

Tuberculosis control in the South-East Asian region: Case Study

While progress has been made globally in reducing the impact of tuberculosis (TB), and while Australia has achieved a TB rate among the lowest reported, the South-East Asian region remains a global TB 'hot spot'. Australia is well placed to help countries in our region deal with TB as we have world-class domestic systems for disease surveillance and control in human and animal health, and a strong track record of cooperation with countries in the region, including on primary health care. Research by a number of Australian research institutions has contributed to regional improvements to TB detection, prevention and treatment, and has demonstrated the possibility of the rapid reduction in TB prevalence within neighbouring countries.



Origin

TB is one of the top 10 causes of death worldwide and has been the leading cause from a single infectious agent. In 2018, an estimated 10 million people fell ill with TB and 1.5 million people died from it. About one-quarter of the world's population are currently infected by TB bacteria but are not yet ill with the disease. However, those infected have a 5-15% lifetime risk of developing active TB disease.

While TB occurs in every part of the world, in 2018 the largest number of new cases (44%) occurred in the South-East Asian region. In Papua New Guinea (PNG), Australia's nearest neighbour, TB kills more people than any other infectious disease, multi-drug resistant TB is widespread and there are occasional cases of extensively drug resistant TB.

The World Health Organization (WHO) *End TB Strategy* focuses on the early detection of TB, the detection of drug-resistant TB and the systematic screening for TB among high-risk groups. It also includes a focus on research and innovation, particularly with respect to the detection and treatment of latent TB infection.



Locally-led TB training in Papua, Indonesia
Credit: Menzies School of Health Research

Grants and Investments

NHMRC
NHMRC funding has contributed significantly to supporting Australia's efforts to eliminate TB, both domestically and within the Asia-Pacific region, including funding to:

- Professor Warwick Britton**
 - Centres of Research Excellence (CRE): 2012, 2018 (TB-CRE)
- Professor Bart Currie**
 - Targeted Call for Research - Northern Australia Tropical Disease Collaborative Research Programme (HOT North): 2017

- Associate Professor Gregory Fox**
 - Early Career Fellowship (ECF): 2013
 - Project Grant: 2015
 - Clinical Career Development Fellowship (CDF): 2018
 - NHMRC, NAFOSTED Joint Call for Collaborative Research Project: 2019

- Professor Ben Marais**
 - Clinical CDF: 2013
 - Practitioner Fellowship: 2018

- Professor Guy Marks**
 - Project Grants: 2013, 2019

- Professor Emma McBryde**
 - Population Health CDF: 2012

- Dr Ella Meumann**
 - Medical/Dental Postgraduate Scholarship: 2016

- Professor Anna Ralph**
 - Clinical CDF: 2018

- Dr James Trauer**
 - Postgraduate Scholarship: 2013
 - Public Health ECF: 2018
 - Project Grant: 2018

- Professor James Triccas**
 - Project Grants: 2013, 2015, 2016

Other grants and investments
Prof McBryde has received support from The Global Fund. A/Prof Fox, Prof Stephen Graham, Prof Ralph and Dr Phillip du Cros have received support from the Department of Foreign Affairs and Trade (DFAT) through the *Health Security Initiative (HSI) for the Indo-Pacific Region* - in Vietnam, PNG, Indonesia, Malaysia - and/or the *Australia Awards - Indonesia*.

Collaboration

The translation of Australian TB research into improved TB detection, prevention and treatment has taken place through a series of collaborations.

The TB-CRE has organised and hosted annual TB Research Symposia since 2010, providing opportunities for Australian and international researchers, clinicians, nurses and others working with TB to showcase their latest findings and to collaborate to improve TB control.

The Australian Tuberculosis Modelling Network (AuTuMN), supported by Global Fund co-financing, has worked with TB programs in China, India, Vietnam, The Philippines, PNG and Fiji to produce open source software for infectious disease control simulation.

The Menzies School of Health Research and the Burnet Institute are collaborating, through the HSI, to deliver regional health system strengthening, through in-country partnerships with:

- The University of Gadjah Mada, the Papuan Health and Community Development Foundation and Mimika District Health Authority in Indonesia.
- The Institute of Medical Research, National Department of Health, Western Province Health Office and the Central Public Health Laboratory in PNG.

The Woolcock Institute of Medical Research has been conducting TB research in Vietnam, involving both local collaborators and a team of Woolcock researchers based in Hanoi and Ca Mau. This work has been undertaken in collaboration with the Vietnam National TB Program and includes a focus on TB screening and case finding.

Trials and Results

The *Active Case-finding in Tuberculosis (ACT)* trials are a series of cluster randomised clinical trials performed in Vietnam by the Woolcock Institute in partnership with the Vietnam National TB Program. The trials evaluated the effectiveness of systematic screening to increase detection of TB in high-risk populations.

The ACT2 trial recruited 25,707 contacts of 10,964 patients with TB in 70 districts of Vietnam. This trial showed that active screening increased case detection by 2.5 times.

The ACT3 trial recruited over 90,000 people in 120 villages of Vietnam, finding a reduction in TB prevalence of 46% with three years of annual screening. It also found a reduction in transmission to children in the community.

The Australian Government funded *Tropical Disease Research Regional Collaboration Initiative (TDRRCI)*, a sister initiative to HOT North, focused on TB and malaria control in Indonesia, Malaysia and PNG.

Under this initiative:

- Pragmatic, low-cost TB interventions were implemented, including symptom screening for TB contacts to achieve active TB case finding and initiation of TB preventive therapy.
- A series of projects were developed and implemented through an operational research capacity building program for TB. These projects provided important local expertise in research development, implementation and publishing in the international literature.

Outcomes and Impact

The scaling-up of active case-finding activities and treatment of TB infection are integral in working towards the global *End TB Strategy* targets.

The ACT2 trial provided the first randomised trial evidence to support contact investigation in high-prevalence settings and will provide important evidence that informs upcoming WHO guidelines for systematic screening. The trial has also led to the scale-up of contact investigation in Vietnam, as a part of a new national policy.

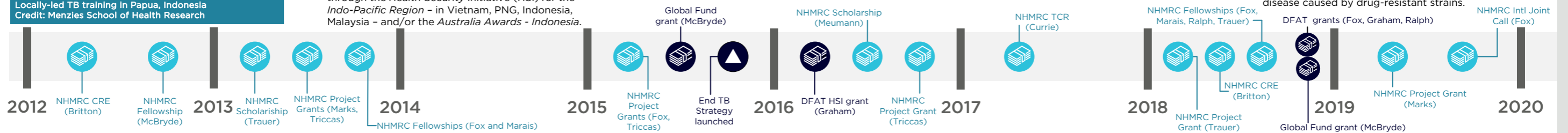
The ACT3 trial has shown a rapid reduction in TB prevalence is possible using new technologies, and provides a new direction for high-burden settings.

Active case-finding work supported through the TDRRCI continues in Indonesia and PNG under the Menzies-led *Stronger Health Systems for multidrug-resistant tuberculosis and malaria project*. The participating district in Indonesia was awarded:

- Best Indonesian TB Program at an Indonesian TB Day awards ceremony, March 2019.
- Best Provincial TB Program in 2018 and 2019.

Knowledge translation activities undertaken by the Menzies School and Burnet Institute have included: training for 76 Indonesian healthcare providers, supported through the *Australia Awards - Indonesia*; and operational research training in Daru, PNG resulting in 12 successfully implemented and locally-led projects.

Future research directions, driven by Australian researchers, include scaling up the use of genome sequences of TB strains to better understand epidemiology locally and internationally; improving access to shorter regimens for treatment of TB infection; and testing all-oral regimens for active TB disease caused by drug-resistant strains.



Woolcock Institute of Medical Research

Professor Guy Marks is head of the Respiratory and Environmental Epidemiology group of the Woolcock Institute, and is also Scientia Professor of Respiratory Medicine at the University of New South Wales.

Associate Professor Gregory Fox is Area Director of TB Services, Sydney Local Health District, is a Research Leader for the Woolcock Institute and jointly leads the Woolcock's Vietnam research team.

The University of Sydney

Professor Warwick Britton was formerly Head of Medicine and Infectious Diseases and Immunology at The University of Sydney and Head of the Tuberculosis Research Program at the Centenary Institute.

Professor Ben Marais is Professor within the Faculty of Medicine and Health at The University of Sydney, he serves on the Executive Committee of the TB-CRE and is a founding member of the Australasian TB Forum.

Professor James Triccas is Head of the Microbial Immunity and Pathogenesis Group at The University of Sydney.

Menzies School of Health Research

Professor Bart Currie leads the Tropical and Emerging Infectious Diseases team at the Menzies School of Health Research and is Director of the HOT North project.

Professor Anna Ralph is Head of the Global Health Division at the Menzies School of Health Research, co-director of Rheumatic Heart Disease Australia and a practising medical specialist at Royal Darwin Hospital.

Dr Ella Meumann is an infectious diseases physician at Royal Darwin Hospital and a researcher at the Menzies School of Health Research.

Burnet Institute

Professor Stephen Graham is Senior Principal Research Fellow at the Burnet Institute. He has provided technical assistance on child TB to national TB control programs in Indonesia, The Philippines, Lao PDR, Myanmar, China and PNG. He also works closely with the World Health Organization in the development of guidelines and training tools for the management of child TB.

Dr James Trauer is Head of the Epidemiology Modelling Unit at Monash University, is a Public Health Physician at the Burnet Institute and was TB Registrar at the Northern Territory Centre for Disease Control.

James Cook University

Professor Emma McBryde is a Professorial Research Fellow in Infectious Disease Epidemiology at the Australian Institute of Tropical Health and Medicine (AITHM) at James Cook University and is Director of AuTuMN.

AuTuMN includes researchers with expertise in TB modelling from other Australian academic institutions including Monash University, The University of Melbourne and the Burnet Institute.