WHO Global Task Force on TB Impact Measurement

Report of the sixth meeting of the full Task Force

19–21 April 2016
Glion-sur-Montreux
Switzerland

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Acknowledgements. This preparation of this report was led by Katherine Floyd, with contributions from Anna Dean, Inés Garcia Baena, Philippe Glaziou, Irwin Law, Ikushi Onozaki, Andrew Siroka, Babis Sismanidis, Hazim Timimi and Matteo Zignol. It was finalized after review by all meeting participants. The funding required by WHO to hold the meeting was provided by the United States Agency for International Development (USAID).

Executive Summary

BACKGROUND

Global targets for reductions in TB disease burden by 2015 were set within the context of the United Nations' Millennium Development Goals (MDGs). The targets were that TB incidence should be falling, and that TB mortality and prevalence rates should be halved by 2015 compared with their levels in 1990. The WHO Global Task Force on TB Impact Measurement was established in 2006, with the aim of ensuring that WHO's assessment of whether 2015 targets were achieved at global, regional and country levels should be as rigorous, robust and consensus-based as possible. The Task Force was convened by the TB Monitoring and Evaluation (TME) unit of WHO's Global TB programme (GTB).

To fulfil its mandate, the Task Force pursued three strategic areas of work during the period 2007–2015. These were:

1. Strengthened surveillance in all countries, towards the ultimate goal of direct measurement of TB incidence and TB mortality using notification and vital registration data, respectively.
2. National TB prevalence surveys in 22 global focus countries.
3. Periodic review and updating of methods used to translate surveillance and survey data into TB disease burden estimates.

WHO published its assessment of whether 2015 global TB targets for reductions in TB incidence, prevalence and mortality were achieved in its 2015 global TB report.[1] This assessment followed a Task Force meeting focused on reviewing methods used by WHO to produce TB disease burden estimates in March 2015. The assessment was well accepted, with no concerns about the published estimates expressed to WHO by Member States.

The MDGs (2000–2015) have been superseded by a new era of Sustainable Development Goals (SDGs) that have an end date of 2030. Similarly, the era of WHO's Stop TB Strategy, which covered the decade 2006–2015 and had the overall goal of achieving the 2015 global TB targets, is over. It has been replaced by the End TB Strategy, which covers the period 2016–2035. In the context of the SDGs and End TB Strategy, the Task Force needed to review and reshape its mandate and strategic areas of work for the post-2015 era, and discuss key components of continued, reshaped and/or new areas of work. A 2.5 day meeting (19–21 April) was organized by GTB/TME for this purpose.

OBJECTIVES

The meeting had five objectives:

1. To review and reshape the mandate and strategic areas of work of the WHO Global Task Force on TB Impact Measurement for the post-2015 era of the SDGs and the End TB Strategy.
2. To review and discuss Task Force efforts to support strengthened TB surveillance such that TB cases and deaths can be directly measured using routine surveillance data from notification and vital registration systems.
3. To review and discuss methods used by WHO to produce estimates of TB disease burden, with particular attention to a) progress made on recommendations from the March 2015 Task Force meeting and b) estimates for drug-resistant TB (rifampicin-resistant TB, MDR-TB, XDR-TB).
4. To review and discuss the role of national TB prevalence surveys 2009–2015 and post-2015.
5. To discuss two new topics under consideration for incorporation within the mandate of the Task Force post-2015: a) surveys of costs faced by TB patients and their households and whether these are catastrophic; b) tools for projections of TB disease burden and case notifications.

[1] World Health Organization. *Global Tuberculosis Report 2015*. Geneva: WHO, 2015.

PARTICIPANTS

Meeting participants (total of 44) included staff from national TB programmes, experts in the fields of epidemiology, statistics and modelling from universities and research institutes, representatives from international technical and funding agencies (Centers for Disease Control and Prevention, USA; European Centre for Disease Control and Prevention; the Global Fund; KNCV Tuberculosis Foundation; Research Institute for TB, Japan; TB Alliance; the Union; USAID; UNITAID), and staff from WHO headquarters as well as Regional and Country Offices.

KEY RECOMMENDATIONS AND OUTCOMES

The key outcomes/recommendations from the meeting are summarized below, for each of the major objectives/topics that were discussed.

1. Mandate and strategic areas of work, 2016–2020

An updated mandate and five strategic areas of work were agreed.

Mandate

To ensure that assessments of progress towards End TB Strategy and SDG targets and milestones at global, regional and country levels are as rigorous, robust and consensus-based as possible.

To guide, promote and support the analysis and use of TB data for policy, planning, and programmatic action.

Strategic areas of work

1. Strengthening national notification systems for direct measurement of TB cases, including drug-resistant TB and HIV-associated TB specifically.

2. Strengthening national vital registration systems for direct measurement of TB deaths.

3. Priority studies to periodically measure TB disease burden, including:
    a. National TB prevalence surveys.
    b. Drug resistance surveys.
    c. Mortality surveys.
    d. Surveys of costs faced by TB patients and their households.

4. Periodic review of methods used by WHO to estimate the burden of TB disease and latent TB infection.

5. Analysis and use of TB data at country level, including:
    a. Disaggregated analyses (e.g. by age, sex, location) to assess inequalities and equity.
    b. Projections of disease burden.
    c. Guidance, tools and capacity building.

The SDG and End TB Strategy targets and milestones referred to in the mandate are the targets (2030, 2035) and milestones (2020, 2025) set for the three high-level indicators i.e. TB incidence, the number of TB deaths and the percentage of TB-affected households that face catastrophic costs as a result of TB disease. Strategic areas of work 1–3 are focused on direct measurement of TB disease burden (epidemiological and, in the case of cost surveys, economic). Strategic area of work 4 is required until all countries have surveillance systems and/or the periodic studies required to provide direct measurements, since indirect methods will be needed to estimate TB incidence and mortality at global, regional and national levels up to the current year.

2. Strengthened TB surveillance

Building on progress made since 2008, which includes the development of a TB surveillance checklist of standards and benchmarks that can be used to systematically assess the extent to which current surveillance systems provide a direct measure of TB cases and TB deaths and the

rollout of this checklist in 41 countries, guides on electronic recording and reporting and inventory studies to measure under-reporting of detected TB cases, support to inventory studies in priority countries, development of guidance on TB epidemiological reviews and a big increase in the use of data from vital registration systems to produce estimates of TB mortality, seven priority areas of work for 2016–2020 were agreed upon. These are listed below.

Strengthening national notification systems for direct measurement of TB cases

1. TB epidemiological reviews including use of the TB surveillance checklist.
2. Regional analysis workshops.
3. Transitioning from paper to electronic case-based surveillance.
4. TB inventory studies to measure under-reporting of detected TB cases.

Strengthening vital registration systems for direct measurement of TB deaths

1. Promote use of vital registration data for measurement of TB deaths.
2. Create and sustain links with relevant stakeholders.
3. Mortality studies to validate the use of vital registration data for measurement of TB deaths.

A key suggestion/recommendation was to establish a dialogue with the 30 high TB burden countries on strengthening TB surveillance, as a basis for setting a target for the number of high TB burden countries that have met all of the TB surveillance checklist standards related to data quality and under-reporting by 2020 (i.e. 8 of the 9 standards for direct measurement of TB cases), and to explore a similar target for the number of countries that meet the standard for vital registration and/or have undertaken a mortality study. It was suggested that this dialogue should be initiated in advance of the End TB Summit, which is being hosted by WHO on an annual basis (the first summit was held in November 2015) and brings together the 30 high TB burden countries as well as technical and financial partners, and concluded at that summit.

The Task Force agreed with the proposed vision for drug resistance surveillance. The vision is that all countries have continuous surveillance systems at least for measurement of rifampicin resistance (for example, based on Xpert MTB/RIF testing) and of additional resistance to fluoroquinolones and second-line injectable agents if rifampicin resistance is detected (for example, based on second-line line probe assays), with ad-hoc surveys approximately every five years to investigate other resistance patterns and the emergence of resistance to new TB drugs using sequencing technologies.

3. Methods used to produce estimates of TB disease burden

Since the Task Force meeting held 31 March–2 April 2015, the main update from WHO was that the methods used to produce the TB disease burden estimates published in the 2015 global TB report were based on the recommendations of that meeting. New estimates of the burden of latent TB infection, developed by a group led by the London School of Hygiene and Tropical Medicine, were then presented, followed by an update from Pete Dodd (Sheffield University) on the latest status of the modelling work he had first presented a year ago. Further details on these two topics are not provided in this report, pending review and publication of journal articles.

For methods to be used to produce country-specific estimates of the incidence of drug-resistant TB for publication in WHO's 2016 global TB report, the general principle that was agreed was that there should not be any dramatic shift from methods used to produce global-level estimates published in 2014 and 2015.

Two specific recommendations were agreed, which were:

1. Use Method I with the suggested refinements listed in the presentation (details in section 4), and in addition to use drug resistance surveillance (DRS) data to cross-check the relative share of relapse/retreatments from notification data, to update the estimated proportion of resistance among relapse cases and to test the hypothesis that levels of MDR-TB are higher in the private sector using data from public-private (PPM) sites.
2. Produce country-level estimates using Method II and compare the two sets of estimates.

Three next steps were also agreed:

1. Advance communication from WHO to countries about the planned publication of country-specific estimates of MDR-TB incidence in the 2016 WHO global TB report is needed. This will be done at the end of June 2016.
2. A small working group on the topic of MDR-TB disease burden estimates was established, composed of the seven people who volunteered.
3. Investigate the possibility of grading of estimates based on data quality, which could accompany published country estimates.

Two alternative approaches that merit investigation in the next 1–2 years are: 1) estimating MDR-TB incidence in two groups only (primary and acquired), which would require additional data, in particular cohort studies to measure the rate of acquisition of resistance during first-line treatment; and 2) development of a deterministic mathematical model to fit estimates of TB incidence and DRS data by country. The latter has been commissioned to Pete Dodd.

4. National TB prevalence surveys 2009–2015 and post-2015

The substantial achievements in the implementation of national TB prevalence surveys 2009–2015 were clearly recognized and applauded.

Post-2015, there was support for three main updates to how surveys are implemented. These were: a) replacement of smear and culture with Xpert, provided this is supported by findings in 2016/17 surveys that will use Xpert and smear/culture in parallel and especially if Xpert Ultra is shown to have performance equivalent to culture in evaluation studies scheduled for 2017; b) strengthened governance/oversight mechanisms, in particular use of Good Clinical Practices (GCP) adapted as appropriate for prevalence surveys; and c) increased investments to ensure timely writing of survey reports and strengthened communication of results and lessons learned.

Epidemiological criteria to identify countries that are potentially eligible to conduct a national TB prevalence survey post-2015 were agreed upon, for two groups of countries: a) countries that implemented a survey 2007–2015; b) countries that did not conduct a survey 2007–2015. The first group includes 24 countries; the criteria for the second group indicate that there are 33 countries that meet epidemiological criteria for considering a first survey. Among these, four stand out in terms of their share of the global TB disease burden: DR Congo (2.5%), India (22%), Mozambique (1.6%) and South Africa (4.7%), all of which either have plans to implement a survey in 2016 or 2017 or are considering it (DR Congo). The remaining 29 countries have <1% of the global burden each. It was highlighted that among countries meeting epidemiological criteria, it is then crucial to assess whether the ten prerequisites (non-epidemiological) for undertaking a survey listed in the "Lime Book" can be fulfilled.

5. Two new topics: surveys of costs faced by TB-affected households, and projections

The main outcomes were that work on projections of TB disease burden will be part of the Task Force's fifth strategic area of work. Surveys of costs faced by TB patients and their households will be part of the Task Force's third strategic area of work.

NEXT STEPS AND A GOAL/ASPIRATION FOR 2020

Next steps identified at the meeting included presentation and discussion about the work of the Task Force at the June 2016 meeting of WHO's Strategic and Technical Advisory Group for TB (STAG-TB), follow-up discussions with the Global Fund regarding funding required to support TB epidemiological reviews and regional analysis workshops that cannot be readily mobilized via country grants, and embarking on a dialogue with the 30 high TB burden countries on the topic of strengthened TB surveillance in the lead up to the End TB Summit in October 2016.

A major goal/aspiration is that in five years' time, progress on TB surveillance will have matched (or exceeded) the impressive progress, showcased at the meeting and beyond what could have been anticipated when 22 global focus countries were identified in December 2007, in the implementation of prevalence surveys.

Introduction

Global targets for reductions in TB disease burden by 2015 were set within the context of the United Nations' Millennium Development Goals (MDGs). The targets were that TB incidence should be falling, and that TB mortality and prevalence rates should be halved by 2015 compared with their levels in 1990. The WHO Global Task Force on TB Impact Measurement was established in 2006, with the aim of ensuring that WHO's assessment of whether 2015 targets were achieved at global, regional and country levels should be as rigorous, robust and consensus-based as possible.

To fulfil its mandate, the Task Force pursued three strategic areas of work during the period 2007–2015. These were:

1. Strengthened surveillance in all countries, towards the ultimate goal of direct measurement of TB incidence and TB mortality using notification and vital registration data, respectively.
2. National TB prevalence surveys in 22 global focus countries.
3. Periodic review and updating of methods used to translate surveillance and survey data into TB disease burden estimates.

These strategic areas of work were taken forward by subgroups of the Task Force, which also periodically met together. A wide range of technical, financial and development agencies, countries and individual experts contributed to the work of the Task Force, with overall guidance, direction and coordination provided by the TB Monitoring and Evaluation (TME) unit of WHO's Global TB programme (GTB).

WHO published its assessment of whether 2015 global TB targets for reductions in TB incidence, prevalence and mortality were achieved in its 2015 global TB report.[2] This assessment followed a Task Force meeting focused on reviewing methods used by WHO to produce TB disease burden estimates in March 2015. The assessment was well accepted, with no concerns about the published estimates expressed to WHO by Member States.

Following their adoption at the UN General Assembly in September 2015, the Sustainable Development Goals (SDGs) have now superseded the MDGs and cover the period 2016–2030. Similarly, the era of WHO's Stop TB Strategy, which covered the decade 2006–2015 and had the overall goal of achieving the 2015 global TB targets, is over. It has been replaced by the End TB Strategy, which covers the period 2016–2035. In the context of the SDGs and End TB Strategy, the Task Force needed to review and reshape its mandate and strategic areas of work for the post-2015 era, and discuss key components of continued, reshaped and/or new areas of work. A 2.5 day meeting (19–21 April) was organized by GTB/TME for this purpose.

This report of the meeting has six major sections, which follow the structure and main topics of the meeting agenda. Each section summarises the main content of the presentation(s), the questions posed for plenary discussion and/or group work, the main recommendations arising from group work and plenary discussion, and where further details can be found. The six sections are:

1. Meeting objectives, expected outcomes, and overall approach.
2. Task Force mandate and strategic areas of work, 2016–2020.
3. Strengthened TB surveillance.
4. Methods to estimate TB disease burden.
5. Prevalence surveys 2009–2015 and post-2015.
6. Two new topics for consideration as part of the Task Force's mandate and strategic areas of work 2016–2020.

The report appendices provide the meeting agenda (7.1) and the list of background documents (7.2).

[2] World Health Organization. *Global Tuberculosis Report 2015*. Geneva: WHO, 2015.

1. Meeting objectives, expected outcomes, and overall approach

1.1 Objectives

Five meeting objectives were defined. These were:

1. To review and reshape the mandate and strategic areas of work of the WHO Global Task Force on TB Impact Measurement for the post-2015 era of the Sustainable Development Goals and the End TB Strategy.

2. To review and discuss Task Force efforts to support strengthened TB surveillance such that TB cases and deaths can be directly measured using routine surveillance data from notification and vital registration systems.

3. To review and discuss methods used by WHO to produce estimates of TB disease burden, with particular attention to a) progress made on recommendations from the March 2015 Task Force meeting and b) estimates for drug-resistant TB (rifampicin-resistant TB, MDR-TB, XDR-TB).

4. To review and discuss the role of national TB prevalence surveys 2009–2015 and post-2015:
    a. Prevalence surveys 2009–2015;
    b. Prevalence surveys post-2015: why, how, where?

5. To discuss two new topics under consideration for incorporation within the mandate of the Task Force post-2015:
    a. Surveys of costs faced by TB patients and their households and whether these are catastrophic;
    b. Tools for projections of TB disease burden and case notifications.

1.2 Expected Outcomes

Five expected outcomes from the meeting were defined. These were:

1. Mandate and strategic areas of work of the Task Force agreed for the period 2016–2020.

2. Task Force well informed about current work related to strengthening TB surveillance, with agreement reached and/or recommendations provided on priority areas of work 2016–2020, updates to Terms of Reference (TOR) for epidemiological reviews, and next steps to expand implementation of TB inventory studies to measure under-reporting of detected TB cases.

3. Task Force well informed about progress made on March 2015 recommendations about methods used by WHO to produce TB burden estimates, consensus on methods to produce estimates of the burden of drug-resistant TB for publication in 2016 and definition of alternative/complementary methods for estimating the burden of drug-resistant TB that should be explored starting in 2016.

4. Task Force well informed about national TB prevalence surveys 2009–2015, with agreement reached on three key topics for future surveys:
    a. Whether prevalence surveys are still needed post-2015, and if so for what purpose;
    b. Major components of surveys that may need to be refined or changed;
    c. Criteria that can be used to assess if a national TB prevalence survey is appropriate.

5. Task Force well informed about emerging work to measure costs faced by TB patients and their households though periodic surveys, and tools for TB-related projections.

1.3 Overall approach

The meeting was structured in five major sessions (approximately one half-day each), with one session for each of the five objectives (for details, see the agenda provided as section 7.1 of the Appendices). Each session began with presentations, and was then followed by either plenary discussion only (Objective 1, Objective 5), by a mixture of group work and plenary discussion (Objectives 2–4, including invited commentaries in plenary for Objective 2). Group and plenary discussions focused on the questions posed in the background documents (listed in section 7.2 of the Appendices) and associated presentations. One member of each group provided feedback in plenary at the end of each session. The main recommendations and/or outcomes from group and plenary discussion were consolidated by TME, summarized as PPT slides and then presented for review and final feedback in the first sessions of Day 2 (mandate and strategic areas of work, strengthened surveillance) and Day 3 (mandate and strategic areas of work, methods to estimate the incidence of drug-resistant TB, prevalence surveys post-2015) of the meeting.

Group work was organized in five groups, each with a facilitator. The groups were designed to ensure that there was a good mixture of perspectives, experience and expertise in each group; the groups had the same participants throughout the meeting.

2. Task Force Mandate and Strategic Areas of Work, 2016–2020

2.1 Overview of presentation

The presentation covered five topics:

1. A reminder about the Task Force's mandate and strategic areas of work during the period 2007–2015 (see also the Introduction to this report);
2. An overview of the SDGs and the End TB Strategy, with particular attention to the three indicators for which high-level targets and milestones have been set;
3. Implications of the SDGs and the End TB Strategy for the Task Force's mandate and strategic areas of work post-2015;
4. Other factors with implications for the Task Force's mandate and strategic areas of work post-2015;
5. A proposal for the mandate and strategic areas of work of the Task Force for the period 2016–2020.

There are 17 SDGs (Figure 1), of which one (SDG3) focuses on health and is defined as "Ensure healthy lives and promote well-being for all at all ages". Under SDG3, Target 3.3 is defined as "By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases". For TB, the indicator selected to track progress is TB incidence (in the current SDG framework, per 1000 population).

A striking feature of the SDG monitoring framework (compared with the MDGs) is that definitions of many indicators require within-country disaggregation: for example, by age, sex, geography (e.g. urban/rural), wealth (e.g. bottom 40%, bottom vs. top income quintiles) and employment status. Some indicators give particular attention to specific subpopulations, including pregnant women, people with disabilities, victims of work-injuries and migrants. These disaggregated indicators will be used to inform assessments of within-country inequality and equity in access to resources, opportunities, services and basic human rights, and identify particular areas or subpopulations where progress is lagging and greater attention is needed.

The End TB Strategy, adopted by all Member States at the 2014 World Health Assembly and covering the period 2016–2035, has the goal of ending the global TB epidemic. The strategy has three high-level indicators for which targets (for 2030 and 2035) and milestones (for 2020 and 2025) have been set (Table 1). The three indicators are the TB incidence rate (as in the SDGs), the number of TB deaths and the percentage of TB-affected households that experience catastrophic costs as a result of TB disease.

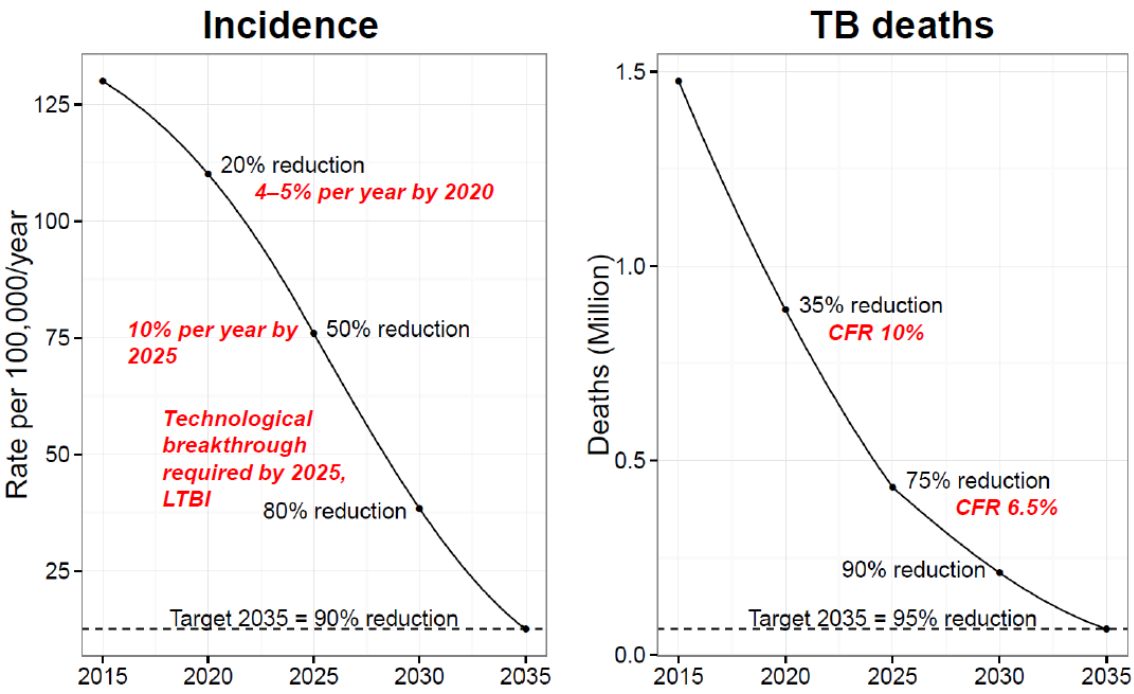
Figure 1: The 17 SDGs

Table 1: The vision, goal, high-level indicators and associated targets and milestones of the End TB Strategy, 2016–2035

VISION	**A WORLD FREE OF TB** – zero deaths, disease and suffering due to TB			
GOAL	**END THE GLOBAL TB EPIDEMIC**			
INDICATORS	**MILESTONES**		**TARGETS**	
	2020	2025	SDG 2030*	End TB 2035
Percentage reduction in the absolute number of TB deaths *(compared with 2015 baseline)*	35%	75%	90%	95%
Percentage reduction in the TB incidence rate *(compared with 2015 baseline)*	20%	50%	80%	90% (approximately 10 per 100,000 population)
Percentage of TB-affected households experiencing catastrophic costs due to TB *(level in 2015 unknown)*	0	0	0	0

The trajectories for TB incidence and deaths required to reach the targets are shown in Figure 2. Reaching the targets and milestones for TB incidence requires the TB incidence rate to be falling at 4–5% per year by 2020, 10% per year by 2025 (equivalent to the best-ever performance historically) and at an accelerated rate (beyond historic levels) after 2025. The latter requires a technological breakthrough by 2025, such that it is possible to reduce the number of cases emerging from the pool of people who are latently infected with *Mycobacterium tuberculosis*. Reaching the milestones and targets for reductions in TB deaths requires not only these declines in TB incidence, but also a lowering of the case fatality ratio (CFR) from a level of 16% in 2015 to 6.5% (the recent average in high-income countries) by 2025.

Figure 2: Trajectories of TB incidence and mortality required to reach End TB Strategy targets and milestones, 2015–2035. CFR = case fatality ratio. LTBI = latent TB infection.



Five major observations and related implications of the SDGs and the End TB Strategy for the Task Force's mandate and strategic areas of work 2016–2020 were identified. These were:

1. TB incidence and TB deaths remain high-level indicators, as they were in the MDGs and the Stop TB Strategy. This means that:
    a. A Task Force strategic area (or areas) of work related to strengthened routine surveillance for direct measurement of TB cases and deaths remains necessary;
    b. A Task Force strategic area of work related to periodic review of methods used to estimate TB disease burden remains necessary. This is because it will be some time before all countries have strong enough surveillance (notification and vital registration) systems to provide direct measurements of TB incidence and TB deaths. In the interim, indirect estimation methods will be required as well.
2. The percentage of TB-affected households facing catastrophic costs is now the third high-level indicator of the global TB strategy (instead of prevalence). This means that:
    a. If the Task Force mandate's remains focused on the best-possible assessment of progress towards high-level targets and milestones, then the Task Force will need to incorporate work related to measurement of costs faced by TB-affected households and whether these are catastrophic into its strategic areas of work.
3. TB prevalence is lower profile than in the MDG and Stop TB Strategy eras. This means that:
    a. Retaining a whole strategic area of work on national TB prevalence surveys may not be justified post-2015.
4. Disaggregation of TB indicators and related assessments of within-country inequalities and equity are higher profile post-2015. This means that:
    a. Disaggregated analyses and related assessments of equity should feature within the Task Force's strategic areas of work.
5. Estimates of the burden of latent TB infection are higher profile compared to the MDG and Stop TB Strategy eras. This means that:
    a. Estimation of the burden of latent TB infection (as well as TB disease) should feature within the Task Force's strategic areas of work.

The four other factors with implications for the Task Force's mandate and strategic areas of work post-2015 that were identified were:

1. Growing demand for disaggregated estimates and analyses at country level for TB specifically. Examples include estimates disaggregated by age and sex, and for drug-resistant TB and well as TB overall (see also section 4); and within-country analyses of TB surveillance and survey data, for example by location, age, sex as well as for specific subpopulations.
2. The importance of the analysis and use of data, as well as data generation. Although analysis and use of data was an important component of Task Force work 2007–2015, this was not explicitly featured in the Task Force's mandate and strategic areas of work.
3. Commonalities between the work of the Task Force and the Global Project on anti-TB drug resistance surveillance. These include the use of both surveillance (as the reference standard) and surveys to measure disease burden and the growing role of rapid tests (see also section 3 and section 5). These commonalities provide a basis for integrating the topic of anti-TB drug resistance surveillance into the work of the Task Force.
4. Growing demand for projections of TB disease burden, using dynamic and statistical modelling approaches. This demand is especially evident from the Global Fund, and tools to support such work at country level are under development (see also section 6).

2.2 Agreed mandate and strategic areas of work following plenary discussion

The draft wording of the mandate and strategic areas of work set out in Background Document 1 was strongly supported, with a few suggested refinements. The final version agreed following plenary discussion and a subsequent review on Day 2 and Day 3 of the meeting is shown below.

2.2.1 Mandate

To ensure that assessments of progress towards End TB Strategy and SDG targets and milestones at global, regional and country levels are as rigorous, robust and consensus-based as possible.

To guide, promote and support the analysis and use of TB data for policy, planning, and programmatic action.

2.2.2 Strategic areas of work

1. Strengthening national notification systems for direct measurement of TB cases, including drug-resistant TB and HIV-associated TB specifically.

2. Strengthening national vital registration systems for direct measurement of TB deaths.

3. Priority studies to periodically measure TB disease burden, including:
    a. National TB prevalence surveys.
    b. Drug resistance surveys.
    c. Mortality surveys.
    d. Surveys of costs faced by TB patients and their households.

4. Periodic review of methods used by WHO to estimate the burden of TB disease and latent TB infection.

5. Analysis and use of TB data at country level, including:
    a. Disaggregated analyses (e.g. by age, sex, location) to assess inequalities and equity.
    b. Projections of disease burden.
    c. Guidance, tools and capacity building.

2.2.3 Explanatory notes, mandate and strategic areas of work

To further explain and justify the mandate and strategic areas of work, the following six points were highlighted (see also the explanatory notes in Background Document 1):

1. The SDG and End TB Strategy targets and milestones referred to in the mandate are the targets (2030, 2035) and milestones (2020, 2025) set for the three high-level indicators i.e. TB incidence, the number of TB deaths and the percentage of TB-affected households that face catastrophic costs as a result of TB disease (see also Table 1). As illustrated in Figure 2, the CFR (mortality divided by incidence) will also be important for assessing progress towards 2020 and 2025 milestones for reductions in TB deaths.

2. Strategic areas of work 1–3 concern direct measurement of TB disease burden.

3. Strategic areas of work 1 and 2 are relevant to all countries, for direct measurement of TB incidence (including for levels of HIV co-infection and drug resistance among TB cases) and TB deaths.

4. Strategic area of work 2 requires linkages with the broader agenda of strengthening civil and vital registration systems, and this is the reason (along with the fact that notification and vital registration are separate systems) for splitting the previous strategic area of work (2007–2015) on strengthened surveillance into two parts (see also section 3).

5. In strategic area of work 3:
    a. National TB prevalence surveys are particularly relevant in: a) high burden countries that still lack any direct measurement of TB disease burden, including for indirect estimates of TB incidence; and b) countries with a baseline survey that can use repeat surveys to directly measure trends and infer impact (see also section 5).
    b. Drug resistance surveys are required every 3–5 years until continuous surveillance based on universal testing is established, and should include measurement of resistance to a wide range of drugs (see also section 3).
    c. Surveys of costs faced by TB patients and their households and assessment of whether these are catastrophic are required every 3–5 years to assess progress towards the End TB Strategy milestones for 2020 and 2025 (see also section 6).

6. Strategic area of work 4 is required until all countries have surveillance systems and/or the periodic studies required to provide direct measurements, since indirect methods will be needed to estimate TB incidence and mortality at global, regional and national levels up to the current year. Post-2015, estimates published by WHO will focus on the period since 2000. Estimates of the number of people latently infected also require indirect estimation approaches.

7. For strategic area of work 5, examples include: standardized terms of reference for country-specific epidemiological reviews, including a) disaggregated analyses (e.g. by age, sex, geography) and related assessments of inequalities and equity and b) projections of disease burden; workshops based on the TB surveillance checklist and handbook on analysis and use of TB data; and guidance and tools (including models) to help countries develop projections of notifications and disease burden under alternative target and intervention scenarios.

2.3 Further details

Further details can be found in Background Document 1 and in the presentation.

3. Strengthening TB Surveillance

3.1 Overview of presentations

There were two presentations. The first was titled "Strengthening TB Surveillance: progress to 2015, priority areas of work for 2016–2020"; the second covered the topic "Drug resistance surveillance: progress to date and emerging innovations".

3.1.1 Strengthening TB surveillance: progress to 2015, priority areas of work 2016–2020

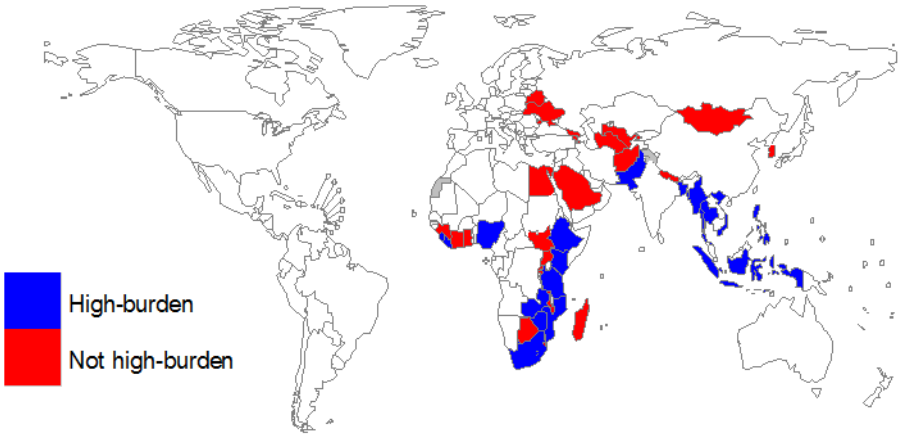
The presentation had two major parts. The first highlighted progress in Task Force work to support strengthened TB surveillance up to the end of 2015. The major examples that were described and explained were:

- Development of a TB surveillance checklist to support systematic assessment and related strengthening (where needed) of TB surveillance. The checklist includes 13 standards and related benchmarks that can be used to assess whether a country's surveillance system meets the standards required to provide direct measurements of TB cases and deaths from notification and vital registration systems respectively, and to inform development and implementation of plans to strengthen surveillance to close identified gaps. Following a two year development process including pilot work in 13 countries, the checklist was ready to be rolled out by January 2013.
- Use of the TB surveillance checklist at country level. By the end of 2015, the checklist had been used by 41 countries,(including 17 of the 30 high TB burden countries[3] (Figure 3), often in association with the preparation of Global Fund concept notes and national TB strategic plans. Common recommendations following completion of the checklist include a need to safeguard and undertake routine analysis of historical subnational surveillance data; to transition from paper-based systems to case-based electronic surveillance; to undertake an inventory study to quantify the level of under-reporting of detected TB cases; and to improve surveillance data for the direct measurement of disease burden associated with drug-resistant TB, HIV-associated TB as well as the disease burden among children.
- Development of a guide on electronic recording and reporting, which was published in 2011. Data reported to WHO in the 2015 round of global TB data collection indicated that 132 countries had case-based surveillance data for TB, and a further 26 countries had such data for drug-resistant TB only. Most of the countries without case-based surveillance were in the African Region.
- Development of a guide on inventory studies to measure under-reporting of detected TB cases. This was published in 2012. By the end of 2015, 9 countries had completed a study. A UNITAID-funded project, implemented by the TB Alliance in collaboration with other partners including WHO and USAID, has included support for the design and/or implementation of inventory studies in a further six countries: China, Indonesia, Pakistan, the Philippines, Thailand and Viet Nam.
- Development of a handbook on understanding and using data at country level. This was published in 2014 and provides practical guidance on the analysis and use of TB surveillance and other relevant data to track the level of and trends in TB disease burden at national and subnational levels, detect outbreaks and inform programmatic action. By the end of 2015, 17 countries had been supported to conduct the analyses recommended in the handbook via regional and national workshops organized by WHO.
- Development of standardized terms of reference and an associated implementation guide for conducting TB epidemiological reviews. These reviews are typically done in advance of or at the same time as a national TB programme review, and are designed to inform understanding of the TB epidemic and related national strategic planning.

[3] The 30 high TB burden countries defined by WHO for 2016–2020 are: Angola, Bangladesh, Brazil, Cambodia, China, Congo, Central African Republic, DPR Korea, DR Congo, Ethiopia, India, Indonesia, Kenya, Lesotho, Liberia, Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, Russian Federation, Sierra Leone, South Africa, Thailand, the United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe.

- Growing use of cause-of-death data from national or sample vital registration systems to produce national estimates of TB deaths. For the 2015 global TB report, estimates of TB deaths for 127 countries were produced using vital registration data, up from only 3 countries in 2008.

Figure 3: Countries that had used the WHO TB surveillance checklist to assess TB surveillance by the end of 2015



The second part of the presentation set out proposed priority areas of work on strengthened TB surveillance for the period 2016–2020. In line with the Task Force strategic areas of work 2016–2020 (section 2), this was done separately for a) TB notification systems and b) vital registration systems. The proposed priority areas of work were:

Strengthening national notification systems for direct measurement of TB cases

1. TB epidemiological reviews.
2. Regional analysis workshops.
3. Transitioning from paper to electronic case-based surveillance.
4. TB inventory studies to measure under-reporting of detected TB cases.
5. Real-time surveillance.

Strengthening vital registration systems for direct measurement of TB deaths

1. Promote use of vital registration data for measurement of TB deaths.
2. Create and sustain links with relevant stakeholders.

3.1.2 Drug resistance surveillance: progress to date and emerging innovations

The presentation covered four topics:

- The Global Project on anti-TB drug resistance surveillance;
- Coverage of surveillance;
- Emerging innovations;
- Conclusions and vision for the future.

The Global Project on anti-TB drug resistance was established in 1994, with two major objectives: 1) to estimate the magnitude of drug resistance; and 2) to determine trends in drug resistance. To date, the focus has been on measurement of multidrug-resistant TB (MDR-TB), defined as resistance to rifampicin and isoniazid. The project is hosted by WHO, with major partners including supranational reference laboratories, the Bill & Melinda Gates Foundation, the Global Fund, the President's Emergency Plan for AIDS Relief (PEPFAR), the Union, USAID, the US Centers for Disease Control, KNCV Tuberculosis Foundation. Since its establishment, five editions of guidelines on drug resistance surveillance have been issued (the latest in 2015) and a series of global reports with the latest data published (four on drug resistance surveillance

specifically between 1997 and 2008, one on multi-drug resistant TB in 2010 and subsequently as part of the annual WHO global TB report). The principles underlying anti-TB drug resistance surveillance were explained.

By the end of 2015, data from continuous surveillance (based on routine diagnostic testing) and surveys were available for 153 countries that account for >95% of the world's population and TB cases (Figure 4). In recent years, typically there have been 10–15 surveys in different stages of preparation or implementation each year. There were 100 countries with at least two measurements of the level of drug resistance, of which 65 had ≥3 measurements. A linear trend (decreasing or increasing) was evident in 12 countries, but assessing trends at global, regional and country levels remains challenging due to different trend patterns and repeat surveys that are not powered to detect differences in the proportions of cases (new and previously treated) with drug-resistant TB. An analysis published in the 2014 WHO global TB report indicated that there was no evidence of changes in the level of MDR-TB at the global level in recent years (remaining stable at about 3.5% among new cases). Coverage of data on resistance to second-line drugs among TB patients with MDR-TB had reached 78 countries by the end of 2015 (Figure 5).

Figure 4: Coverage surveillance data on resistance to isoniazid and rifampicin by the end of 2015

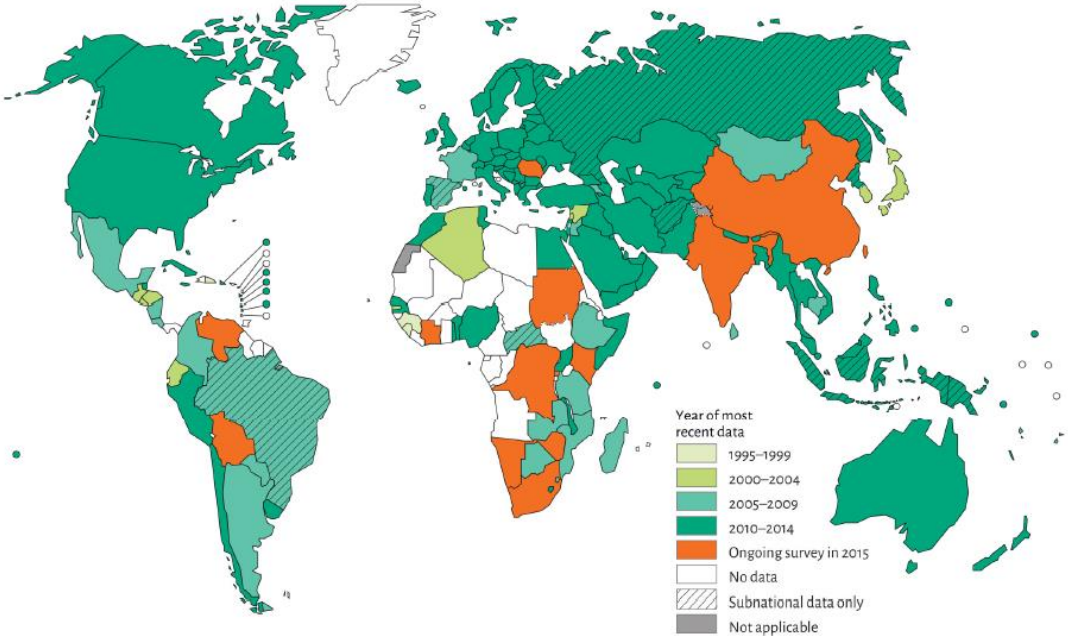


Figure 5: Coverage of surveillance data on resistance to second-line anti-TB drugs by the end of 2015

Two major innovations were highlighted: the use of molecular tests, and the use of sequencing technologies. Since its endorsement by WHO in December 2010, Xpert MTB/RIF has provided an opportunity to simplify surveillance of drug resistance (by reducing the number of culture tests required and hence lowering demands on laboratory staff capacity and time, and reducing the challenges associated with transportation of samples) and accelerate progress towards universal testing for rifampicin resistance. Line probe assays (LPAs) can also be used in surveys. By April 2016, Xpert MTB/RIF had been used in six surveys and its use was planned in seven upcoming surveys. LPAs had been used in five surveys. Sequencing technologies have been introduced to surveillance of anti-TB drug resistance surveillance in a recent multi-country project implemented by WHO with funding from the Bill & Melinda Gates Foundation and USAID. This project has focused on the first-ever nationally-representative measurements of resistance to pyrazinamide and fluoroquinolones, which may be part of new TB treatment regimens. Sequencing is the most accurate molecular test available, allows high and rapid throughput (about 200 strains in 3–4 days) and is cheaper than conventional phenotypic testing. Current evidence suggests that test accuracy may be equivalent to phenotypic testing for rifampicin and pyrazinamide, but lower sensitivity for isoniazid, fluoroquinolones and aminoglycosides. Accuracy in testing for new TB drugs (bedaquiline and delamanid) has yet to be studied. Lower sensitivity for some drugs notwithstanding, a recent WHO Expert Meeting on policy guidance for drug susceptibility testing agreed that such tests could be used for surveillance purposes, with test results corrected for known biases.

The suggested vision for surveillance of anti-TB drug resistance surveillance is that all countries have continuous surveillance systems at least for measurement of rifampicin resistance (for example, based on Xpert MTB/RIF testing) and of additional resistance to fluoroquinolones and second-line injectable agents if rifampicin resistance is detected (for example, based on second-line LPAs), with ad-hoc surveys approximately every five years to investigate other resistance patterns and the emergence of resistance to new TB drugs using sequencing technologies.

3.2 Questions for discussion in group work and plenary

Questions related to strengthening TB surveillance were first discussed in groups and then in plenary. Questions related to surveillance of drug-resistant TB were discussed in plenary only.

3.2.1 Strengthening TB surveillance: progress to 2015, priority areas of work 2016–2020

Five questions were posed for discussion in group work and plenary. These were:

1. Do you agree with the proposed priority areas of work for 2016–2020 for (i) notification and (ii) vital registration systems? If not, what additions or modifications would you suggest?
2. Do you think there should be country prioritization in all or some of these areas of work? If so, on what basis?
3. Do you agree with the major proposed updates to the ToRs for TB epidemiological reviews? If not, what additions or modifications are proposed?
4. What are the key steps the Task Force recommends to expand implementation of inventory studies?
5. Which individuals and/or agencies are willing to contribute to each of the proposed priority areas of work?

3.2.2 Drug resistance surveillance: progress to date and emerging innovations

The question posed for plenary discussion was whether the Task Force agreed with the proposed vision for drug resistance surveillance i.e. a) the establishment of national continuous surveillance systems for at least rifampicin resistance and b) implementation of ad-hoc surveys for investigating patterns of resistance to a wider range of drugs.

3.3 Recommendations/outcomes from group work and plenary discussion

The main recommendations/outcomes from group work and plenary discussion are summarized below.

3.3.1 Strengthening TB surveillance: progress to 2015, priority areas of work 2016–2020

Seven priority areas of work were agreed upon: four for strengthening national notification systems for direct measurement of TB cases, and three for strengthening national vital registration systems for direct measurement of TB deaths. These are listed below.

Strengthening national notification systems for direct measurement of TB cases

1. TB epidemiological reviews including use of the TB surveillance checklist.
2. Regional analysis workshops.
3. Transitioning from paper to electronic case-based surveillance.
4. TB inventory studies to measure under-reporting of detected TB cases.

Strengthening vital registration systems for direct measurement of TB deaths

1. Promote use of vital registration data for measurement of TB deaths.
2. Create and sustain links with relevant stakeholders.
3. Mortality studies to validate the use of vital registration data for measurement of TB deaths.

While it was agreed that real-time surveillance is important, especially in low-incidence countries, this was not felt to be a *priority* area of work for the Task Force. The topic should nonetheless be featured in documentation related to Task Force work (e.g. an updated version of the 2009 Policy Paper[4] that set out the recommendations of the Task Force for 2009–2015).

For the second priority area of work related to vital registration systems, examples of stakeholders that were identified were maternal and child health (MCH) community, civil and vital registration (CRVS) community, child health and mortality prevention surveillance network (CHAMPS).

Country prioritization from the global perspective was considered important. It was agreed that high TB burden countries should be considered for all areas or work, and within this list that inventory studies should be prioritized in countries with a large private sector. Further prioritization and customization of a package of activities should be based on the results from the TB surveillance checklist and epidemiological reviews, and expressed demand from countries.

A key suggestion/recommendation was to establish a dialogue with the 30 high TB burden countries on strengthening TB surveillance, as a basis for setting a target for the number of high TB burden countries that have met all of the TB surveillance checklist standards related to data quality and under-reporting by 2020 (i.e. 8 of the 9 standards for direct measurement of TB cases), and to explore a similar target for the number of countries that meet the standard for vital registration and/or have undertaken a mortality study. It was suggested that this dialogue should be initiated in advance of the End TB Summit, which is being hosted by WHO on an annual basis (the first summit was held in November 2015) and brings together the 30 high TB burden countries as well as technical and financial partners, and concluded at that summit.

There was agreement that the major updates needed to the ToRs for TB epidemiological reviews are to include content related to the End TB Strategy's three high-level indicators and the top-ten indicators that have been defined for measuring progress in specific components of the Strategy,

[4] *TB impact measurement: policy and recommendations for how to assess the epidemiological burden of TB and the impact of TB control*. Geneva, World Health Organization, 2009 (Stop TB policy paper no. 2; WHO/HTM/TB/2009.416). Available at www.who.int/tb/publications/2009/impactmeasurementpolicy/

disaggregated analyses to assess inequalities and equity in line with the SDG agenda, and how to develop projections of TB disease burden.

Other suggestions related to the ToRs for TB epidemiological reviews were to:

- Add an Executive Summary as a deliverable;
- Give more emphasis to subnational analysis;
- Add a task related to debriefing of high-level officials;
- Include a checklist that sets out the data required to complete all elements of a TB epidemiological review;
- Add text to indicate the ideal timing of a TB epidemiological review.

To expand implementation of inventory studies to measure the under-reporting of detected TB cases, one recommendation was to systematically include these studies in plans developed as part of Challenge TB, if they are identified to be needed following completion of the TB surveillance checklist/TB epidemiological review. Improving communication to key stakeholders about the value of inventory studies, for example using a two-page fact sheet that could feature case studies that showcase how results can be used to inform programmatic action, was also recommended.

The major technical and financial partners involved in supporting TB prevention and care confirmed their interest in contributing to the priority areas of work.

Additional points to highlight that arose during plenary discussion were:

- The original priority areas of work that were proposed were based on experience with implementation of the TB surveillance checklist in 41 countries, regular country dialogue, workshops and lessons learned from the work of the Task Force since 2007.
- TB epidemiological reviews are for countries.
- It is essential to make sure that core TB surveillance indicators are not lost when TB-specific recording and reporting systems are integrated into wider health information systems. There is ongoing work to develop a case-based DHIS2 TB module that includes core TB surveillance indicators.
- Current lack of committed funding for TB epidemiological reviews is a major constraint/threat to progress in this area of work. It was indicated that the Global Fund may be able to address this issue, and there should be follow-up discussion between WHO and the Global Fund to explore options after the meeting.

3.3.2 Drug resistance surveillance: progress to date and emerging innovations

The Task Force agreed with the proposed vision for drug resistance surveillance.

3.4 Further details

Further details can be found in Background Documents 2a-c (available here: 2a, 2b, 2c) and Background Document 2g (available here), and in the two presentations (available here: p1, p2). Background Documents 2d-f were journal articles submitted for publication at the time of the meeting, and will be made available online following their publication.

4. Methods to Estimate TB Disease Burden

4.1 Overview of presentations

The main objective of this session of the meeting was to review and discuss methods for estimating the incidence of drug-resistant TB. The first part of the session was also used to present updates on work related to estimates of TB disease burden that had followed directly from the Task Force meeting held a year earlier, in March/April 2015.

4.1.1 Updates since the Task Force meeting on methods to estimate TB disease burden held 31 March–2 April

In advance of WHO's publication of estimates of TB disease burden 1990–2015 and associated assessment of whether 2015 global TB targets for reductions in TB incidence, prevalence and mortality were met, a Task Force meeting was held 31 March–2 April to discuss the methods to be used to produce these estimates. Ongoing or future work related to estimates of the burden of latent TB infection and development of a dynamic model to produce various types of TB disease burden estimates (including for drug-resistant TB and TB in children specifically) was also presented and discussed. Although not the main focus of the April 2016 Task Force meeting, the first part of the session on TB burden estimates was used to provide updates on work done since the March/April 2015 meeting.

The main update from WHO was that the methods used to produce the TB disease burden estimates published in the 2015 global TB report, and associated assessment of whether 2015 global TB targets were met, were based on the recommendations of the March/April 2015 Task Force meeting (see also Background Document 3a).

Rein Houben then presented new estimates of the burden of latent TB infection, which have been developed by a group led by the London School of Hygiene and Tropical Medicine with a paper submitted for publication. Pete Dodd (Sheffield University) then provided an update on the latest status of the modelling work he had first presented at the March/April 2015 Task Force meeting. In the past year, this had been extended to include an HIV/ART structure, and to produce estimates of the burden of drug-resistant TB in children; estimates of the latter have been submitted for publication. Further details regarding the work on these two topics are not provided in this report, pending review and publication of journal articles.

4.1.2 Estimates of the burden of drug-resistant TB

The presentation opened by highlighting that estimates of the disease burden caused by multidrug-resistant TB (MDR-TB) specifically are important for programmatic, planning and budgeting purposes. This is because compared with drug-susceptible TB, treatment of MDR-TB is much longer, more toxic, higher cost and has poorer outcomes (50% treatment success rate globally). It was also pointed out that the same methods can be used to estimate the burden of MDR-TB and the burden of rifampicin-resistant TB (RR-TB), and that the latter may be more relevant in future for two reasons: 1) the scale-up of Xpert and related increase in diagnosis of RR-TB (as opposed to MDR-TB); and 2) that the treatment recommended in WHO treatment guidelines is the same for RR-TB and MDR-TB.

The rest of the presentation then covered three topics:

1. A brief history of MDR-TB disease burden estimates published by WHO;
2. Current methods used by WHO to estimate the incidence of MDR-TB at global level, and their strengths and limitations related to production of country-level estimates; and
3. Alternative methods for estimating country-level MDR-TB incidence that could be considered in future.

Historically, five major indicators have been used to describe the burden for MDR-TB:

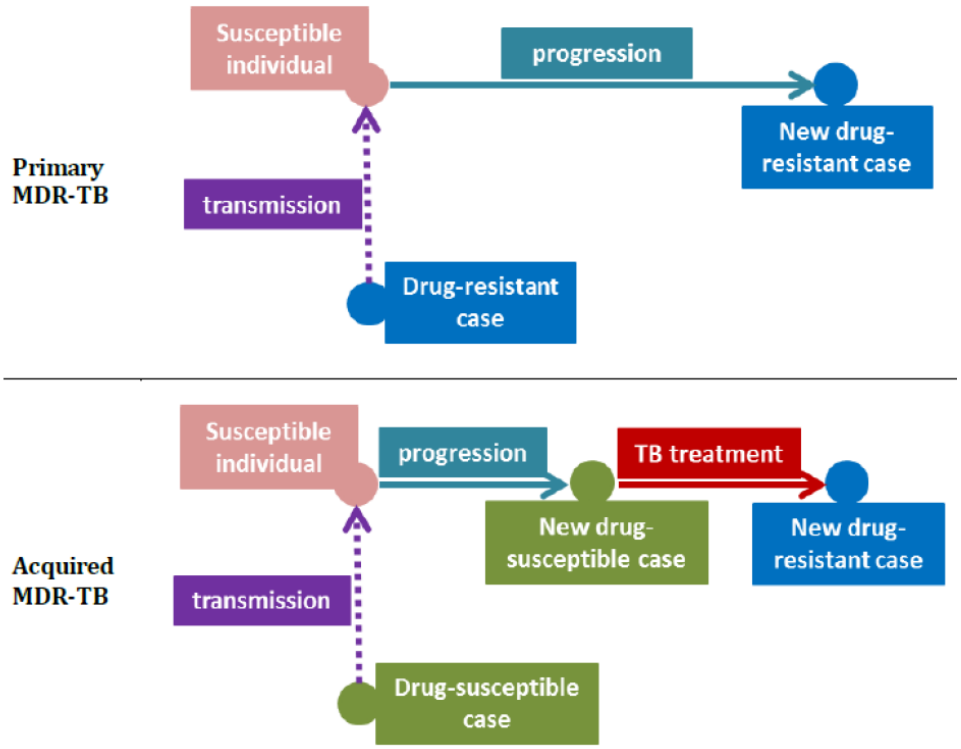
- The proportion of new and previously treated TB cases that have MDR-TB;

- The estimated number of MDR-TB cases among notified pulmonary TB cases;
- The incidence and prevalence of MDR-TB, and mortality caused by MDR-TB.

Country-level estimates of MDR-TB incidence were first published in a 2010 WHO global report on MDR-TB surveillance and response. Such estimates were not included in subsequent global TB reports (2011–2015) following concerns expressed by countries and some WHO Regional Offices that programmatic efforts were not being appropriately reflected, given that incidence includes cases that have not been detected as well as cases that could not be diagnosed with available tests. Reports in these years instead focused on comparisons of the number of MDR-TB cases detected and treated with estimates of the number of MDR-TB cases among notified cases of pulmonary TB. This approach was reinforced following a half-day discussion on indicators to be used for assessing progress in the response to MDR-TB at a global MDR-TB stakeholders meeting in October 2013. Key recommendations from that meeting were to use country-level estimates of the number of MDR among notified pulmonary TB cases for programmatic purposes (including planning, budgeting and monitoring), and a global level estimate of MDR-TB incidence for advocacy purposes. These recommendations were also endorsed by WHO's Strategic and Technical Advisory Group for TB (STAG-TB) in June 2014.

In the past two years, there has been growing and intensifying demand for WHO to publish country-specific estimates of the MDR-TB incidence, in particular from major donor agencies (including the Global Fund, which uses such estimates in a disease burden formula that is one input to country-specific funding allocations), the Stop TB Partnership secretariat and civil society. For this reason, WHO plans to publish country level estimates in the 2016 WHO global TB report, but a review of methods was needed first. The rest of the presentation thus focused on methods for producing estimates of the incidence of MDR-TB at country level.

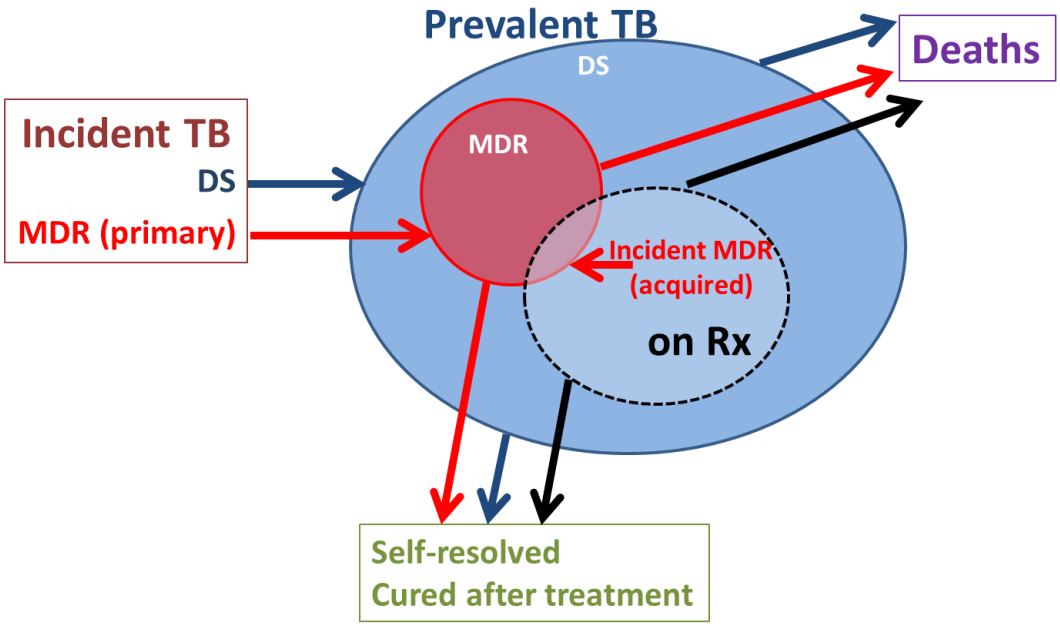
Figure 6: The two mechanisms that lead to MDR-TB



It was explained that MDR-TB incidence comprises a sub-group of incident TB previously infected with MDR strains (primary MDR-TB) and a sub-group of drug-susceptible TB cases who acquire MDR-TB through exposure to TB drugs (acquired MDR-TB). TB dynamics disaggregated by drug susceptibility status were illustrated diagrammatically (Figure 6, Figure 7). Incident TB cases that are drug susceptible to all first line anti-TB drugs (DS) or that have MDR-

TB (primary) feed into the pool of prevalent TB cases (DS and MDR respectively), of which a proportion is on first line treatment (Rx) at any given point in time. From the cases on treatment, an additional sub-group of incident MDR-TB (acquired) cases feeds into the pool of prevalent cases of MDR-TB. Prevalent cases die (with or without treatment), self-resolve without treatment, cure with treatment, or remain chronic prevalent cases.

Figure 7: An overview of TB dynamics disaggregated by drug susceptibility status DS=drug-susceptible to all first-line anti-TB drugs; MDR=multidrug-resistant; Rx=first-line treatment



Much of the data required for direct measurement of MDR-TB incidence are not available. Instead, key parameters need to be approximated using alternative data sources that provide indirect estimates (for example, that the level of MDR-TB among notified TB cases approximates the level of MDR-TB among incident TB cases). The two different methods for producing indirect estimates that have been used at the global level were then explained.

Method I approximates total MDR-TB incidence by first adding the estimated number of MDR-TB cases among three distinct types of TB case notifications: new all forms (about 58% of total incidence), relapse all forms (about 27% of total incidence), and all retreatments that are not relapses (about 15% of total incidence). All three estimates are then inflated upwards by the estimated amount of incident cases not identified by surveillance systems, for all forms of TB. Limitations of this method that were identified included: the non-representativeness of key parameters; some double-counting of cases (retreatments might have already been counted in the new or relapse categories); the assumption that data from drug resistance surveillance that typically does not cover the private sector applies to all incident TB cases; and the use of the same inflation factor for all three groups of cases (arguably, MDR-TB cases among those previously treated would be more likely to be captured by the surveillance system compared with new cases). Country-level estimates have the additional limitation that country-level values are not available for some parameters. Three ways to improve estimates based on this method were suggested: updating a previous literature review to inform values used for key parameters; refinements to the inflation factor used for retreatments that are not relapses, for example based on findings from inventory studies; and an approach to correct for the double-counting of cases.

Method II estimates MDR-TB incidence as the number of MDR-TB deaths divided by the MDR-TB case fatality rate (CFR), with the CFR calculated as the weighted average of the CFR among treated and untreated MDR-TB patients. The data gaps that affect this method were identified, and it was also emphasized that this method results in wider uncertainty intervals, thus affecting their value for programmatic purposes.

Two suggestions for alternative methods that could be explored in future (but not in time for the 2016 global TB report) were made. The first would estimate MDR-TB incidence in two groups only: primary and acquired. This would require additional data: in particular, cohort studies to measure the rate of acquisition of resistance during first-line treatment. The second was the development of a deterministic mathematical model to fit estimates of TB incidence and DRS data by country.

4.2 Questions for discussion in group work and plenary

Three questions were posed for discussion in group work and plenary. These were:

1. What methodological approach would you recommend for producing country-specific estimates of MDR-TB incidence to be published in WHO's 2016 global TB report?
2. For the two major approaches presented in the document for the estimation of MDR-TB incidence, are there any specific improvements that you would recommend that could be implemented by July 2016?
3. Are there other approaches (alternatives to methods I and II) that you think should be explored in the next 1–2 years?

4.3 Recommendations/outcomes from group work and plenary discussion

For questions 1 and 2, the general principle recommended was to not make a dramatic shift in methods for 2016. Two specific suggestions were made, which were:

1. Use Method I with the suggested refinements listed in the presentation, and in addition use DRS data to:
    - Cross-check the relative share of relapse/retreatments from notification data;
    - Update the estimated proportion of resistance among relapse cases used in Method I;
    - Test the hypothesis that levels of MDR-TB are higher in the private sector using data from public-private (PPM) sites.
2. Produce country-level estimates using Method II and compare the two sets of estimates.

For question 3, it was recommended that both alternative approaches merited further investigation. For the deterministic mathematical model specifically, it was agreed that this work would be commissioned to one of the Task Force members: Pete Dodd from the University of Sheffield.

Three other next steps were also agreed:

1. Advance communication from WHO to all Member States regarding the planned publication of country-specific estimates of MDR-TB incidence in the 2016 WHO global TB report is needed.
    - GTB/TME plans to send estimates to countries for review, with customised communication as appropriate, by the end of June 2016.
    - This communication will include a specific request for countries to advise GTB/TME if there are any additional data available to inform their estimates.
2. A small working group on the topic of MDR-TB disease burden estimates will be established. Task Force members who volunteered were: Draurio Barreira, Ted Cohen, Pete Dodd, Philippe Glaziou, Babis Sismanidis, Matteo Zignol and William Wells.
3. Investigate the possibility of developing a grading of estimates based on data quality, which could accompany published country estimates.

4.4 Further details

Further details can be found in Background Document 3b and in the presentation.

5. Prevalence Surveys 2009–2015 and post-2015

5.1 Overview of presentations

There were three presentations. The first was titled "National TB prevalence surveys 2009–2015"; the second "Main findings and recommendations from USAID-commissioned independent review of prevalence surveys"; and the third "Prevalence surveys post-2015: how, where?".

5.1.1 Prevalence surveys 2009–2015

The presentation had three main parts. The first provided an overview of progress made in implementing surveys 2009–2015 and documenting results and lessons learned, in the context that national TB prevalence surveys in 22 global focus countries was one of the Task Force's three strategic areas of work during the period 2007–2015. The second summarized the methods used in these surveys and ten key results and associated lessons learned. The third highlighted major challenges faced.

There was a "boom" in prevalence surveys from 2009 to 2015 (Figure 8), compared with typically one or no survey per year in previous years (back to 1990). By the end of 2015, 17 of the 22 global focus countries had completed a survey or were due to do so shortly (Figure 9).[5] An additional 6 countries had completed a survey and three global focus countries were due to start a survey in 2016. Only two of the original 22 global focus countries had not implemented a survey and had no plan to do so (Mali and Sierra Leone).

Figure 8: Prevalence surveys implemented 1990–2015. Asian countries in green, African countries in blue.

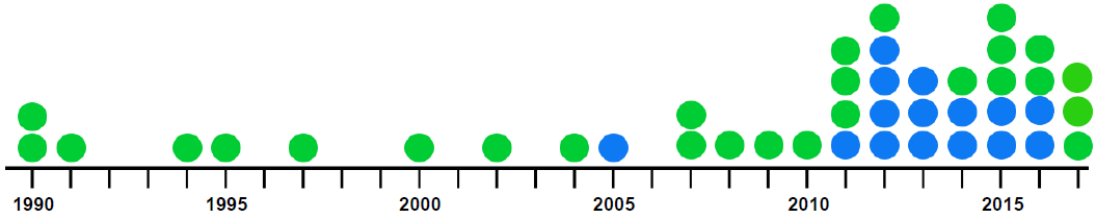
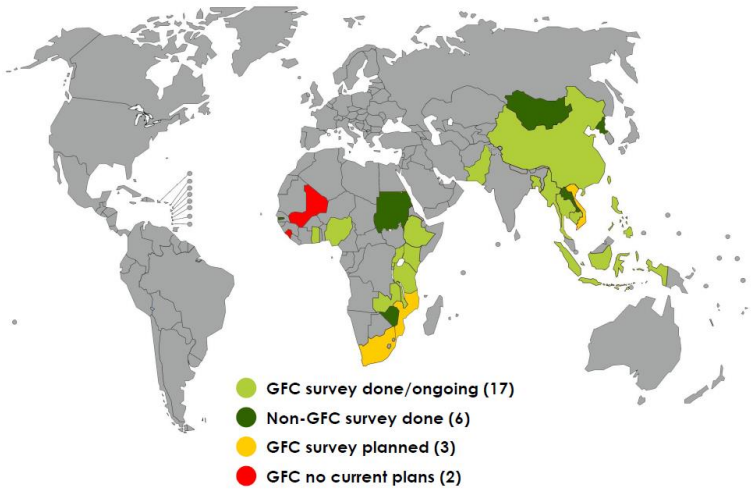


Figure 9: Progress in implementation of national TB prevalence surveys in global focus countries (GFC) and other countries (non-GFC), 2009–2015



[5] In the order in which the surveys were done, these countries are: Myanmar (2009-2010); China (2010); Cambodia, Ethiopia and Pakistan (2011); Nigeria, Rwanda, Tanzania and Thailand (2012); Malawi, Ghana (2013); Indonesia (2013-2014); Zambia (2014); Uganda (2015); Bangladesh (due to be completed in 2016); Kenya (due to be completed in 2016); and the Philippines (2016, following three previous surveys, the last in 2007).

The publications (reports and journal articles) that have been published from the surveys that had been completed by the end of 2015, and progress made in establishing a data repository for prevalence survey data and documents (e.g. protocols, standard operating procedures, reports, journal articles) and in developing a comprehensive book that will showcase the results and lesson learned from surveys 2009–2015, were then described and explained.

In terms of methods, all surveys implemented 2009–2015 used consistent screening and diagnostic algorithms, and were guided by the recommendations in the WHO TB prevalence survey handbook (2nd edition, 2011 "Lime Book"). The key role of many technical partners and country-country collaboration in facilitating and ensuring the quality of surveys through direct technical assistance and sharing of experience and expertise (for example, via workshops, study tours, training opportunities and mid-survey reviews) was highlighted.

Key results were presented for ten topics, as follows:

1. TB prevalence: smear-positive pulmonary TB and bacteriologically confirmed pulmonary TB, in adults. Considerable variation among countries is evident, with the highest prevalence rates in Asia and high proportions of bacteriologically confirmed cases that were sputum smear-negative in all countries.
2. Comparison of estimates of TB prevalence (all forms, all ages) based on survey results with pre-survey estimates published by WHO. Estimates based on survey results have almost always been more precise (narrower uncertainty intervals), and are often within the uncertainty range of pre-survey estimates. Exceptions were Lao PDR, Indonesia, Malawi and Ghana (higher estimates beyond the upper limit of the previous uncertainty interval) and Gambia (lower estimate below the lower limit of the previous uncertainty interval).
3. Trends in TB prevalence in the four countries where repeat surveys have been done. Surveys in China, Cambodia, the Philippines and Republic of Korea show that TB prevalence (per 100,000 population) can be halved in a decade.
4. Distribution of TB prevalence by sex. TB prevalence has been found to be systematically higher among men, especially in Asian countries.
5. Distribution of TB prevalence by age. An ageing epidemic (in terms of prevalence per 100,000 population) is evident in Asian countries, with a more mixed picture in African countries. In some countries, the absolute number of cases is also highest in older age groups (for example, Cambodia, China and Thailand).
6. Reporting and detection gaps illustrated by prevalence surveys. When the prevalence of smear-positive TB (P) is compared with notifications of smear-positive TB (N), the P:N ratio is systematically higher for men and for HIV-negative people (compared with people living with HIV). Some countries (for example, Nigeria) have strikingly high P:N ratios.
7. The proportion of prevalent cases that met symptom screening criteria. Typically, 30–50% of cases did not meet the symptom screening criteria, both for those with smear-positive and bacteriologically-confirmed TB. These figures were up to 70–80% in a few countries (for example, Cambodia, China and Thailand).
8. Health-care seeking behaviour among bacteriologically confirmed TB cases that reported symptoms meeting screening criteria. Many symptomatic participants found to have bacteriologically confirmed TB during surveys (but who had not previously been diagnosed) had sought care prior to the survey.
9. Place of treatment, for those on TB treatment at the time of the survey. In several countries, high proportions of people on TB treatment were receiving care in the private or nongovernmental sectors, in both African and Asian countries (with the highest proportion being over 40% in Indonesia). Very low proportions were observed in three countries: China, Sudan and Zambia.
10. The performance of sputum-smear microscopy. A high proportion of survey participants that were eligible for sputum examination and had a sputum smear-positive result were found unlikely to have TB (based on a culture or molecular test).

The main implications of these results were the summarized as follows:

1. Surveys can demonstrate:
    a. The true burden (accurate) of TB disease;
    b. Reductions in disease burden with repeat surveys, and in turn provide evidence about intervention impact and service access;
    c. That some countries can do better with available interventions;
    d. Transmission dynamics (age and sex).
2. Survey results provide a platform to revisit policy:
    a. Reliance on smear microscopy in the context of active case finding needs to be reassessed;
    b. Screening and diagnostic algorithms used in routine clinical care and active case finding, including the role of chest X-ray, need to be revisited.

The major challenges faced in surveys implemented 2009–2015 were highlighted. These were:

1. More than 50% of surveys had problems with culture examinations. Low rates of culture confirmation of smear-positive TB cases (<85%) were observed in 11 of the 19 surveys, and it has proved difficult to standardise culture techniques between and within countries. A transition to molecular tests (already used alongside smear microscopy and culture in 8 surveys) in future surveys.
2. Delays in the time taken to complete survey preparations and to disseminate results following the completion of field operations. The median time to prepare a survey was three years (ranging from 8 months to 6.5 years). Delays were mostly due to the time taken to procure X-ray equipment and/or strengthen laboratory capacity and/or identify a suitable implementing agency.
3. Data management. Many countries faced challenges with data management, and in five of these there were major problems. Problems included transcription errors, poor archiving of documents and chest X-rays, and non-relational datasets that did not match.

5.1.2 Main findings and recommendations from USAID-commissioned independent review of prevalence surveys

The presentation started with an overarching statement that the independent assessment had been extremely positive about the value of national TB prevalence surveys and that the achievements in implementing these surveys in recent years were very impressive.

The independent assessment was a collaboration between USAID and the Bill & Melinda Gates Foundation, undertaken by a multidisciplinary team of consultants with a focus on surveys conducted since 2009 and including three country visits (to Cambodia, Ethiopia and Ghana).

Major recommendations from the independent assessment team were highlighted, acknowledging that some of these were already reflected in recent surveys or were being actively considered. The nine major recommendations were:

1. Surveys should be simplified through greater standardization, including incorporation of new technical developments such as Xpert MTB/RIF. It was recognized that bar codes, electronic data collection and management, and use of Xpert MTB/RIF had already been used in several surveys, while revised screening algorithms, the role of computer-assisted diagnosis and use of Xpert Ultra and the Omni platform were given as examples of topics meriting further discussion.
2. The Task Force should lead efforts to obtain external input from groups conducting other large surveys to explore innovations in sampling and analysis that could improve quality and efficiency. Specific examples were to include a laboratory expert within the prevalence survey subgroup of the Task Force,[6] that use of computer-assisted diagnosis for TB may benefit from wider work related to computer-assisted diagnosis of other lung

[6] Laboratory experts were regularly included in Task Force work on prevalence surveys, starting with the development of the laboratory chapter in the Lime Book.

conditions; and that experts in biomarker collection and analysis for population-based surveys might have useful insights.

3. Prevalence surveys should adhere to Good Clinical Practice (GCP). This includes establishment of a body to provide independent oversight, for example using an entity such as a Data Safety and Monitoring Board (DSMB). Such an entity can help to avoid real or perceived conflicts of interest among those providing technical assistance.
4. TB prevalence survey data need to be used more broadly to provide a better understanding of TB epidemiology and to strengthen national and international TB control efforts. Examples given were a need to support national TB programmes to act on findings, including revision of screening algorithms, reallocation of resources, investments in laboratory infrastructure and overall improvements in the way in which results are communicated.
5. Opportunities for synergies with HIV and non-communicable disease programmes should be sought to take advantage of the quality sampling of national TB prevalence surveys and to provide political and financial support for them. It was noted that several surveys had included questions on smoking behaviour and that Botswana was considering conducting a joint TB and HIV prevalence survey.
6. Development and execution of a detailed communication strategy, including plans for report writing and wide dissemination and identification of local advocates should be built into all surveys, with funds used to facilitate more rapid generation of reports and greater dissemination of findings to a broader audience. This was highlighted to be a "high priority" topic for action.
7. Funding for surveys must be closely coordinated to avoid delays, with the timing of surveys better synchronized with the Global Fund application process. It was commented that this can be difficult to do, but that best practices and lessons learned could be identified and featured in the next edition of the Lime Book.
8. Serial surveys may provide highly useful data to monitor trends and evaluation programme activities, but guidelines should be developed outlining under what conditions and with what frequency they should be considered. It was recognized that the Task Force has already been clear on the timing of repeat surveys but it was indicated that there was less clarity about how to account for different methodologies between one survey and the next.[7]
9. Continued investments should be made in surveillance, including exploration of the value of sentinel surveillance as an alternative to periodic surveys. Ongoing investments in strengthening surveillance were stated to be a priority, with use of the WHO TB surveillance checklist of standards and benchmarks (see also section 3) to support this identified as critical.

5.1.3 Prevalence surveys post-2015: how, where?

The presentation started with a reminder about the major challenges faced in surveys implemented 2009–2015, based on a systematic assessment conducted by WHO (Background document 4d). The tabular summary of the results of this assessment, included in Background document 4e, is shown in Table 2. As already highlighted in the first presentation (see section 5.1.1), the three major challenges were 1) problems with culture (which underperformed in 58% of surveys), 2) substandard data management in some surveys, and 3) suboptimal use of results, with the time to publish a report taking more than one year after the completion of field operations in almost half of all surveys and with about one fifth of countries experiencing delays in results being accepted by national authorities.

Four major changes to survey methods (the "how") were proposed for discussion. These were:

1. Use of Xpert MTB/RIF instead of sputum smear microscopy and culture, with associated analytical adjustments to account for its differing specificity and sensitivity compared

[7] There is some guidance on this is the chapter on repeat surveys in the Lime Book. This chapter could also be expanded in future based on experience since the book was published in 2011.

with culture. Rapid tests are easier to implement than culture, and in the near future it is possible that the new Xpert Ultra cartridge will have performance comparable to culture.

2. Strengthened governance/oversight mechanisms. Things that go beyond practices in recent surveys include systematic training on good clinical practices (GCP), highly standardized and systematic monitoring by external monitors with regular reporting to an independent data monitoring committee established by the survey sponsor(s), and an onsite survey monitor.
3. Adherence to Good Clinical Data Management Practices. It was recognized that many recommended practices have already been adhered to in surveys. Good practices that were highlighted included regular validation of the database, an audit trail for any corrections, maintaining copies of records in source documents and a record repository.
4. Increased resources for reporting and use of results. Past experience shows that higher budgets and more staff time are needed for reporting production, and that possible results and their implications need to be anticipated and discussed with national authorities in advance, to help ensure confidence that results are reliable and to facilitate early acceptance and use of results. Appropriate and timely engagement with the media are also important.

Table 2. Major challenges observed in national prevalence surveys completed 2009–2015

Challenges	Number of surveys affected*
Preparations	
Time taken to complete survey preparations (i.e. ≥3 years from decision to implement to start of field operations	14/19
Delays due to chest X-ray procurement	7/19
Delays due to upgrading laboratory capacity	3/18
Field and central operations	
Low participation rates (<80%)	5/19
Delays in case management	7/16
Laboratory	
Low culture confirmation among smear-positive study cases (<85%)	11/19
Failure of biosafety cabinet	1/19
Laboratory protocol violations	6/19
Data management	
Inadequate data management plan	6/19
Major data management problems during field operations that were not resolved during field operations	5/19
Considerable time taken to clean data (1+ year)	5/19
Dissemination of results	
Long delays (>1 year) before survey results accepted by public health authorities	4/19
Long delays in producing the final report of the survey (1+ year)	8/18

* The total number of countries in the denominator varies because information was not available for all surveys at the time this document was prepared.

The analytical methods that would be needed to adjust survey results based on Xpert MTB/RIF (or a similar rapid test) were explained, for two major survey designs. The first survey design was screening based on symptoms and chest X-ray (as in recent surveys) followed by Xpert MTB/RIF testing for all those screening positive. The second survey design was as for the first survey design, plus use of a different diagnostic test to confirm or rule out TB disease (in addition to use of Xpert MTB/RIF). A possible third design – Xpert MTB/RIF testing for all survey participants, with no screening – was also noted as potentially relevant to countries in which screening using chest X-ray is difficult or impossible for logistic reasons (e.g. difficulties in transporting X-ray equipment to many clusters).

In terms of where national TB prevalence surveys are worth considering post-2015, two groups of countries and associated epidemiological criteria were suggested (Table 3).

Table 3. Suggested epidemiological criteria for assessing whether a country could consider implementing a prevalence survey post-2015, for two major groups of countries

Criteria	Explanations
Group 1 - Countries that conducted a national prevalence survey, 2007-2015* (Figure 10)	
1. Estimated prevalence of bacteriologically confirmed TB ≥2.5 per 1000 population aged ≥15 years during the previous survey: *and* 2. >5 years since the last survey.*	• Sample size small enough (less than 70,000 individuals) to make surveys feasible in terms of cost and logistics; • Time between surveys sufficient to allow a statistically meaningful comparison of prevalence.
Group 2 - Countries that did not implement a national prevalence survey 2007–2015 (Figure 11)	
1. Estimated TB incidence** ≥1.5 per 1000 population/year (all forms, all ages); *and* 2. No nationwide vital registration system with standard coding of causes of deaths; *and* 3. Infant mortality rate > 10/1000 live births.	• Sample size** small enough (less than 70,000 individuals) to make surveys feasible in terms of cost and logistics, accounting for added uncertainty due to the use of rapid molecular tests with performance that may be inferior to culture; • No reliable direct measurement of TB disease burden; • Indirect indicator of low access to quality health services as defined in the Standards and Benchmarks for TB surveillance and vital registration.

* Surveys conducted prior to 2000 may lack comparability with surveys implemented according to the screening and diagnostic algorithm recommended in the *Lime Book*. A WHO workshop held in Cambodia in 2012 recommended a period of 7–10 years between two surveys. Designs 1–3 of a planned survey may be adapted to include microscopic examination of smears performed in laboratory confirmed cases to allow comparability of results with the previous survey.
** Country-specific prevalence estimates may not be published by WHO post-2015, except for countries with prevalence survey results. For sample size determinations, prevalence in the age group ≥15 years may be predicted from incidence.

The countries in each group are shown in Figure 10 and Figure 11.

Figure 10: Countries that conducted a national prevalence survey, 2007–2015 (n=24)

In Group 1, it was recognised that China and Thailand are unlikely to conduct another national survey given the relatively low TB burden in terms of rates, the possibility of direct measurement of trends from surveillance data and the expected low participation among urban/mobile populations. However, a subnational survey could be considered, for example in Western China

or North Eastern Thailand. A repeat survey may also not be appropriate in Gambia and Rwanda, due to their low TB disease burden.

Figure 11: Countries that did not conduct a national prevalence survey 2007–2015 that met the proposed Group 2 criteria in 2015 (n=33)

For any country that meets the epidemiological criteria shown in Table 3, it was stressed that survey feasibility must also be carefully assessed. As set out in the Lime Book, the following prerequisites must be in place for a survey to be feasible:

1. There is strong commitment and leadership from the NTP, Ministry of Health and a core group of professionals;
2. A suitable institute, organization or agency to lead and manage the survey can be identified;
3. There is adequate laboratory capacity;
4. X-ray equipment can comply with the regulations of the national regulatory authority;
5. Reliable and timely procurement and logistics is possible;
6. Funding is available;
7. Security in the field for survey teams and participants can be assured;
8. Data management can be done according to recommended standards;
9. Community participation is likely to be sufficiently high, including in urban areas;
10. External support and technical assistance are available if needed. This is likely to be especially important for countries implementing a survey for the first time.

5.2 Questions for discussion in group work and plenary

Five questions were posed for discussion in group work and plenary. These were:

1. Do you recommend that national prevalence surveys should be conducted post-2015?

If yes:

2. Do you agree with the suggested updates to survey methods, in particular:
    - Use of Xpert® MTB/RIF (hereafter Xpert) instead of smear microscopy and culture, with adjustments to survey results until Xpert has equivalent performance to culture;
    - Strengthening of overall governance/oversight mechanisms including more formal arrangements for survey monitoring and related actions by implementers and sponsors;
    - Ensuring Good Clinical Data Management Practices, including quality control at each stage of data handling to ensure that all data are reliable and have been processed correctly;
    - Investment of more resources in the work required once results are finalised, especially to ensure the timely production of survey reports and effective communication of findings and their implications.
3. Do you have any suggestions for other improvements to survey methods?

4. Do you agree with the proposed criteria for identifying which countries should consider a national survey post-2015, or would you propose modifications to these criteria?
5. Should there be any country prioritisation within groups 1 and 2, from a regional and/or global perspective?

5.3 Recommendations/outcomes from group work and plenary discussion

There was strong agreement about the value of national TB prevalence surveys and the substantial achievements in implementing such surveys 2009–2015 were applauded. It was agreed that surveys would continue to be needed between 2016 and 2020.

In terms of proposed updates to survey methods, there was agreement replacing sputum smear microscopy and culture with Xpert MTB/RIF (or equivalent or better molecular test), with the following caveats:

- This transition should await results from ongoing surveys in Bangladesh, Kenya and the Philippines, which are using Xpert MTB/RIF and culture in parallel. Surveys implemented in 2016 or 2017 should use both culture and Xpert MTB/RIF, pending results from evaluation of the new Xpert Ultra cartridge (scheduled for 2017);
- Research may be needed to assess the specificity and sensitivity of Xpert (MTB/RIF or Ultra) in the general population, since this may be different compared with clinical settings given the on-average earlier stage of disease. If Xpert Ultra is found to have equivalent performance to culture in evaluations scheduled for 2017, such research may not be necessary.
- Surveys should use Xpert Ultra instead of Xpert MTB/RIF if this is found to have equivalent or superior performance. Evidence on the former is expected by the end of 2016.
- In countries where the recommended screening algorithm based on chest X-ray and symptoms is not feasible due to logistic challenges with transportation of X-ray equipment to many clusters, the third design (see section 5.1.3) based on screening of all survey participants using Xpert could be the best option. The main examples among countries actively considering a national TB prevalence survey are DR Congo and Nepal.

There was agreement on strengthening overall governance/oversight mechanisms including more formal arrangements for survey monitoring and related actions by implementers and sponsors, and with use of Good Clinical Data Management practices. Two of the five groups expressed some concern that GCP-type practices could impede surveys if they were too demanding, while a third group was surprised that sponsors had not previously insisted upon such practices (in particular an independent data monitoring committee and an on-site monitor) given the amount of resources invested. It was noted that USAID had already commissioned some work to provide suggestions about how GCP could be implemented in the context of national prevalence surveys.

There was agreement that funding for report production and associated efforts to communicate and disseminate results should be included in the survey budget from the outset. It was also suggested that a standard template could help with report writing and that a standard database that would generate standard sets of figures and tables could also help.

There were no other major suggestions for other improvements to survey methods, although it was noted that computer-assisted diagnosis was worth reviewing and that HIV testing should be considered in all surveys (HIV testing and/or reporting had been done in six African surveys to date).

There was general agreement with the epidemiological criteria proposed for identifying countries where a national TB prevalence survey is worth considering. However, the following points or questions were raised for further consideration:

- Group 1:
    - Five years is too short an interval between surveys.

- Is a rate of 250 per 100,000 population too high? (This excludes China, Gambia, Rwanda, Sudan and Thailand).

- Group 2:
  - Should a cut-off in terms of the absolute number of cases be used? For reference, this information has been added to the original table included in Background document 4e in Table 4 below.
  - The indicator used for access to health care is indirect.

In terms of country prioritization:

- It was observed that there was a risk that countries listed in each group might think that they "need to do a survey", while the language used in subsequent guidance material should also not discourage countries from considering a survey.
- Countries need to meet the perquisites for conducting a survey listed in the Lime Book in addition to epidemiological criteria.
- From a global perspective, it was highlighted that four countries stand out in terms of their share of the global TB disease burden: India (22%), South Africa (4.7%), DR Congo (2.7%) and Mozambique (1.6%). All of these countries already have plans to implement a survey. Other countries each account for <1% of the global TB incidence.

Table 4: Countries that did not conduct a national prevalence survey 2007–2015 but that met the proposed Group 2 criteria in 2014, and their contribution to global TB incidence.

Country	Proportion (%) of estimated global incidence (2014)	Absolute number (in 1000s) (range) of incident TB cases (2014)	Country	Proportion (%) of estimated global incidence (2014)	Absolute number (in 1000s) (range) of incident TB cases (2014)
Afghanistan	0.6	60 (53-67)	Kiribati	<0.1	0.6 (0.5-0.7)
Angola	0.9	90 (58-130)	Lesotho	0.2	18 (13-24)
Bhutan	0.0	1.3 (1.1-1.4)	Liberia	0.1	14 (12-15)
Botswana	0.1	8.5 (8.0-9.1)	Madagascar	0.6	55 (49-62)
Cameroon	0.5	50 (44-56)	Marshall Islands	<0.1	0.2 (0.1-0.2)
Central African Republic	0.2	18 (16-20)	Micronesia	<0.1	0.2 (0.1-0.4)
Chad	0.2	22 (19-24)	**Mozambique**	1.6	150 (120-180)
Cote d'Ivoire	0.4	36 (33-40)	Namibia	0.1	13 (12-15)
Congo	0.2	17 (15-19)	Nepal	0.5	44 (39-50)
DR Congo	2.5	240 (220-270)	Papua New Guinea	0.3	31 (23-41)
Djibouti	0.1	5.4 (4.8-6.1)	Sierra Leone	0.2	20 (15-25)
Equatorial Guinea	<0.1	1.3 (1.2-1.5)	Somalia	0.3	29 (25-32)
Gabon	0.1	7.5 (6.6-8.4)	**South Africa**	4.7	450 (400-510)
Guinea	0.2	22 (19-24)	Swaziland	0.1	9.3 (6.8-12)
Guinea-Bissau	0.1	6.6 (4.7-8.9)	Timor-Leste	0.1	5.8 (4.8-6.9)
Haiti	0.2	21 (19-24)	Tuvalu	<0.1	<0.1 (<0.1-<0.1)
India	22.4	2200 (2000-2300)			

5.4 Further details

Further details can be found in Background Documents 4a-b (available here: 4a, 4b) and Background Documents 4e-f (available here: 4e, 4f), and in the three presentations (available here: p1, p2, p3). Background Document 4c, which provided the draft abstract, figures and tables from a paper summarizing the results and lessons learned from prevalence surveys in Africa 2010–2015, will be made available online following its publication. Background Document 4d, which summarized the main challenges faced in surveys implemented 2009–2015, will be made available online following further review and discussion with country survey teams.

6. Two New Topics for consideration as part of the Task Force's Mandate and Strategic Areas of Work 2016–2020

6.1 Overview of presentations

There were two presentations. The first was titled "TB disease burden and intervention impact: TIME dynamic model"; the second covered the topic "Measuring patient costs to monitor progress towards the target to eliminate catastrophic costs and help design social protection and universal health coverage".

6.1.1 TB disease burden and intervention impact TIME dynamic model

The presentation was in three main parts. The first gave an overview of the TIME model, including its rationale and content; the second explained its use at country level to date; and the third discussed next steps.

"TIME Impact" is an epidemiological transmission model that has been developed by Avenir Health and the London School of Hygiene and Tropical Medicine, with funding from USAID, the Bill & Melinda Gates Foundation and the Global Fund. It can be used to help understand the TB epidemic in a country, to explore the future trajectory of the epidemic and intervention impact under alternative scenarios and to use these analyses to inform the development of national strategic plans and funding proposals (including "investment cases"). There has been growing and intensifying demand for projections of TB disease burden and intervention impact, and associated "investment cases", especially in the context of Global Fund concept notes (see also section 2).

Model parameters include those related to the natural history of TB, the HIV epidemic and provision of antiretroviral treatment (ART), drug resistance, treatment history and age. TIME Impact can be used alongside related modules in the OneHealth tool (TIME Estimates, which is based on estimates published by WHO) and other modules (e.g. TIME Economics) that are under development.

To date, there are two countries that have undertaken considerable work with TIME Impact: Ghana and South Africa (to help build a joint TB and HIV investment case, including at provincial level). Four additional countries have benefited from some training in how to use TIME Impact: Bangladesh, Sudan, Viet Nam and Zambia, in all cases related to the development of Global Fund concept notes and/or to inform the reprogramming of grants, and have used it to varying extents. Partners of Avenir Health have provided some training in Latin America. A regional workshop to provide training for TB policy makers from Indonesia, Myanmar and Viet Nam was held in early 2016.

The main challenges faced to date have been identifying the right individuals to train and participate in work related to the development of model scenarios and the application of results, sustaining interactions between those with expertise in TIME Impact and those using it at country level, obtaining the data required to inform the model and potential misspecification of the model and associated misuse of results.

In terms of next steps, in particular related to the work of the Task Force, it was highlighted that TIME Impact is relevant to development of projections at country level, including development of related capacity, guidance and tools (strategic area of work 5), and that it can also be used within TB epidemiological reviews.

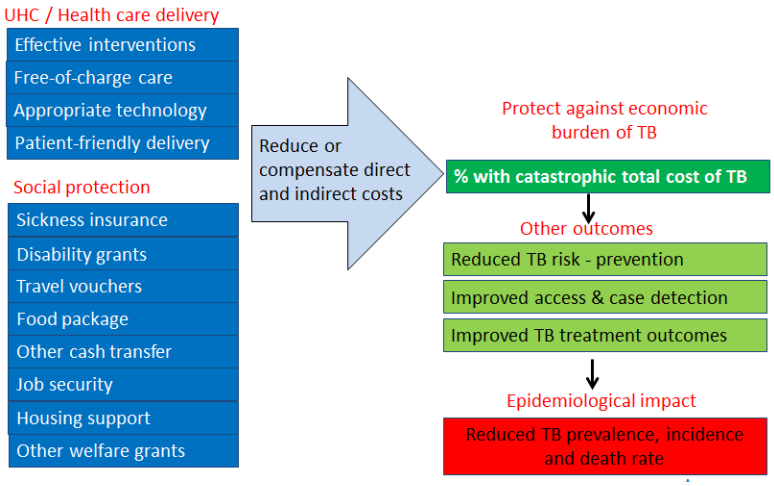
6.1.2 Measuring patient costs to monitor progress towards the target to eliminate catastrophic costs and help design social protection and Universal Health Coverage (UHC)

The presentation covered five main topics:

1. The rationale for surveys to measure the costs faced by TB patients and their household and related assessment of whether costs are catastrophic, and associated definition of terms;
2. The generic protocol and associated questionnaire that have been developed for cost surveys and assessment of whether costs are catastrophic;
3. Progress to date in implementing surveys;
4. Development of a handbook to provide guidance on the design, implementation, analysis and reporting of cost surveys;
5. Expanding the group of experts contributing to the planning, design, implementation, analysis and reporting of surveys.

The percentage of TB patients and their households that experience catastrophic costs as a result of TB disease is one of the three high-level, overarching indicators of the End TB Strategy, with a 2020 milestone of zero (section 2). This target is in line with the broader goal (and SDG target) of achieving UHC. Achievement of the 2020 milestone requires not only access to effective TB diagnosis and treatment that is free at the point of access, but also social protection to protect people from income losses and non-medical expenditures (hence the emphasis on UHC and social protection in the End TB Strategy). This is illustrated in Figure 12.

Figure 12: The relationship between UHC, social protection and costs faced by TB patients and their households



Two working definitions of catastrophic costs were explained.

Definition 1: Total costs (indirect and direct combined) faced by TB patients and their households exceed a given threshold (e.g. 20%) of the household's income.

Definition 2: The percentage of TB patients and their households that experience dissaving (i.e. taking out a loan, or selling property or livestock to face health costs associated with the TB disease).

The second definition is less demanding from a data perspective, but requires further testing to confirm whether or not it is a good proxy measure for whether TB patients and their households experience catastrophic costs.

The distinction between "catastrophic health expenditures" (an indicator used by the World Bank and WHO) and "catastrophic costs due to TB" (the End TB Strategy indicator approved by the World Health Assembly in May 2014) was explained. "Catastrophic health expenditures" are defined as out-of-pocket payments for health care (for all conditions) that exceed a given fraction

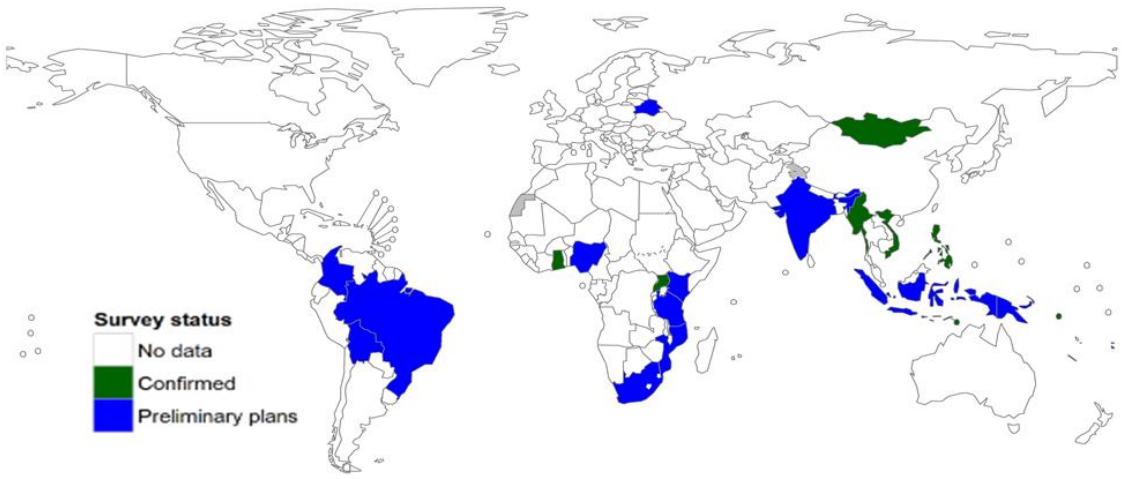
of a household's total consumption (or non-food). This indicator can be measured in general household surveys that include collection of data on payments for health care by all household members. "Catastrophic costs due to TB" is defined as the total amount of TB-related direct medical, direct nonmedical and indirect costs as a result of TB disease exceeding a fraction of annual household income. It can be assessed through facility-based surveys, with findings illustrating the extent to which UHC and social protection are in place and informing policy and programmatic action to close identified gaps.

A generic protocol to guide the design, implementation and analysis of cost surveys has been developed. This builds on the patient cost tool previously developed as part of the USAID-supported TB Coalition for Technical Assistance (TBCTA). A Task Force was established in 2014 to adapt and update this tool for measurement of the End TB Strategy indicator. The methods set out in the protocol are designed to achieve four objectives:

1. Document costs and identify the main cost drivers, to inform policy;
2. Monitor progress towards the 2020 milestone that no TB patients and their households face catastrophic costs as a result of TB disease;
3. Determine the correlation between facing costs above different thresholds of annual household income and dissaving, in order to assess if the measure of dissaving can be used as a proxy for whether catastrophic costs are experienced;
4. Determine the association between cost and treatment outcome (using routine cohort data).

Surveys are cross-sectional and facility-based, and require a sample of 500–1000 TB patients that have been on treatment for at least 2 weeks. Facilities are selected using random cluster probability proportional to size sampling; a facility's chance of being selected is proportional to the number of patients treated at that facility. Within each facility, patients are asked to take part in the survey consecutively. Data collected at one point in time are then used to estimate costs (direct and indirect) during the time periods that cannot be captured at the time of the survey. The expected time required for data collection is 2–3 months, with a total of 5–6 months from initial planning to finalization of results. The survey questionnaire being used in the first round of surveys (field-testing version) has 130 questions and takes 40–60 minutes per patient to complete; an e-survey tool has been developed to facilitate data entry and subsequent analysis. In at least the first round of surveys, two approaches will be used to estimate the costs associated with time losses (human capital and output-based methods).

Figure 13: Countries with definite or provisional plans to implement a survey of costs faced by TB patients and their households, in April 2016



An outline of the planned handbook on survey methods (to be developed later in 2016 and early 2017) was shown and other major next steps were highlighted. These were:

- Field testing of the generic protocol and questionnaire in 2016;
- Revision/finalisation of the generic protocol (late 2016 – early 2017);
- First results from a series of surveys will be featured in the 2017 global TB report.

The overall aim is that a survey should have been done in all 30 high TB burden countries before 2020. The status of confirmed or provisional plans in April 2016 to implement a survey is shown in Figure 13.

The presentation concluded with a call for members of the Global Task Force on TB Impact Measurement to become involved in survey preparation, implementation, and analysis, use and dissemination of findings.

6.2 Discussion in plenary

6.2.1 TB disease burden & intervention impact: TIME dynamic model

The main points made in plenary discussion were:

- Effective use of TIME Impact is dependent on input data. Improving the data available to feed the model is essential. The minimum data inputs that are required are provided at http://tbmodelling.lshtm.ac.uk/time/.
- TIME Impact is one model, but others are also available or under development. The TB Modelling and Analysis Consortium (TB-MAC), which brings together various modelling groups, is not promoting one specific tool/model.
- TIME Impact is not suitable for use in low-incidence countries because it is based on the assumption of homogenous mixing, whereas in low TB burden countries the epidemic is concentrated in specific areas and/or populations (high risk groups).

6.2.2 Measuring patient costs to monitor progress towards the target to eliminate catastrophic costs and help design social protection and Universal Health Coverage (UHC)

Several questions were asked about the methodological aspects of cost surveys. It was explained that these are questions that have also been extensively discussed in the task force that was established specifically to work on the development of a generic protocol and questionnaire. The various issues raised are well recognized and methods will be updated based on experience in the first round of surveys. There were expressions of interest to contribute to the proposed handbook, and clear interest in embarking on such surveys in the European Region was expressed (for example, Belarus in 2016).

6.3 Recommendations/outcomes from plenary discussion

The main outcomes were that work on projections of TB disease burden will be part of the Task Force's fifth strategic area of work (see section 2). Surveys of costs faced by TB patients and their households will be part of the Task Force's third strategic area of work (see also section 2). Staff from WHO's Global TB Programme will follow up with people who expressed interest in contributing to review of survey protocols and to the development of a handbook on measurement of costs faced by TB patients and their households.

6.4 Further details

Further details can be found in Background Documents 5a-g (available here: 5a, 5b, 5c, 5d, 5e, 5f, 5g) and in the two presentations (available here: p1, p2). The TIME model is available at http://tbmodelling.lshtm.ac.uk/time/. Further information on cost surveys can also be requested from the Global TB Programme at tbdata@who.int.

7. Appendices

7.1 Final meeting agenda

DAY 1: Tuesday 19 April 2016

Time	Topic	Presenter
08.30 – 09:00	Registration	
09:00 – 09:15	Welcome and introduction of participants Declaration of conflict of interest	Jaap Broekmans (Chair)
09:15 – 09:30	Meeting objectives and expected outcomes Review and adoption of agenda	Katherine Floyd Jaap Broekmans
Objective 1. Task Force mandate and strategic areas of work, 2016–2020		
09:30 – 10:00	**Presentation**: The WHO Global Task Force on TB Impact Measurement: proposed mandate and strategic areas of work 2016–2020 **(Background document #1)**	Katherine Floyd
10:00 – 10.45	**Discussion**	All in plenary
10:45 – 11:00 Coffee break		
Objective 2. Strengthening TB surveillance: progress to date, discussion of topics that are currently high priority		
11:00 – 12:00	**Presentation including Q&A:** Strengthening surveillance towards the ultimate goal of direct measurement of TB cases and deaths from notification and vital registration data: Task Force work to date, proposed priority areas of work 2016–2020 and questions for discussion **(Background document #2a)** Including specific reference to: 1) regional analysis workshops using full range of resources developed by the Task Force **(Background document #2b)** 2) epidemiological reviews – draft implementation guide and suggested updates to TORs **(Background document #2c)** 3) inventory studies to measure under-reporting of detected TB cases **(Background document #2d)**	Babis Sismanidis
12:00 – 12:45	**Commentaries and perspectives**	Emily Bloss, Martien Borgdorff, Charlotte Colvin, Eveline Klinkenberg, Marieke van der Werf
12:45 – 14:00 Lunch		
14:00 – 14:45	**Presentation including Q&A**: Drug resistance surveillance: progress to date and emerging innovations **(Background document #2e, 2f, 2g)**	Matteo Zignol Anna Dean
14.45 – 15:45	**Group work on strengthening surveillance (four groups) (based on standard template/set of questions)**	All in groups
15:45 – 16:00 Tea break		
16:00 – 18:00	**Group work continued, followed by feedback in plenary**	All in groups

DAY 2: Wednesday 20 April 2016

Time	Topic	Presenter
09:00 – 10:00	Summary of main discussion/outcomes from Day 1	Jaap Broekmans Katherine Floyd Babis Sismanidis
Objective 3. Methods to estimate TB disease burden: progress since March 2015 meeting, review of methods to produce estimates for drug-resistant TB		
10:00 – 11:00	**Presentations including interactive Q&A**: Methods to estimate TB disease burden: progress since March 2015 **(Background document #3a)**	Katherine Floyd Pete Dodd Rein Houben
11:00 – 11:15 Coffee break		
11:15 – 11:45	**Presentation including interactive Q&A**: Methods to estimate the disease burden caused by drug-resistant TB **(Background document #3b)**	Babis Sismanidis
11:45 – 12:45	**Group work including final feedback in plenary**	All in groups
12:45 – 14:00 Lunch		
Objective 4. National TB prevalence surveys 2009–2015 and post-2015		
14:00 – 15:30	**Presentations followed by questions for clarification**: National TB prevalence surveys 2009–2015 **(Background documents #4a-4d)** Main findings and recommendations from USAID-commissioned independent review of prevalence surveys **(Background document #4f)** Prevalence surveys post-2015: why, how, where? **(Background document #4e)**	Ikushi Onozaki Irwin Law Charlotte Colvin Ken Castro Philippe Glaziou
15:30 – 15:45 Tea break		
15:45 – 18:00	**Group work on prevalence surveys post-2015 (four groups) followed by feedback in plenary**	All in groups

DAY 3: Thursday 21 April 2016

Time	Topic	Presenter
09:00 – 9:45	Summary of main discussion/outcomes from Day 2	Katherine Floyd Babis Sismanidis Irwin Law
Objective 5. Emerging work to measure costs faced by TB patients and their households though periodic surveys, and tools for TB-related projections		
09:45 – 10:30	**Presentation followed by Q&A and discussion**: TB disease burden & intervention impact – TIME dynamical model (background/rationale, progress-to-date, next steps) **(Background document #5f)**	Rein Houben
10:30 – 10:45 Coffee break		
10:45 –12:00	**Presentation followed by Q&A and discussion:** Surveys of costs faced by TB patients and their households and whether these are catastrophic: why, how, where and progress to date **(Background documents #5a-e)**	Knut Lonnroth Inés Garcia Baena
12:00 –12:30	Summary of meeting outcomes and concluding remarks	Jaap Broekmans Katherine Floyd
12:30 – 14:00 Lunch followed by departure		

7.2 List of background documents

No.	Background document	No. of pages[1]
1.	**Proposed mandate and strategic areas of work 2016-2020**	16
2.	**Strengthening TB surveillance**	
	a. Strengthening tuberculosis surveillance: rationale and proposed areas of work 2016–2020	8
	b. Regional analysis workshops – concept note, draft agenda	7
	c. TB epidemiological reviews – draft implementation guide, proposed updates to current TORs	43
	d. TB inventory studies – viewpoint (draft journal article) *CONFIDENTIAL*	8
	Drug resistance surveillance	
	e. Twenty years of global surveillance of anti-tuberculosis drug resistance (draft journal article) *CONFIDENTIAL*	14
	f. Population-based resistance of *M.tb* isolates to PZA & fluoroquinolones – results from a multi-country project (draft journal article) *CONFIDENTIAL*	13
	g. Future direction of surveillance of anti-TB drug resistance in the End TB era	7
3.	**Current WHO methods to estimate TB disease burden**	
	a. Executive summary of report of the 3rd meeting of the TB estimates subgroup, April 2015	1
	b. Methods used to estimate the burden of drug-resistant TB (MDR-TB, RR-TB, XDR-TB)	24
4.	**TB prevalence surveys**	
	a. Results and lessons learned from surveys in Asia 1990–2012 – journal article	18
	b. Overview of results and programmatic/policy implications – PPT from STAG-TB meeting June 2015	6
	c. Results and lessons learned from surveys in Africa 2010–2015 – figures, tables and abstract for draft journal article *CONFIDENTIAL*	14
	d. Tabular summary of challenges faced in the 19 surveys implemented 2009–2015 *CONFIDENTIAL*	7
	e. Prevalence surveys post-2015 – why, where, how?	27
	f. Independent USAID review: findings & recommendations	138
5.	**Surveys of costs faced by TB patients and their households and whether these are catastrophic**	
	a. Generic protocol and questionnaire	96
	b. Financial burden for tuberculosis patients in low- and middle-income countries: a systematic review	13
	c. Beyond UHC: monitoring health and social protection coverage in TB	10
	d. Defining catastrophic costs and comparing their importance for adverse TB outcome with MDR	17
	e. What can dissaving tell us about catastrophic costs?	8
	Tools for projections	
	f. TB disease burden & intervention impact – TIME dynamical model: background, progress-to-date, next steps	42
	g. Projections of TB case notifications	1

[1] Including appendices and references

Background papers marked confidential will be made available on the Task Force website once they have been published (2d, 2f, 2g, 4c) or once they have been reviewed by countries (4d).