Report on TB Modelling and Analysis Consortium activities
TB MAC; 2017_06_08

This report covers activities up to end Dec 2016. Impacts can extend after Dec 2016.

The TB Modelling and Analysis Consortium aims to improve global TB control by coordinating and promoting mathematical modelling and other quantitative research activities to provide scientific support for policy decisions and implementation. A summary of our activities towards this aim follows:

1. Identifying high priority research questions concerning TB control that require input from mathematical modelling or other quantitative research

- We convened seven international meetings that brought together TB modellers and other experts to discuss high priority TB topics:
    1. *Optimising TB Control in High HIV Prevalence Settings*, South Africa, 2012
    2. *Impact and cost-effectiveness of current and future diagnostics for TB*, The Netherlands, 2013
    3. *Rational introduction of new drugs and regimens*, China, 2013
    4. *Post-2015 global TB targets #1* USA 2014 (methods and preliminary results)
    5. *Post-2015 global TB targets #2* London 2014 (epidemiological results, economics methods)
    6. *Post-2015 global TB targets # 3* Switzerland 2015 (economic results)
    7. *Modelling socio-economic determinants and interventions for TB* USA 2015
- The first three meetings successfully generated a list of modelling research priorities and allocated funding. Meeting 4-6 focussed on the post-2015 Targets project the first multi-model exercise in TB, which explored the epidemiological and economic challenges involved in reaching the post-2015 WHO global TB targets. The results are widely recognised to be a major advance in the use of TB modelling for policy discussions, and highlighted key areas for future study and data collection. The last meeting (#7) explored the potential of modelling to understand the impact of social and structural determinants of TB care and prevention, which is a key area of interest for WHO-GTB's End TB Strategy, and part of the global Sustainable Development Goals agenda.

2. Facilitating sharing of data, information and expertise to achieve consensus on current knowledge and knowledge gaps, methodological standards and current best practice for TB control decision making

- We carried out systematic reviews of key modelling literature prior to most meetings and posted them on the TB MAC website.
    ○ TB modelling in high HIV prevalence areas,
    ○ TB math & economic modelling
    ○ TB diagnostics modelling
- We have provided analytic and methodological input at key meetings & committees, including, the UNAIDS reference group, the External Review of the Global Fund Distribution of Funding by Disease, the WHO post-2015 Global Targets and the post-2015 WHO TB Research Agenda, at STAG TB, the StopTB Global Plan 2016-2020, the Global Fund Lives Saved Modelling, the Critical

Path to TB Drug Regimens Initiative, the TB Alliance, the Aeras Economic Working Group for Vaccine Research, the newly formed WHO TB Vaccine Technical Expert Group, the WHO Global Task Force on TB Impact Measurement (in 2015 and 2016), the meeting on Country-Level TB modelling tools to Support Policy and Program Implementation (2015, Washington DC), and the Modelling Roadmap meeting (2016, Washington DC).

- Methods developed and used to produce country level TB/HIV Mortality estimates in the WHO TB and UNAIDS reports from 2013+.
- We coordinated the multi-modelling-groups in detailed analytic work to explore if and how we can reach the post-2015 WHO global TB targets.
- TB MAC has also created and run an *Introductory TB modelling postgraduate course.* This was first run at the IUATLD conference in 2013 and re-run in 2014, 2015, 2016 and 2017 (forthcoming).
- TB data from the TB Targets exercise for China, India and South Africa was contributed to an exercise by the Department of Health Systems Governance and Financing in WHO, estimating resource needs across diseases in LMIC (manuscript submitted to The Lancet)

3. Funding small analytical/modelling research projects

- TB MAC identified need for, and allocated initial seed development funding for new modelling tool 'TIME'. TB MAC cut its links with TIME in May 2015 because of the conflict of interest of TB MAC focussing effort on one modelling tool. Support for TIME development and application is now from KNCV and USAID who use TIME in their technical support programme across a number of countries. TIME is developed and implemented with technical assistance partner (Avenir Health, previously Futures) with scale up capacity to apply in multiple countries. TIME has been piloted in Global Fund country workshops to support rational generation of concept notes for the New Funding Model. Countries that need to submit joint TB/HIV concept notes benefit from the close integration of the UNAIDS HIV models and TIME. TB/HIV mortality results from the model have been published in the annual WHO and UNAIDS reports from 2013 onwards.
- TB MAC has set up a competitive and independent process to scope, identify and fund small modelling projects. Projects funded so far include:
  - *The feasibility of CRP as TB triage test for identifying individuals who require confirmatory testing for pulmonary TB (*Anja van't Hoog*, AIGHD)*
  - *Modelling to support the scale-up of TB case detection within countries* (Josh Salomon, Harvard)
  - *Modelling to Understand the Epidemiological Impact and Market Impact of Harmonized Regimens for MDR-TB* (Lisa Smith, William Davidson Institute)
  - *Cross-regimen translational modeling platform for linking non-clinical and early clinical studies in TB drug development* (Rada Savic, UCSF)
  - *Mathematical models to improve drug dosing for limiting persistence in M. tuberculosis* (Pia Schulz zur Wiesch, Harvard)
  - *Exploring the impact of active case finding* (Nick Menzies, Harvard)
  - *Treatment for latent tuberculosis infection (LTBI): in what settings is the greatest impact on the burden of active TB seen?* (Romain Ragonnet, Melbourne)
  - *Mathematical modelling for TB burden estimation* (Pete Dodd, University of Sheffield)

- ○ *Modelling multidrug-resistant fitness cost and genotypic heterogeneity to accurately define tuberculosis program treatment targets* (Gwen Knight, Imperial College London)
  - ○ *Informing decision making for universal access to quality tuberculosis care in India – an operational epidemic / economic modelling framework* (David Dowdy, Johns Hopkins University)
  - ○ *Social Protection to enhance the control of TB - Modelling Consortium (S-PROTECT)* (Delia Boccia, LSHTM)
  - ○ *Assessing the impact of poverty and DOTS programme coverage on tuberculosis epidemiology in Yunnan, China for integration into a modelling framework* (Richard Coker, LSHTM)

4. Disseminating results and tools to key stakeholders including TB control programmes and donors

- Meeting reports
  - ○ Results from the meeting discussions are rapidly made available through meeting reports at the TB MAC website after each meeting.
- Peer-reviewed publications
  - ○ 11 academic papers have been been published open-access:
    - ■ *"How Can Mathematical Models Advance TB Control in High HIV Prevalence Settings?"* IJTLD, 2014.
    - ■ *"Impact and cost-effectiveness of current and future tuberculosis diagnostics: the contribution of modelling"* IJTLD, 2014.
    - ■ *Modeling of Novel Diagnostic Strategies for Active Tuberculosis - A Systematic Review: Current Practices and Recommendations,* Plos One, 2014
    - ■ *The impact of antiretroviral therapy on mortality during tuberculosis treatment: a systematic review and meta-analysis.* Plos One 2014
    - ■ *Using the TIME model in Spectrum to estimate tuberculosis-HIV incidence and mortality,* AIDS, 2014
    - ■ *Feasibility of achieving the 2025 WHO global tuberculosis targets in South Africa, China, and India: a combined analysis of 11 mathematical models.* Lancet Global Health 2016
    - ■ *Cost-effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa: a combined analysis of nine models.* Lancet Global Health, 2016
    - ■ Benefits of continuous isoniazid preventive therapy may outweigh resistance risks in a declining tuberculosis/HIV coepidemic AIDS, 2016
    - ■ Is IPT more effective in high-burden settings? Modelling the effect of tuberculosis incidence on IPT impact IJTLD, 2017
    - ■ Pedrazzoli et al, Modelling the social and structural determinants of TB: opportunities and challenges (Accepted)
  - ○ 5 more manuscripts are review or in preparation
    - ■ **Under review**: Verguet et al, Catastrophic health costs averted by TB control: findings for India and South Africa from a modeling study (Lancet Global Health)

- ■ **In preparation**: Menzies et al. [The potential for new diagnostics to improve TB case detection: a transmission dynamic model of nine high-burden countries](#)
- ■ **In preparation**: Bilinski et al. [Efficiency of tuberculosis control strategies targeted toward high-risk groups](#)
- ■ **In preparation**: Menzies et al, title TBC (TB MAC Targets project - approaches to optimisation of intervention scenarios)
- ■ **In preparation**: Gomez et al, title Modelling the cost of TB interventions at scale: Applied cost functions (TB MAC Targets project - Cost curves during intervention coverage scale-up)

● Post-2015 Targets work focussed on China, India and South Africa. Results have been disseminated and incorporated into ongoing activities in South Africa through the TB Think Tank. Results were disseminated to the India RNTCP in 2015, and to the China NTP in 2016.

● Conference symposia
  ○ TB MAC has organised conference symposia at the IUATLD conference
    - ■ *How Can Mathematical Models Advance TB Control in High HIV Prevalence Settings?* (Paris, 2013)
    - ■ *Can we reach the post-2015 WHO global TB targets?* (Barcelona, 2014)
    - ■ *[Modelling to support TB control policy in the era of the End TB Strategy](#)* (South Africa, 2015)
    - ■ *[Modelling to overcome resistance to TB drugs and to the End TB Strategy](#)* (UK, 2016)
    - ■ *[Modelling to support acceleration toward elimination](#)* (Mexico, forthcoming 2017)

● With Partners
  ○ *'TIME' – a new country-level user-friendly TB modelling tool for decision & policy makers*
    - ■ As mentioned above, through early engagement with stakeholders, country representatives, and the modelling community, a clear need for a country-level user-friendly TB modelling tool was identified. TB MAC allocated initial seed development funding for new modelling tool 'TIME' within the Spectrum software run by Avenir Health. TB MAC links with TIME were cut in May 2015 because of conflict of the interest. Now funded by USAID and KNCV. Key stakeholders, including GTB, Stop TB partnership, UNAIDS and Global Fund are actively engaged.
    - ■ The newly developed tool, TIME (TB Impact Model and Estimates), has a module for TB/HIV estimation to generate country level HIV-associated TB incidence and mortality estimates, which are used by WHO-GTB and USAID. TIME Impact, a new dynamic TB impact model, allows for projection of trends and intervention impact estimation. The TIME Impact model is also linked to the OneHealth Costing Tool to explore budget implications, and generate budgets for domestic and international funding applications. After engaging with GTB, the TB component of OneHealth has been updated to mirror the current WHO/GTB budgeting and planning tool.
    - ■ TIME v3.0 is currently available for download via the dedicated website (www.timemodelling.org). TIME has been widely used by countries in the past and

current Global Fund funding cycles, including Indonesia, Viet Nam, Nigeria and South Africa.