TB Modelling and Analysis Consortium

TB Modelling and Analysis Consortium (TB MAC) / World Health Organisation (WHO)

Annual meeting

Country-level modelling & TB Case Detection

Glion, Switzerland
18-22 September 2017

Meeting Report

www.tb-mac.org

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Executive summary

The TB Modelling and Analysis Consortium (TB MAC) is an initiative to improve global tuberculosis (TB) control by coordinating and promoting mathematical modelling and other quantitative research activities.

At our eighth meeting, held in September 2017 in Glion, Switzerland, our aims were twofold. The first of these was to introduce a variety of initiatives to support country-level TB modelling, including guidance for country-level TB modelling, a catalogue of models currently available to conduct such modelling, and several planned and ongoing projects to close data gaps around the epidemiological and economic impacts of TB control interventions. Our second aim was to create a forum to facilitate discussions on how to improve current epidemiological and economic modeling efforts related to TB case detection. We brought together experts from different fields, including social epidemiologists and epidemiological modellers, health economists, and representatives from policy bodies, including GFATM, USAID, World Bank and WHO to discuss these bodies of work and shape the direction of future efforts in this area.

The meeting centered around presentations contributed by a range of participants, followed by whole- and small-group discussions that saw significant engagement from all present, culminating in a number of useful and concrete suggestions for the future direction of various pieces of work.

1.1 TB Modelling and Analysis Consortium (TB MAC)

Background

The complex natural history of TB, range of possible interventions and great variation in epidemiological settings, mean that TB policy makers and donors face great uncertainty when prioritising TB control activities.

This uncertainty can be reduced and quantified, and the cost-effectiveness of different strategies compared, using mathematical modelling and other quantitative research activities. Several groups of modellers worked separately on issues such as the impact of new diagnostics, drugs and vaccines, but although this work has contributed greatly to understanding the transmission and control of TB, the influence of the work was weakened by a lack of coordination, information-sharing, consensus building and prioritisation.

This led to critical research gaps and conflicting policy recommendations which served TB control poorly. Policy making and resource allocation must be based on scientific consensus derived from best analytic inputs, which draw on data and models in epidemiology, economics, demography and related disciplines. The TB Modelling and Analysis Consortium (TB MAC, www.tb-mac.org) aims to improve the interaction between quantitative researchers, policy makers, TB programmes and donors to improve global control. A first meeting focussed on TB control in high HIV settings. TB MAC's focus then shifted to diagnostics and drugs, followed by a multi-model comparison exercise to evaluate the feasibility of the End TB Strategy targets in China, India and South Africa, and subsequently a consideration of the socio-economic determinants of TB.

TB MAC Aim

To reduce the global burden of TB by increasing the effectiveness and efficiency of TB control policy and practice at global and country level.

TB MAC Objectives

1) Create improved coordination, knowledge sharing and management within the TB community
2) Create new high quality modelling guidelines and resources
3) Develop better informed TA/decision making communities and modellers

1.2 TB MAC meeting 8: First TB MAC/WHO annual meeting

Background to meeting

In its first annual meeting, TB MAC sought to address each of its 3 main objectives, as well as strengthen its link with WHO through work on the modelling stream within the WHO - Global TB Programme TB Impact Measurement Task Force, where results from the meeting will fed back to the wider Task Force meeting.

In order to contribute towards TB MAC's objectives of sharing of knowledge (objective 1) and better informed communities (objective 3), the meeting brought together participants from a number of different viewpoints, including funding agencies, technical assistance organisations, country representatives, epidemiologists and modellers, as well as those outside the field of TB. These participants would initially discuss key resources that TB MAC had been developing (objective 2), including a guidance document for applying modelling to inform country-level TB decision making and a catalogue of currently available models. In addition, proposals and projects to strengthen the data available for models to inform country decision-making, from both an epidemiological and cost perspective, were put forward for discussion and feedback.

In the second part of the meeting, as part of objective 1 the TB MAC Research Group was charged with identifying a key area of interest to discuss during the annual meeting. Following a community-wide consultation process, modelling of case detection was chosen. A similar group of participants from a range of backgrounds (with a significant overlap in participants from the first part of the meeting) was brought together to discuss the challenges and future direction of modelling case detection, from a range of perspectives.

Structure and process of meeting

The 2017 TB MAC/WHO annual meeting focused on four topics:

1) **Country-level modelling guidance and catalogue**
    - *Monday 18th and Tuesday 19th September 09:00 - 17:00*

   A discussion around two separate documents: (i) guidance covering principles and good practices of country-level TB modelling, and (ii) a catalogue and characterisation of country-level TB models available to project epidemiological burden, intervention impact and allocative efficiency.

2) **Epidemiological data collection / collation for model parameterisation for country-level resource allocation decision making**
    - *Wednesday 20th September 09:30 - 12:30*

   A discussion of epidemiological and programmatic data gaps reducing the objectivity of country-level TB models used for resource allocation decision making, as well as a draft framework for data collation/collection to fill these evidence gaps.

3) **Cost data needs of epidemiological models**
    - *Wednesday 20th September 13:30 - 17:00*

A discussion of cost data gaps reducing the objectivity of country-level TB models used for resource allocation decision making, as well as initiatives to improve cost data availability and use for modelling.

4) **Modeling TB case detection: challenges and ways forward**
    - *Thursday 21st 08:30 to Friday 22nd 16:00*

A discussion of model design, empirical needs, theoretical constructs and economic principles required to improve model estimates of the epidemiological end economic impacts of TB case detection strategies.

1.3 Country-level modelling guidance and catalogue (DAYS 1-2)

1.3.1 Background

The use of mathematical modelling to inform and support TB policy-making has been encouraged by major funders and adopted by several high-burden countries. These quantitative planning exercises are undertaken to improve the impact of TB funding and support funding applications. In recent years a number of technical assistance providers have developed mathematical models and technical assistance capacity to support in-country TB policy decisions, and it is expected that the demand for technical assistance to support TB modelling will increase. Motivated by this growing role of mathematical modelling in TB policy-making, and the apparent heterogeneity in modelling approaches and results, TB MAC was asked to develop **guidance** (see link for draft document presented at meeting) for country-level TB modelling, as well as a **catalogue** (see link for draft document presented at meeting) of models that are currently engaged in this process. This work has been developed by TB MAC in collaboration with key global stakeholders including the World Health Organisation, the Global Fund against AIDS, TB and Malaria (GFATM), the Bill and Melinda Gates Foundation, the Stop TB Partnership, the World Bank, and USAID.

The documents focus on the use of mathematical models to support national TB policy and planning, including GFATM funding applications. They cover both the epidemiological and economic aspects of modelling, to capture all considerations that arise as part of projecting future epidemiological outcomes, evaluating the consequences of competing policy options, cost estimation, and analyses of cost-effectiveness and allocative efficiency.

The aim of the guidance document is to provide concrete, pragmatic guidance for how TB modelling and related technical assistance is undertaken to support country decision-making. The document describes ten principles for country-level TB modelling. These principles cover the design and estimation of the mathematical models themselves, as well as the approaches used to identify and synthesize evidence, and incorporate modelling into the process of policy identification and comparison. The principles are intended to apply to the estimation of both epidemiological and economic outcomes, and be relevant to any country-level TB modelling exercise undertaken to inform policy making. Each principle is accompanied by several ‘good practices’ for operationalizing these principles. These practices suggest concrete steps that could be taken for implementing the principles.

The aim of the catalogue is to provide a characterisation of five models that can currently provide country-level estimates of TB epidemiology, as well as the health impact of competing policy alternatives and guidance on optimal resource allocation or the exploration of incremental cost-effectiveness. The catalogue covers in detail six aspects of the models, including the epidemiological and cost model, the policy options that can be represented by the model, the approach to optimal portfolio selection, the approach to technical assistance and a history of previous applications of the model.

As a part of the TB MAC meeting, two days were spent introducing these documents and discussing changes that could be made to them to increase their utility.

1.3.2 Aims and objectives

Aim: Elicit feedback on the guidance and catalogue documents, their adoption and dissemination

Objective 1: Discuss the guidance document principles
Objective 2: Discuss the catalogue overall structure
Objective 3: Discuss finalisation, adoption and dissemination of both documents

1.3.3 Summary

Day 1 Summary

The morning session was chaired by Ted Cohen, and began with an introduction to the entire week, followed by an outline of the guidance document by Nick Menzies (see slides 1, 2, 3, 4). This was followed by a series of discussions each around one principle outlined in the guidance. Each principle was introduced by a discussant, before an open group discussion was held on ways in which the principle could be amended or extended in order to better capture the realities of country-level TB modelling.

The first principle, **Relevance**, was introduced by Michael Kimmerling, and discussion centered around the inclusion of text on the entry point to the process, including identifying the evidentiary need and identifying modelling as a potential approach to fill this need. In addition, it was suggested that here, as well as throughout the text, the abstract principles and best practices would benefit from concrete examples, which could be used to illustrate how these principles might be operationalized in typical country applications. The second principle, **Realism**, was introduced by Jeff Eaton. The role of modelling when evidence was weak was discussed, as well as potential approaches. The overall conclusion was that the onus is on modellers to highlight uncertainties in their results, and this should be reflected in the guidance. The possibility of external review of model results and assumptions post-analysis was also explored.

The afternoon session, chaired by Katherine Floyd, continued discussion of the principles contained in the modelling guidance. The third principle, **Appropriateness**, was introduced by Ted Cohen. The focus of discussions centered on the text itself, identifying the need for clarity on the concept of unnecessary complexity within a model, and judging model design against intended use. The fourth principle, **Evidence synthesis**, was introduced by Liz Corbett, and focused on the type of evidence that should be sought and how to go about this, including defining a checklist of common minimum data needs. The fifth and sixth principles, **Validation/Contextualisation** and **Valuation**, were introduced by Pete Dodd (the latter on behalf of Paul Revill). The first of these principles brought up the issue of external validation of models, as well as the possibility of periodic model comparisons and formalising generic model metrics to ensure the satisfactory operation of models. The latter principle generated much debate on the use of a rich set of results, with the conclusion that while this may be useful, it is also important to highlight a specific summary measure and time horizon. In general this principle was felt to be much more detailed than earlier principles, and might require some rewording. Discussion around the principle of **Transparency**, introduced by Philippe Glaziou, centered on the production of an outline reporting format, as well as the inclusion of a section on roles and responsibilities for various parties involved in the

modelling process. The eighth principle, of **Timeliness**, was introduced by Lori Bollinger. This discussion also included comment on the flowchart of the modelling process (see figure in the document), which was felt to be isolated from the rest of the document and needed better incorporation within the text.

The ninth principle, **Country ownership**, was introduced by Abiodun Hassan. This was emphasized as an extremely important principle, and led to discussion around the language used throughout the text, which could be edited to emphasize the country stakeholder viewpoint to a greater degree. It was also noted that this principle might refer instead to institutional ownership within countries, as it is important that the most appropriate individuals and institutions within a country be involved in the modelling process. The final principle, **Iteration**, was introduced by Mehran Hosseini on behalf of Johannes Hunger. The discussion of this principle distinguished the need for iteration during the course of an individual modelling application (for example, through development of the modelling question) as compared to iteration between applications (for example, through continued engagement between modellers and country stakeholders to include the possibility of revision of results).

Day 2 Summary

The morning session, chaired by Jaap Broekmans, began with a summary of the previous day's discussions around the guidance document, including key changes to be made to the document based on this input. This was followed by an introduction to the model catalogue by Finn McQuaid (see slides). An open discussion of the structure of the catalogue was then held. Key suggested changes included the addition of a narrative introduction, that outlined the various models, the various sections of the catalogue and its purpose. A central concern was that this introduction should be focussed on the needs of country decision-makers considering which model to adopt for an upcoming planning process. It was also suggested that the catalogue include a greater level of detail on historical applications for each model (including the addition of references who could be approached from a country perspective) as well as additional details on model limitations.

The afternoon session focused on the steps to finalisation of both documents, as well as the pathway to their adoption and dissemination. Representatives from USAID, WHO, GFATM, BMGF, WB and the Vietnam NTP each gave a short presentation on how they felt dissemination/adoption would be best achieved for the modelling guidance. This included publication as a formal WHO report and brochures, as well as the WHO GTB website and preparation of a slide deck that could be used to introduce the document. Additional avenues for dissemination included through country offices, implementing partners, regional workshops and by referencing the document in individual applications.

1.3.4 Outcomes and next steps

The meeting generated a large number of suggestions about how to strengthen and finalize the modelling guidance and catalogue, and approaches to ensure that the documents are widely adopted.

The guidance writing group (Nick Menzies, Rein Houben, Gaby Gomez and Finn McQuaid), in consultation with the TB MAC Committee, will undertake edits to the modelling guidance and catalogue to incorporate the suggestions made at the meeting, including text edits, inclusions of examples, and development of related materials (slide decks, checklists). The revised documents will go through a final review before being finalized by the end of 2017. The modelling guidance will be presented at the WHO Task Force meeting in late February 2018.

1.4 Epidemiological data collection/collation for model parameterisation for country-level resource allocation decision making (DAY 3)

1.4.1 Background

This session focussed on epidemiological and programmatic data gaps commonly encountered when models are used for country level resource allocation.

TB policy analysis is increasingly being employed to evaluate questions around allocative efficiency -- for example, what is the marginal benefit of increased spending on competing parts of the TB program budget? What portfolio of TB services would maximize health outcomes for a given budget constraint? For these analyses to provide valid answers to these types of evaluation questions, evidence is needed on the marginal change in program costs and epidemiological impact produced by defined changes in the TB policy portfolio (e.g. addition of new interventions/activities, or changes in the coverage or scope of existing interventions/activities). This evidence needs to be reasonably precise, as the optimal portfolio identified in the evaluation will be determined by the ratio of marginal costs to marginal benefits for competing policies. If these values are incorrect a sub-optimal policy is likely to be chosen. While the outcomes of routine interventions (e.g. treatment of drug-sensitive active TB) are well documented, much less information is available on programmatic activities designed to improve the coverage and/or quality of these routine interventions. However, these activities are commonly the focus of TB budgeting decisions, as they represent an important subset of approaches for improving program impact, in addition to the introduction of new technologies, or adoption of new interventions.

During the TB MAC ‘Targets’ exercise, it became clear that empirical evidence on the impact of these programmatic actions is scarce or missing. For example, what are the actions that could be undertaken to increase the number of cases that present for screening, and what are the incremental impact and cost of these actions? Answers to these questions are essential to assess/evaluate the cost-effectiveness of a policy to improve retention along the TB care cascade, through a model or other tool, yet empirical evidence to answer these questions is commonly missing in the course of a country-level planning exercise. This evidence gap is particularly acute for proposed interventions (i.e. not yet being implemented), but critically also apply to current program operations. Slow progress has been made on filling these critical data gap since these issues were first highlighted in 2014, despite the increasing willingness of countries to use models for country level resource allocation decision making.

This session discussed the programmatic and epidemiological data gaps related to TB modelling and program planning, and how these could be resolved by a number of planned and proposed initiatives.

1.4.2 Aims and objectives

Aim: Obtain feedback on a proposed initiative to close data gaps and direction for future work

Objective 1: Define some common epi data gaps encountered during country-level TB modelling, and common approaches taken to resolve these issues
Objective 2: Describe and discuss a proposal for reducing data gaps

1.4.3 Summary

The session was introduced by presentations from Nick Menzies and Finn McQuaid. Nick Menzies described a schema of the causal linkages commonly included in TB models, with policy descriptions linked to programmatic actions, linked to changes in the distribution of services received by TB target populations, linked to proximal health impacts, linked to distal health impacts. Nick identified the historical practice of some modelling applications, which described policies in terms of their impact on coverage and similar programmatic outcomes (rather than specific activities), and how these approaches made it difficult to gauge the plausibility and resource implications of proposed policies. Finn McQuaid discussed examples of evidence gaps and assumptions made by different expert participants during the TB Targets modelling exercise, as well as examples from the published literature. Additional comments made during this introduction stressed the utility of pilot projects for informing modeling assumptions prior to wide scale-up, and the difficulty of making an investment case when this initial programmatic data is unavailable.

After this introduction, Babis Sismanidis (WHO-GTB) gave a presentation on the collection, analysis and use of data for TB policy and planning, based on current approaches used by countries, as well as WHO-GTB plans to support these efforts. Much of this work is organized through the TB Global Impact Measurement Task Force, which has a mandate to (1) ensure the assessment of progress towards End TB Targets is rigorous, robust, and consensus-based; and (2) guide, promote, and support analysis and use of TB data. This is achieved through (a) strengthening notifications, (b) strengthening vital registration, (c) priority studies to measure TB burden, (d) refinement of burden estimation methods, and (e) analysis/use of country-level TB data. This last point was the most relevant to this session. Babis described the this platform, which provides dashboards with sub-national monitoring data & time trends, and outlined plans for future work to ensure tools are completed, address existing data gaps, coordinate/provide technical assistance, translate findings into action, build national and regional capacity, and ensure findings complement NSPs and funding applications. This work is not focussed on data generation, but instead about data use, to harness the available TB data (including DHS, HS utilization data), and ensure it is appropriately used for decision making.

In the next session Rein Houben outlined a proposal to address data gaps in the context of TB modelling applications. The proposed work would be undertaken in two phases - collation of existing data and mapping remaining data gaps (Phase 1), followed by an open request for proposals to collect data to fill key remaining gaps (Phase 2). Phase 1 would identify the relevant data gaps across the care cascades, and collate all existing data that might be available from funding organisations (e.g. GFATM), NTPs, NGOs and local research activities, which could include ongoing modeling efforts. Under this proposal TB MAC would generate the work description and framework for these posts, as part of the TB MAC 2017

work plan. Deliverables would include an overview of data gaps mapped onto the TB care cascade (see figure 1 for example), as well as completed data gaps from collated data. If any high priority data gaps were identified that could not be filled through collating existing data, these would be used to generate a set of Request For Applications (RFAs) for Phase 2. Philippe Glaziou discussed this proposal in the context of some observations about the quality of routine TB data, providing examples on how some of these data sources differ from the quantities we would like to have to monitor the epidemic and inform modelling. Discussion from this session revolved around the various data gaps that exist, and how their relative importance will depend on the research question being addressed. In the context of resource allocation and policy choice, unit costs and programmatic factors were generally agreed to be some of the most important areas for better information. For predicting disease trends the limited information on underlying disease epidemiology was also seen to be important.

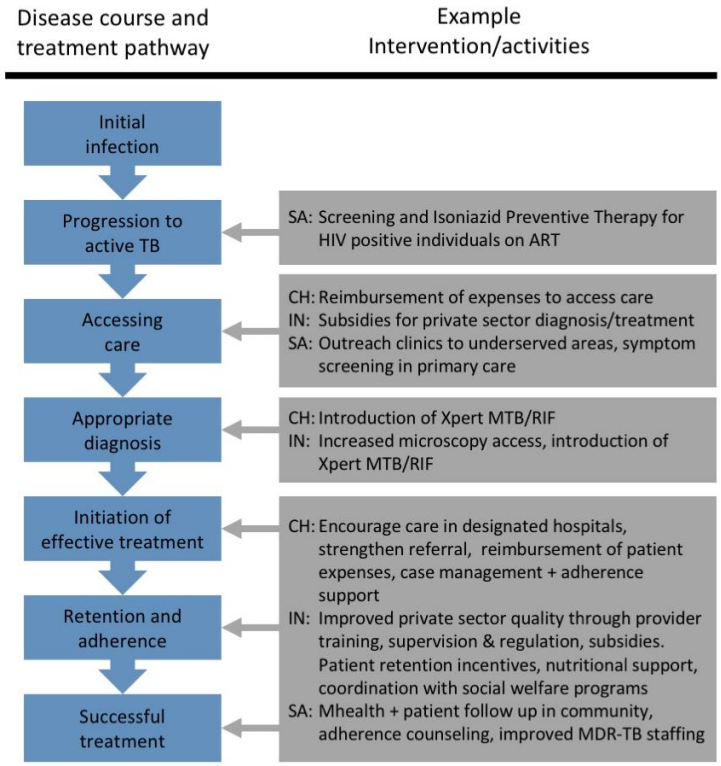

Figure 1: Example care cascade and interventions (From TB MAC Targets exercise).

1.4.4 Outcomes and next steps

There was wide agreement that there is a need for better evidence on programmatic aspects of TB policy for the purpose of modelling, and the quality of modelling could be improved by more careful and explicit representation of programmatic changes implied by candidate policies. The proposal itself was deemed to be encouraging but insufficiently specific, and it was felt that it should be revised in light of the morning's discussion to better describe data to be collated, how these would be analyzed, and how the analytic products would be used by models. Additional issues to be considered would be (a) the extent to which any estimates could be considered generalizable, and (b) the biases inherent in programmatic data, and how these would be considered.

1.5 Cost data needs of epidemiological models of TB (DAY 3)

1.5.1 Background

Recent systematic reviews (published and ongoing) have highlighted that TB unit cost estimates are outdated, not available for most high burden countries, and not representative of delivery modalities rapidly evolving or new technologies emerging. In particular, there have been no unit cost estimate for any TB intervention or service published since 2010 in over 50% of countries within the three high burden (TB, MDR, HIV/TB) lists from a patient, provider, or societal perspective. We also observe a marked variation in cost data availability between countries where unit cost estimates are available: some countries, such as South Africa, have a significant number (>10) of recent studies informing policymaking, while other countries, such as countries with high MDR TB burden, have substantially less data from a provider perspective and almost no data from a patient perspective related to prevention, diagnosis or treatment of MDR-TB. Cost estimates for diagnosis or treatment of LTBI are available in few high and upper middle income countries only, while cost data on social protection or patient support initiatives are also scarce across all settings.

Secondly, there have been few (multi or single-country) multi-site studies conducted to derive empirically cost functions; and there is limited information to help parameterise these functions when modelling resource allocation for TB interventions. For reasons of data scarcity, currently, modelling groups evaluating these questions either apply an assumption of linearity of costs (single constant unit cost per unit of output), build mechanistic cost functions to include assumptions of varying marginal costs at different levels of service delivery, or fit theoretically-defined cost functions to observed data (one or two data points at times). Improvement to these approaches are urgently needed and dependent, among others, on data availability.

1.5.2 Aims and objectives

Aim: Introduce the Global Health Cost Consortium

Objective 1: Describe current cost data availability for modelling, including ongoing initiatives
Objective 2: Obtain feedback on current and future work to improve availability, accessibility and use of cost data

1.5.3 Summary

This session was jointly organised by the GHCC and TB MAC. The session started by discussing current use of cost data as well as current initiatives to improve quality, availability, and use of this information in TB epidemiological models. Major cost initiatives described included the VALUE-TB and WHO Catastrophic costs initiatives. VALUE-TB aims to provide a comprehensive set of unit costs for TB services (health service) data across 5 countries (China, Ethiopia, India, Kenya, and Philippines) to develop a sustainable framework (in terms of tools and processes) for TB cost data collection at the country level. There is strong centralized guidance and the project is set up in partnership with WHO

working through the National TB Programmes. Country leadership is essential to the study design, data collection and data use, where the aim is to enable countries to continue future regular (2 yearly cycles) costing efforts. The project lasts from 2017-2019 and all data will be made available on the GHCC data repository at the end of the project. The WHO-TB catastrophic costs initiative aims to provide comprehensive (patient) cost data across 20 countries. This is also an initiative that aims to improve the availability of cost data but also future quality of data. For that purpose, WHO-TB leads the development of standard indicators and measurement approaches for the monitoring of progress against the post-2015 TB target of "no TB-affected family facing catastrophic costs due to TB" by 2020. For implementation of the study, WHO-TB is collaborating with local NTPs to undertake nationally representative patient costs surveys. These are facility-based patient surveys, usually 500-1000 patients (min. 20 clusters). Data collection is underway – 4 countries have completed the surveys.

The Global Health Cost Consortium (GHCC) was then introduced. GHCC is an initiative by the University of Washington, UCSF, LSHTM, INSP, Avenir Health and UCT working closely with GFATM, PEPFAR and WHO-TB. It aims to improve the interpretation and use of cost information in resource needs estimates, investment planning and efficiency improvement for HIV and TB. It will be producing several products (reference case, standardised tools for data collection, guidance on methods, unit cost study repository, and a dynamic costing tool). The reference case (see link) is a set of 'acceptable' principles and methodological guidance on how to achieve those principles, and includes both theory and evidence based guidance. Part of this effort is the standardisation of TB-specific interventions with additional guidance where available on reporting standards (including a framework for standardisation of interventions, units, activities, and inputs).

Feedback was then sought from the modellers present in particular on the framework proposed for standardisation of interventions, units, activities, and inputs. This consultation is part of a broader round of consultations with other partners (as shown in Figure 2). It feeds into the country piloting process part of VALUE TB and will ultimately inform the final layout and content of the GHCC tools.

The proposed layout of GHCC tools (UCSR and UCost) as well as the format of data and tools to be made available for modellers was then presented.

Feedback from the group identified that it would be helpful to complement the standardisation of interventions, units, activities and inputs with an explanation of definitions (ie definitions of case finding strategies, explicit enumeration of all available interventions). A high level of disaggregation into activities will be useful as long as these activities can be mapped to model outputs. A high level of disaggregation of units into inputs will be useful for modelling groups considering more mechanistic approaches to cost functions and for the estimation of unit costs of new interventions (when these have not been introduced).

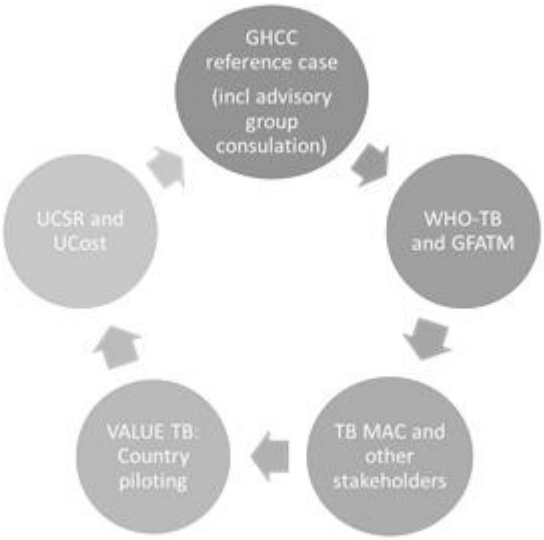

Figure 2: Feedback process for standardisation of interventions, units, activities, and inputs.

A second discussion revolved around the fact that models potentially have the capacity to include cost functions in their analyses – some mechanistic based on model outputs, some theoretical functions based on coverage. Data presented in ways that can accommodate those two approaches would be appreciated. In terms of the tools, transparency and accessibility for users to be able to understand and extract the components they wish to use is key, while there is a need for guidance on how to include costs into models and for continued support from the GHCC when using the online tools.

1.5.4 Outcomes and next steps

In the short term, GHCC will compare the proposed framework to GFATM's new reporting form. Modellers were also requested to provide any further additional feedback on the standardisation framework proposed and the tool formats (UCSR and UCost). GHCC will include feedback from modellers before an advisory group meeting in November for presentation there and feedback to TB MAC after meeting.

In the medium term, GHCC will work with modelling groups to map their outputs to the units proposed. At the same time, GHCC/TB MAC (attendees to the workshop) will work towards a position paper on TB cost data needs and availability for priority setting using transmission modelling.

1.6 Modelling TB case detection: challenges and ways forward (DAYS 4-5)

1.6.1 Background

The meeting took place over two days: Day 1 was dedicated to epidemiological considerations for models of TB case detection (coordinated by David Dowdy), and Day 2 was dedicated to health systems and economic considerations (coordinated by Hojoon Sohn). Both days began with scientific presentation sessions, were followed by small group sessions, and concluded with a general discussion among the entire group focused on synthesis and a way forward.

1.6.2 Aims and objectives

Aim: To create a forum that brings together experts to facilitate discussions on how to improve current epidemiological and economic modeling efforts related to TB case detection. Fund 1-2 small projects related to modeling of case detection (through a Request for Applications with a closing date of October 31, 2017)

Objective 1: To identify the most important themes/gaps that need to be addressed in order to improve models of TB case detection
Objective 2: To identify tangible next steps (manuscripts, training programs, communications, etc.) that can lead to better models of TB case detection in the future

1.6.3 Summary

Day 1 Summary

The first session, entitled “how to model the epidemiological impact of TB case detection”, was chaired by Nick Menzies. Major themes that emerged included the representation of TB case detection within epidemiological models by James Trauer (see slides), the chronology of transmission with respect to TB natural history and the potential importance of chronic coughers as individuals who are both likely to be more infectious throughout the subclinical period and less likely to seek care by Hanif Esmail (see slides), and the importance of considering the role of “false positives” (people without TB who nonetheless receive a positive test for TB - later suggested that we use the term “misdiagnosis” rather than “false positive”) by Rein Houben (see slides). Olivia Oxlade also presented empirical and historical data on TB epidemiology in the Inuit. Discussion after the session focused largely on the role of misdiagnosis - for example, whether we should be considering these individuals on the basis of DALY/QALY losses, patient costs, potential worse outcomes of other illnesses, or as a ratio of misdiagnoses to TB deaths averted.

The second session, entitled “role of novel diagnostic tests in TB case detection”, was chaired by Michael Kimerling. Major themes that emerged from this session included the lack of current convincing evidence that active case finding actually lowers M.tb transmission on a population level by Katharina Kranzer (see slides 1, 2, 3, 4), the distinction between detecting cases earlier in their disease course versus detecting earlier forms of TB disease by Samuel Schumacher (see slides), and the importance of context and linkage to other data (e.g., from interventional studies and prevalence surveys) in developing better models of TB

case detection (see slides). Bradley Wagner presented data from a model of incipient TB case detection in South Africa. Discussion after this session was somewhat more muted but focused largely on the role of empiric treatment and the importance of considering context in TB case detection models.

The third session, entitled “modeling TB case detection in heterogeneous epidemiological and economic contexts”, was chaired by Ted Cohen. Major themes that emerged included the potential for unobserved heterogeneities to result in overestimation of the impact of TB interventions such as case detection by Gabriela Gomes and the use of heterogeneities to better target interventions to highest-risk populations by Nim Pathy (see slides). Sourya Shrestha presented modeling results to illustrate how heterogeneities might impact dual epidemics (e.g., HIV and TB), and Jon Zelner presented data and modeling results related to spatial heterogeneities in TB transmission in Peru. Discussion after this session focused largely on the distinction between observed and unobserved heterogeneities, how the former may result in models overestimating the impact of interventions (and thus should be incorporated into those models) while the latter can help to develop targeted interventions that augment the impact of interventions.

Small groups were asked to provide thoughts on the most important themes from the day and best ways to move forward, in terms of logistical things that could be done to ensure that models of TB case detection were better as a result of the meeting. Major themes included the role of false positives/misdiagnosis, importance of including heterogeneity (or the importance of determining when heterogeneity is important to consider), and the need to collect additional data on context and from ongoing interventional studies/prevalence surveys. Next steps are summarized below.

Day 2 Summary

David Dowdy opened with a recap of Day 1, and Hojoon Sohn gave an introduction to Day 2. After that, the fourth session, entitled “health systems thinking and strengthening for TB case detection”, chaired by David Dowdy, began. Major themes included thinking about the role of case detection in a 2x2 space of people versus time/natural history (see slides), the role of operational modeling with an example given from the Philippines by Bertie Squire (see slides), systems dynamics models with an example from Georgia by Karin Diaconu (see slides), and agent-based models of TB case detection with an example from India (see slides). Discussion was focused on individual presentations, and included vigorous interest in the various types of health systems models, how to appropriately engage stakeholders in the process, the challenges of including the complexity of health systems in such models, the cost of constructing detailed health systems models, and how better to engage with the broader health systems research community.

The fifth session, entitled “economics of TB case detection”, was chaired by Hojoon Sohn. This session included only two scientific presentations. Fiammetta Bozzani gave a summary of work done in collaboration with the TB Think Tank in South Africa, which included the incorporation of constraints to identify the TB screening interventions most likely to be cost-effective as incorporated in the “real world” of the South African health system. Nicole Fraser-Hurt and Gerard Abou Jaoude then gave an overview of the Optima TB model and its use to aid in resource allocation decisions related to TB control in Gauteng province, South Africa. This was followed by a panel discussion, led by Anna Vassall, in which panelists gave

their input on the differences in model type and the matching of appropriate model type to the appropriate question, as well as what the most important additional pieces of data would be to improve health systems models of TB case detection going forward.

Small groups were again asked to provide thoughts on the most important themes from the day and best ways to move forward. Major themes included the importance of considering health systems in models of TB case detection, the need to better bridge the gap between our current expertise and that of individuals engaged in health systems models, the challenges of finding an appropriate balance between simplicity and complexity in such models, and the importance of including constraints to better estimate real-world impact. Next steps are summarized below.

1.6.2 Outcomes and next steps

In the small group discussions for each day, participants were asked to provide suggestions for next steps. These suggestions largely fell into three categories: perspective-style manuscripts, other written works for use to the TB community, and engagement with specific groups/stakeholders. With respect to manuscripts, the following four ideas were the ones that participants settled upon:

(1) Deeper dive into the implications of TB misdiagnosis (particularly "false positives" - people without TB who are wrongly diagnosed as having TB)
(2) Exploration of heterogeneity as it pertains to TB case detection - what do we mean by heterogeneity, what types of heterogeneity exist, when is heterogeneity likely to be most important, etc.
(3) The importance of context in models of TB case detection - reconciling simple/broad models with detailed/implementation models, understanding the role of the existing diagnostic and epidemiological setting, etc.
(4) The role of health systems thinking (and modeling) in evaluating TB case detection, including data needs and a way to improve these efforts

An email has been sent out to all participants to solicit interest in taking these ideas forward (and in leading those efforts). Those topics that garner the most support will be organized into writing teams in November, after we ensure there is no overlap with the RFA.

For an additional written piece of work, it was suggested that participants might develop a "toolkit" document that could be used to illustrate the types of data that would be most helpful to models if added on to prevalence surveys, interventional studies, etc.

In terms of engaging with other stakeholders, Daniel Chin and David Dowdy have already created a link with TB-REACH to discuss plans for interfacing modelers with individuals who are carrying out TB-REACH projects. David Dowdy and Bertie Squire have begun a conversation about how to engage TB modelers with the health systems community, specifically the Health Systems Global conference in 2018 (in Liverpool).

Finally, the RFA closing date is October 31, 2017. We encouraged participants to take the ideas from this meeting and craft them into proposals for the RFA.

In summary, the TB Modeling Research Group not only succeeded in bringing together a diverse group of individuals - including experienced TB modelers, policymakers and other stakeholders, and people with expertise in related fields (e.g., health systems) - but we also have a clear path forward from this meeting, in terms of how to realistically improve models of TB case detection going forward.

APPENDICES

2.1 Participant List
2.2 Meeting Agenda
2.3 GHCC Project Brief

Appendix 2.1 Participant List

Name	Organisation	Email address
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Appendix 2.2 Meeting Agenda

TB MAC / WHO Annual Meeting
18th to 22nd September 2017
Victoria Hotel, Glion, Switzerland

Topic #1
Country level modelling guidance
Monday 18th and Tuesday 19th September
09:30 - 17:00

Background

The first 2 days of the meeting will focus on reviewing an advanced draft of new guidance on country level modelling, and a catalogue of country-level TB models.

The guidance covers 10 principles of good modelling practice in the country-level policy decision context, each with a set of good practices.

The catalogue provides an inventory of TB modelling packages that are available for projections of disease burden under different intervention scenarios and associated assessment of allocative efficiency. The inventory will characterize these packages according to standard criteria, with the aim of helping potential users to make an informed judgement about which package may suit their policy/programmatic requirements.

Meeting Aims/Objectives

- Feedback / comments and achieving consensus on the guidance document
- Feedback / comments and buy-in on the model catalogue
- Agreed path towards adoption and dissemination of the guidance and catalogue

Leads: Finn McQuaid / Nick Menzies - presentations
Rein Houben - organisation

Agenda

When	What	Who
Mon AM		Chair - Ted Cohen
09:30-09:50	Introduction to overall meeting	Richard White / Katherine Floyd
09:50-10:05	Introduction to the guidance/catalogue sessions	Finn McQuaid (intro), attendees (comments)
10:05-10:30	Guidance synopsis+questions for clarifications	Nick Menzies
10:30-11:00	*Break*	
11:00-12:00	1 Relevance 2 Realism	Michael Kimerling Jeff Eaton

12:00-13:00	*Lunch*	
Mon PM		Chair - Katherine Floyd
13:00-14:00	3 Appropriateness 4 Evidence Synthesis	Ted Cohen Liz Corbett
14:00-15:00	5 Validation 6 Valuation	Pete Dodd Pete Dodd (for Paul Revill)
15:00-15:30	*Break*	
15:30-16:30	7 Transparency 8 Timeliness	Philippe Glaziou Lori Bollinger
16:30-17:30	9 Country ownership 10 Iteration	Abiodun Hassan Johannes Hunger
Tue AM		Chair - Jaap Broekmans
09:30-10:15	Guidance - summary of changes	Nick Menzies
10:15-11:00	Model catalogue: intro + process + clarifications	Finn McQuaid (intro), all (comments)
11:00-11:30	*Break*	
11:30-12:15	Catalogue - Open discussion	Finn McQuaid
12:15-13:15	*Lunch*	
Tue PM		Chair - Richard White
13:15-13:45	Catalogue: summary of main changes requested	Finn McQuaid
13:45-14:15	Guidance + catalogue 1. Next steps to finalisation 2. Updating proposal	Nick Menzies
14:15-15:00	3. Path to adoption / dissemination. How can we make these docs used/useful? ● Aim - summary of each stakeholder's potential dissemination and use of guidance and catalogue	USAID - Sevim Ahmedov WHO-GTB - Katherine Floyd WB - David Wilson GFATM - Johannes Hunger BMGF - Daniel Chin Country - Dr Hoa (VN)
15:00-1515	Close	Nick Menzies
15:15-15:45	*Coffee- close of day*	

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Topic #2

Epidemiological data collection / collation for model parameterisation for country level resource allocation decision making
Wednesday 20th September 2017
09:30 - 12:30

Background
This session will focus on epidemiological and programmatic data gaps commonly encountered when models are used for country level resource allocation. TB modelling for resource allocation decision making requires evidence on the series of links between policy adoption and intended health impacts, yet it is not uncommon during individual applications that empirical evidence is not available, and assumptions are made based on expert opinion. This can detract from the objectivity and reproducibility of modelled analyses. This session will discuss this problem and workshop potential solutions, including a draft framework for data collation/collection to fill these evidence gaps.

Meeting Aims / Objectives
Define common epi data gaps encountered during country-level TB modelling, and common approaches for resolving this issue. Describe proposal for reducing data gaps. Obtain feedback and direction for future work.

Lead: Nick Menzies

Agenda

When	What	Who
Wed AM		Chair: Daniel Chin
9:30-9:40	Introduction, session overview	Nick Menzies
9:40-10:00	Commonly encountered evidence gaps for model-based TB resource allocation	Finn McQuaid
10:00-10:30	Collection, analysis and use of data for TB policy and planning	Babis Sismanidis
10:30-11:00	*Break*	
11:00-11:30	Proposal for filling data gaps for TB policy modelling	Rein Houben
11:30-12.30	Discussant comments Open discussion	Philippe Glaziou

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Topic #3
Cost data needs of epidemiological models
Wednesday 20th September 2017
13:30 - 17:00

Background
This session is jointly organised by the Global Health Cost Consortium (GHCC) and TB MAC. It will focus on the discussion of initiatives to improve cost data availability and use for modelling.

Meeting Aims/Objectives
- Describe current cost data availability for modelling, including ongoing initiatives: GHCC (improving data quality), VALUE TB (improving data availability - health service costs), WHO catastrophic cost initiative (improving data availability - patient costs)
- Introduce the Global Health Cost Consortium aims, processes and products
- Obtain feedback on current and future work to improve availability, accessibility and use of cost data

Co-Organisers: Gabriela Gomez (TB MAC/GHCC); Carol Levin (GHCC); Lori Bollinger (GHCC); Anna Vassall (TB MAC/GHCC); Nick Menzies (TB MAC)

Meeting materials: GHCC overview leaflet

When	What	Who
13:30	Introduction to the afternoon work	Chair: David Dowdy
13:35-14:00	Current use and availability of cost data	Presenter: Gabriela Gomez
14:00-14-30	Global Health Cost Consortium	Presenter: Carol Levin
14:30-14:45	Introduction of group discussion	Presenter: Carol Levin
14:45-15:15	Break	
15:15-16:45	Open discussions: - Standardisation of interventions/units/inputs - UCSR, UCost presentations	Presenter: Gabriela Gomez Presenter: Lori Bollinger

16:45-17:00	Next steps for GHCC	Presenter: Carol Levin

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Topic #4
TB MAC Modelling Research Group Meeting
Modeling TB case detection: challenges and ways forward
Thursday 21st 08:30 to Friday 22nd 16:00

Background

With the ambitious goal to end the global TB epidemic by 2030, improving TB case detection will be a critical component in the global and local strategy for TB control. While there are many innovative interventions that have demonstrated the ability to increase the number of cases detected, translating these increases in case detection into estimates of epidemiological and economic impact remains a major challenge. Considering the Sustainable Development Goals, it is also important for models to consider the sustainability of TB case detection efforts. Specific issues relevant to modeling TB case detection include: (a) the role of subclinical and bacteriologically negative TB in transmission and detection; (b) the role of novel diagnostic tests in TB case detection; (c) modeling TB case detection in heterogeneous (e.g., local or country level) contexts; (d) strengthening health systems to support TB case detection; and (e) cost, cost-effectiveness, financing, and affordability of TB case detection. This meeting will, therefore, aim to advance thinking with respect to model design, empirical data needs, theoretical constructs, and economic principles as applied to incorporating these factors into high-quality and effective models evaluating interventions evaluating TB case-detection strategies.

Meeting Aims/Objectives

The primary objectives of this meeting are to create a forum that brings together experts to facilitate discussions on how to improve current epidemiological and economic modeling efforts related to TB case detection. We also aim to fund one or two projects (via a single RFA) that will improve the current *status quo* with respect to modeling the (epidemiological or economic) impact of TB case detection.

Structure: The meeting will include five 90-minute sessions (three on Day 1 and two on Day 2) consisting of a mixture of formal scientific presentations and breakout discussions. The second half of Day 2 will be a full-group structured synthesis discussion where the group discusses key questions related to the modeling of TB case detection, as well as potential ways forward.

Lead: David Dowdy

Agenda

Session 1: How to model the epidemiological impact of TB case detection

- Considering different types of case detection and the uncertain epidemiological role of subclinical and/or bacteriologically negative TB

Session 2: Role of novel diagnostic tests in TB case detection

- What are the implications of the changing diagnostic landscape for models of case detection, considering the discussion in Session 1

Session 3: Modeling TB case detection in heterogeneous epidemiological and economic contexts

- Considering the different needs/end users of such models, the role of case detection in models evaluating multiple different interventions, and the variety of local and country-level contexts (including socioeconomic factors) in which TB case detection efforts might be performed

Session 4: Health systems thinking and strengthening for TB case detection

- Modeling such considerations as integration of TB case detection into broader and complex systems, involvement of NGO and private sectors, and operational/human resource needs

Session 5: Economics of TB case detection

- Considering the health systems issues discussed in Session 4, heterogeneity discussed in Session 3, also integrating concerns of accurate costing, efficiency, equity, affordability, and financing

Date: Thursday, September 21st, 2017
Attendees: Small groups will be pre-designated

Agenda

When	What	Who
8:30 – 9:00	*Introductions and scope/goals of the meeting*	David Dowdy
AM part 1	*Session 1:* How to model the epidemiological impact of TB case detection	Chair: Nick Menzies
9:00 – 10:00	Incorporating case detection into epidemiological models of TB	James Trauer
	Modeling TB Control in the Inuit in Northern Canada : 1950- today	Olivia Oxlade
	Conceptualizing subclinical TB and its role in transmission at the population level	Hanif Esmail
	Comparing case detection against other interventions in TB models	Rein Houben
10:00 – 10:30	Questions & Discussion	All participants
10:30 – 10:45	*Break*	
AM part 2	*Session 2:* Role of novel diagnostic tests in TB case detection	Chair: Michael Kimerling
10:45 – 11:45	Will new diagnostics impact on transmission?	Katharina Kranzer
	Detecting cases earlier and detecting earlier cases: potential synergies and risks	Samuel Schumacher
	How should diagnostics for incipient TB be utilized to reduce population-level transmission?	Bradley Wagner
	Modeling the role of novel TB diagnostics: black and white or shades of gray?	David Dowdy

11:45 – 12:15	Questions & Discussion	All participants
12:15 – 13:15	*Lunch*	
PM part 1	*Session 3:* Modeling TB case detection in heterogeneous epidemiological and economic contexts	Chair: Ted Cohen
13:15 – 14:15	Data requirements and key considerations for incorporating heterogeneity into models of TB case detection	Sourya Shrestha
	The role of unobserved heterogeneity in modeling TB case detection	Gabriela Gomes
	The importance of the social context in modeling TB case detection	Jon Zelner
	Modeling the impact of TB case detection in diverse countries: the SEARO experience	Nim Pathy
14:15 – 15:15	Questions & Discussion	All participants
15:15 – 15:30	*Break*	
PM part 2	Small group discussions and session(s) feedback	Chair: David Dowdy
15:30 – 16:15	Small group discussions (5 groups)	Break into five small groups to summarize key take-home messages
16:15 – 16:30	5 minute summary	Group representatives
16:30 – 16:50	Group discussion	All participants
16:50 – 17:00	Wrap up & summary	David Dowdy
End of the day		

Date: Friday, September 22nd, 2017
Attendees: Small groups will be pre-designated

Agenda

When	What	Who
8:30 – 8:45	Recap of day 1	David Dowdy
8:45 – 9:00	Introduction to day 2	Hojoon Sohn
AM part 1	*Session 4:* Health systems thinking and strengthening for TB case detection	Coordinator: Hojoon Sohn Chair: David Dowdy
9:00 – 10:00	Incorporating health systems into epidemiological models of TB case detection: what are the major considerations?	Pete Dodd
	Thinking about health systems as a determinant of the impact and cost-effectiveness of TB case detection	Bertie Squire
	Health service delivery in high-burden settings: what are the major considerations for models of TB case detection?	Karin Diaconu
	It's time to think about health systems factors more closely: what and how do the health systems factors influence the costs and effectiveness of TB intervention(s)?	Hojoon Sohn
10:00 – 10:30	Questions & Discussion	All participants
10:30 – 10:45	*Break*	
AM part 2	*Session 5:* Economics of TB case detection	Co-ordinator: Hojoon Sohn Chair: Anna Vassall
10:45 – 11:45	Optimizing the allocative efficiency of TB case detection interventions: what are the key considerations?	Nicole Fraser-Hurt and Gerard Abou Jaoude

	Data considerations for models of the economics of TB case detection	Fiammetta Bozzani
	Panel Discussions**:** Dealing with data availabilities and opportunities to improve empiric data collection for health systems, economic, and financing modeling for TB case detection	Chair: Anna Vassall Panel: Session 4 & 5 speakers + Ines Garcia
11:45 – 12:15	Questions & Discussion	All participants
12:15 – 13:15	*Lunch*	
PM	Small group discussions and session(s) feedback	Coordinator: Hojoon Sohn
13:15 – 14:15	Small group discussions	Break into five small groups to summarize key take-home messages
14:15 – 14:30	5 minute summary	Group representative
14:30 – 15:15	Group discussion (specific to day 2 topics)	Chair: Hojoon Sohn
15:15 – 16:00	Next steps & closing: Group discussion about next steps and areas for further methods development	Chair: David Dowdy

Appendix 2.3 GHCC Project Brief

Link to document.