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**tbcentre**

LONDON  
SCHOOL of  
HYGIENE  
& TROPICAL  
MEDICINE



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Cover image: active case finding in  
Blantyre, Malawi, courtesy of Liz Corbett

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**Improving health worldwide**

**TB Centre Biennial Report 2015**

# Foreword: working to tackle the intractable challenges of tuberculosis



**Baron Peter Piot** *Director and Professor of Global Health*  
London School of Hygiene & Tropical Medicine

Despite significant progress in recent decades, tuberculosis continues to be a major cause of mortality in many parts of the world, and in some areas, even in high-income countries including the UK, it is on the rise once more. This resurgence is caused by two major challenges: people living with HIV, which greatly increases the risk of developing active TB disease, and the emergence of multi drug-resistant forms of TB that are extremely difficult to treat.

Our School has for many years been at the forefront of tuberculosis research, diagnosis and treatment, working in collaboration with government agencies, universities and civil society partners across more than 70 projects in around 40 countries worldwide.

In recent years, the TB Centre at the School has become established as a collaborative hub to further develop and co-ordinate this work. Thanks to the leadership of David Moore, and now Helen Fletcher, the Centre is growing to encompass all aspects of research from laboratory science in host and pathogen biology, deciphering the genetic code of drug resistant strains, to implementing new control strategies.

This report highlights some of the projects, partnerships and areas in which the Centre is engaged. There is much to do, and as always the biggest challenge is to persuade governments and funders to work together and act strategically to build effective health systems and services. TB has throughout history been closely linked with poverty, and its control will come through sustained public health and socio-economic interventions that improve people's quality of life.

I hope you will be inspired by what you read here to support the work of the TB Centre and join us in the common goal to understand, control, and ultimately eliminate this disease.

*DDW*

# About the TB Centre

TB kills more people worldwide than any other disease. In 2014, 9.6 million people contracted TB and 1.5 million died from the disease. However, the number of people with a new diagnosis of TB has fallen by an average of 1.5% per year since 2000, and ending the disease by 2030 is among the health targets of the newly adopted Sustainable Development Goals. This is a daunting task, but if researchers, governments, NGOs, industry and funders respond now, working together we can achieve it.

The TB Centre at the London School of Hygiene & Tropical Medicine brings together more than 120 laboratory scientists, clinicians, epidemiologists, statisticians, public health specialists and policy-makers. Our shared purpose is to reduce the global burden of TB, through high quality research, education and knowledge translation.

## Innovation

Through consultancy work, research meetings, seminars and journal clubs, we disseminate our work and generate new ideas. Members of the TB Centre are global leaders in areas including:

- clinical trial design
- epidemiology
- tracing of TB transmission using molecular tools
- host-pathogen interactions
- development and implementation of new diagnostics
- mathematical modelling
- health economics
- health systems research



*Helen Fletcher*



*Katherine Fielding*

## Collaboration

We work in more than 20 countries with high prevalence of TB across Asia, Africa and Latin America, and our researchers are strongly integrated with local academic institutions, governments and international organisations.

## Investing in the future

We are committed to training the next generations of TB researchers, and have an active student community within the TB Centre. Our collective goal is to generate new knowledge, and to transfer the highest quality research into policy and practice, and ultimately real-world impact. We invite you to join us.

**Helen Fletcher**, Director, TB Centre  
**Katherine Fielding**, Deputy Director, TB Centre  
<http://tb.lshtm.ac.uk>  
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*This publication was collated and edited by Steve Smith, Helen Fletcher, David Moore and Patrick Wilson, November 2015.*

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*Staff collecting TB data electronically, courtesy of ZAMSTAR (see page 6)*

*Staff at TB Centre retreat in Canterbury, November 2015, by Kristian Godfrey*

# Clinical trials: towards effective diagnosis and treatment

Progress towards rapid and reliable diagnosis followed by effective drug treatment is vital in the effort to control tuberculosis. TB Centre investigators have been awarded funding for a number of major clinical trials which aim to effect this progress.



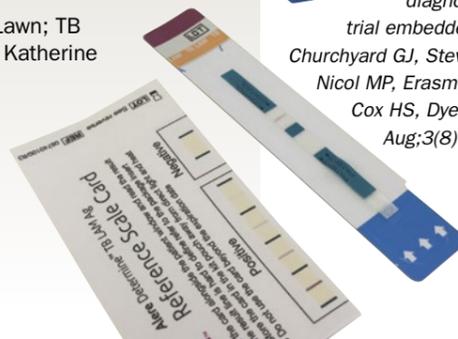
## Rapid urine-based screening for TB to reduce AIDS-related mortality in hospitalised patients in Africa

Post-mortem studies show that TB is the cause of between one-third and two-thirds of adult HIV/AIDS-related deaths recorded in health facilities in sub-Saharan Africa. However, around one half of these TB cases are undiagnosed at the time of death, highlighting the urgent need for new diagnostic approaches. Background studies conducted in Cape Town by Stephen Lawn show that a large majority of TB cases can be rapidly diagnosed from a urine sample within the first 24 hours of acute hospital admission, using a combination of two techniques: *Determine TB-LAM lateral-flow urine test* and *Xpert MTB/RIF* testing of concentrated urine.

The three-year Screening for Tuberculosis to Reduce AIDS-Related Mortality in Hospitalized Patients in Africa (STAMP) study, started in 2015, is an individually-randomised controlled trial that will assess the clinical outcomes of standard sputum-based testing with Xpert MTB/RIF plus additional urine-based screening, compared with the standard screening alone. Funded by a UK Medical Research Council, Department for International Development and Wellcome Trust Global Clinical Trials Scheme grant award of £2.1 million over three years, the trial is underway in both Malawi and KwaZulu Natal, South Africa.

**Principal Investigator:** Stephen D. Lawn; **TB Centre co-investigators:** Liz Corbett, Katherine Fielding, Clare Flach

STAMP trial images courtesy of Zomba Central Hospital, Malawi



## TB Fast Track: evaluating empirical TB treatment for people with HIV

TB is the most leading cause of death among people with HIV worldwide, and limited data suggest that this remains true of people starting antiretroviral therapy. However, the diagnosis of TB is difficult and may be missed altogether. People with low CD4 cell counts in particular are less likely to be diagnosed using sputum-based tests, because of low mycobacterial concentration or inability to produce sputum.

TB Fast Track is a cluster-randomised trial that aims to evaluate the effects of targeted empirical TB treatment on early mortality in people with HIV accessing antiretroviral therapy in clinics in South Africa. The intervention uses a point-of-care technology-based algorithm to rapidly identify individuals at high risk, and ensure they start TB treatment, followed by antiretroviral therapy. Mortality in the intervention group will be compared to that among adults managed according to standard practice based on South African guidelines.

TB Fast Track is funded by a UK Medical Research Council, Department for International Development and Wellcome Trust Global Clinical Trials Scheme grant award of £3.2 million.

**Principal Investigator:** Alison Grant; **TB Centre co-investigators:** Katherine Fielding, Anna Vassall

## The XTEND study: evaluating Xpert MTB/RIF as a first line TB test in South Africa

The XTEND study evaluated the impact of the new diagnostic test Xpert MTB/RIF in the context of its national roll-out in South Africa. It was a cluster-randomised trial, in which study clinics were randomised to early implementation of Xpert MTB/RIF as their first-line TB diagnostic test, while control clinics continued to use smear microscopy, which is the standard test. The study included over 4,600 people giving sputum to be tested for TB.

The results, recently published in *Lancet Global Health*, showed that mortality at six months was not lower in study clinics using Xpert MTB/RIF than in the control clinics using microscopy, and the number of people starting TB treatment by six months was also not changed. However the proportion of people with a confirmed TB diagnosis was higher in the clinics using Xpert. These results imply that implementation of a new diagnostic test with higher sensitivity may not, in isolation, improve patient outcomes for drug-sensitive TB. Improved outcomes may need better tests, but also better linkage to TB and HIV care.



*Xpert MTB/RIF versus sputum microscopy as the initial diagnostic test for tuberculosis: a cluster-randomised trial embedded in South African roll-out of Xpert MTB/RIF.* Churchyard GJ, Stevens WS, Mametja LD, McCarthy KM, Chihota V, Nicol MP, Erasmus LK, Ndjeka NO, Mvusi L, Vassall A, Sinanovic E, Cox HS, Dye C, Grant AD, Fielding KL. *Lancet Global Health* 2015 Aug;3(8):e450-7.



The launch of the TBVAC2020 consortium, courtesy of The TB Vaccine Initiative

## The quest for new and improved TB vaccines

The current vaccine against tuberculosis, Bacille Calmette Guerin (BCG) is nearly a century old and does not provide effective protection against TB, especially in high incidence settings where it is most needed. To eventually eliminate TB, we need a new, highly efficacious vaccine. The TB Vaccine Initiative consortium (TBVAC2020) has been granted 24.6 million euros from the European Horizon 2020 programme and other government sources to advance new TB vaccine candidates from discovery to clinical development. Three TB Centre principal investigators, Hazel Dockrell, Gregory Bancroft and Helen Fletcher, are leading on three separate projects as part of a consortium of 40 research institutes, pioneering innovative approaches to vaccine development.

### Discovery and development of TB biomarkers of protection

The Biomarkers of Protection work package of TBVAC2020 aims to optimise the measurement of candidate biomarkers and develop methods such as the Mycobacterial Growth Inhibition assay, which indicate the level of immunity a person has against TB. Host immune responses will be correlated with TB disease risk and the effect of helminth worm infections on mycobacterial growth inhibition will be analysed.

**TB Centre members:** Helen Fletcher, Andrea Zelmer, Hazel Dockrell, Steven Smith, Mateusz Hasso Agopsowicz, Shaheda Anwar

### Standardised pre-clinical models for candidate TB vaccine evaluation

This component of the TBVAC2020 research programme at the School will provide standardised head-to-head testing of candidate TB vaccines. Testing for both safety and efficacy will be performed using immune deficient mice.

**TB Centre members:** Gregory Bancroft, Felipe Cia

### Preclinical Model Development

People are often affected by conditions that increase their risk of developing TB. These conditions include HIV, obesity and diabetes. New animal models will be developed to better reflect these human conditions that are associated with increased TB disease risk. This will improve our chances of identifying vaccines to protect vulnerable populations.

**TB Centre members:** Helen Fletcher, Andrea Zelmer



TB infected mouse lung tissue, courtesy of research student Maria Podinovskaia



Field workers testing Xpert MTB/RIF as a first-line TB diagnostic tool, photo courtesy of the XTEND study

# Selected TB Centre activities around the world

## Multi-drug resistant TB and interaction with diabetes in Peru

In addition to ongoing diagnostic, epidemiological and genomic studies largely focussed on multi-drug resistant TB in Peru, Centre researchers are working with partners at Universidad Peruana Cayetano Heredia (UPCH) in Lima on the EU-funded TANDEM consortium project. The association between TB and diabetes mellitus is being investigated using established laboratory and community-based research platforms here and at partner sites in Indonesia, Romania and South Africa. Both the School and UPCH are core partners in the global TB genomics programme known as CRyPTIC, the Comprehensive Resistance Prediction for Tuberculosis International Consortium, led by the University of Oxford and funded by the Bill & Melinda Gates Foundation.



Photo courtesy of Rebecca Kanter

Contact: [David Moore](#)

## HIV-related TB in Malawi: clinical trials on diagnosis, treatment and outcomes

The Malawi-Liverpool-Wellcome Trust and College of Medicine in Blantyre hosts many TB Centre investigators and projects including four major randomised controlled trials of diagnostic interventions, funded by the UK Medical Research Council, Department for International Development and Wellcome Trust Global Clinical Trials Scheme, as well as the US National Institutes of Health and Helse Nord.



Photo courtesy of Liz Corbett

The site also undertakes comprehensive extended monitoring and evaluation of all registering TB patients in Blantyre City. A recently developed online app known as "ePAL" – the electronic Participant Locator – enables accurate identification of TB hotspots. The centre also has a strong social science theme, for example studying masculinity as a barrier to seeking TB treatment and medical care.

Contacts: [Marriott Niiwasa](#), [Clare Flach](#), [Rebecca Harris](#) and [Liz Corbett](#)

## Malawi Epidemiology and Intervention Research Unit

The Karonga Prevention Study, now part of the Malawi Epidemiology and Intervention Research Unit, is using traditional epidemiology and whole genome sequencing on long-term population-based data to find out how and where TB transmission occurs, whether some strains are more transmissible or virulent than others, and how TB interacts with HIV.

Contacts: [Judith Glynn](#) and [Mia Crampin](#)

## Clinical trials looking at immunological reactions in leprosy

Work in Ethiopia on leprosy has involved clinical trials looking at ciclosporin as a treatment for immunological reactions in leprosy, assessing reaction severity scale and quality of life tools, as well as observational studies in patients co-infected with HIV and leprosy. This work has contributed towards an important project with the Ministry of Health in Ethiopia mapping leprosy.



Photo courtesy of Saba Lambert

Contacts: [Saba Lambert](#) and [Diana Lockwood](#)

## HIV-related TB co-infection in Brazil

A two-year clinical trial with individual randomisation led by epidemiologists from the Oswald Cruz Foundation in Recife, Brazil and the School started in March 2014. The objective is to estimate the incremental cost-effectiveness of a protocol for screening and diagnosis of TB in HIV patients. The study includes screening by clinical algorithm, followed by diagnosis with gene Xpert MTB/RIF, sputum smear microscopy and chest X-ray.



Photo courtesy of Noemia Teixeira-Filha

Contact: [Noemia Teixeira-Filha](#)

## Treatment trials for drug-sensitive and drug-resistant TB

A recently completed trial in adults with drug-sensitive pulmonary TB in five countries in Africa showed that a four-month experimental treatment with the drug gatifloxacin was not as effective as the standard treatment with ethambutol for six months. These results were published in the New England Journal of Medicine in 2014, and we are now working with Médecins Sans Frontières on a new trial using bedaquiline and pretomanid.

Contacts: [Katherine Fielding](#), [Elizabeth Allen](#) and [Dave Moore](#)

## Africa Centre TB programme

KwaZulu-Natal has very high TB incidence, and the highest prevalence of multi-drug resistant TB in South Africa. Here, the Africa Centre, in which the School is a key collaborator, is developing a multidisciplinary research programme in order to understand TB transmission, and develop interventions to interrupt it. Initial projects include a TB treatment cohort including multi-drug resistant TB, using epidemiological, geospatial and molecular data to understand TB transmission networks; and a study to estimate the incidence of TB infection among adolescents.

Contacts: [Alison Grant](#) and [Richard Lessells](#)

## The immunology of TB in adults and infants

We have several projects around the immunology of TB in both adults and infants, funded by the UK Medical Research Council, The Wellcome Trust and the European Union. In adults, we have a particular interest in the B cell immune response to TB, and also in clinical trials of new TB vaccines. In infants, we have two projects looking at whether the latent TB infection status of pregnant mothers affects their children's response to BCG following birth, including a randomised controlled trial of delayed BCG, to determine whether BCG non-specifically stimulates the infant innate immune system to protect against unrelated infections.

Contacts: [Stephen Cose](#), [Sarah Prentice](#) and [Alison Elliott](#)

## Health systems and policy research

Members of the TB Centre have collaborated on two important studies in South Asia, and are engaging in further research with policy makers. In Pakistan we collaborated with the National TB Programme on an important cohort study which showed that treatment outcomes were similar for multi-drug resistant TB patients treated using locally procured drugs and international quality assured drugs. We also conducted a multi-country analysis of private sector engagement in TB management across South Asia.



Photo courtesy of WHO/Rochkind

Contact: [Mishal Khan](#)

## Interlinked Projects in Myanmar and Yunnan Province, China

In Myanmar, TB Centre researchers are undertaking a case control study to determine risk factors associated with multi-drug resistant TB. In Yunnan, qualitative research is addressing questions of access and stigma amongst patients with TB and the role of gender in seeking health services. We are also analysing the costs and cost-effectiveness of community-based multi-drug resistant TB treatment programmes. These projects are funded by USAID, and we are working in collaboration with FHI360, Myanmar National TB Programme and Yunnan Centre for Disease Control.



Photo courtesy of Richard Coker

Contacts: [Richard Coker](#) and [Mishal Khan](#)

## Leprosy projects in India

Patients with leprosy and neuropathic pain report a poor quality of life and psychological wellbeing. In a project looking at nerve damage characteristics and somatosensory profiles of leprosy patients in low-resource settings, School researchers have identified a novel profile of sensory loss to thermal and mechanical sense, combined with preservation of vibration sense. They have also shown that adding azathioprine to leprosy immune-suppression does not improve patient outcomes, an important negative result.

Contacts: [Omer Haroun](#) and [Diana Lockwood](#)

## Research Programme on TB control

In a five year collaboration between the School, Saw Swee Hock School of Public Health, University of Singapore, the Cambodia National Institute of Public Health and TB Programme, and Phnom Penh University of Health Sciences, researchers are conducting a series of linked projects in qualitative methods, epidemiology, genomics, transmission dynamics modelling and health economics. The overarching goal is to define a variety of options to reform Cambodia's TB Programme and interventions, and to assess their likely impact and costs over the next 15 years.

Contacts: [Richard Coker](#) and [Mishal Khan](#)

## Improving adherence to treatment for drug-sensitive TB

Mobile text messaging and medication monitors have the potential to improve adherence to TB treatment and reduce the need for directly observed treatment. Researchers from the School and the National Center for Tuberculosis Control and Prevention in China conducted a cluster-randomised trial in four provinces in China, to assess the effectiveness of these interventions. Patients either received text message reminders, an electronic medication monitor, both, or no reminders for their six month treatment period. Patients receiving no reminders missed 30% of their medication doses and patients receiving text messages missed 27%. However, patients with an electronic medication monitor box – which beeps if not opened at the agreed time – only missed 17% of doses, and those who received both text messages and medication monitors missed just 14%, clearly demonstrating effectiveness. A second study is now underway, using a more robust medication monitor and examining clinical outcomes. These studies are funded by the Bill & Melinda Gates Foundation.



Photo courtesy of Tim Quijano / Flickr

Contacts: [Katherine Fielding](#) and [James Lewis](#)

## TB programmes in Zambia

Zambart is a major research collaboration between the School and the University of Zambia. Current Zambart studies include a TB vaccine trial with Aeras and GlaxoSmithKline, diagnostics studies of Quantiferon plus, a TB and meningitis study, and a study of the relationship between TB, HIV and diabetes, as well as HPTN071/PopART which looks at TB in the context of universal test and treat for HIV.

Contacts: [Helen Ayles](#)

Note: The lines and points on the map indicate in which areas these projects are based. They are not meant to be geographically accurate.

# Towards better control of HIV-related TB

The Consortium to Respond Effectively to the AIDS/TB Epidemic (CREATE) is an international research consortium funded by the Bill & Melinda Gates Foundation to assess the impact of novel strategies for controlling HIV-related TB. It has funded three large cluster-randomised trials including the ZAMSTAR and Thibela TB studies, in which TB Centre researchers have leading roles.

## Thibela TB: mass screening and treatment in mining communities

The Thibela TB study was conducted in South African goldmines where notification rates of people with TB in 2008 were 3,000 per 100,000 miners, despite a control programme in the mines following international guidelines, and regular radiological screening. Since conventional control methods were not working in this setting, we investigated a radical method to control TB. Thibela TB, which is “Prevent TB” in Sesotho, took the approach of screening the whole workforce for TB, treating those diagnosed and providing preventive therapy (nine months of anti-TB drug isoniazid) for those eligible. This intervention was compared with the current standard of care, and we assessed the overall impact on TB incidence and prevalence.

The Thibela TB study has generated 23 publications including contributions to a supplement in *AIDS* in 2010, and we continue to analyse data. Safety data and our experiences of implementing isoniazid preventive therapy has contributed to the roll-out of preventive therapy for people living with HIV. Our main findings, published in the *New England Journal of Medicine* in 2014, disappointingly showed the intervention did not improve TB control at the population-level in these gold mines. A large scale mathematical modelling exercise helped to explain our results and suggested that a much more intensive “combination prevention” approach will be needed to improve TB control in the mines.

Churchyard GJ, Fielding KL, Lewis JJ, Coetzee L, Corbett EL, Godfrey-Faussett P, Hayes RJ, Chaisson RE, Grant AD; Thibela TB Study Team. A trial of mass isoniazid preventive therapy for tuberculosis control. *New Engl J Med*. 2014; 370(4):301-10.

Vynnycky E, Sumner T, Fielding KL, Lewis JJ, Cox AP, Hayes RJ, Corbett EL, Churchyard GJ, Grant AD, White RG. Tuberculosis control in South African gold mines: mathematical modeling of a trial of community-wide isoniazid preventive therapy. *Am J Epidemiol*. 2015 Apr 15;181(8):619-32.

## The ZAMSTAR trial: community TB testing and counselling

The Zambia and South Africa tuberculosis and AIDS reduction study (ZAMSTAR) was a cluster-randomised trial of two interventions to reduce the burden of TB at community-level. One was improved community-wide TB testing and the other a household-level intervention to provide TB and HIV counselling to facilitate prompt diagnosis and treatment. The trial was conducted in 24 communities in Zambia and the Western Cape province of South Africa, in partnership with the Zambia AIDS Related TB (ZAMBART) Project and the Desmond Tutu TB Centre at Stellenbosch.

Around a million people were involved in the trial at a cost of less than one US dollar per person per year. The study’s main finding, published in *the Lancet*, showed that the household intervention may have reduced prevalence of TB in adults, and that children in the communities that received household counselling were half as likely to become infected with TB.

*“In these communities, TB and HIV affect the entire household, so you need to involve not only the TB patient but his or her entire family. If adults are not diagnosed and treated, they can infect children”*

Helen Ayles, ZAMSTAR Principal Investigator

Data from the trial have already been instrumental in shaping World Health Organization guidelines, both for screening for active TB among people living with HIV and for community TB screening.

Ayles H, Muyoyeta M, Du Toit E, Schaap A, Floyd S, Simwinga M, Shanaube K, Chishinga N, Bond V, Dunbar R, De Haas P, James A, Gey van Pittius NC, Claassens M, Fielding K, Fenty J, Sismanidis C, Hayes RJ, Beyers N, Godfrey-Faussett P. Effect of household and community interventions on the burden of tuberculosis in southern Africa: the ZAMSTAR community-randomised trial. *Lancet*. 2013 Oct 5;382(9899):1183-94.

Murray EJ, Bond VA, Marais BJ, Godfrey-Faussett P, Ayles HM, Beyers N. High levels of vulnerability and anticipated stigma reduce the impetus for tuberculosis diagnosis in Cape Town, South Africa. *Health Policy Plan*. 2013 Jul;28(4):410-8.



Thibela TB project with gold miners in South Africa (see page 6), photo courtesy The Aurum Institute

# TB Modelling and Analysis Consortium

The TB Modelling and Analysis Consortium (TB MAC) is a global community of TB modellers who provide quantitative support for TB policy decisions and implementation. By promoting collaboration and funding research projects, TB MAC has since its inception in 2012 been of great influence in policy debates, and developing the global field of TB modelling.

On the global policy level, TB MAC has updated the World Health Organization methods used to estimate the amount of HIV-related TB globally, and provided input on technical discussions that resulted in the decision by the Global Fund to Fight AIDS, TB and Malaria not to reduce the proportion of funds it allocates to TB. In recent years, TB MAC has also supported the development of tools to integrate modelling into country-level policy discussions. These have been used in collaborations with UNAIDS, the World Health Organization, and the governments of Vietnam, Ghana, South Africa.

In response to the post-2015 End TB Strategy, TB MAC has led the first multi-model TB comparison exercise to assess the feasibility of the new targets of 50% reduction in TB incidence and 75% reduction in TB mortality by 2025 for China, India and South Africa. This work coordinated the efforts of 11 modelling groups, a team of economists and representatives from the

country National TB Programmes and advocacy communities. Results from this work have informed policy discussions, in particular in South Africa, where the work has influenced budgets and operational research priorities. The modelling is being used in South Africa in their first ever combined TB and HIV Investment Case.

The consortium is open to anyone who is interested in quantitative methods to improve TB policy and practice. It is funded by a grant to the School from the Bill & Melinda Gates Foundation.

**TB centre members:** Richard White, Rein Houben, Christina Albertsen, Anna Vassall

Houben, R. M., D. W. Dowdy, A. Vassall, T. Cohen, M. P. Nicol, R. M. Granich, J. E. Shea, P. Eckhoff, C. Dye, M. E. Kimerling, R. G. White and T. M. T-H. m. participants (2014). “How can mathematical models advance tuberculosis control in high HIV prevalence settings?” *Int J Tuberc Lung Dis* 18(5): 509-514.

Zwerling, A., R. G. White, A. Vassall, T. Cohen, D. W. Dowdy and R. M. G. J. Houben (2014). “Modeling of Novel Diagnostic Strategies for Active Tuberculosis – A Systematic Review: Current Practices and Recommendations.” *PLoS ONE* 9(10): e110558.



Field workers at Ndirande clinic, Malawi, courtesy of Liz Corbett

## Interactions between TB and diabetes

### Diabetes associated with increased risk of TB in the United Kingdom

Researchers at the TB Centre have used UK electronic routine health records to study the association between diabetes and TB. The project used data taken from general practice consultations and records for up to six million patients over more than 20 years and produced a cohort of more than a quarter of a million patients with diabetes, who were compared with a control group and followed up for incident TB disease. Despite the UK having a very effective primary health care system that incentivises high quality care for chronic diseases such as diabetes, the increased risk of TB was still evident. The study showed that those accessing the least amount of diabetes care were at the greatest risk for TB. The findings have implications for UK national policy proposing to provide high risk groups access to TB screening and treatment in primary care settings.

**TB Centre members:** Louise Pealing, David Moore

*Risk of tuberculosis in patients with diabetes: population based cohort study using the UK Clinical Practice Research Datalink. Louise Pealing, Kevin Wing, Rohini Mathur, David Prieto-Merino, Liam Smeeth, David A J Moore. BMC Medicine 06/2015; 13(1):135.*

### TB and diabetes mellitus in TANDEM

Diabetes increases the risk of TB and seems to impair response to TB treatment. [The TANDEM Consortium](#), funded by the European Union, is investigating the links between TB and type 2 diabetes. Through field work in Peru, South Africa, Romania and Indonesia, TANDEM will determine the most cost-effective approaches to screening for diabetes in TB patients and for TB in diabetes patients. Together with partners in the Netherlands, Germany and New Zealand, molecular interactions between *M. tuberculosis infection* and diabetes are being elucidated using fat cells, macrophages, global gene expression analysis and genetic analysis. The TANDEM consortium is funded by a four year European Union grant award of 5.9 million euros.

**TB Centre members:** Hazel Dockrell, Jackie Cliff, Clare Eckold, David Moore, Ulla Griffiths, Yoko Laurence

*TANDEM: understanding diabetes and tuberculosis. Reinout van Crevel and Hazel M. Dockrell; TANDEM Consortium. Lancet Diabetes Endocrinol, 2014; 2(4):270-2.*

## Taught courses and research degrees relating to TB

### Distance learning TB module

The TB module is part of the School's Infectious Diseases MSc distance learning course. It is multidisciplinary, with biology, pathology and immunology balanced with considerations of broader social and ethical issues. The study material is delivered in digital format, with interactive exercises, figures and animations, and a team of 15 tutors supports learning via virtual learning environment discussion forums. Our student body is highly diverse, with approximately 120 students registered each year from around 40 countries worldwide. For full details, visit [www.lshtm.ac.uk](http://www.lshtm.ac.uk) or contact module organiser [jackie.cliff@lshtm.ac.uk](mailto:jackie.cliff@lshtm.ac.uk).

### Current PhD students working on TB-related projects

| Student                  | Project title   |
|--------------------------|---|
| Mateusz Hasso Agopsowicz | Epigenetics and immune responses to BCG vaccine   |
| Shaheda Anwar            | Impact of helminth infection on antimycobacterial Immune responses in UK migrants   |
| Katherine Horton         | Understanding and assessing the potential impact and cost-effectiveness of targeting men in systematic screening for tuberculosis   |
| Sean M. Cavany           | Optimising contact tracing for tuberculosis in England  |
| Sophie Rhodes            | Developing a mathematical modelling framework to predict the best dose in humans for TB vaccines using animal data  |
| Rebecca Harris           | Informing clinical development of novel TB vaccines through mathematical modelling and development of novel epidemiological tools.  |
| Natascha Meunier         | Characterising bovine tuberculosis in and around the Queen Elizabeth National Park, Uganda  |
| Clare Eckold             | Host blood gene expression changes through tuberculosis treatment: effect of HIV or type 2 diabetes co-morbidity  |
| Sarah Lou Bailey         | Understanding the threat of diabetes mellitus to tuberculosis control in sub-Saharan Africa: the impact of HIV and diabetes control   |
| Noemia Teixeira-Filha    | The treatment of HIV/AIDS in Brazil: economic evaluation of strategies for screening and diagnosis of tuberculosis in people living with HIV/AIDS and the use of antiretroviral therapies as a way to reduce morbidity and mortality of tuberculosis in this population |
| Yoko Laurence            | Economic evaluation of screening and treatment strategies for concurrent TB and DM in Indonesia, Peru and Romania   |
| Lisa Stockdale           | Measuring the impact of vaccination on TB drug efficacy   |
| Satria A. Prabowo        | Investigation of therapeutic vaccination strategy for tuberculosis in an <i>ex-vivo</i> mycobacterial growth inhibition assay   |
| Charlotte Sarfas         | Influence of age on the T-cell immune response in BCG vaccinated Rhesus macaques  |
| Ivanice Freire           | Incidence risk of progression to tuberculosis in migrants with fibrotic lesions suggestive of post-TB scarring  |
| Patrick Nguipdop-Djomo   | Re-emergence of tuberculosis in Western high-income low incidence countries: Levels of BCG vaccines derived protection, and the role of social deprivation  |
| Joilda Nery Silva        | Effect of a cash transfer programme on tuberculosis incidence, and treatment success in Brazil  |
| William Rudgard          | Estimate the potential mitigation effect of social protection on TB catastrophic costs  |
| Palwasha Khan            | Investigating <i>Mycobacterium tuberculosis</i> transmission in rural Malawi  |
| Ankur Gupta-Wright       | Hospitalised patients with HIV-associated TB diagnosed by rapid urine-based diagnostic assays: an investigation of factors associated with mortality  |
| Yasmeen Hanifa           | A study of the frequency and underlying causes for "TB symptoms" in patients attending for HIV care in South Africa   |
| Aaron Karat              | Prevalence of TB and other treatable diseases at autopsy in South Africa  |
| Patrice Akusa Mawa       | The impact of maternal infection with <i>Mycobacterium tuberculosis</i> on the infant response to BCG immunisation  |
| Sarah Prentice           | Does neonatal BCG vaccination provide protection against heterologous pathogens by stimulating the innate immune system?  |
| Amera Khan               | Determining the feasibility and acceptability of implementing a latent TB infection testing and treatment program at overseas panel sites for US bound immigrants   |
| Jody Phelan              | Tuberculosis host and pathogen genomics   |
| Sedona Sweeny            | Improving methods to evaluate the poverty impact of disease   |
| Debora Pedrazzoli        | Impact of socioeconomic determinants on TB control  |
| Marek Lalli              | Modelling the dynamics and impact of targeted interventions for high-risk groups for National Strategic Plans against tuberculosis: development and application of a modelling tool for in-country decision making  |



*TANDEM project worker screening for diabetes in TB patients in Lima, Peru, courtesy of Cesar Ugarte*