gene therapy and vaccine development for TB.

Keywords: SOCS3, STATS3, Protective immunity, cytokines, TB patients, healthy contacts.

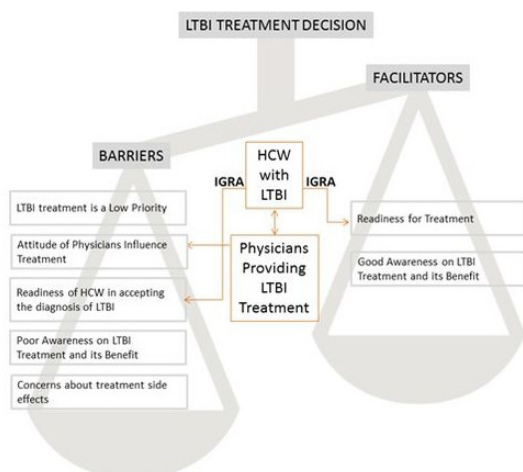
TBS-EP-51 Facilitators and Barriers to Latent Tuberculosis Treatment Uptake among Primary Health Care Workers in Malaysia- A Qualitative Study

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Introduction: Healthcare workers (HCW) have an increased risk of active and latent TB infection (LTBI) compared to the general population due to increased workplace exposure to mycobacterium tuberculosis.

There are differing recommendations on treating HCW with LTBI, which has resulted in a lack of treatment being received in this high-risk group in Malaysia. This study aimed to explore the facilitators and barriers to LTBI treatment among HCW in Malaysia.

Methods: This was a qualitative study using Focus Group Discussions and In-depth Interviews on HCW who were diagnosed with LTBI via Tuberculin Skin Test or Interferon Gamma Release Assay (IGRA) in primary healthcare clinics in Selangor, Malaysia. A semi structured topic guide was used to guide the interview. The interviews were audio-recorded, transcribed verbatim and analysed thematically.



Results: 18 HCW participated. Five themes emerged: i) Treatment for LTBI is viewed as a low life priority, ii) Attitude of treating physicians influenced treatment decision, iii) Readiness of HCW in accepting the diagnosis, iv) Awareness of LTBI treatment and its benefit, and, v) Concerns about treatment side effects.

Treatment for LTBI treatment was not viewed as a priority by the HCW diagnosed with LTBI or the treating physicians. The lukewarm attitude of treating physicians towards LTBI treatment during consultation influenced treatment decisions. IGRA can facilitate the readiness to accept diagnosis and treatment. Poor awareness on LTBI treatment and its benefit and medication side effect are barriers to treatment.

Conclusion: Treating physicians and HCW diagnosed with LTBI need to be educated on the importance of LTBI treatment in order to increase the uptake of LTBI treatment. Addressing the barriers to treatment and enhancing facilitators can assist policymakers to safeguard the health of HCW.

TBS-EP-52 Factor influencing the quality of life among Covid survivors in Riau Province, Indonesia - Post covid infection vaccination improving survivors' quality of life.

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Objective: To assess the status of health-related quality of life (HRQOL) among survivors and to analyze the factors associated with HRQOL of survivors.

Methods: The cross-sectional study was conducted among 468 and 285 survivors living in rural and urban in Riau Province, Indonesia, respectively on August 2021. The St George Respiratory Questionnaire (SGRQ) was asking to survivors and the Total score which reflects the proxy for quality of life was assessed. Quantile regression with the respect to 50th percentile was used to analyze the influencing factors of SGRQ score.

Results: There is a significant association for the factors of living in rural, being female, having an underlying medical condition, and getting hospitalization during treatment, which has the total score 4.77, 2.43, 7.22, and 21.27 higher than urban, males, not having an underlying medical condition and not getting hospitalization, respectively. Moreover, having the full vaccination has a score - 3,96 in total score significantly.

Conclusion: Survivors who living in Rural, being female, underlying medical conditions, hospitalization are the factors influencing lower HRQOL, while getting fully vaccinations is giving benefit to increase HRQOL. This study results can provide the targeted recommendations for improvement of HRQOL of survivors.

Predictors	Levels	Symptom domain	Activity domain	Impacts domain	Total Domain
Region of residence	Rural	2.56* (2.56-2.56)	2.98 (0.25-1.46)	3.99* (3.43-5.87)	4.77* (3.06-5.54)
	Urban	0	0	0	0
Sex group	Female		2.98 (0.17-3.97)	3.82 (0.16-4.22)	2.43* (1.27-3.86)
	Male		0	0	0
Comorbid disease	Yes	8.74* (4.23-14.65)	15.84* (3.73-30.20)	4.40 (-0.07-9.83)	7.22* (3.12-17.57)
	No	0	0	0	0
Vaccinated dose received	Fully vaccinated		-2.98* (-8.68 - -1.61)	-3.99* (-5.90 - -3.15)	-3.96* (-5.87 - -2.88)
	Partial vaccinated		-2.98* (-7.86 - -2.83)	-3.84* (-4.32 - -0.25)	-3.00 (-5.15 - -0.61)
	Unvaccinated		0	0	0
Treatment result	Hospitalization	19.45* (15.65-29.09)	32.62* (22.21-38.95)	15.00* (10.51-19.42)	21.27* (16.22-24.51)
	Mild	9.71* (9.71-9.71)	2.09 (0.51-4.30)	3.97* (2.99-4.31)	5.18* (4.74-6.43)
	Asymptomatic	0	0	0	0

Table.

TBS-EP-53 Factors shaping access to TB testing among adolescents living with Human Immunodeficiency Virus in the Eastern Cape, South Africa

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Background: South Africa has the largest population of adolescents living with HIV (ALHIV) in the world, who are at greater risk of TB-related morbidity and mortality. Research on TB has largely overlooked ALHIV, resulting in knowledge and service provision gaps. This paper provides insights into access to TB testing among ALHIV.

Methods: This longitudinal study, in the Eastern Cape, n=933 ALHIV (10-19 years old) were included in the analysis (90% of baseline sample, retained at second and third interview). The selection of social factors was informed by a literature review and filtered using the Ecological Model and the People Centered Model of TB Care. Multivariate analysis models, using R statistical software, and a stepwise approach identified significant factors at wave 2, wave 3 cross-sections and across both time points.

Results: 55.1% of ALHIV were female, 24% lived ruraly, 78.13% vertically acquired HIV, 58.3% (wave 2) and 37.6% (wave 3) reported having a TB symptom in the past year, 32.9% (wave 2) and 36.3% (wave 3) had a TB symptom and did not have a TB test. Being older (OR 1.43, CI 1.06-1.92, p 0.02), female (OR 1.34, CI 1.02-

1.75, p 0.03), in a relationship at both time points (OR 1.79, CI 1.23-2.62, p 0.002), and having had a viral load test in the past year at both time points (OR 1.50, CI 1.11-2.02, p 0.008) were associated with higher odds of TB testing.

Having TB symptoms (wave 2: OR 1.69, CI 1.27-2.26, p<0.00, wave 3: OR 1.67, CI 1.26-2.22, p<0.001) was strongly associated with testing for TB at each time point, suggesting screening processes are in place but can be improved in facilities where ALHIV receive care. Factors linked to housing, TB exposure risk and mobile phone access were associated with improved TB testing on cross-sectional analysis.

TBS-EP-54 Impact of COVID-19 disruptions on global BCG coverage and paediatric TB mortality: a modelling study

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Background: The impact of COVID-19 disruptions on global BCG coverage and paediatric TB mortality is unknown. We estimated the impact of COVID-19 disruptions on global BCG coverage and paediatric TB mortality, to guide mitigation measures.

Methods: We used data from multiple sources to estimate global COVID-19-disrupted BCG vaccination coverage. With a static mathematical model, we estimated the global number of additional paediatric TB deaths in the first 15 years of life due to delayed/missed vaccinations in 14 scenarios varying in duration of disruption, and magnitude and timing of catch-up.

Results: We estimated a global 25% reduction in BCG coverage within the COVID disruption period. The best-case scenario [3-month disruption, 100% catch-up within 3 months) resulted in an additional 886 (0.5%) paediatric TB deaths, and the worst-case scenario [6-month disruption with no catch-up) resulted in an additional 33,074 (17%) deaths. The magnitude of catch-up was found to be the most influential variable in minimising excess paediatric TB mortality.

Conclusions: Ensuring catch-up vaccination of missed children is a critical priority. BCG catch-up alongside other routine vaccines may be a feasible way to achieve catch-up without separate campaigns. Urgent action is required to support countries with recovering vaccination coverage to minimise paediatric TB deaths.

TBS-EP-55 Impaired lung function among new patients successfully treated for pulmonary tuberculosis in Ballabgarh and Mohna Tuberculosis Units, Faridabad, Haryana, India.

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Introduction: India contributes to 27% of global TB cases with an incidence rate of 193 per lakh population leading to increase in burden of post pulmonary TB sequelae predominantly obstructive and restrictive chronic lung impairments.

Methodology: A cross sectional study was conducted among 140 new drug sensitive pulmonary TB patients from urban and rural Tuberculosis Units of Ballabgarh (70 participants) and Mohna (70 participants) respectively, between December 2020- March 2021.

Adult (age >18 years) new pulmonary TB cases who had successfully completed Anti Tubercular Treatment (ATT) between October 2019- October 2020 were included in the study.

The participants underwent pulmonary function test (PFT) using a portable spirometer to estimate the prevalence of impaired lung function (ILF) i.e., obstructive, restrictive or mixed lung impairment. Multivariable logistic regression was applied to identify the risk factors for lung impairment after successful treatment for TB.

Results: 140 participants were included in the analysis. Median (IQR) age at enrolment was 30(23-45). 83(59.3%) of the participants were males. 62(44%) of the cases had impaired lung function with a reversible airflow obstruction and restrictive lung impairment was detected in 19(13.6%) cases each. Irreversible post broncho-dilator airflow obstruction was detected in 13(9.3%) of the cases and 11(7.9%) had mixed lung impairment. ILF was associated with age >30 years (aOR=2.2; 95% CI=1.1-4.6, p=0.03), high AFB sputum grade at diagnosis (aOR=13.0, 95% CI=4.6-37.2, p<0.01) and if PFT was conducted was after 6 months since treatment completion (aOR=2.8, 95% CI=1.0-5.1, p=0.04).

Conclusion: We found a high prevalence of impaired lung function in new drug sensitive pulmonary TB patients. Screening for post pulmonary TB sequelae such as impaired lung function should be included in the long time follow up of pulmonary TB cases in the National Tuberculosis Elimination Program.

TBS-EP-56 Implementing GeneXpert increases TB case detection amongst prisoners with opioid dependence with and without HIV coinfection in Malaysia

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Background: Prisons are recognized as high-risk settings for tuberculosis transmission, yet data on TB burden among prisoners is scarce. In Malaysia, existing guidelines require newly admitted prisoners to be screened for TB upon entry, with sputum culture as the gold standard. We report on TB screening yield and the benefit of implementing GeneXpert in a Malaysian prison.

Methods: Prisoners with opioid use disorder (OUD) living with and without HIV entering Kajang prison in Kuala Lumpur, Malaysia between August 2017 and September 2021, underwent screening for active TB disease including WHO symptom screen, and sputum for AFB smear, culture, and Xpert MTB/Rif. Chest radiography was performed for those with symptoms. Active TB was defined as positive AFB, culture (BACTEC MGIT 960 liquid culture) or Xpert.

Results: Among 495 (63.87%) enrollees, all were men, median age was 42 years (IQR 36-48), 385 (77.8%) were employed prior to incarceration, 280 (56.3%) were coinfecting with Hepatitis C, and 79 (15.9%) were coinfecting with HIV.

Microbiologically confirmed *M.tuberculosis* was identified in 35 (14%). In 20 (57%), AFB/Culture confirmed the diagnosis, while GeneXpert identified an additional 15 (43%) cases, decreasing the number needed to screen from 25 to 14.

Among those with active TB (n=35), the majority (33; 94.2%) were HIV negative. Active TB was associated with increasing age (p=0.001) and CRP (p=0.01), while methamphetamine use (p=0.053) and HIV disease (p=0.052) were borderline correlates.

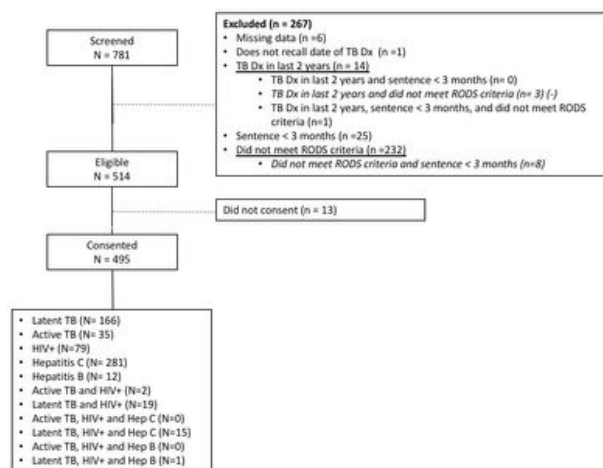


Figure. Participant flow chart.

Conclusions: Case finding among prisoners with OUD resulted in an extremely high TB case notification rate. Implementation of Xpert increased case detection and decreased the number needed to screen. The majority of TB cases among prisoners occurred in those without HIV, supporting the need for screening all incarcerated individuals. Innovative strategies to scale Xpert are needed to rapidly diagnose and disrupt epidemic propagation within Malaysian prisons.

TBS-EP-57 Inventory study on completeness of national tuberculosis case notifications 2018 in Poland

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Background: Evaluating the completeness of tuberculosis (TB) notification data is important for monitoring of TB surveillance systems, and estimating the disease burden is crucial for selecting appropriate TB control strategies. Therefore, we conducted an inventory study to calculate TB underreporting in Poland in 2018.

Methods: We compared records in the Polish national TB notification system with the records of diagnostic laboratories and calculated the observed as well as the modelled underreporting using the Capture-Recapture method. As data-protection restrictions limited the acquisition of a third case-based dataset, we implemented a double-pronged inventory study approach: we compared data of hospitalized TB patients from the National Health Fund (NHF; national health insurance), aggregated by administrative units (“voivodeships”), sex and age, to the notification data, which provided an independent estimation of reporting completeness.

Results: The observed underreporting based on notification and laboratory data from 2018 equaled 11%: laboratories reported 534 TB patients more in addition to the 4,075 patients notified in both data sources in 2018. Of these 534 patients not present in the TB notification system for 2018, 456 were subsequently identified in the system as having being notified in the years 2019 and 2017, reducing the number of patients not notified at all to 78, and the modelled TB underreporting to 2.2%. The underreporting based on the aggregated NHF data varied between voivodeships, sexes and age groups, equaling 4.5% nationwide.

Conclusions: Our results suggest that over 95% of estimated TB cases in Poland are captured within the TB surveillance system and that the TB notification rate is likely a good proxy of the TB incidence in Poland. However, significant reporting delays can cause discrepancies between data sources for a given year. This could be improved by the already planned change from a paper-based to an overall electronic reporting system.

TBS-EP-58 LTBI treatment: To Take or Not to Take? A Qualitative Exploration

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Introduction: To reduce Tuberculosis (TB) related mortality; various guidelines have recommended treating Latent Tuberculosis (LTBI). As part of the end TB strategy, the Ministry of Health Malaysia (MOH) has started to aggressively treat LTBI among high risk populations. Studies showed that many factors influenced treatment uptake among patients.

This study aimed to explore the facilitators and barriers that may influence patients’ decision to or not to receive treatment for LTBI.

Methods: Patients diagnosed with LTBI were purposively recruited based on age, gender, occupation and treatment decisions from primary healthcare clinics in Petaling District, Selangor Malaysia. Face to face in-depth interviews were conducted prior to the COVID-19 pandemic and phone interview with audio recording during the pandemic. A semi structured topic guide was developed based on the Common-Sense Model of Self-Regulation (CSM-SR) and literature review. Audio recordings were transcribed verbatim and analyzed thematically.

Results: 26 interviews were conducted, six themes emerged: Treatment decision was influenced by internal factors such as participants’ poor knowledge and misconception, and their perceived susceptibility to LTBI; external factors such as healthcare practitioners’ (HCP) competency and consultation skills and participants surrendering their treatment decision to HCP. Participants’ own perception of stigma with LTBI and stigma from the community also influenced the decision-making process.

Conclusion: Patients with LTBI had poor awareness and knowledge regarding the disease resulting in a reliance on HCP to make treatment decision for them. Primary HCP need to equip themselves with knowledge and consultation skills to guide their patients in their decision-making process.

There is an urgent need to reevaluate the existing screening and treatment program for LTBI to ensure increased uptake of treatment in high risk populations.

TBS-EP-59 Optimized doses of rifampicin: a systematic review and Bayesian meta-analysis

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Introduction: First-line anti-tuberculous treatment has not changed for several decades. Some studies suggest that higher doses of rifampicin than the standard ones could optimize the outcomes without compromising the safety of patients.

Methods: We performed a systematic review of the literature published between 2010 and 2020. We selected prospective clinical studies, using rifampicin doses above 10mg/kg/day, extracting data about safety, efficacy and pharmacokinetics. Due to the multiple comparisons and uneven designs, we performed a network meta-analysis with a Bayesian approach.

Results: We obtained nine studies through the literature review, and added two studies published in 2007. The eleven studies report data from 2093 participants, evaluating eight different rifampicin doses ranging from 13 to 35mg/kg/day. Overall, 1208 participants received doses higher than 10mg/kg/day, 113 above 30mg/kg/day.

Safety: high doses did not increase the risk of overall and hepatic AE grade 3 or higher. The Surface Under the Cumulative Ranking Curve Analysis did not show an orderly increase between the dose and the probability of severe AE. There were no reports of hypersensitivity reactions.

Efficacy: increasing doses seem to increase the EBA at 5 days but not at 14 days, except for doses of 30mg/kg/day or higher. Increasing doses of rifampicin have in-

creasing probabilities for SCC by week 8, although with wide credibility intervals for the risk ratio. Similar results were found for cure, mortality (in TB meningitis), and recurrence.

Pharmacokinetics: most studies reported pharmacokinetic data, including complete curves from 206 participants (Figure 1).

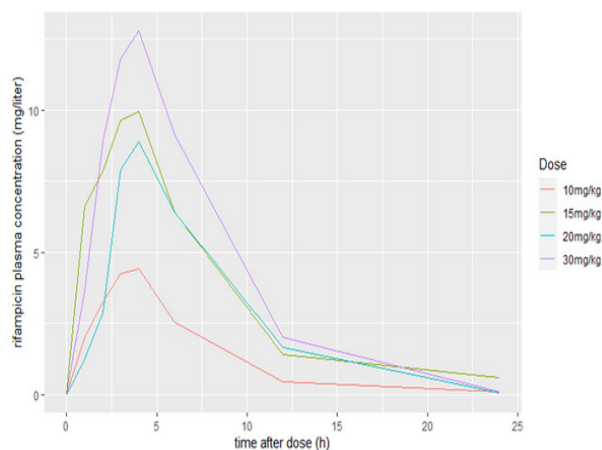


Figure 1.

The increase in the maximum concentration and the 24-hour area under the curve are exponential with increasing doses of rifampicin, but the time to the maximum concentration remains stable and the half-life increases slightly.

Conclusion: Rifampicin doses up to 35mg/kg/day are safe and seem to increase the microbiological efficacy as compared to doses of 10mg/kg/day.

TBS-EP-60 Population Pharmacokinetics of Pyrazinamide in Study 31/ACTG A5349 (S31/ A5349)

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Pyrazinamide (PZA) is a key component of treatment for tuberculosis (TB). Currently, PZA dosing is based on weight, and may be suboptimal. Dose optimization demands characterization of significant covariates and sub-populations at risk for underexposure. Based on the largest-to-date PZA database from S31/ACTG A5349 (NCT02410772), we evaluated PZA population pharmacokinetics (PK) and significant covariates to identify an optimal dosing approach.

We analyzed data from 2096 S31/A5349 participants who received weight-banded PZA dosing ranging from 1000 to 2000 mg. We performed population PK model-

ing using NONMEM (version 7.4). We tested multiple structural models with different absorption processes followed by covariate relationships investigation using stepwise covariate modeling. We validated the final PK model by visual predictive checks and bootstrapping. Lastly, we compared simulated exposure for 1500 mg flat dosing and WHO weight-banded dosing.

We found great variability in PZA PK exposure, with area under the curve (AUC) ranging from 155 to 916 (median 311) mg^{*}h/L. Bioavailability (F1) of PZA was dose-dependent. Using 1000 mg as reference, F1 of 1500 mg and 2000 mg were at 0.806 (relative standard error (RSE), 1%) and 0.71 (RSE 3%), respectively.

Female subjects had higher F1 by 15.9% (RSE 10%) compared to male. Subjects with diabetes had a 13.1% (RSE 40%) higher clearance than those without. The volume of distribution in subjects at age 17 was 8.5% (RSE 23%) higher than those at age 60 years.

Most importantly, we found no association of body weight with clearance where AUC in subjects weighed at 42 kg and 70 kg largely overlapped with each other (Figure 1). PZA AUC in above-mentioned subgroups were illustrated in Figure 1.

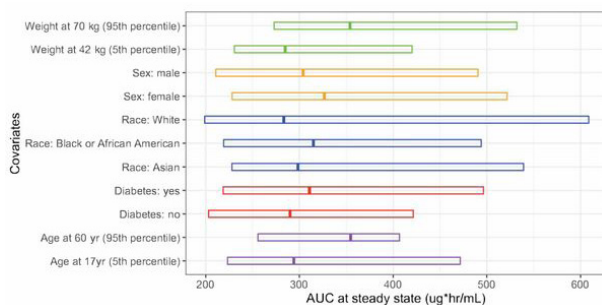


Figure 1.

Compared to WHO weight-banded dosing, flat dosing at 1500 mg achieved equitable PZA exposure across all weights. A more precise stratified dosing algorithm should consider race, sex, age and presence of diabetes.

TBS-EP-61 Preclinical in vivo assessment of replacing linezolid for inhaled spectinamide 1599 in the Nix-TB regimen

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Tuberculosis (TB) patients with highly drug-resistant forms of TB have limited treatment options. The Nix-TB trial (NCT02333799) is testing three-oral-drugs, namely bedaquiline (B), pretomanid (Pa) and linezolid (L) combined as "BPAL regimen" for treatment of drug-resistant-TB. Current Nix-TB data is showing that BPAL regimen leads to excellent favorable outcomes however some toxic effects are observed. Linezolid is a protein inhibitor with known toxicities under prolonged therapy. Spectinamide 1599 (1599) is another potent protein synthesis inhibitor of *Mycobacterium tuberculosis* (Mtb) without known adverse effects and cross-resistance with other TB drugs and is currently in preclinical studies as inhalational therapy for TB.

Here, we hypothesize that inhaled 1599 has similar or higher efficacy than linezolid if combined with BPA (BPAS regimen). The BPAL and BPAS regimens were tested in Balb/c and C3HeB/FeJ mice infected with a low dose aerosol infection of Mtb. The bacterial burdens in lungs and spleens were determined at 2 (Balb/c) and 4 weeks (Balb/c and C3HeB/FeJ) post-treatment.

The results showed that when compared to untreated control, the bacterial burdens in lungs of BPAL and BPAS treated Balb/c mice were decreased by >1 and 5 log₁₀ CFU after 2 and 4 weeks of treatment respectively and no statistically significant differences were observed in CFUs between treatment groups. In C3HeB/FeJ mice, 4 weeks of BPAL and BPAS treatment decreased the bacterial burden by >3 log₁₀CFU compared to untreated control with no statistically significant differences between treatment groups.

Comparative analysis of the cytokine profile in bone marrow, plasma, and lung homogenate samples from C3HeB/FeJ treatment groups showed statistically significant differences at bone marrow level. BPAL treated animals had higher concentration of proinflammatory cytokines and chemokines compared to BPAS group.

We concluded that inhaled 1599 is a potential replacement for linezolid if combined as BPAS regimen and further studies are warranted.

TBS-EP-62 Repurposing Deferoxamine B drug against drug-resistant tubercle bacillus

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FDA-approved repurposing of drugs strategy aids in rapid therapeutic solutions. The existing drugs are screened for a new effective purpose reducing the drug development cost and time.

This study focuses on one such drug viz Deferoxamine-B (DFO-B) used to treat thalassaemic patients. DFO-B is a siderophore that chelates excess iron from the blood of these patients who need blood transfusion regularly.

Drug-resistant tuberculosis is a threat in India and as per the WHO statistics for 2019, TB affects 193 people per 100,000 population, which is alarming.

In this *in vitro* study, the potential of DFO-B as an anti-tubercle agent was evaluated. *Mycobacterium tuberculosis (Mtb)* produces endogenous mycobactin and carboxymycobactin that help in its growth by the supply of chelated iron from the environment. DFO-B is an exogenous siderophore to *Mtb* that cannot be utilized by the pathogen for its growth.

To study the effect of DFO-B against drug-resistant tubercle bacilli, six isolates of Extremely Drug-Resistant *Mtb* (XDR-*Mtb*) were used. The drug susceptibility was evaluated by the Mycobacteria Growth Indicator Tube-Drug Sensitivity Test. For the XDR-*Mtb* isolates, DFO-B alone inhibited five out of the six isolates tested. The MIC of DFO-B decreased when used in synergism with either of these antituberculosis drugs such as isoniazid, rifampicin, amikacin, moxifloxacin. The work is ongoing, and many isolates will be tested for statistically valid results.

These preliminary results indicate a potential new application of DFO-B and would be useful as an adjunct to anti-TB drugs in overcoming the drug-resistance problem of *Mtb* in India and other countries. This study is an endeavor towards the End TB by 2030 strategy of the WHO.

TBS-EP-63 SARS-CoV-2 viral load in the respiratory particles expelled by COVID-19 patients in the wake of second-wave in Mumbai, India- What's new?

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The second wave of COVID-19 infections in India was driven by the SARS-CoV-2 variants, with the Delta variant becoming predominant strain in India and much of the world. With advent of vaccination and the rapid homogenous spread of variants, it is important to understand the correlates of its transmission. Our earlier study during the first wave showed that capturing respiratory particles expelled by COVID-19 patients may reflect individual transmission risk.

In this study, respiratory particles of 54 vaccinated and unvaccinated home-isolated patients from Mumbai with SARS-CoV-2 positivity were captured on adapted N-95 masks between July and Aug 2021. Viral RNA was quantified using rRT-PCR in masks and concomitantly collected nasopharyngeal swab (NPS) samples and compared with our reported mask results from 31 patients from the 2020 wave.

A significantly high proportion (92.5%; 50/54) of COVID-19 patients were mask-positive with low mask, and NPS Ct values 31 (IQR 27-34) and 23 (IQR 20-27) in 2021 compared to 42% mask positivity and Ct values (37 IQR 33-38-mask and 29 IQR 24-31-NPS) in the 2020 wave (p<0.0001). The mask positivity rate among fully vaccinated patients was 90% (28/31).

Moreover, 26/50 mask-positive patients were high viral emitters (expelled >1,000 viral particles in 30 min), of which 15 were fully vaccinated. A subset of samples sequenced (n=12) showed dominance of the Delta variant. The study showed a 2.2-fold increase in mask positivity and a 3.3-fold increase in high viral emitters after the second wave compared to the first in Mumbai.

High viral loads in respiratory particles expelled by patients noted in the study may explain the current high transmission rates. Importantly, the risk of transmission from vaccinated and unvaccinated individuals appears similar. Although vaccination is undeniably beneficial for reducing disease severity, the study fortifies the emphasis on masking and behavioral norms for the foreseeable future.

TBS-EP-64 Standardization of stool concentration method for molecular detection of tuberculosis

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Background: The inability of children to expectorate sputum and paucibacillary status of *M.tuberculosis* (MTB) in them increases diagnostic complexity of tuberculosis disease in pediatric population. Xpert testing of preprocessed stool proves to be promising method for detection of MTB and its rifampicin resistance in pediatric population.

However, current diagnostic algorithms still require further DST to other drugs. In this study, we aimed to standardize a stool concentration method for detection of MTB and its drug resistance to isoniazid by line probe assay.

Methods: A total of 10 children attending Institute of Child health, Chennai for complaints other than respiratory infections were included in the study. The stool from them was spiked with H37Rv in 5 different dilutions (1:1, 1:10, 1:100, 1:1000, and 1:10,000). Spiked samples (50) were subjected to 1% chlorhexidine treatment and concentrated with Brij 35 solution. The concentrated solution was washed twice and filtered using glass wool syringe filters. All the filtrates were subjected to smear microscopy, solid culture, Xpert Ultra testing and DNA extraction for Line probe assay.

Results: Out of 10 samples, growth was seen in 4 samples (neat) at 3rd week of inoculation with 3-8 colonies in two samples and 1+ growth in two samples. There was no growth in other dilutions. In smear microscopy, bacilli could be seen in 8 samples (1:1 and 1:10). Xpert ultra testing could detect MTB in all dilutions of stool with "MTB detected low" in 1:1 and 1:10, "MTB detected very low" in 1:100 and 1:1000 and "MTB detected trace" in 1:10,000 dilutions. Similarly line probe assay could detect MTB and its rifampicin and isoniazid sensitivity in all samples and dilutions.

Conclusion: The protocol standardized in this study proves to be better working in molecular detection of MTB. However for culture and smear testing, further refinement is needed.

TBS-EP-65 TB22 – a 22 gene signature for diagnosing TB

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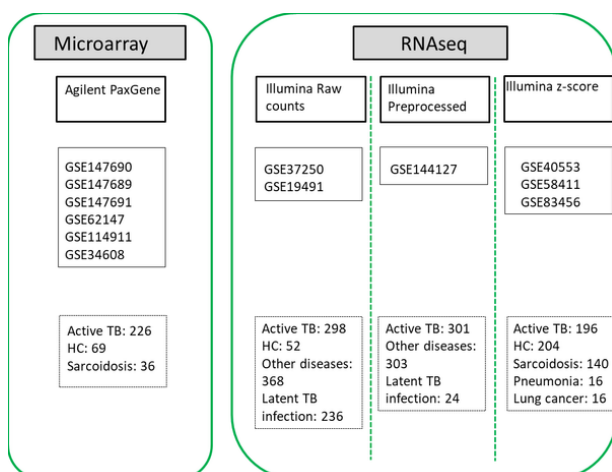
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Background: In 2019, more than 10 million tuberculosis (TB) cases were diagnosed. Early diagnosis of TB is one of the most important measures to contain the disease and RNA-based diagnostics showed to be promising as future diagnostic tool. We recently described a whole blood RNA-based score (TB22) for individual therapy duration. Here, we describe the diagnostic performance of TB22 to identify patients with active TB.

Methods: We used open-access RNA-datasets (RNA-seq, microarray) identified in the GEO-database in the context of tuberculosis in HIV positive and negative patients. The datasets were pooled according to data structure and were the starting point for further analyses (See Figure 1). In addition, 23 additional TB-related RNA signatures were identified for performance comparison with TB22.

Results: TB22 and the Qian signature showed the best diagnostic performance in microarray-datasets with AUC =0.96 (95%-CI 0.92-0.99) to distinguish between active TB vs. other diseases (OD) and healthy controls (HC). TB22 showed similar performance to discriminate between individuals with latent and active TB with an AUC=0.89 (95%-CI 0.84-0.95), compared to the Hoang signature with an AUC=0.89 (95%-CI 0.83-0.94) and the Zak signature with an AUC=0.89 (95%-CI 0.82-0.95).

To distinguish between active TB and HC and ODs, TB22 showed a performance with an AUC=0.90 (95%-CI 0.85 - 0.95) in the RNAseq dataset, which was also the best performance for this comparison. A specialized TB22 model for patients with HIV co-infection showed a diagnostic accuracy with an AUC of 0.94 (95%-CI: 0.86–1) while a model optimized for HIV negative patients yielded an AUC of 0.92 (0.87 - 0.96).



Conclusion: TB22 is not only promising as therapy monitoring tool and to conduct individualized therapy durations in MDR-TB patients, but also for the diagnosis of active TB in patients with and without HIV co-infection.

TBS-EP-66 Sub-inhibitory drug exposure selects diverse resistant populations in *Mycobacterium tuberculosis* complex bacteria

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In order to enhance TB diagnostics, rapid molecular tests are being developed with robust mutation catalogues. Developing such catalogues is aided by *in vitro* mutant selection and characterization. Unfortunately, current *in vitro* selection models often miss low-level, clinically relevant mutant populations. We hypothesized that by exposing *Mtbc* bacteria to low-levels of antibiotics, we might select more fit – clinically relevant variants, due to competition with susceptible and heteroresistant populations.

In this study, the *Mtbc* lab strain H37Rv was exposed to sub-inhibitory concentrations of bedaquiline or clofazimine over 20 days. Mutant colonies were then selected and characterized by phenotypic assays, and whole genome sequencing on the short-read Illumina® and long-read PacBio® platforms.

In total, 215 mutant clones were characterized, which included 64 unique variants. Over 95% of these variants implicated the efflux pump regulator - *Rv0678*; with the remaining affecting the direct target of bedaquiline - *atpE*. Competition experiments revealed that *atpE* mutations have major fitness implications, whereas *Rv0678* mutations may not. Interestingly, 13 mutants did not harbor a variant in any known resistance associated genes. Through long-read sequencing and *de novo* gene assembly, we identified a large-scale gene rearrangement effectively cutting *Rv0678* in half.

Here, we demonstrated the potential of employing a weak selection pressure - *in vitro* model, for the selection of resistant clones. Furthermore, we observed the first large genomic inversion in an *Mtbc* strain *in vitro*, which implicated drug resistance.

In the end, we hope that this model can be applied to new and less well-known drugs, to elucidate unknown resistance mechanisms, and bolster mutation catalogues for genotypic resistance prediction.

TBS-EP-67 Survey on the management of tuberculosis with monoresistance to first-line drugs in Spanish centers

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Introduction: Isolated resistance to first-line drugs is the preceding stage to multi-drug resistant tuberculosis (MDR-TB). However, the optimal management of these cases is still unclear.

Methods: We performed a survey about the management of tuberculosis with isolated resistance to isoniazid, rifampicin, and pyrazinamide addressed to clinicians and microbiologists with expertise in the diagnosis and management of patients with tuberculosis from Spanish centers from September 2019 to January 2020. The survey included questions about the interpretation of the genetic and phenotypic drug susceptibility tests, regimen composition, and regimen duration in different hypothetical scenarios. Data collection was performed online with the REDCap platform.

Results: Eighteen centers answered the survey. Regarding isoniazid monoresistance, there were 24 different treatment regimens, and 28 different durations (from 6 to 12 months). In 14/24 regimens, the participants considered the use of fluoroquinolones, 11/24 high-dose isoniazid, and none high-dose rifampicin. When genotype and phenotype susceptibility results did not agree, 4/18 participants consider more important the genotypic results, 2/18 consider more important the phenotypic, but most participants would consider all situations as full resistance. Twelve regimens and 16 durations were proposed for rifampicin monoresistance. Ten out of 12 regimens contained fluoroquinolones, 3/12 high-dose isoniazid, 1/12 high-dose rifampicin (phenotypic resistance without mutations in *rpoB*), 4/12 were MDR-TB, all including injectable drugs. There were 6 regimens for the treatment of pyrazinamide monoresistance, 3/6 using fluoroquinolones.

Conclusion: This exploratory survey shows great uncertainty in the management of first-line drug monoresistance in tuberculosis. More high-quality studies are needed to inform patient care.

TBS-EP-68 The blood monocyte/lymphocyte ratio in children with pulmonary tuberculosis from families with cases of COVID 19 and tuberculosis

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According to the World Health Organization, 1,190 thousand children fell ill with tuberculosis (TB) in 2019. Monocyte/lymphocyte ratio is simple indicator of the prognosis of cardiovascular diseases and other diseases, but it has not yet been investigated in children with pulmonary TB from families with TB cases and COVID-19. The purpose of this study was studying the monocyte/lymphocyte ratio in children with pulmonary TB from families with TB cases and from families with cases of COVID-19 and TB.

The study was conducted in two groups of children. The first group included 10 children from families with TB cases. The second group included 10 children from families where cases of COVID-19 were initially registered, and then TB cases were registered.

The following criteria were considered in the analysis: tuberculosis verified by the bacteriological method and/or radiological method, COVID-19 verified by confirmed by a positive COVID-19 RT-PCR assay result and computed tomography chest. The blood cell counts in children were studied before the start of treatment. The monocyte/lymphocyte ratio was calculated. The comparison was carried out by calculating Student's t test. Both groups did not differ by quantity of boys and girls. Each group included 5 boys (50 %) and 5 girls (50 %). The average age of children in both groups was the same: in the first group – 9.3 ± 4.3 years, in the second group – 9.3 ± 4.3 years.

The monocyte/lymphocyte ratio was 0.21 ± 0.10 in the first group, in the second group – 0.32 ± 0.12 . The difference is significant $P < 0.05$.

In our study, we found that the monocyte/lymphocyte ratio was higher in children with pulmonary TB from families with cases of COVID-19 and TB compared with children from families with TB cases. Further research is needed to establish the prognostic value of the monocyte/lymphocyte ratio in children with COVID-19 and TB.

TBS-EP-69 The Global Health Impact Project: The Tuberculosis Model

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Information is the key to optimizing the allocation of health resources and to extending access to essential medicines. Presently, there is no comprehensive tool for estimating the effects of different health interventions, which undermines the ability to prioritize investments.

This model presents one of the first systematic efforts to measure the benefits of health interventions using publicly available data. The Global Health Impact (GHI) index calculates the amount of death and disability averted by key medicines globally using data on:

- 1) Outcomes in the absence of treatment,
- 2) The effectiveness of treatment, and,
- 3) How many people who need treatment access it.

The index is a model that measures impact to evaluate performance, set targets, and guide the distribution of resources. The tuberculosis model utilizes public data on the available drug treatments for TB to assess the disease burden by number of disability-adjusted life years (DALYs) globally.

The data on TB can be looked at by drug, country or company, providing a deeper look into how different drugs are having an impact, where there is a higher need for treatment, and how companies' products are distributed around the world.

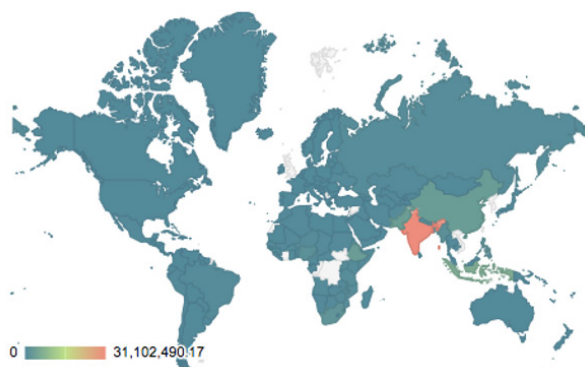


Figure. Estimated disability adjusted life years lost in the absence of treatment.

TBS-EP-70 In silico bioprospecting of anti-tuberculosis activity in *Phyllanthus emblica* L. and identification of lead molecules

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Introduction: Tuberculosis (TB) remains one of the top ten cause of death worldwide and leading cause of death from a single infectious agent. The emergence of Multi Drug Resistance and Totally Drug Resistance bacterial strains necessitate novel drugs. *Phyllanthus emblica* L. has been used in traditional medicine to treat TB but its efficacy is not validated.

Aim: To validate anti-tuberculosis activity and identification of lead molecules in *Phyllanthus emblica* L. through *in silico* approach.

Methods: A total of 106 phytochemicals from *Phyllanthus emblica* were docked with each of the four promising target proteins *viz.* mycolyltransferase antigen protein 85C (Ag85C/FbpC) involved in cord factor synthesis, filamentous temperature sensitive Z (FtsZ) involved in bacterial cell division, pantothenate kinase (PanK) involved in co-enzyme A pathway and decaprenylphosphoryl β -D-ribofuranose-2 epimerase (DprE1) involved in the synthesis of virulent factor arabinan using the tool AutoDock VINA 1.1.2.

The phytochemicals which showed $\Delta G_{bind} \leq -6$ Kcal/mol when docked with the foregoing targets were selected as active/hit molecules. The protein-ligand binding interactions, drug-likeness, toxicity and ADMET properties of the active molecules were analyzed and identify the best lead.

Results: Out of 106 phytochemicals screened, 62 have inhibitory activity on all the four target proteins. The number of active molecules obtained against the selected targets *viz.* Ag85C, FtsZ, PanK and DprE1 was 75, 82, 86 and 89 respectively. Further analysis of protein-ligand binding interactions, drug-likeness, toxicity and ADMET properties revealed that the compounds rutin and eriodictyol have desirable properties to recommend as the best lead molecules.

Conclusion: The results substantiate the traditional use of *Phyllanthus emblica* against tuberculosis. However, identified lead molecules are to be further evaluated through *in vitro* and *in vivo* experiments.

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