

# **TB Modelling and Analysis Consortium (TB MAC)**

## **TB MAC Global post-2015 TB Targets**

Geneva, Switzerland

27-28 April 2015

### **Meeting Report**

**[www.tb-mac.org](http://www.tb-mac.org)**

## TABLE OF CONTENTS

### Contents

Executive summary .....	3
TB Modelling and Analysis Consortium (TB MAC) .....	5
Summary of TB MAC meeting 6: global post-2015 TB Targets Exercise .....	6
Summary of presentations and discussion - Day 1 .....	8
Summary of presentations and discussion - Day 2 .....	14
APPENDICES .....	19

## 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.

Our sixth meeting was dedicated to economic aspects of a multi-model exercise that aims to focus efforts of modellers, economists and other experts to assess the new post-2015 GTB global TB targets (which interventions, at what scale, and what resources are required to reach them) in South Africa, India and China.

During the meeting 43 representatives from participating epidemiological models, economists, country TB programmes and other stakeholder organisations came together to discuss results, explore the lessons learned and set out the path of the economic work of TB MAC going forward. The meeting was informed by presentations on: the TB Targets methods; the TB Targets impact and economic results; a short summary of the TIME model, as an example of a resource allocation model; a review of current cost data; a presentation on incorporating poverty metrics into TB resource allocation; a summary of recent evidence on the cost-effectiveness of single interventions; and, an overview of the reference case for economic evaluation. Using these presentations as a basis, the group was asked to make suggestions to finalise the TB Targets work (these are listed in detail in the main text pages 10 and 11 below), but also, more broadly, make recommendations for TB MAC's support for the use of models for economic analysis going forward.

In summary, the following suggestions were made for TB MAC to consider supporting going forward. These suggestions do not mean that TB MAC should conduct this work; in most cases these priorities may serve to enable and encourage the broader modelling community to develop work in the following areas. The areas highlighted by the meeting participants were as follows:

- a) TB MAC should play a role in highlighting and further **defining the cost data requirements for the use of models in economic analysis**; and support the use of standardised unit cost estimates. A particular data gap was identified, from the TB Targets work, for more data on both the costs and effects of interventions to support TB service/ programme performance (eg. interventions to support adherence, improve social protection and the public private mix). In addition, there was a strong call to critically evaluate empirical methods for cost data collection to ensure that they were efficient and feasible. The focus should be on developing rapid methods for priority countries, and to conduct data collection on a regular basis in selected high burden countries.
- b) TB MAC should **support analytical work on cost model development**, specifically in the areas of incorporating cost functions and health systems/programmatic costs into TB resource allocation models.
- c) TB MAC should encourage further **debate and exploration of the minimum requirements for epidemiological models to be fit for purpose for different forms and applications of economic analysis**.
- d) TB MAC should encourage modellers and economists to further **develop models for economic analysis** to: better capture false-positive TB diagnoses, presumptive TB cases, DALYs (post cure) and complex diagnostic algorithms; and further define appropriate calibration/ stratification requirements of models to assess the cost-effectiveness of different interventions.
- e) TB MAC should encourage **debate in the modelling community of the relative strengths of different types of models (or hybrids of models) for different forms and applications of economic analysis**; with a particular attention to models that are able to incorporate implementation/ constraints/ health systems issues. It will important to encourage communication between those conducting economic analyses for

product developers and those working at the country level, who may capture more operational issues. Analytically there is space for more work to be done to understand the relationship between technical and allocative efficiency and to further identify the key areas of uncertainty influencing resource allocation results.

- f) TB MAC should **enable work in the area of incorporating poverty metrics in the economic analysis** of TB control interventions using models. There needs to be further debate and work on appropriate, transparent and feasible metrics and thresholds for these non-health outcomes, and engagement of economists who work across the health sector and beyond.
- g) TB-MAC can facilitate the **sharing of lessons on engagement with decision makers to support resource allocation and planning**, in particular the development of methods to properly and simply convey uncertainty; to learn lessons for different approaches to engagement; to develop tools to bridge model outputs with country/donor planning processes; and to further develop analyses to appeal to audiences beyond the NTPs.
- h) TB MAC should encourage further expanding the **use of modelling in a broader range of economic analyses**, with a particular focus on areas like budget impact.
- i) TB MAC should continue to **encourage health economists to participate and engage with modellers** by: a) informing them of what is happening in TB modelling; b) making the work of TB MAC more interesting to economists who are not solely focussed on one type of model or analysis; c) acting as a broker to bring interdisciplinary team together to provide solutions.

# 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 co-ordination, information-sharing, consensus building and prioritisation.

This led to critical research gaps and conflicting policy recommendations that 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](http://www.tb-mac.org)) aims to improve the interaction between quantitative researchers, policy makers, TB programmes and donors to improve global control. Meetings thus far (see [website](#)) have focused on how modelling can support TB control in high HIV settings, the development, deployment and evaluation of novel TB diagnostics, and rational introduction of new TB regimens.

## TB MAC Aim

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.

## TB MAC Objectives

- 1) **Identify research questions** concerning TB control that require input from mathematical modelling or other quantitative research
- 2) Facilitate **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
- 3) **Fund** small analytical /modelling research projects
- 4) **Disseminate results and tools** to key stakeholders including TB control programmes and donors

## Summary of TB MAC meeting 6: global post-2015 TB Targets Exercise

This report describes the sixth TB MAC meeting in Geneva, Switzerland which was the final meeting on the multi-model exercise organised by TB MAC to explore the Global post-2015 TB Targets. The meeting was also an opportunity to reflect and define the involvement of TB MAC in economic analysis going forward.

### *Objectives of TB Targets exercise*

The objective of the TB Targets exercise is to answer two research questions, one with a specific epidemiological focus (I), and the second with a clear economic perspective (II), which builds on the results found in (I).

- I. What would be the health impact (on TB incidence, mortality, DALYs) if a list of existing/near-existing interventions is scaled up to ambitious but feasible levels by 2025 in South Africa, India and China?
- II. What would be the costs and cost effectiveness of the alternative strategies, and the optimal strategies under different budget/resource constraints?

### *Background to meeting*

The post-2015 WHO Global TB Programme Strategy was ratified by the World Health Assembly on 19th May 2014. The WHO 'End TB strategy 2016-2035' has a vision of a 'world free of TB (zero deaths, disease or suffering due to TB)' and the goal of 'Ending the Global TB Epidemic' by 2035, defined as fewer than 10/100,000 cases. Intermediate targets (TB incidence reduced by 50%, mortality reduces by 75%) were proposed for 2025. These new global targets raise many questions. They were said to be ambitious to drive innovation and resource mobilisation, whilst feasible, but how achievable are they at the individual-country level? And which interventions, at what scale, and what resources would be required to achieve these targets?

In this sixth TB MAC meeting we aimed to:

1. Disseminate initial results of the TB Targets exercise
2. Identify key lessons learned from the TB Targets work
3. Outline the state of art in the economic analysis of TB control
4. Identify and prioritise the key technical, content and capacity gaps in the economic analysis of TB control, (including data and analysis needs)
5. Identify specific actions to enhance the appropriate use of models in the economic analysis of TB control
6. Determine the areas where improving links between infectious disease modellers and economists through the TB MAC consortium, can enhance the economic analysis of TB control

### *Structure and process of meeting*

The meeting was structured into two days, please see appendix 2.1 for the final agenda. Day 1 focussed on the TB Targets and multi-intervention resource allocation models. Day 1 started with presentations on the TB Targets results. This was followed in the afternoon with presentations on the TIME model and on the availability of cost data. The day ended with group work and a panel discussion to help the group define the main areas for future model development and data collection needs.

Day 2 focussed on possible extensions/developments of these models. The day began with a presentation and discussion of poverty outcomes and societal costs. This was followed by a presentation of the lessons learned from economic evaluations of single interventions. These evaluations tend to be based around intervention studies and trials and/or use detailed models of specific interventions (that may go into more detail than models used to assess the cost-effectiveness of multiple interventions). This was followed by a short presentation on the reference case for economic evaluation, supported by BMGF. Finally, there was group work and discussion to further refine and explore areas for future work and TB MAC support.

# Summary of presentations and discussion - Day 1

## *Introduction to TB MAC, the TB Targets exercise and the meeting objectives*

*Anna Vassall, Richard White*

These two presentations outlined the scope of the meeting and its objectives (as described above). In addition, participants were asked to consider the following 'big picture' questions as they were considering the presentations throughout the day.

- What the main lessons of the TB Targets work for the different countries?
- How can use and understanding of resource allocation models be enhanced?
- Are the results fit for different purpose/use (resource allocation, resource requirements, budgeting, advocacy)?
- Where do the models need further work? (interventions, outputs, model structure)
- Are the costing models fit for purpose? (interventions, outputs, model structure)
- What approach should be adopted when cost data are not available? (extrapolation, ingredients costing, rapid primary data collection, selected primary data collection)
- What approach should be adopted to appropriately consider health systems investments, high coverage, programmatic and above service level costs?
- How to be transparent about uncertainty?

## *Presentation of final impact results for the TB Targets exercise*

*Rein Houben*

A presentation was made of the final impact results of the TB Targets exercise. Results from 11 models were presented and an explanation provided of the approach taken in terms of data, calibration and intervention definition. The TB Targets project focused on existing or near-existing tools (no game-changing vaccine, diagnostic or drug regimen sufficiently far in pipeline), and modelled two 'ambitious but feasible' scenarios: one defined by country experts and one by advocates. The interventions modelled included: improved access, improved diagnosis, linkage to care, improved treatment success, forms of active case finding and preventative therapy. Social determinants and interventions were not modelled, nor was active case finding in high risk groups. The precise definition of the interventions varied substantially by country. The results will be submitted for publication later in the year.

A number of observations/ questions were raised by the meeting participants. It was noted that the modelling did not account for the effect of other (non-TB control) determinants of TB incidence and mortality such as general economic growth, reduction of vulnerability etc.; whereas the post-2015 targets were set taking account of overall history/trend of incidence. There was concern that some of the advocate-defined interventions—such as mass screening with preventative therapy—were not based on current tools or evidence on cost-effectiveness. There was a request that as declines in incidence seem to happen earlier in some situations to have results available also for 2020 (in addition to 2025). It was also noted that there was more certainty around treatment outcomes than the impact of improved diagnostics; and a repeated concern about the exclusion from the analysis of intervention for key populations. There was a discussion as to whether the results from these three countries were representative enough to inform global decisions. And finally, there was a request to translate these results into action at the country level.



## *Introduction to economic work for the TB Targets exercise*

*Anna Vassall*

This presentation introduced the economic approach to the TB Targets work. The following **sub-objectives** are defined for the economic aspect of the TB Targets work:

What is the cost-effectiveness of a combination of (near-existing/ existing) TB control interventions that can be scaled up between 2015 and 2025?

What is the cost of this combination of interventions, over time and by payer?

What combination of interventions is most cost-effective under different budget constraints?

How are the costs and cost-effectiveness of this combination of interventions impacted by different assumptions about global prices, key policy decisions, adherence and efficacy of the interventions?

The broad approach was to be inclusive – and that all models included in final impact results are included in economic analysis. It was noted that the analysis was limited by the lack of primary data on the costs and effects of some interventions, as well as remote country engagement. The economic work though expanded on previous efforts by taking a societal perspective – and benefitted from recent primary data collection on patient-incurred costs.

From the economic perspective interventions were divided into four types:

- TB service performance improvements (e.g. improve initial default, success rate)
  - Technology change (e.g. replace smear microscopy with Xpert)
  - System change (e.g. support public private mix)
  - Enabling (e.g. actions to support adherence and/or quality of case management)
- Expanding TB service coverage of ‘new’ approaches (e.g. expanding active case detection)
- Expanding TB service coverage (e.g. expanding MDR treatment coverage)
- Health systems improvements (e.g. increased to primary health care)

Key challenges were to ensure that the interventions were being modelled consistently by all modelling groups and that these interventions matched the efficacy assumptions being used to implement the intervention in each model. This had required extensive work with the modelling teams and country experts. The challenge was most substantial in the case for the interventions to improve TB service performance (such as incentives to improve adherence), where there is little evidence on how much it would cost / how effective it would be in different settings.

Three core challenges were also identified in using infectious disease models to estimate costs. Firstly, many previous analyses had focussed on disease outcomes rather than changes in levels of TB service provision. For example, TB screening is provided for many false positive TB cases, which has no epidemiological impact but has a huge cost impact. This was often not addressed in the models, with few being able to provide the numbers of persons needing to be screened. Secondly, the extent of detail on service provision (for example around the diagnostic algorithm) was currently insufficient in many models to directly be used to estimate costs. Finally, calibration to epidemiological outputs was sometimes insufficient to arrive at an informative level of certainty for economic purposes. For example many of the models exhibit a large degree of uncertainty around MDR-TB treatment; this may be less important in terms of general TB incidence, but can lead to large variation in costs.

Most of these challenges had been addressed during the process. There were comments at the end of the importance of using standardised unit cost estimates for each of the model outputs that are comparable across settings. A general comment was also made that none of the scenarios addressed misallocation of resources under the current mix of interventions (and that all the scenarios are aspirational...), and so efficiency improvements may not have been fully considered.

### *Presentation of results and plenary discussion*

#### *Nick Menzies – presentation of DALYs averted and model outputs (service levels)*

These presentations began with a detailed summary of the methods used to calculate DALYs and define the necessary model outputs for the estimation of incremental cost-effectiveness ratios. A number of challenges were highlighted, in that not all models produce the same outputs: most notably for DALYS, the models produced different health states (e.g. some models have simplified HIV categorization) and age structures. It was also noted that as stochastic models exhibit random variation in results, so estimates of total deaths averted are noisy; and in this case the YLL component of DALYs estimated from TB specific deaths averted, so this became important. A limitation was noted, in that although there is potential to carry out additional sensitivity analyses to revise disability weights, it was not possible to estimate DALYs from TB sequelae post treatment, because models are not producing results on the epidemiology of sequelae.

Selected results of the main model outputs (in terms of levels of services) were presented. These will be submitted for publication later in the year. A few take-home points were highlighted: a) the short-term effect was notably different from the long-term effect for a lot of these outcomes (ie. long-term reductions in resource utilization); b) the results were highly context dependent; c) there was substantial uncertainty in multiple dimensions, with some important contrasts between different models, reflecting real uncertainty about how these interventions will impact the epidemic.

Several comments were made. Firstly it was highlighted that more programmatic effort may have to be made as burden declines and this should be reflected in the cost models attached to these model outputs. Secondly, there was a discussion around using a base case comparator as ‘business as usual’ rather than a ‘do nothing’ base case where there is no investment. Finally, a comment was made to reconsider the disease weight for TB following TB cure – as those who have had TB may incur disability in later life.

#### *Gabriela Gomez – presentation of cost and cost-effectiveness results*

The main study findings on costs and cost-effectiveness were presented; these will be submitted for publication later in the year. The results presented for South Africa were final, but for India and China the opportunity was used to further discuss the costs and inputs used.

The following comments were raised by the participants: Firstly, the challenges of estimating the costs and efficacy for some interventions, given the lack of data, particularly around adherence and the public private mix were discussed. Secondly it was noted that one of the models, with huge variation in DALY estimates, seemed like stochastic error problems and these results would need further scrutiny. Concern was also raised about how to present results where there was a ‘patchwork’ in the ranking table, should we be concluding that policy makers should be deeply suspicious of results from all models? Or do we explain that this reflects current uncertainty.

There was a comment that the baseline cost estimates for South Africa seemed low, and a recommendation to refer to the 2007 WHO expenditure tracking work (although it was noted that hospitalisation levels were likely to have been higher then). There was a surprise given the lack of impact of Xpert on MDR-TB treatment costs in China and a

comment that the societal perspective will be critical in China – a lot of patients in China aren't accessing treatment because they dropped out because of high costs. It was also noted that India now has a new algorithm where Xpert plays a larger role. Also, it was noted to be careful about the assumption that public sector is good quality and private sector is poor quality - some evidence that public treatment is creating drug resistance. The issue of transfers of costs from patients to providers was raised and how best to reflect this in an economic evaluation framework. Several participants felt it would be useful to understand in more detail how the models projected different costs / cost drivers between different modelling results.

### ***Presentation of TIME and TIME Economics***

*Rein Houben and Carel Pretorius*

A short presentation was made of TIME and TIME Economics. The presentation began by highlighting the need for resource allocation models that can be used at the country level. It was noted that HIV work in this area had been successful, but that there was a need for a TB-HIV tool as well, and that the TB MAC remit included supporting the development of these models. The use of these models depends on country need. At present TIME Data is not ready yet. TIME Estimates is up and running and a report on estimates has been published. TIME Impact covers four TB disease states and a number of target based or activity-based interventions. It also delivers specific outputs for resource allocation. TIME Economics assesses cost-effectiveness and resources needs. There are a number of case studies where TIME used, including South Africa, Ethiopia and Bangladesh.

### ***Presentation of cost data availability***

*Yoko Lawrence and Inés Garcia Baena*

There were two presentations made on patient and provider cost data. These highlighted substantial gaps in both provider and patient/household costs. In summary, there was a range of data on treatment costs, but much was out of date and may not reflect current treatment practices. There was some discussion on whether the gap was most substantial in MDR-TB treatment or first line / retreatment regimens. There are less data on the former, but some participants felt that it was easier to extrapolate MDR-TB treatment costs across settings. There were much less data on the costs of diagnosis and detection; although there was a range of unit cost information on different tests. However, there were few data available on the overall costs of diagnostic algorithms in different settings. Finally there were little/no data on the costs of other interventions, or costs to improve TB service performance – including many of the interventions included in the TB Targets process as being key to reaching the post-2015 targets.

### ***Group work and Panel Discussion: Country and Global Perspectives***

Following the presentations above the meeting divided into three groups: a user group, who discussed the following questions:

- What are the priority 'economic uses' of TB Targets/ TIME (resource allocation, resource requirements, budgeting, advocacy) in the coming two years?

- What are the key improvements/ approaches/ actions required to support use and understanding of TB resource allocation models at the country level? List two concrete improvements.
- Should and how can any uncertainty be presented to decision makers? Provide an example, or list of issues.

A modelling group, who discussed:

- Are the TB models (as discussed at this meeting) fit for resource allocation (or other economic purposes)? Which areas (interventions, outputs, model structure) require either immediate or long term development? List two specific areas.
- How can modelers (and economists) be more transparent about uncertainty? What are the key technical developments required? List two areas.

And two economic groups, who discussed:

- Are the TB costing models fit for purpose? (interventions, outputs, model structure). What are the priority areas for future development? List two priority areas.
- What are the options for including health systems investments, high coverage, programmatic and above-service level costs in analyses? Are there specific linkages, or pieces of work that can assist in this effort? List two approaches or links with other efforts.
- Discuss the pros and cons of different approaches to missing TB cost data? (extrapolation, ingredients costing, rapid primary data collection, selected primary data collection).
- Recommended concrete actions, either in terms of data collection or methods development, required to achieve the above?

The feedback of these groups was then presented to panel to provide a response. This panel included: *Katherine Floyd, WHO; Micheal Borotwitz, GFATM; Kathy Fierkart (KNCV); Susmita Chatterjee (PHFHI, India), Sun Qiang (China), Triya Dinihari (NTP, Indonesia).*

### The user group

The user group felt that the key target audiences for resource allocation models were: funders (eg. GFATM preparing for next replenishment cycle); b) policy makers (WHO for messaging and timing for cost savings); c) country implementers (Indonesia – advocacy tool to reach beyond MOH and NTP; China – patient cost and drivers and issues of insurance to increase national health support).

The group recommended not to present uncertainty formally when presenting results, but to raise awareness and address this through long-term engagement with policy makers. The panel also felt that modellers should present high-level uncertainty only to policy makers who had a good level of understanding of models. It was also mentioned that having results from different models is confusing; and not to be too concerned about uncertainty as the bar is low. Emphasis was placed on ensuring that the models are simple and clear. Further audiences such as financiers and insurers were also highlighted as important to reach.

### The modelling group

The modelling group felt that it was important to consider uncertainty in the primary outcome measure, and to understand that some models may be more sensitive to some parameters than others. This group felt that transparent communication to policy makers about uncertainty is essential, but needs to be done in a way to clarify investment

decisions rather than 'muddy waters'. When deciding whether infectious disease models are fit for purpose it is important to that a model is relevant for a particular setting and for a particular purpose e.g. budgeting or particular high-burden groups, and to ensure iterative feedback mechanism for users at all stages. The panel felt that there remains some quality issues to address before models can be widely used, but highlighted that this is more to do with data to inform models (at a national level). These data may be available, but the question is how to access them. There was a call to ensure that the community allows for models that are less standardised and more complex to capture new interventions and approaches.

### The economic group

This group identified that there were two types of economic model that could inform resource allocation; general infectious disease models that may be designed to deal with multiple interventions (as presented in day 1) or single intervention models that may have been developed for a specific study. Within the latter group, there were models that examine cohorts (often used to extend outcomes over time of clinical trial cohorts) and those which included reductions in secondary infections. Each form of model has different strengths and weaknesses and a discussion was had on the time horizon and complexity required for different economic analyses/ decisions.

Likewise there are a number of costing models/ tools available: OneHealth, Excel spreadsheets (ingredient approach), Excel with focus more on unit cost -> i.e. accounting approach – that also were suitable in different situations. It was noted that currently cost functions are often not used, but are key when assessing expanded coverage (as with the TB Targets), so none of the current models are yet wholly fit for purpose.

The dearth in costing data was discussed, but it was acknowledged that it is far from ideal to spend 1 to 2 years collecting data. New methods need to be developed for 'rapid' costing, if the models are to be fit for purpose for country level decision making. It was noted that when provider costs are collected, patient cost data should also be collected. National Health Accounting NHA data can be used from sub-accounts that may bring in additional data; and possibly NTP Reviews could be a potential channel for collecting cost data (but some members thought there were concerns in using NTP only data). There needs to be further guidance on how to extrapolate costs from one setting to another. It should be noted some services are more suited for extrapolation than others. WHO-CHOICE data was also discussed. It is often used but there were substantial concerns about sources, utility and maintenance of this database.

The panel commented that use of cost functions is a perennial and important issue. Another key gap was health systems/ programmatic costs; OneHealth can do that but only if country fills it in for all areas, not just TB. It was acknowledged that it was very challenging to create a tool that was sufficiently fit for purpose to plan finances, but simple and flexible for use across countries. For national use, costing by service level may also affect usefulness of model (e.g. hospital, PHC, community), but has substantial data requirements. The panel also commented on the lack of data, both in terms of the age of studies and the small sample sizes. In settings like China the challenges of capturing full costs from providers, insurers and patients was seen as an important concern. Given the need was great, there was a question as to where to start? It was suggested to focus on priority countries and do data collection on regular basis for these selected, high burden countries. The work of the JLN Costing Network (costing subgroup, representing 7 countries) involved in developing a practical costing manual (including India and Indonesia) was highlighted as a possible example to follow.

## Summary of presentations and discussion - Day 2

### *Incorporating poverty and equity*

*Stephane Verguet*

This presentation reported on the results of the poverty analysis included as part of the TB Targets work. The work was commissioned in the context of Universal Health Coverage (UHC), and incorporates costs incurred by patients/households. For TB – direct costs are large, but indirect costs can also be substantial, so the focus of this exercise is on out of pocket (OOP) direct medical, OOP direct non-medical, indirect costs. The work refers to several measures of financial risk protection: catastrophic expenditures (eg. Xu et al.); impoverishing expenditures (Wagstaff and van Doorslaer 2003); Value of insurance provided (Verguet). The approach uses the outputs from models (e.g. number of people on treatment, MDR treatment, deaths) and then randomly assigns that individual to a household with a given annual income and OOP costs; assuming that there is twelve times more TB in bottom income quintile. The work is done for South Africa and the numerator (unit patient costs) drawn from the XTEND study plus estimate of funeral costs from Collins and Leibbrandt (2007). The denominator (household income) is drawn from Gamma distribution based on gross national product (GDP) per capita and Gini index. Preliminary results were presented and will be submitted for publication by the end of the year.

The group commented that this work may help inform one of WHO's priority with prevalence surveys, to measure catastrophic expenditures. It was noted that the pursuit of UHC extends beyond catastrophic health expenditure to include catastrophic health 'costs' in general; the analysis presented was in line with this approach. Challenges remain on how to calculate productivity and a question was made about considering the household as the unit of analysis. This was a particular concern among how to include the economic impact on the unemployed or situations where multiple households share a single breadwinner. It was also noted that funeral estimates are most likely a quite substantial underestimate of household costs of a breadwinner dying. There were some comments on how the distribution of patient expenditures was defined; and to consider adapting the analysis to reflect that this was not uniform among patients across income groups. The importance of including pre-diagnosis costs was also highlighted.

### *Updates in economic evaluations of new technologies*

*David Dowdy*

This presentation summarised the key lessons learned from the last few years of economic evaluations of single interventions. Several key issues were highlighted.

Firstly, the importance of understanding the baseline practice. For example, there is only going to be impact from a diagnostic test if that test is used in a certain way (ie. test done properly, patient receives results etc.). How the use of a new diagnostic test may either be influenced by the baseline practice is often unclear. Moreover, there is a risk that as modellers do a disservice to the standard of care. The actual standard of care may be better than most models credit. Eg patients who look the sickest may actually receive empiric therapy. This is one of the key findings from the various trials and economic evaluations around Xpert roll-out. Similar work with drugs shows same effect – a model from one paper assumed that if you didn't complete every dose of therapy you got no benefit; in reality there is still a chance of cure if you are on drugs for less time. This led to more than 2-fold overestimation of impact as compared to standard of care.

The standard of care is also key for estimating incremental costs. Recent work finds that new tools may actually end up being less expensive than we previously thought. Increased upfront costs are balanced by reduction in downstream costs (ie. less overtreatment from more specific diagnosis). In some case this cost reduction is more important than any impact, for example recent work on PaMZ predicts that the overall cost for PaMZ regimen is lower due to averted expenditure in the future, particularly a reduction in patient costs.

Secondly, the effect of implementation on cost-effectiveness of new tools also is critical. Models often assume linear scale-up. In reality, this might be very different. New tools may end up being targeted to those who need them the least, or some new technology (eg. SMS) may be easier to implement than current standard of care. The placement of the technology is also key data from Uganda, looking at actual Xpert implementation finds that a median 25 tests performed each month. Putting this into an economic model gives a very different result.

Thirdly, recent years have seen a great incorporation of societal costs in cost-effectiveness analysis. This raises the question of whether we should treat costs incurred by patients as the same as costs incurred by the health system?, when patients have so much less capacity to pay. This is currently being examined by bio-ethicists at Johns Hopkins (Merritt, Zwerling et al), working on incorporating social justice assessment into CEA. New tools have different purposes – they may not always be designed to be cost-effective, but they may be designed to increase access, to rule out TB in people with cough, to improve equity, advocacy and engagement of civil society.

The group responded with several observations. It was noted firstly that, in addition to supported resource allocation, these findings need to be fed back to the product development process – we should prevent silos between those conducting economic analyses for product developers and those working at the country level. Secondly, these analyses may call for different modelling approaches; particularly including delivery and operational aspects in cost-effectiveness analysis.

Thirdly, it was suggested that implementation aspects are important because we can get economic estimates wrong, but we should also go beyond that and suggest implementation itself invokes a series of choices that should then be subject to decision analysis. It's only meaningful to say what is the cost-effectiveness of this particular way of implementing a particular new drug etc, rather than asking what is cost-effectiveness of the drug in general. We should focus on analysing strategies rather than of technologies. But this is a question of homogeneity – once you start to account for implementation you find our ability to generalize will be much less. This will cause a shift in how we talk about cost-effectiveness, and will have profound implications on the way we do our business of CEA (will need much more localized analysis, more analysis of a strategy rather than a tool).

Fourthly, it was noted that implementation does not just vary across settings, but also across time. For some regarding Xpert these findings are not the end of the story – implementation practices may take time to change/ adjust – and it is important to follow up with new empirical data to understand dynamic effect when you approach modelling systems, just as with diseases. Finally, from a user perspective it was commented that although the discussion is academically interesting, it is not possible to run a model of every tool in every country. Countries will need to make decisions on this, and need to know what impact it makes on their budget. Is there a way of translating this into a simpler model that can give some guidance on budget impact at country level across settings?

### *Reference case for economic evaluation*

*Damian Walker*

This presentation outlined the reference case for economic evaluation, supported by BMGF. The rationale for this case was that BMGF does not catalogue the economic evaluations they support nor the findings from these studies; does

not know the extent to which the studies we fund are used or useful; and to date has not required grantees to use common methods or reporting standards. Therefore BMGF funded the Methods of Economic Evaluation Project (MEEP) with NICE International. This included a critical review of published economic evaluations funded by BMGF; and developed version 1 of reference case. Key issues notes were inconsistent methods and reporting standards observed in BMGF-funded economic evaluations observed, in terms of uncertainty, time horizon, perspective, comparators, affordability, equity and DALY standards. 11 principles (universal) were identified, but particular methodological specifications aren't necessarily always given. Reporting standards are prescriptive.

What next for reference case? There is to be a process of embedding this into grant applications. (currently in soft-launch). In the future there will be a technical panel that will check for adherence (and potentially withhold payment or give additional grant until it's proven the evaluation has adhered to guidelines). DFID is interested in adopting this, have also spoken with Global Fund, GAVI, USAID. No other funders have these methods in place either. The reference case can provide a framework for methodological research as well. Grant to Tufts Medical Center to expand their CEA registry to include studies using DALYs, launch of Global Health CEA registry. There is further work to engage low and middle income countries to build priority-setting institutions (w/ IDSI and DFID)

The group asked for clarification on how this reference case relates to other guidelines. Mark Sculpher from York is acting within MEEP as a sort of bridge with other groups –and this orientation is clearly for LMICs. It was noted that country-specific NICE-like bodies are a good plan, but there remain substantial capacity constraints at country level. There should be efforts to bring together all groups of grantees that include economists working with modellers to come up with a list of common issues affecting EEs alongside transmission models (HIV, TB, malaria, NTDs ...). Finally, it was also noted that CEA is increasingly important for Global Fund and much more standardised guidance is required around how to finance interventions, what should be covered under national health insurance, etc... and these questions can be informed by this type of analysis.

### *Group work and plenary feedback*

Following the presentations above the meeting divided into three groups: a user group, who discussed the following questions:

- Should and what poverty/equity assessment be part of either resource allocation models or CEAs? Who are the key stakeholders? And what metrics may most appeal?
- Are there any key areas of interest in single CEA interventions (or particular areas of development) that are not currently being met?
- What are to support do NTPs need to use and understand TB CEAs? Identify either links to other activities, or activities that TB –MAC may consider (or mobilise/collaborate with others to do) improve the use of model based economic evaluation.

The modelling group discussed the following questions:

- Are the different models in TB MAC currently able to examine poverty and equity issues? Is this something of interest?
- What are the key lessons learned from recent economic evaluations of new technologies that may inform future modelling efforts and technical development of models? List two areas for possible further work.



- What support do modelers need to achieve reference case standards in CEA? (including linking to other efforts)? Identify concrete areas that TB MAC could support (or link with other efforts)

The two economic groups discussed the following questions:

- What poverty metrics should be considered? Identify metrics that could be used for the TB Targets exercise specifically, but also discuss other approaches (distribution cost-effectiveness, if considered important) that TB MAC or other could explore going forward
- What are the steps that need to be taken to incorporate 'real world constraints' and link detailed economic evaluations to broader resource allocation work?
- How can TB MAC best encourage the participation of economists in its activities? List two concrete activities.

### The user group

The user group agreed that a poverty or equity assessment was useful. It could be one of the most powerful tools of convincing funders and global community to invest in TB interventions. A poverty analysis could be important for both public funders and national insurers. The metrics that have most appeal are those on catastrophic expenditures; but there was concern about the unit of analysis (e.g. patient, household). This would need to make sense to the local context. In China for example it may be more useful by extended family. There was a strong interest in the work on single interventions, but the importance of looking at interventions in combination, such as bringing new diagnostics out, along with say new drugs (for MDR-TB) was raised. There was also interest in optimising the entire case detection algorithm. There was a strong argument made for support to NTPs needed, but this should include different types of economic analysis including areas like budget impact. The plenary discussion re-iterated that models that appeal beyond TB are required to convince the MoHs and Treasuries. The case was also made to not 'reinvent the wheel' and use existing metrics to assess poverty impact.

### The modelling group

There was a strong interest in incorporating poverty and equity in current models, but concern about thresholds. Are current thresholds arbitrary? If arbitrary, then should be standardized. It was noted it was difficult to validate the comparison between each interventions, but should modellers and economists should carefully validate each step, especially distributional assumptions, e.g. by using patient cost surveys. There was little consensus on whether the lessons learned from recent CEAs pointed primarily to a model or data issue? Model contextualisation is needed but not sure if can be done. At a minimum it is important to be explicit about contextual assumptions in model for those using results. Even if modellers don't have context understanding, this is still need to validate outcome. There was a discussion on how important is it to have stratified models – and this is an area that needs more enquiry. The process of dialogue with decision makers was also considered critical - but it would be useful to compare and discuss what processes may be most effective. The plenary discussion highlighted the importance of considering health systems models; and being clear up front what is the primary economic purpose of the model. There was some debate on how 'good' models needs to be to be useful to a decision making process; and again the importance of an iterative process of engagement with decision makers was highlighted. However, it was also noted that what decision makers consider to be a good model outcome may be at odds with validity of model.

## The economic group

The economic group was not satisfied with any of the poverty metrics, even though all were discussed. They felt that different metrics can be used for different audiences. It was felt that catastrophic costs and poverty are more communicable to policy makers but miss people below poverty line. Extended Cost-Effectiveness Analysis (ECEA) was felt to be too complex for many decision makers. The social justice metric sounded interesting, but still needs development. Overall it was felt there was much room to improve metrics in this area but also data collection needed – as it was necessary to include enough data in patient cost surveys to calculate various metrics. Incorporating implementation or real world constraints was also felt to be critical, but hard to identify which of these may be most important. This highlights the importance of working closely with countries in any analysis, as it is important that they set the economic focus and agenda in this respect.

Analytically there was much more work to be done to understand the relationship between technical and allocative efficiency – and the key uncertainties driving resource allocation. There is a critical gap in capacity to take results in resource allocation models and translate them into budgets to implement interventions. TB MAC should continue to encourage health economists to participate and engage with modellers by: a) informing them of what is happening; b) making the work of TB MAC more interesting to economists who have broader interests than one type of model or analysis; and c) acting as a broker to bring interdisciplinary team together to provide solutions. For the future it is important to be aware and collaborative of other disease specific activities focusing on economics – share methods with those groups and contribute to global work – e.g. global poverty measure due to disease; focus on less data hungry methods to generate cost methods; and finally further examine how we define poverty and the justification for using specific metrics or thresholds. The plenary discussion highlighted that TB is leading the way in incorporating poverty metrics in modelling and, while other disease areas have moved further ahead in examining health systems, none have yet a good simple method.

## APPENDICES

### Meeting Agenda

<b>DAY 1 – Monday 27<sup>th</sup> April 2015</b>		
<b>Morning Session</b>	<b>Chair:</b> Michael Kimerling <b>Reporters:</b> Sedona Sweeney / Fiammetta Bozzani	
<b><u>SESSION 1 - PRESENTING THE TB TARGETS – OVERVIEW</u></b>		
<b>09:00-09:30</b>	<b>Introduction to TB MAC, the TB Targets exercise and the meeting objectives</b> Introductions, overview presentation and time for clarifications	Anna Vassall Richard White
<b>09:30-10:15</b>	<b>Presentation of Final Epi results</b> Presentation of the models, interventions and main epi results and time for clarifications	Rein Houben
<b>10:15-10:30</b>	<b>Introduction to Economic Work</b> Presentation of economic methods	Anna Vassall
<b>10:30-11:00</b>	<b>TEA BREAK</b>	
<b><u>SESSION 2 - PRESENTING THE TB TARGETS – ECONOMIC RESULTS</u></b>		
<b>11:00-12:30</b>	<b>Presentation of results and plenary discussion</b> Presentation of TB MAC economic results	Nick Menzies Gabi Gomez
<b>12:30-13:30</b>	<b>LUNCH</b>	
<b>Afternoon Session</b>	<b>Chair:</b> Bertie Squire <b>Reporters:</b> Andrew Siroka / Yoko Laurence	
<b><u>SESSION 3 - USE OF RESOURCE ALLOCATION MODELS AT THE COUNTRY LEVEL</u></b>		
<b>13:30-14:15</b>	<b>Presentation of TIME and TIME Economics</b> Presentation and clarifications	Carel Pretorius Rein Houben Tom Sumner
<b>14:15-14:45</b>	<b>Presentation on current cost data availability and issues</b> Presentation and clarifications	Anna Vassall Ines Garcia Baena
<b>14:45-15:00</b>	<b>TEA BREAK</b>	
<b>15:00-16:00</b>	<b>Group Work</b> Discussion and recommendations of main gaps (use, data, technical) required to improve the resource allocation models (TB Targets work, TIME, and other models)	
<b>16:00-17:00</b>	<b>Panel Discussion: Country and Global Perspectives</b> Key gaps and the way forward: Michael Borowitz, Katherine Floyd, Kathy Fierkart, Susmita Chatterjee, Sun Qiang, Triya Dinihari	

**DAY 2 – Tuesday 28<sup>th</sup> April 2015****Morning Session****Chair:** Josh Salomon**Reporters:** Sedona Sweeney / Fiammetta Bozzani**SESSION 4 - DEVELOPMENTS IN THE ECONOMICS OF TB CONTROL**

**09:00-09:45**    **Incorporating poverty and equity**    Stephane Verguet  
Presentation and discussion

**09:45-11:00**    **Updates in economic evaluations of new technologies**    David Dowdy  
Presentation and discussion

**11:00-11:15**    **TEA BREAK**

**SESSION 5 - IDENTIFYING GAPS AND THE WAY FORWARD**

**11.15-11.45**    **Reference Case for Economic Evaluation**    Damian Walker

**11:45-12:30**    **Group Work**  
Identifying key gaps in use, knowledge and capacity in TB economics (with a specific focus on economic evaluation using modelling)

**12:30-13:30**    **LUNCH**

**Afternoon Session****Chair:** Anna Vassall**Reporters:** Andrew Siroka / Yoko Laurence

**13:30-14:30**    **Plenary Feedback**  
Feedback of group work  
The way forward and recommendations to TB MAC going forward to support the use of models in economic analysis

**CLOSURE**

## Participant List

<b>Andrew Kennedy</b>	The Global Fund to Fight AIDS, Tuberculosis and Malaria
<b>Andrew Siroka</b>	World Health Organization
<b>Anna Vassall</b>	London School of Hygiene and Tropical Medicine
<b>Bawa Wuryaningtyas</b>	National Tuberculosis Programme, Indonesia
<b>Bertie Squire</b>	Liverpool School of Tropical Medicine
<b>Carel Pretorius</b>	Avenir Health
<b>Christian Lienhardt</b>	World Health Organization
<b>Claudia Denkinger</b>	Foundation for Innovative New Diagnostics
<b>Damian Walker</b>	The Bill & Melinda Gates Foundation
<b>David Dowdy</b>	Johns Hopkins Bloomberg School of Public Health
<b>Don Mudzengi</b>	The Aurum Institute
<b>Eliud Wandwalo</b>	The Global Fund to Fight AIDS, Tuberculosis and Malaria
<b>Elvis Gama</b>	Liverpool School of Tropical Medicine
<b>Fiammetta Bozzani</b>	London School of Hygiene and Tropical Medicine
<b>Gabriela Gomez</b>	Amsterdam Institute for Global Health and Development
<b>Grace Huynh</b>	Institute for Disease Modelling
<b>Ines Garcia Baena</b>	World Health Organization
<b>Jose Izolza Licea</b>	UNAIDS (Joint United Nations Programme on HIV/AIDS)
<b>Josh Salomon</b>	Harvard School of Public Health
<b>Katherine Floyd</b>	World Health Organization
<b>Kathy Fiekert</b>	KNCV Tuberculosis Foundation
<b>Knut Lonnoth</b>	World Health Organization
<b>Lucica Ditiu</b>	Stop TB
<b>Matt Hamilton</b>	Futures Institute
<b>Matthew Jowett</b>	World Health Organization
<b>Mehran Hosseini</b>	The Global Fund to Fight AIDS, Tuberculosis and Malaria
<b>Michael Borowitz</b>	The Global Fund to Fight AIDS, Tuberculosis and Malaria
<b>Michael Kimerling</b>	KNCV Tuberculosis Foundation
<b>Nick Menzies</b>	Harvard University
<b>Nimalan Arinaminpathy</b>	Imperial College London / Public Health Foundation of India
<b>Philip Eckhoff</b>	Institute for Disease Modelling
<b>Rein Houben</b>	London School of Hygiene and Tropical Medicine
<b>Richard White</b>	London School of Hygiene and Tropical Medicine
<b>Romain Ragonnet</b>	University of Melbourne
<b>Sahu Suvanand</b>	World Health Organization
<b>Sedona Sweeney</b>	London School of Hygiene and Tropical Medicine
<b>Shufang Zhang</b>	The Global Fund to Fight AIDS, Tuberculosis and Malaria

<b>Stephane Verguet</b>	Harvard University
<b>Sun Qiang</b>	Shandong University, China
<b>Susmita Chatterjee</b>	Public Health Foundation of India
<b>Tom Sumner</b>	London School of Hygiene and Tropical Medicine
<b>Triya Dinihari</b>	National Tuberculosis Programme, Indonesia
<b>Yoko Laurence</b>	London School of Hygiene and Tropical Medicine