ACE-CF: Artificial Intelligence to Control Exacerbations in adult CF

Led by: Andres Floto, Charles Haworth, and Lucy Gale, Royal Papworth Hospital, Cambridge; John Winn and Damian Sutcliffe, Microsoft Research Institute, Cambridge and Kirsty Hill, Magic Bullet (Social Enterprise company)

Additional adult CF centres: Jamie Duckers, Cardiff (All Wales), Gordon MacGregor, Glasgow (SW Scotland), Robert Gray, Edinburgh (South East Scotland), Damian Downey, Belfast (All NI) and Caroline Elston (KCL, London)

Scan to find out more about the LifeArc Chronic Respiratory Infection Translational Challenge

Summary

AI to improve healthcare

Meeting unmet medical/societal/financial needs

Chronic health conditions place an increasingly heavy burden on patients, healthcare professionals and payers. Existing standards of care are inflexible and do not adapt well to the enormous variation in patient need. We have successfully explored alternative care models for Cystic Fibrosis (CF) by using blue-toothed devices for home-monitoring for CF. Supervised machine learning using these anonymised datasets has created a predictive algorithm (research tool) able to identify a worsening in condition, up to 10 days before the clinical team. We are now planning to provide directly to patients the algorithm outputs to inform a safe but more flexible and more timely approach to keeping people healthy.

SmartCareCF – Project Breathe

ACE-CF building on 10 years past success

SmartCareCF: First exploratory study (Funded by CF Trust, EPSRC, Microsoft Research Institute). Multicentre non-interventional study (148 people) established acceptability of home-based monitoring using blue-toothed devices. Data only returned to patient.

Key success: Machine learning analytics used data to develop Predictive Algorithm for APEs.

Project Breathe: Second study (Funded by CF Foundation (USA), EPSRC & HDR UK. Multicentre study:

i. Create a tool for adults with CF to inform and assist self-management
ii. With consent, home-based data provided to CF centre to assist clinical decision-making
iii. Validate and refine predictive algorithm as research project

Next steps: Supported by LifeArc

Improve and Widen

ACE-CF: Formal clinical trial to test Predictive Algorithm in Real Time to provide self-management tool to adults with CF. Co-funded by LifeArc and NIHR (AI in Healthcare competition). MHRA registration.

Further research funded by LifeArc:

i. **Plug and Play:** Testing novel sensors. Can passive sensors enrich existing data acquisition devices?
ii. **Bronchiectasis:** Can learnings in CF be applied to other chronic respiratory conditions? Study at Royal Papworth Hospital led by Dr Charles Haworth

AI in Healthcare competition

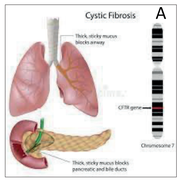
Background

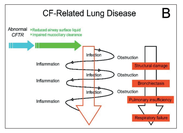
Cystic Fibrosis

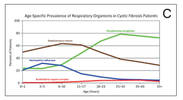
- Result of genetic mutations in the CFTR encoding gene. Now routinely diagnosed at birth. Multisystem condition
- Chronic condition characterised by long periods of stability interrupted by lung infection and inflammation (Acute Pulmonary Exacerbations: APE)
- Enormous person-to person variability in nature of CF complications and the way these progress
- Cycles of infection/inflammation cause progressive lung damage and associated loss of lung function
- Lungs become chronically infected with pathogens such as Pseudomonas aeriginosa, Mycobacterium abscessus
- In 50's CF was entirely paediatric condition with 80% mortality by age 5 years. Incremental improvements in life expectancy: so by 2020, > 50% of people with CF were adults
- Clinical care managed exclusively by CF Centres

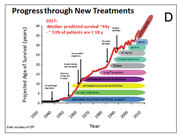
Unsustainable model of care

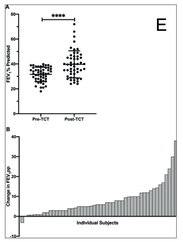
- Burden of care identified as key issue for people with CF (James Lind Alliance consultation)
- Standards of care come at significant costs to the individual, healthcare professionals and payers
- Existing adult CF centres under increasing strain following rise in life expectancy
- From 2012-2022, new genotype-dependent disease-modifying drugs are now available to >90% of CF people
- Significant differences in response to these drugs between individuals
- Drugs improve well-being, reduce the rate of lung function loss BUT APEs are still an issue albeit at lower frequency











Features of CF

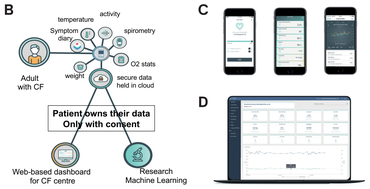
A. Multisystem genetic condition
B. CF loss of lung function over time following repeat cycles of lung infection and inflammation (APEs)
C. Majority of adults have chronic infection in lungs
D. Growth in life expectancy since 1950's
E. Variation in response to triple therapy. Waterfall plot from Phase 3 study with Highly Effective Modulator Therapy Reporting of average rise in lung function masks underlying enormous individual variation

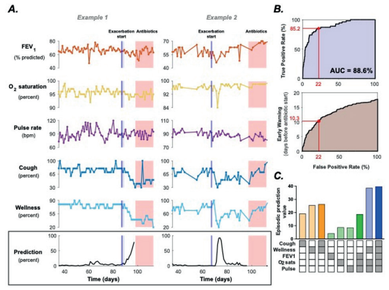
SmartCareCF/Project Breathe

Established

- Feasibility and acceptability of using blue-toothed devices at home to monitor CF
- Easy access to data. Individuals download Breathe App on to their smart phone (Android or iOS)
- High level of user acceptability and engagement with App design
- People with CF feel empowered: seeing own data results in a "Nudge effect
- With an individual's consent, data can be visualised by CF Centre multidisciplinary team
- Home-based monitoring can safely change care model – move away from existing one-size-fits-all
- Passive data acquisition improves frequent data capture
- Machine learning applied to frequent home-based data can predict the onset of an APE up to 10 days in advance

Project Breathe:
A. Patient centric
B. Data collection
C. Display of data on phone
D. Web-based dashboard for CF Centre





Predicting the onset of acute pulmonary exacerbations using machine learning

We trained and then tested a probabilistic logistic regression classifier to predict impending APEs. (A) Examples of the algorithm output (black box) during two APEs, showing: input signal data from measurements of FEV1, O2 saturations, pulse rate, cough, and wellness (above); the probability peak and distribution for the machine learning-predicted start of the exacerbation (vertical dark blue lines and light blue area respectively); and the duration of antibiotic treatment (pink area). (B) Performance metrics for the predictive algorithm showing: (top) episodic ROC curve, with an area under the curve (AUC) of 88·6% (blue) and a true positive rate of 85·2% at a false positive rate (FPR) of 22% (red); and (bottom) the early warning time (relative to current treatment start date) over the full range of false positive rates, showing 10·3 days of early warning at a FPR of 22% (red). (C) The relative contribution of raw and derivatised signals from symptoms scores (yellow), physiological sensors (green) or both (blue). Damian Sutcliffe, unpublished

ACE-CF

- Formal clinical trial to test value of predictive algorithm to adults with CF. Recruitment due to start early 2023
- Current work focus Quality of life is primary outcome
- i) Validating Predictive Algorithm and converting a research tool to one acceptable to CF adults
  - a) Machine learning in real time, b) how to display meaningfully, c) user experience ++ Patient engagement at all stages of design, d) b testing prior to start of trial, v) MHRA involvement
- ii) Clinical trial planning

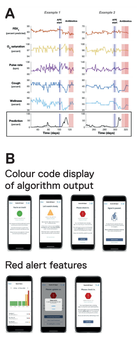


Fig. 6.11 Simulated production usage of the Predictive Classifier using Project Breathe data, for two participants (on Highly Effective Modulator Therapy) over 80 days of their respective study periods, each including an APE event. It shows the input signal data for the 5 core measures, along with the corresponding predicted risk that an APE has started (day-to-day volatility in the measures. In both cases, shortly after the APE starts, the predicted risk from the mode framed at the bottom). The probability peak and 90% confidence bounds for the Alignment Model predicted start of the exacerbation (vertical dark blue lines and light blue area respectively), and the duration of antibiotic treatments (IV in pink) are superimposed for context. During periods of stability, the predicted risk of an APE is low, with some variance due to the normal l increases rapidly. (Damian Sutcliffe, unpublished)

Plug and Play

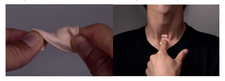
- Testing of various novel devices alongside existing Project Breathe
- Novel devices: To improve frequency and quality of data observations
  - i) Passive data acquisition (e.g. Smart watch) better than active (e.g. spirometry)
  - ii) Data quality = noise of data
- Both likely to improve confidence of predictive algorith
- Examples below: On-going discussions with LifeArc to source additional devices in academia and biotech

Bedside passive measure of overnight respiratory rate (Circada)

Breathe biopsy (Owlstone)

Vocal assessment (Sonde Health)

Micro engineered pliable skin patch for cough, temp, cardiovascular and respiratory (Sonica)



Bronchiectasis

- Can this approach be applied to other chronic respiratory conditions?
- Study to test home-monitoring in 50 patients with non-CF bronchiectasis
- i) Feasibility and acceptability ii) machine learning of anonymised data to create predictive algorithm for pulmonary exacerbations