

INDEPENDENT ASSESSMENT OF NATIONAL TB PREVALENCE SURVEYS CONDUCTED BETWEEN 2009–2015



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PREFACE

Tuberculosis (TB) prevalence surveys provide the most accurate measure of the burden of disease and data for monitoring disease trends over time. The results of these surveys are also used to calibrate mathematical models to forecast the extent and burden of TB around the globe. Thus, the Global Fund for AIDS, Tuberculosis, and Malaria (Global Fund), the United States Agency for International Development (USAID), and other global partners have justified expenditures to implement national TB prevalence surveys in high burden countries during recent years. Countries have received excellent technical guidance and leadership from the World Health Organization (WHO), Global TB Programme (*nee* Stop TB Department). TB prevalence surveys represent a major undertaking of monetary and human resources to ensure appropriate sample sizes and unbiased estimates of TB burden among the surveyed populations.

A substantial investment by the Global Fund, USAID, and other global technical partners have enabled an increase in the number of national TB prevalence surveys being implemented in high TB burden countries since 2009. In the 1990s and most of the 2000s, ≤ 1 national TB prevalence survey was implemented each year. However, between 2009 and 2016, it is expected that approximately 25 countries will have implemented national TB prevalence surveys; this includes 16 that were completed between 2009 and 2014.

To account for these investments, identify and share lessons gained, and ultimately inform, streamline, and facilitate future surveys, USAID partnered with the Bill and Melinda Gates Foundation (BMGF) to commission a team of multidisciplinary experts to conduct an independent and systematic assessment of the national TB prevalence surveys that have been undertaken over the past five years. This report of the assessment identifies the crucial value of TB prevalence surveys and provides a series of recommendations for the implementation of future surveys.

We are grateful to the team of expert consultants for their dedication, commitment, objectivity, attention to detail, and practical recommendations. We also thank our colleagues in WHO's Global TB Programme, Tuberculosis Monitoring and Evaluation Unit, who provided extensive support for the assessment and responded to numerous requests for information. Last, but not least, we are grateful to the many stakeholders at global and national level who took time to share their perspectives with the team of expert consultants and agreed to participate in this assessment. We look forward to using these recommendations to inform crucial future investments in surveillance systems, along with the design and implementation of forthcoming surveys in a manner that accelerates access and use of the results for decision-making, policy-derivation, and to account for, and monitor progress in the global battle against TB.



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ACRONYMS

AIDS	Acquired immunodeficiency syndrome
CAD	Computer-assisted diagnosis
CDC	Centers for Disease Control and Prevention (US)
CXR	Chest radiographs
DHS	Demographic and Health Surveys
DOTS	Directly-observed therapy
DST	Drug susceptibility testing
FM	Fluorescent microscopy
GCP	Good Clinical Practice
GDF	Global Drug Facility
Global Fund	Global Fund for AIDS TB and Malaria
HIV	Human immuno-deficiency virus
IUATLD	International Union Against Tuberculosis and Lung Disease
JICA	Japan International Cooperation Agency
KNCV	Koninklijke Nederlandse Centrale Vereniging tot bestrijding der Tuberculose
Lao PDR	Lao People's Democratic Republic
LED	Light-emitting diode (used in microscopes)
LJ	Lowenstein-Jensen (a media used for TB culture)
MGIT	Mycobacterial growth indicator tube (TB culture method)
MOH	Ministry of Health
MTB	<i>Mycobacterium tuberculosis</i>
NFM	Global Fund New Funding Model
NGO	Non-governmental organization
NHANES	US National Health and Nutrition Examination Survey
NHIS	US National Health Information Survey
NTM	Non-tuberculosis mycobacterium
NTP	National tuberculosis program
NTRL	National tuberculosis reference laboratory
PEPFAR	Presidents Emergency Program for AIDS Response (US)
QA	Quality assurance
RIF	Rifampin
RIT	Japanese Research Institute of Tuberculosis
STOP TB	Partnership of 1300 organizations that support the fight against TB
TA	Technical assistance
TB	Tuberculosis
TB CAP	US Tuberculosis Control Assistance Program
TB CARE	USAID/PEPFAR funded program for TB, HIV, and TB drug resistance
USAID	United States Agency for International Development
USG	United States Government
WHO	World Health Organization
ZN	Ziel-Neelsen (a method for staining sputum smears for microscopy)

INDEPENDENT ASSESSMENT OF NATIONAL TB PREVALENCE SURVEYS CONDUCTED BETWEEN 2009–2015

EXECUTIVE SUMMARY

Background

National tuberculosis (TB) prevalence surveys provide an essential means by which countries gather data to estimate the national prevalence of TB disease, understand program successes and limitations (e.g. why persons with active TB have not been diagnosed or reported to the National TB Program (NTP)), and assess the impact of national TB programs and policies. As part of a broader effort to improve TB measurement, the World Health Organization (WHO) convened a Global Task Force on TB Impact Measurement in 2006 which included country representatives and their technical and financial partners. Due to the paucity of country-level data on TB prevalence, the Global Task Force designated national prevalence surveys in 21 global focus countries as one of its top priorities.

The WHO has played a central role in coordinating the development of survey methodology and providing country support; under its leadership, 16 national surveys were completed between 2009 and 2014, and several more are currently under way. Due to their scope and complex methodological and sampling considerations, these surveys require considerable human and financial resources, as well as external technical assistance to be conducted successfully. Survey costs, exclusive of bilateral technical assistance, have ranged from slightly under one million to over 5 million US dollars. To date, these surveys have yielded extremely valuable data on the burden of TB including trends when repeat surveys have been conducted as well as insights into the limitations of current NTP screening algorithms, health seeking behavior, and other important insights into program performance. As the global TB community and individual NTPs gain more experience with these surveys, it becomes increasingly crucial to identify and share lessons learned, with an eye towards informing, streamlining and facilitating future surveys.

For these reasons, the U.S. Agency for International Development (USAID) and the Bill & Melinda Gates Foundation supported an independent assessment of surveys conducted since 2009. The purpose of the assessment was to review the overall approach to survey design, to better understand countries' experiences with survey preparation and implementation, as well as analysis and reporting, in order to inform recommendations on how to make future surveys more effective and efficient. The team also sought to better delineate the role national prevalence surveys should play in ongoing efforts to improve the measurement of TB burden.

Methods

In mid-2015, an independent assessment team developed a set of study questions corresponding to the assessment objectives and identified available data sources. The assessment consisted of three elements: a desk review of available documents from countries that had completed surveys, qualitative interviews with key international stakeholders and the country NTP managers, and team visits to three select countries to conduct an in-depth assessment of survey achievements and challenges.

Desk reviews were conducted for all 16 countries that had completed surveys between 2009 and 2014. These included: Cambodia, China, Gambia, Ghana, Ethiopia, Indonesia, Laos, Myanmar, Malawi, Nigeria, Pakistan, Rwanda, Sudan, Tanzania, Thailand, and Zambia.

Interviews with key stakeholders were conducted using interview guides tailored to the role that each played in the surveys. Persons interviewed included:

- NTP managers from countries that completed surveys between 2009 and 2014.
- WHO staff who have played a lead role in providing global guidance and coordination of technical support to countries implementing national TB prevalence surveys.
- Staff from international donor agencies that have supported national TB prevalence surveys, in particular the Global Fund for AIDS, TB, and Malaria (Global Fund) and USAID (including staff from headquarters and country missions).
- International experts who have provided guidance and support to surveys, including staff from technical agencies that are members of the Global Task Force and independent consultants.

The survey team conducted site visits in Cambodia, Ethiopia, and Ghana.

Summary of findings

The data collection and analysis sought to provide insight into the following high-priority questions about the planning, implementation, and analysis of national TB prevalence surveys.

What was the impetus to conduct the surveys?

Most countries reported that they conducted surveys to achieve a more accurate estimate of the burden of TB disease. The ultimate decision to conduct a prevalence survey appeared to be largely internal rather than the result of external influence from WHO or donors. However, in the case of some of the highest burden countries, these institutions also appeared to have played a pivotal role in promoting survey implementation.

Who implemented the surveys, and what was the role of the NTP?

Because TB surveys are resource intensive (from both a human and financial perspective), they have the potential to disrupt routine NTP program activities. As a result, the level of direct NTP engagement in survey activities can vary substantially. In two countries, the NTP led the surveys and used existing NTP personnel to conduct the survey. In an additional four, the NTP involvement was more peripheral, with the surveys implemented by government research units or by local research institutions. In the remaining 10 countries, the NTP took a leadership role and was closely involved in the oversight and monitoring, and frequently also in writing the report, though the survey was conducted by staff specifically hired for the study or an implementing research institution.

Did non-NTP leadership or involvement affect how well the results were accepted or how quickly the reports were generated?

There is a general belief that more robust NTP involvement in survey implementation leads to greater national-level acceptance and more rapid generation of reports. With a few exceptions, the results have been largely accepted by the countries. In countries that had higher-than-expected rates, the potential political implications and other factors had greater impact on their

acceptance than whether or not the NTP was directly involved. Final reports have been published in the two countries in which the NTP performed the survey and the four in which the survey was performed by an external implementing agency, while in four of the 10 countries in which the NTP played a leadership role but hired external staff or engaged an institution to conduct the survey, final reports are still pending.

Most surveys involved extensive networks of external technical and funding partners. What issues arose in working with these partners?

External technical assistance from WHO and other technical agencies who are members of the Global Task Force was deemed an essential element of success and was greatly appreciated. Most countries received technical assistance from WHO as well as external partners such as Koninklijke Nederlandse Centrale Vereniging tot bestrijding der Tuberculose (KNCV Tuberculosis Foundation), The United States Centers for Disease Control and Prevention (CDC), and the Japanese Research Institute of Tuberculosis (RIT); no major problems were noted in the coordination of this assistance. However, in one of the countries in which WHO was more peripherally involved in providing technical assistance, concerns about the prevalence estimates created tension between WHO, the technical partner, and the country.

Some stakeholders (technical partners as well as funders) felt that it would be useful if other members of the Global Task Force played a more active role in survey oversight, both given their complexity and the dual role of WHO in monitoring the studies and ensuring that recommendations are followed. Were these stakeholders to play a bigger role, the feeling of involvement and ‘ownership’ by other members of the Global Task Force may increase and thus influence the likelihood that survey results are used for advocacy and funding purposes.

Most of the surveys were funded by the Global Fund for AIDS, TB, and Malaria (Global Fund), with additional funding from bilateral donors, most notably U.S. Agency for International Development (USAID) and Japan International Cooperation Agency (JICA), usually in the form of technical support. Procuring and aligning funding from multiple donors was a major challenge for many of the countries and also an important cause of survey delays. Once the surveys began, donors in several countries were approached for additional funds when shortfalls occurred. The need to tap multiple donors commonly created issues related to different approval and disbursement timelines, as well as varied reporting requirements. In some cases, these challenges were an obstacle to survey implementation.

To what extent did the surveys foster South-South technical collaboration and build international capacity in surveys and operations research?

An important positive outcome of the surveys has been the development of South-South collaborations. Countries that had conducted successful surveys provided technical assistance to other countries in survey planning and implementation. In addition, opportunities to visit countries with surveys in progress proved extremely valuable for countries about to launch their own surveys, and created valuable links between TB programs.

The experience of conducting the surveys also increased national capacity for additional survey efforts and for conducting operations research. The experience functioned to build the skills and confidence of NTP program staff and fostered relationships with national research institutes.

How much technical support do WHO and its partners provide?

TB prevalence surveys require a high degree of technical assistance (TA), as few countries have the requisite local expertise and experience to manage these enormous and complex undertakings. Most countries received considerable and universally appreciated technical support from WHO as well as external partners, including KNCV, CDC, and RIT. In most settings, WHO appears to have played a more central role in providing and coordinating project support from its partners, however, in a few countries, the primary technical support was provided by institutions such as KNCV. The types of TA that were provided included protocol development, resource mobilization, project management, laboratory support, radiology training and reading, quality control, data management and analysis, and report writing.

Overall, data analysis has required considerable external technical assistance; few of the countries have been able to accomplish this activity on their own. Even with the WHO data analysis workshops, country teams have heavily depended on WHO and other external involvement to arrive at the prevalence estimations and conduct additional analyses.

Technical support for these surveys is both intensive and costly. External visits usually range from 3-7 days, and often exceed 20 visits over the course of the survey, and in some instances, technical staff has been placed full-time in country to provide survey support. Beyond the in-country support, remote support has been provided for some countries in the form of quality assurance reading of chest radiographs (CXR). The costs of this technical assistance has not been factored in many survey budgets because it is covered through direct agreements between technical partners and donors. However, this support likely exceeds \$100,000 per survey, not including the salaries of staff providing the assistance.

In addition to providing technical support, an important role of the WHO-led Global Task Force has been to foster mutual support and learning between countries through activities such as the periodic Global Task Force meetings. Despite these opportunities for sharing, more recent surveys still are experiencing some of the same previously identified challenges and have not acted on key lessons learned (e.g., digital data capture, HIV testing).

What was actually learned from these surveys about TB prevalence and incidence?

An enormous amount has been learned about TB prevalence from these surveys, both at the national and international level. In six of the 16 countries, the results of the survey indicated a burden that was more than 30% lower than the point prevalence anticipated at the time of the survey, while in one country, the estimate was more than 30% higher. Both the survey estimates and their confidence limits differed from previous estimates, and the confidence intervals from the surveys were generally considerably tighter than those produced by modeling.

TB incidence rates and the global number of cases are the most commonly used measures of TB burden, but are virtually impossible to measure directly or reliably in the absence of high-quality reporting systems. Until recently, notification data combined with expert opinion have been used in most countries to develop these estimates. The sample size that would be needed to measure incidence is prohibitive, but incidence can be derived from prevalence by making assumptions about duration of disease or using modeling techniques. The availability of the prevalence survey data for several high-burden counties has resulted in major revisions in the key TB indicators.

The changes in WHO estimated TB incidence rates based on the TB prevalence survey data, especially from the high-burden countries of Indonesia and Nigeria, has had a profound effect on the global number of estimated TB cases. Findings from these high burden countries have resulted in an upward adjustment of the estimated number of incident TB cases worldwide from 8.5 million to 9.6 million. This has had important implications for advocacy, fund-raising, and program activities.

What do stakeholders perceive as the value of the estimates produced by the prevalence surveys?

A consistent theme of the stakeholder interviews was the enormous value of having accurate data. Many described the surveys as “game changers” that gave more realistic estimates based on actual data. These more accurate estimates are deemed essential for planning, targeting, advocacy, and funding purposes. Several stakeholders also commented on the finding that the number of cases was far more than had been obtained through previous estimation methods, which influenced the visibility and relative importance of TB as a major public health issue both within countries and on a global scale.

Beyond the national prevalence estimates, what other information useful to national TB programs came from the surveys?

In addition to prevalence estimates, surveys provided countries with additional information about the proportion of cases on treatment, the validity of current case-finding algorithms, health-seeking behaviors among persons with presumptive TB, characteristics of persons with TB who had not been previously diagnosed, and prevalence of non-TB mycobacteria. In some countries, data were collected on socioeconomic status and behavioral risk factors such as smoking among TB patients. Information on HIV status, when collected, provided insight into the TB/HIV co-epidemics.

Although useful information was collected that better defined the epidemic and improved targeting and diagnostic strategies and algorithms, these results were not always included in the final reports or actively communicated to stakeholders and others who can benefit from this knowledge. As a result, several stakeholders expressed the unfortunate impression that the surveys were providing essentially a single number (TB prevalence).

How did the countries use these data, and have changes in practice or policy resulted from the findings?

The NTP managers reported that they used the data from the prevalence surveys to make decisions about the implementation and design of their national TB programs. Although several of the proposed changes have not yet resulted in actual policy changes due to a variety of factors (e.g. timing, funding, political leverage), the intended changes based on survey results have included the following:

- General updates to national strategic plans, goals, targets, and priorities that form the basis for the Global Fund New Funding Model (NFM) application
- Focus on newly identified population groups or geographic areas at higher risk
- Increase in emphasis on and activities related to active case finding and case detection
- Increased focus on the private sector and its role in TB case detection and treatment
- Modifications to screening criteria and algorithms (especially in response to identification of cases who were symptom-screen negative, as well as smear negative, culture positive cases)

- Implementation of GeneXpert (Xpert® MTB/RIF)
- Increased use of digital X-rays

In many cases, NTP managers commented that the data from the surveys gave them the power to influence change for TB priorities, strategies, etc. within their countries. Finally, the data are being used to secure additional resources and funds for TB activities.

The asynchrony between the completion of the analyses and funding cycles for Global Fund has limited or delayed the implementation of the changes in some countries. This suggests that, to optimize the usefulness of the surveys, further attention should be paid to aligning these cycles wherever possible.

What additional benefits did the NTP managers report from participation in the survey?

The NTP directors cited a number of additional benefits that accrued from participation in the surveys. These included capacity building for the NTP, radiology, and laboratory staff; durable goods (such as vehicles, mobile CXR units, etc.) that were recycled for program purposes; and the strengthening of capacity to conduct active case finding, and building survey and research skills. In addition, surveys often improved communication among in-country divisions and institutions.

Were the surveys leveraged for other purposes?

These surveys likely represent the largest and highest quality adult health surveys in the countries in which they have been conducted. However, the focus in almost all cases has been exclusively on TB. Collecting HIV data as part of TB prevalence surveys would provide greater insights into the co-epidemics and has been shown to be feasible. Additionally, there is an increasing interest in leveraging these activities to provide insight about non-communicable diseases, and address a lack of recent population-based data on the prevalence of conditions such as diabetes and hypertension and associated behaviors, such as smoking. However, few countries have collected non-TB data from all or a sub-sample of the survey population, and even fewer reported these results. Most of the NTP managers felt that it would be possible and useful to include other diseases or conditions in future surveys if carefully organized.

What are the staffing needs to conduct a quality survey that is completed in a reasonable time and on budget, and without disrupting routine NTP activities?

TB prevalence surveys are labor intensive. In general, each survey generally required the following:

- An executive or steering committee consisting of about 10-20 experts
- A technical committee/technical advisory group of 20-30 persons (representing the various competencies such as census, radiology, and bacteriology, and data management)
- Several (3-6) fixed survey teams consisting of 10-15 staff
- A local support team with an additional 10-15 staff in each cluster

A commonly identified bottleneck was staff skilled in reading CXR, as well as providing quality control for these readings. Laboratories represented a second major bottleneck, as the volume of specimens far exceeds the routine burden of the TB programs, and experience in managing large numbers of cultures may be limited. Some degree of routine program activity disruption occurred in most countries, especially in laboratories, but the level of disruption varied widely.

What measures were put in place to monitor quality?

All protocols included extensive descriptions of quality control measures. Such quality control was deemed particularly essential for CXR readings as well as for sputum and culture. However, it was often difficult to ascertain the extent to which the quality measures had been implemented during field operation since results for these QA/QC measures were infrequently presented in the final survey report.

What were the primary issues encountered in processing the laboratory specimens?

Ultimately, quality of the surveys is closely related to the quality of the laboratory data, as both false positive and false negative readings can have an important impact on prevalence estimates. Laboratory procedures were highly variable from country to country, making cross-country comparisons problematic. These may have also affected the prevalence estimates.

In addition to issues with standardization, many NTP managers reported that handling the large volume of specimens presented a major challenge for ongoing laboratory activities. The maintenance of laboratory equipment and transporting specimens to the central laboratories for processing represented additional important field-level challenges.

What issues were encountered in data entry, management, and analysis?

In the countries for which data were available on actual survey time lines, the time between completion of field data collection and presentation of results to the Ministry ranged from 3-20 months. Bar coding and electronic data entry was associated with shorter data turnaround times in some, but not all, countries. In general, countries with the shortest turn-around times gave considerable thought to the design and flow of questionnaires and numeric coding of data responses, and used bar coding and electronic data entry.

Several countries struggled to create a cleaned and validated data set for analysis. Accurate linking of the clinical, radiological, and laboratory data is critical, and paper-based systems are particularly prone to errors in data linkage. Validation of lab results and/or CXR readings delayed the availability of the final database for several countries. In most countries, data analysis depended heavily on external TA by WHO staff and other groups, as well as the biannual analysis workshops held at WHO in Geneva, Switzerland. Most countries could have not completed the data analysis by themselves. With few exceptions, analysis was limited to the overall TB prevalence estimates, by sub-groups, and health-seeking behaviors.

How was the actual quality of the surveys?

Overall quality of the data was based on a number of different aspects, including the response rates, accuracy of data collection, a low rate of false-negative CXR, consistent numbers of specimens from patients who had symptoms or positive CXR, high quality smear microscopy, careful culture procedures, and meticulous data entry and management. As mentioned above, it was not always possible to examine the relative contribution of each of these factors based on data presented in the final reports. Variation in the number of participants with a valid outcome and the subsequent extensive amount of imputation that was required in some countries with lower response rates may have led to either over- or under-estimation of the TB rates. The available data did not allow to quantify the potential effect of the imputation.

To what extent did the surveys produce reliable and credible data?

With some exceptions, the surveys had overall response rates greater than 80%, although rates as low as 57% were recorded. However, even studies with reasonable overall response rates had very low participation in certain subgroups and clusters. The imputation that was used to adjust for non-response may produce over- or under-estimates, and sensitivity analyses were not routinely performed. Other issues affecting validity include the rate of false-negative x-ray readings, the numbers of specimens obtained from each suspect case, contamination rates, and aggressive decontamination.

To what extent are the data comparable between countries?

Greater standardization of methods and the development of an international database that included primary data from prevalence surveys would allow groups to examine larger issues in TB epidemiology and the effects of programs on TB rates. At present, chest radiograph readings as well as microscopy and culture results are affected by the techniques used, local skills, and other factors such as decontamination practices and media content. These factors limit direct comparisons between countries.

Were there time and budget overruns?

The surveys took a minimum of two years to complete from protocol development to report publication, with an upper limit of 10 years. The greatest variability was in the preparation time, which ranged from 5 months to 6 years, and the analysis and reporting stages, which ranged from 5 months to more than 2.5 years.

The time from protocol development to survey initiation was often affected by difficulties in obtaining funding and problems in procuring and importing equipment. The reasons behind delays in analysis and reporting included time for completion of quality control activities and resolution of discrepancies, delays in data cleaning and analysis, and factors such as political considerations, concerns over data quality, lack of funding for writing and printing, staff turnover, lack of skilled staff, and low priority for busy NTP managers.

Initial budgets ranged from 0.9 million to over 5 million US dollars (USD), and the costs per participant ranged from \$19 to \$116 USD. It was difficult to evaluate cost overruns since these data are not readily available. In general, hiring external staff or contracting with research bodies increased cost, as did digital CXR and bar coding and electronic data entry. Not typically included were the costs of technical assistance visits, which added tens of thousands of dollars. For those countries for which detailed budget information was available, either from the protocol or the final report, fieldwork was the most costly element, followed by acquisition of radiological equipment and mobile vans.

To what extent did the data reach the countries' health leadership?

In virtually all countries for which there was information available, methods used for disseminating survey results included briefing government officials and various level of the NTP program. Workshops involving donors, NGO, and the press were common, often timed with the release of the official survey report. However, few if any of the programs appeared to have specifically developed a communication plan for the survey; this would include proactively

identifying the groups with which they would communicate, the message, the timing, and the modalities of communication, as well as reservation of funding for these activities.

What considerations should be taken into account in future activities?

There is a willingness and interest on the part of most stakeholders to find better ways of doing the surveys, including standardizing data entry and processing, using innovative methods such as automated x-ray readings, implementing GeneXpert Ultra (projected availability mid 2016) instead of culture as the diagnostic test for those with positive symptom screens or CXR, bar coding, and moving to continuous, rather than periodic, surveys.

Many countries, including several that are not on the list of high-impact countries, have expressed interest in conducting surveys, which is likely to put a major strain on available technical resources and have serious financial implications. Countries have also expressed an interest in repeat surveys, although a number of technical and financial concerns have been raised. The need also remains to improve surveillance programs, which would obviate the need for these surveys and/or explore alternative, less costly strategies to assess the TB burden.

Conclusions and recommendations:

TB prevalence surveys represent the most ambitious and complex health surveys in the world. WHO and its technical partners as well as the Global Fund have played a critical role in spearheading and funding these efforts, and countries have been highly committed to successfully completing them. The surveys have been game-changers and are universally valued in the TB world. At the same time, however, the surveys are highly complex, expensive, require massive external technical assistance, and are subject to problems with radiography, laboratory testing, data management, and analysis. There are ways in which they can be further improved to not only increase their quality but also their value for money. Going forward, the following key issues need to be addressed:

- 1) The surveys should be simplified through greater standardization. New technical developments such as the use of GeneXpert MTB/RIF should be incorporated to simplify and streamline the surveys.**
- 2) The Global Task Force should lead efforts to obtain external input from groups conducting other such large surveys to explore innovations in sampling and analysis that could improve quality and increase efficiency.**
- 3) Prevalence surveys are expensive with important consequences for policy and funding, and therefore should adhere to Good Clinical Practice (GCP) principles.**
- 4) TB prevalence survey data needs to be used more broadly to provide a better understanding of TB epidemiology and strengthen national and international TB control efforts.**

- 5) Opportunities for synergies with HIV and non-communicable disease programs should be sought to take advantage of the quality sampling and to provide political and financial support for the surveys.**
- 6) The 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, and funds should be provided to facilitate more rapid generation of reports and greater dissemination of results to a broader audience.**
- 7) Funding for the surveys must be closely coordinated to avoid delays, and the timing of surveys should be better synchronized with the Global Fund application process so that funding can be obtained in a timely way to make TB program changes based on survey results.**
- 8) Serial surveys may provide highly useful data to monitor trends and evaluate program activities, but guidelines should be developed outlining under what conditions, and with which frequency, they should be considered.**
- 9) Continued investments should be made in surveillance, and efforts explored to examine sentinel surveillance as an alternative to periodic surveys.**

MAIN REPORT

Background

The WHO Global Task Force on TB Impact Measurement was established in 2006 with a mandate to ensure the best possible assessment of whether 2015 global targets for reductions in disease burden are achieved¹. At the end of 2007, the Task Force agreed on three major strategic areas of work, one of which was national TB prevalence surveys in 22 global focus countries.² The main objective of these surveys is to estimate the national prevalence of TB disease, with a key secondary objective of better understanding why and how persons with active TB miss being diagnosed and/or reported to the National TB Program (NTP).

WHO, with input from a subgroup of the Global Task Force that included representatives from countries and their technical and financial partners, developed an updated handbook on national TB prevalence surveys which was published in 2011. The handbook, known as the Lime Book, included comprehensive guidance on survey design, implementation, analysis and reporting,³ and subsequent updates to this guidance have been made available through web appendices, papers and informal communications. WHO has been extremely active in providing global guidance and coordination of technical support to the 22 global focus countries. Support has also been provided to other countries, such as the Gambia, Laos PDR, Mongolia, Sudan and Zimbabwe, but designated lower priority. Support to surveys has included organizing global, regional, and national workshops and training opportunities; peer-review of survey protocols; mid-term survey reviews; exchange visits; and country missions related to all aspects of surveys, conducted by experts from technical agencies, national experts who have played a lead or key role in previous surveys, and independent consultants.

As a result of these efforts, the number of annual TB prevalence surveys has increased substantially in recent years. In the 1990s and most of the 2000s, the number of annual surveys ranged from 0-2, while between 2009 and 2016, 27 surveys were conducted or planned, 16 of which had been completed when this independent assessment began mid-2015. Most countries have conducted surveys for the first time, or for the first time in accordance with recommended WHO methods, although three countries (Cambodia, China, the Philippines) have conducted repeat surveys.

This increased number of national TB prevalence surveys has necessarily been accompanied by a substantial increase in investment of human and financial resources. Survey costs, exclusive of bilateral technical assistance, have ranged from slightly under one million to over 5 million USD. The majority of funding for surveys conducted between 2009 and 2015 has been provided through Global Fund grants. Contributions from domestic sources in some countries, as well as USAID (as part of the TB CARE project), other United States Government (USG) funds, and other bilateral donors. Most of the funding for technical assistance to countries has been provided by USAID (via PEPFAR grants, TB CAP, TB CARE, and Challenge TB projects, as well as an umbrella grant to WHO), by the government of Japan, and the Global Fund. USAID projects (e.g. DELIVER and TO 2015) have also provided procurement and logistical support.

¹ For fuller details, see www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en/

² These are: Bangladesh, Burma, Cambodia, China, Indonesia, Pakistan, Philippines, Thailand, Viet Nam (Asia) Ethiopia, Ghana, Kenya, Malawi, Mali, Mozambique, Nigeria, Rwanda, Tanzania, Uganda, Sierra Leone, South Africa, Zambia (Africa). The criteria used to select these countries are explained in the WHO handbook on national TB prevalence surveys.

³ Tuberculosis prevalence surveys: a handbook. World Health Organization, 2010 (WHO/HTM/TB/2010.17). Available at: www.who.int/tb/advisory_bodies/impact_measurement_taskforce/resources/documents/thelimebook

To date, surveys have yielded extremely valuable data on the burden of TB in high burden settings (including trends in countries that have conducted repeat surveys) and led to substantial revisions in the estimated number of incident TB cases worldwide. The surveys have also provided insights into the limitations of current NTP screening algorithms and health seeking behavior in different country contexts. Further details are available in survey reports, published papers, papers that are in press or in preparation,⁴ and on the Task Force website. Examples have also been highlighted in the annual WHO global TB report (see Chapter 2 of the 2010–2014 editions of this report). In coming years, international donors will need to make strategic decisions about the level of investment in surveys and ensure accountability for recent investments.

As the global TB community and individual NTPs gain more experience with these surveys, it becomes increasingly important to identify and share lessons learned with a goal of improving the implementation, efficiency, and effectiveness of future surveys. At the same time, new technologies and innovative ways to collect and analyze data for population-based surveys are, or will become, available in the near future. Stakeholders will benefit from an in depth exploration of how TB prevalence surveys could incorporate these new methods and innovations to address ongoing challenges. In addition to the use of improved rapid diagnostic technologies such as GeneXpert MTB/RIF®, there are opportunities to consistently collect data on co-morbidities such as diabetes and HIV, as well as second line drug resistance (in selected settings). There may also be opportunities to improve data management to address concerns about the timeliness and use of survey results.

For these reasons, USAID and the Bill & Melinda Gates Foundation supported an independent assessment of surveys from 2009 to the present. The scope of work is provided in Annex 1.

Objectives

1. To review the survey design of national TB prevalence surveys, including the processes used to develop and finalize survey design, and their main strengths and weaknesses.
2. To review experience with survey preparations and actual implementation (including but not limited to procurement, survey management and staffing, the clinical and laboratory aspects of field and central survey operations, data management), and identify the main strengths, challenges faced and how they were addressed, and lessons learned.
3. To review experience with analysis of data and reporting of results from prevalence surveys, including the processes used to produce final results and disseminate/use these results, and identify the main strengths, challenges faced and how they were addressed, and lessons learned.
4. To produce three in-depth country case studies that highlight key aspects of survey design, preparations, implementation, analysis and reporting of results.
5. To consider how surveys could be modified in future to make processes (from design to reporting) more effective and efficient, including via the use of new technologies.
6. To consider the future role of prevalence surveys in efforts to improve measurement of the absolute burden of TB disease and trends in this burden.

Methods

A two-day meeting of independent assessment team members was held in Paris in July, 2015 that included detailed presentations on the rationale, history, methods, and results of the TB prevalence surveys by WHO staff and a discussion of proposed assessment methods (Annex 2). At this time, a timeline was also developed for the project. Subsequently, the assessment team developed an analytic

⁴ For a full list, see the latest quarterly update on prevalence surveys issued by the Task Force subgroup. For Asian surveys implemented 1990–2012, see “National TB prevalence surveys in Asia 1990–2012: An overview of results and lessons learned” (in press, available from WHO Global TB Programme on request).

plan that consisted of a set of study questions corresponding to the study objectives (Annex 3) and identified the data sources that would be used as inputs for each question (Annex 4). The assessment consisted of three elements:

- A desk review of the sixteen countries that had completed surveys between 2009 and 2014: Cambodia, China, Gambia, Ghana, Ethiopia, Indonesia, Laos, Myanmar, Malawi, Nigeria, Pakistan, Rwanda, Sudan, Tanzania, Thailand, and Zambia
- Qualitative interviews with key international stakeholders and the NTP managers from countries that had conducted surveys
- Team visits to three countries to conduct an in-depth assessment of survey achievements and challenges.

The desk reviews included key documents provided by the WHO TB Monitoring and Evaluation staff, which were used to conduct standardized data abstraction for each country (see Annex 5 for abstraction form). Documents reviewed included survey protocols, reports from missions by technical advisors, reports from mid-term survey reviews and other relevant/informative trip reports, workshop agendas, background documents and presentations, quarterly survey progress updates issued by the WHO Global Task Force on TB Impact Measurement, summaries developed by WHO on key methodologic variables and outcomes, WHO publications, and final survey reports (see Bibliography for a list of the sources used). The number of documents available for each country ranged from 3-10. Final reports, which were considered the most complete and reliable data source for most of the items abstracted, were not available for several of the countries, although in some cases, draft versions were informally shared with the study team for data verification purposes. Documents from each country were reviewed by a primary and a secondary reviewer from the study team. WHO TB Monitoring and Evaluation staff provided the needed information for certain key variables for which data were not readily available.

Interviews with key stakeholders were conducted using interview guides tailored to the role that each individual played in the surveys (see Annex 6). Persons interviewed included:

- WHO staff who have played a lead role in providing global guidance and coordination of technical support to countries implementing national TB prevalence surveys
- Staff from international donor agencies that have supported national TB prevalence surveys, in particular the Global Fund and USAID (including staff from headquarters and country missions)
- International experts who have provided guidance and support to surveys (including those from technical agencies and independent consultants)
- NTP managers from most of countries that completed surveys between 2009 and 2014

Sixteen stakeholders were interviewed (see Annex 7 for a list of those interviewed). Because of the extreme heterogeneity of the respondents and the opportunistic nature of the sampling, results are not presented quantitatively but by employing anonymous direct quotations. A summary of the themes and key quotes are included in annex 9.

Current or previous NTP managers from the 16 countries were contacted, and interviews were completed for 10 of the 16 (Cambodia, Ghana, Ethiopia, Indonesia, Myanmar, Malawi, Nigeria, Tanzania, Thailand, and Zambia; see Annex 8). Transcripts of the responses to each question were reviewed by each person interviewed. In addition to presenting anonymous illustrative quotes in this report, results are presented quantitatively, where relevant, as the number who expressed certain views. Detailed transcripts or summaries of the responses are presented in Annex 10.

The assessment included site visits to Cambodia, Ethiopia, and Ghana, which represented countries in various stages of implementation. Ghana had recently completed a survey, while Ethiopia had completed a survey several years earlier and was contemplating another, and Cambodia had already conducted a repeat survey. The choice of two African and one Asian country offered the opportunity to examine

differences in regional capacity and experience. All three were among the 22 global focus countries. During these visits, interviews were conducted with staff who had played a key role in leading and managing surveys, including survey principal investigators, survey coordinators, national TB program managers, survey data managers and laboratory staff. In addition, senior officials of Ministries of Health and the country office representatives from USAID and other donor agencies were also interviewed. See Annex 11 for detailed reports from each country visit.

Responses to evaluation questions

What was the impetus to conduct the surveys?

Most countries reported that they conducted surveys to achieve a more accurate estimate of the burden of TB disease. Several countries wanted to obtain baseline data to measure the impact of planned interventions, while others that had already performed surveys wanted to evaluate the effectiveness of their program activities. The ultimate decision to conduct a prevalence survey appeared to be largely internal rather than the result of external influence from WHO or donors. However, in the case of some of the highest burden countries, these institutions also appeared to have played a pivotal role in promoting survey implementation.

Who implemented the surveys, and what was the role of the NTP?

In a limited number of countries in Asia, including Lao and Cambodia, the NTP led the surveys and used existing NTP personnel to conduct the survey. In two Asian and two African countries, the NTP was not the central implementing partner and their involvement was more peripheral; these surveys were implemented by government research units or by local research institutions. In the remaining ten countries, the NTP was actively engaged in the conduct of the surveys, taking a leadership role and being closely involved in the oversight and monitoring of survey activities and frequently in writing the report, though staff specifically hired for the study by the NTP or a research institution conducted the actual survey.

Did non-NTP leadership or involvement affect how well the results were accepted, or how quickly the reports were generated?

With a few exceptions, the data have been largely accepted by the countries, and in the one case where there was a clear delay in acceptance by the government, the potential political implications of the much higher prevalence than expected in combination with changes in NTP management as well as at MOH key staff appears to have weighed more heavily than the peripheral role of the NTP in conducting the survey. The two countries in which the NTP conducted the survey itself completed the reports in a timely way, although in one of these countries, there is no final published report in the country's language. Among the ten countries in which the NTP had a leadership role but hired staff or engaged a research institution, four had not published final reports by the end of 2015 even though their surveys had been completed by 2013 or earlier. The four countries where the NTP was not the implementing agency have all published reports and did not appear to experience major problems with acceptance of results.

Most surveys involved extensive networks of external technical and funding partners. What issues arose in working with these partners?

External technical assistance from WHO and other technical agencies who are members of the Global Task Force was deemed essential to the success of the surveys and was greatly appreciated. Most countries received technical assistance from WHO as well as external partners (KNCV, CDC, RIT), and no major problems were noted in the coordination of this assistance. However, in one of the countries where WHO was more peripherally involved in providing technical assistance, concerns were raised over the prevalence figures generated that created tension between WHO, the technical partner, and the country.

Some stakeholders (technical partners as well as funders) felt that it would be useful if other members of the Global Task Force played a more active role in survey oversight, both given their complexity and the dual role of WHO in monitoring the studies and ensuring that recommendations are followed. As eloquently expressed by one of the stakeholders:

“We need to look at prevalence surveys as large research projects. They need a steering committee with independent members, and a data monitoring group, as is done in clinical trials. Someone also needs to have political leverage to solve problems in the field. [In some surveys, they have] noticed problems right from the start. The way the monitoring was set up was that WHO was overseeing, and teams visited and recommendations were made, but the recommendations are not always acted upon because no pressure is placed on the country. [We] should have advisory group reporting to the donors to make sure things are happening... WHO is doing a great job and is technically proficient, but they are under fire because they are always put in a monitoring position. Having a strong independent advisory group could help protect them. “

This expanded role for stakeholders, who would be independent and not involved in the survey implementation, would also respond to criticisms that the surveys have been “in the hands of a small number of experts”. This could increase the feeling of involvement and ‘ownership’ by other members of the Global Task Force and thus the likelihood that survey results would be even more widely used for advocacy and funding purposes.

Most of the surveys were funded by the Global Fund for AIDS, TB, and Malaria (Global Fund), with additional funding from bilateral donors, most notably USAID and JICA, usually for technical support. Ensuring funding from multiple donors was a major challenge for many of the countries and also an important cause of survey delays. Once the surveys began, donors in several countries were approached for additional funds when shortfalls occurred. The need to tap multiple donors created issues of different timelines for approval and disbursement and different reporting requirements and was an obstacle to survey implementation for some.

The status of current and proposed surveys is discussed in quarterly meetings that include Global Fund, WHO, STOP TB and various donors. Such coordination should help to resolve some of the challenges encountered which resulted in delays in assembling funding, though it will not fully resolve issues of coordinating additional sources of funding.

To what extent did the surveys foster South-South technical collaboration and build national and international capacity in surveys and operations research?

A highly positive outcome of the surveys has been the development of South-South collaborations. In particular, the Cambodian TB survey team has provided substantive support to other surveys in both Africa and Asia, and the Ethiopian survey staff continues to provide technical assistance to other countries conducting surveys. In addition to the technical advisors, the opportunities to visit countries with surveys in progress has proved extremely valuable for countries that were preparing to conduct their own surveys and created valuable links between TB programs.

The experience of conducting the surveys also increased capacity for additional survey efforts and for conducting operations research through building the skills and confidence of the NTP program staff and fostering relationships with national research institutes. As stated by one of the stakeholders:

“We were always complaining that there wasn’t research capacity in country and that the researchers were doing less relevant work for the NTP, but now they have been contracted by the NTP [to conduct the surveys] and they are establishing a working relationship for the future.”

An additional means of increasing capacity has been to identify a person, ideally within the NTP, who can use the experience of conducting and writing up the survey results as a PhD thesis. For example, the University of Amsterdam has a flexible program that permits short-term course work and encourages such efforts. This program has worked well in some countries as a way of both increasing capacity and ensuring that the surveys are written up in a timely way.

How much technical support do WHO and its partners provide?

WHO and its partners and consultants under the umbrella of the Global Task Force have provided considerable and universally appreciated support to the surveys. In Cambodia, for example, RIT Japan, financed by JICA, had three full-time staff members on site, including a project manager who also managed the project budget. In addition, a Japanese expert provided radiology quality control, and analysis was largely conducted by the RIT/JICA consultant in close collaboration with the country team. Other partners (WHO, TB CARE /USAID) were also involved in field monitoring visits, and an external review mission of the survey was conducted by WHO and CDC staff during field activities. In other settings, WHO appears to have played a more exclusive role in project support, while in a few countries, the primary technical support was provided by institutions such as KNCV.

Intensive external technical support is required to conduct these studies. In Ghana, for example, 24 consultant visits, averaging in length from 3–7 days (and sometimes longer), were undertaken during the various phases of the project. These visits included WHO staff as well as WHO-funded consultants from Italy, Germany, and Ethiopia. In Rwanda, the number of external visits totaled 18 between 2010 and 2014 and the principal investigator and survey coordinator visited Cambodia to observe survey operations in the field. Two external monitoring missions were conducted by CDC and WHO; these also served as demonstration visits for neighboring countries planning TB prevalence surveys. In Zambia, there were 19 visits between 2012 and

2014 by the lead technical partner as well as a visit by WHO, an external monitoring mission and a study tour. In Ghana, 26 technical and monitoring missions were conducted over the course of the survey, and in other countries, more than 20 visits were not unusual. Beyond the in-country support, remote support has been provided for some countries in the form of quality assurance reading of chest radiographs (CXR). The costs of technical assistance have not been factored into many survey budgets because it is covered through direct agreements between technical partners and donors. In Zambia and Rwanda, for example, these technical costs were on the order of \$150-200,000 including salaries and consultant fees.

Overall, data analysis has required considerable external technical assistance; few of the countries have been able to accomplish this activity on their own. Even with the WHO data analysis workshops, country teams have heavily depended on WHO and other external involvement to arrive at the prevalence estimations and conduct additional analyses. For some countries there has also been heavy external involvement in writing the survey report.

In addition to providing technical support, an important role of the WHO-led Global Task Force⁵ has been to foster mutual support and learning between countries. Sharing of survey experiences is enhanced by the periodic Global Task Force meetings in Geneva, as well as protocol and data analysis workshops and survey coordinator workshops. During these meetings, countries share their survey status, challenges and plans for mitigation. This discussion fosters an active exchange of experience. However, despite these efforts, more recent surveys still are experiencing some of the same challenges of others and have not taken up key lessons learned (e.g., digital data capture, HIV testing). One goal would be to improve the effectiveness of these conversations in capturing these lessons and ensuring that they are applied as additional countries launch their surveys. It is possible that a more standardized survey blueprint, such as that used in the Demographic and Health Surveys, might help prevent some common problems, decrease the need for intense external assistance, and lead to fewer concerns regarding data analysis and interpretation.

What was actually learned from these surveys about TB prevalence and incidence?

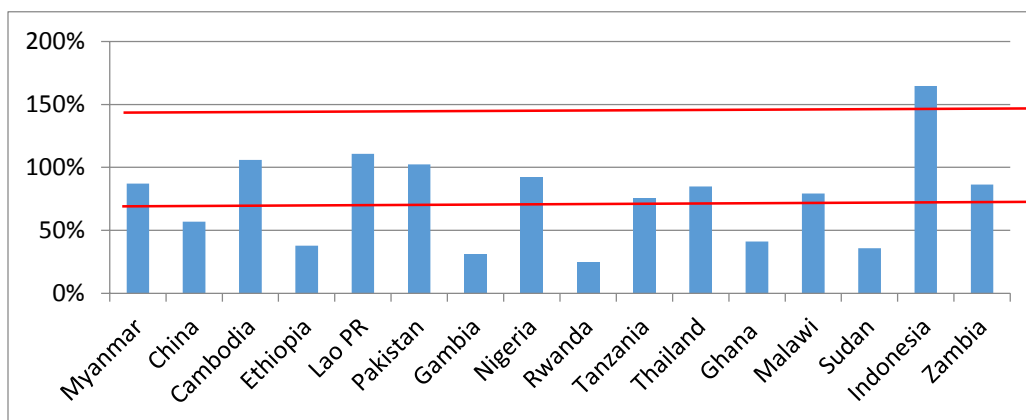
An enormous amount has been learned about TB prevalence from these surveys, both at national and global level. To assess the extent to which the surveys produced estimates of TB prevalence that differed from the estimates from WHO and elsewhere assumed at the time of study design, we examined the ratio of the point prevalence obtained from the surveys to the prevalence figure used for the sample size assumptions when the survey was designed. In six of the 16 countries, the results of the survey indicated a burden that was more than 30% lower than the anticipated point prevalence estimate, while in one country, the estimate was more than 30% higher (Figure 1).

Directly measuring incidence requires enormous sample sizes that are not feasible in a survey context. Prevalence estimation requires high but still feasible sample sizes, and incidence can be estimated from prevalence data by making assumptions about duration of disease or using

⁵ http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en/

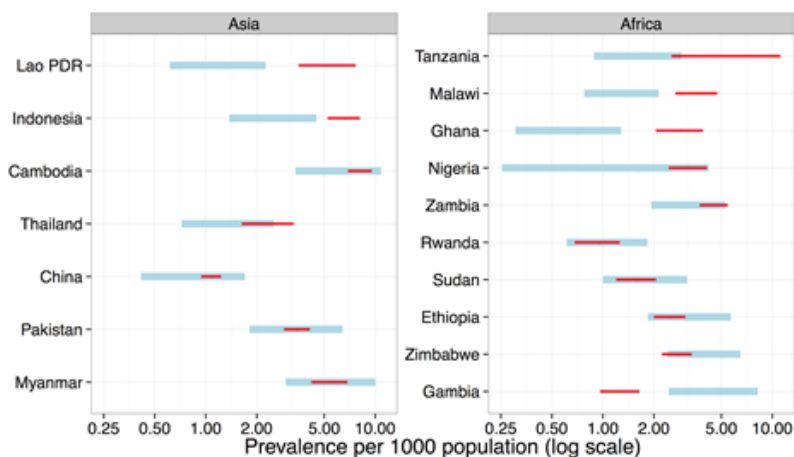
modeling techniques. The availability of the prevalence survey data for several high-burden countries has resulted in major revisions in incidence and other key TB indicators.

Figure 1: Ratios of TB prevalence obtained from the survey and estimated/assumed TB prevalence at the time of survey design for countries performing surveys between 2009 and 2014 (observed/expected *100%)



An additional illustration of the importance of survey findings for those surveys conducted between 2009 and 2014 is the extent to which the estimates and their confidence limits from the survey (shown in red) differed from WHO estimated values at the time of the survey (shown in blue; see Figure 2). Furthermore, the confidence intervals from the prevalence estimated based on the surveys were generally considerably tighter than those from the WHO estimates.

Figure 2. Pre- and post-survey prevalence estimates for countries conducting surveys between 2009 and 2014 (source: WHO presentation, 2016 Cape Town IUATLD meeting)



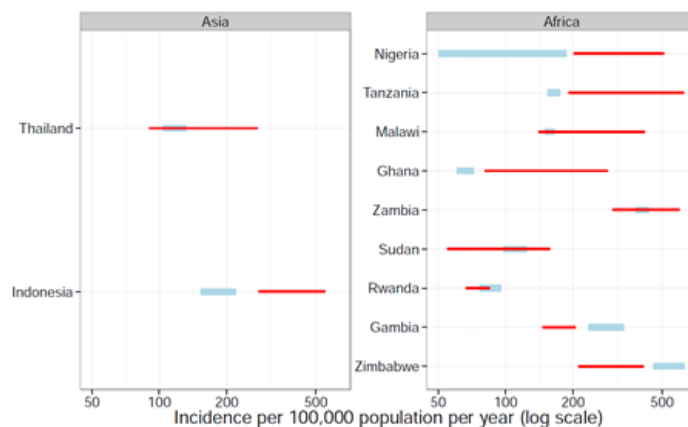
What impact have the surveys had on global estimates of TB?

TB incidence rates and the global number of cases are the most commonly used measures of TB burden, but are virtually impossible to measure directly or reliably in the absence of high-quality reporting systems. Until recently, most countries used notification data combined with expert

opinion to develop these estimates⁶. As mentioned previously, incidence can be derived from prevalence by making assumptions about duration of disease and/or by using modeling techniques. The availability of prevalence survey data for several high-burden countries has resulted in major revisions in estimated incidence rates.

Pre- and post-survey incidence estimates are provided in Figure 3. The 95% confidence interval around incidence estimates from the surveys is displayed in red, while the 95% confidence intervals around WHO estimates at the time of the surveys is displayed in blue. These findings demonstrate that the incidence estimates derived from prevalence survey data are higher than the pre-survey estimates in four, and lower in two, of the countries that conducted surveys between 2012 and 2014. The confidence intervals are broader, suggesting that expert opinion estimates often don't approximate actual burden, and highlights the uncertainties inherent in estimating disease duration. According to the most recent WHO figures, 46% of global incidence is now derived from prevalence values obtained by the TB Prevalence Surveys.

Figure 3. Pre- and post-survey incidence estimates, 2012-2014. (source: WHO)



The changes in incidence rates based on the survey data, especially for the high-burden countries of Indonesia and Nigeria, has had a profound effect on the estimated global number of TB cases. Findings from these high burden countries have resulted in an increase in the estimated number of TB cases worldwide from 8.5 million to 9.6 million, which has had profound implications for countries, and for global advocacy, fund-raising, and program activities.

What do stakeholders perceive as the value of the estimates produced by the prevalence surveys?

A consistent theme of the stakeholder interviews was the enormous value of having more accurate data, as reflected in the following sample of quotations. Many described the surveys as “game changers” that gave more realistic estimates based on actual data. These more accurate estimates are deemed essential for national planning, targeting, advocacy, and funding purposes. Several stakeholders also commented on the finding that the number of cases was far higher than

⁶ http://www.who.int/tb/publications/global_report/gtbr14_online_technical_appendix.pdf.

those previously derived using estimation methods, thus changing the visibility and relative importance of TB as a major public health issue within countries but also on a more global scale

“[The surveys] are essential to our work, especially as we talk about getting more and more grounded in facts rather than estimates based on estimates based on estimates.”

“You get more data –we thought we were fighting a little snake, but we are really fighting Godzilla.”

“Numbers have become critical for funding allocations but also for advocacy. When you estimate mortality [using the new prevalence estimates], you get many more cases and deaths. TB and HIV both [were] killing the same number of people, but in reality TB probably killed more than HIV worldwide [in the past decade].”

“You recuperate [survey costs] rapidly in terms of efficiencies in how you run your program. [There’s a] much more focused program and better use of resources if data are accurate...”

“[Country X] is an example—[finding a high rate] was really painful and caused turmoil at government level, but it has given visibility to TB and [the government knows] the world is looking at them.”

Serial surveys have proven to be particularly valuable. In both Cambodia and China, repeat surveys produced data documenting reductions in prevalence, offering critical evidence that DOTS strategy may have contributed to the decline. These repeat surveys also helped to identify areas where additional improvements were needed.

“The three most recent China surveys, 1990, 2000, and 2010, coincided with pre-DOTs, halfway through moderate quality DOTs in half the country, and full scale up with good coverage by 2010. You can clearly and convincingly see that the data are really strongly supportive of changes that have occurred in TB control.”

All ten NTP managers interviewed felt that the studies provided valuable information that has allowed them to better understand their TB situation and, as a result, design their TB programs. However, in many cases, the findings were not immediately usable for the Global Fund application process as survey results were not available in time for the 2014-2016 funding cycle. Although these numbers can be included in the 2017-2019 applications, the opportunity to obtain additional funding to diagnose and treat a greater number of cases was missed in some countries where the results of the incidence and prevalence estimates from the survey were not available for use in the Global Fund new funding model (NFM) application. This is a particularly relevant issue in countries where the survey produced estimates higher than the assumed values. While all countries were eventually able to use their survey data as the basis for new strategic plans, and therefore as part of the Global Fund NFM application process, it emphasizes the importance of strategic planning the timing of surveys and ensuring rapid analysis of results.

Beyond the national prevalence estimates, what other information useful to national TB programs came from the surveys?

In addition to the prevalence estimates, the surveys provided countries with additional information about 1) the geographic distribution, clinical, and/or demographic characteristics of TB cases 2) the proportion of known and new cases on treatment; 3) the validity of current case-finding algorithms; 4) health-seeking behaviors among persons with presumptive TB; 5) prevalence of non-TB mycobacteria, and in some cases an indication of the levels of drug resistance; and 6) additional data, such as behavioral risk factors including smoking, alcohol use among TB cases and non-cases, as well as insight into the TB/HIV co-epidemics for countries that conducted HIV testing.

Geographic distribution, clinical, and/or demographic characteristics of TB cases

All 16 surveys had sample sizes that were adequate to obtain a single national estimate rather than to provide estimates by geographic subunit. However, some countries (i.e. Nigeria and Zambia) had more cases than anticipated, which resulted in the possibility of producing provincial/state estimates. Although these estimates had wide and often overlapping confidence intervals, they did provide evidence of regional variation.

Almost all countries performed stratified sampling for urban/rural areas, and sometimes for additional strata (i.e., pastoralist in Ethiopia, nomadic in Sudan, semi-urban in Malawi and Tanzania) with the goal of obtaining a more accurate national estimate and decreasing the required sample size. Most of the countries used the strata-specific estimates to identify areas or groups with higher TB burden.

The data were also used to identify the symptoms most commonly associated with bacteriologically positive TB; this was useful for clinical training and development of appropriate screening algorithms. In addition, countries compared rates by age group and gender, and in some cases by wealth status, education, or occupation. These additional analyses have been useful for program planning, especially where countries estimated patient diagnostic rate (PDR)⁷ to obtain an indication of relative underdiagnoses or under-reporting of specific groups. Often, data were triangulated with other sources such as the TB registers.

Proportion of previously detected cases

Countries collected information about treatment history and care seeking from those with TB symptoms. Using these data, it was possible to assess the percentage of bacteriologically confirmed cases who had been previously treated or were currently on treatment in the NTP and elsewhere, as well as cases which had not been detected by the program prior to the survey. In China, the relative proportion of new and previously treated cases changed over time, indicating the success of the DOTS strategy. The following represents an example of the impact of such findings on the National Strategic Plan:

“Because the prevalence survey showed lots of missed cases, [the NTP] plans on moving to GeneXpert and CXR as screening tool...and more sensitive screening in outpatient care—persons with cough + one more symptom get an evaluation. These changes have been included in National Strategic Plan.” (A stakeholder)

⁷ Borgdorff M, Emerg Infect Dis. 2004 Sep; 10(9): 1523–1528

Limitations of current case-finding algorithms

The surveys allowed programs to examine the sensitivity of their diagnostic algorithms for detecting active TB among those with smear- or bacteriologically-positive TB. Some countries performed these analyses and have reconsidered their algorithms, especially regarding duration of cough. In Cambodia, for example, the country changed its algorithm from the single symptom, cough greater than two weeks, to a four-symptom screening algorithm that consisted of cough, fever, weight loss, and/or night sweats for > 2 weeks.

Health seeking behavior

All countries collected data on health-seeking behaviors for individuals with a positive symptom screen for TB, providing important data regarding TB cases who should have been detected by the country's case-finding methods and diagnostic algorithm. Some countries also collected this information on individuals who were currently on treatment and/or who had been previously treated. In many cases, findings were revealing and resulted in changes in programmatic approaches to case finding and in diagnostic algorithms. In some countries, the main finding was that many of the patients who had gone undiagnosed had been previously seen by government health providers; in others, a substantial portion of patients had sought care in the private sector or even in pharmacies. Additionally, patients who smoked and had chronic cough did not always seek care.

“We went into hard to reach areas, we learned a lot about the TB problem first hand... We learned a lot about our case-detection (the data itself was very important and informative) but we also learned the reasons for the high prevalence. Access to care is quite an issue here. And there are capacity limitations – many of our health workers are missing the diagnosis. So we learned a lot about why the prevalence is so high.” (NTP manager)

Laboratory findings

Use of culture in many of the countries revealed unexpectedly high proportions of non-tuberculous mycobacterium (NTM), which has implications for diagnosis and treatment. In some countries, the proportion of NTM exceeded 15%, suggesting that MTB-specific testing with technologies such as the GeneXpert MTB/RIF assay may be warranted in spite of their greater costs. This finding needs further investigation to determine whether the NTM detected is an environmental artifact or has public health significance and whether it impacts routine TB case detection in a manner that warrants action. This issue is particularly relevant if countries base their plans for increased case-finding activities on the use of sputum smear microscopy.

Drug resistance surveillance is usually performed on a large sample of specimens from new and previously treated TB cases. Although the sampling frame and sample sizes are different from those recommended in the WHO guidelines for surveillance of drug resistance—most TB prevalence surveys have only 100-200 identified TB cases--the data obtained on samples tested from the prevalence surveys can nonetheless yield valuable information on drug resistance patterns among prevalent TB cases by treatment status. Findings from the survey can provide a base for sample size calculations for future surveys, especially for countries without a history of drug resistance surveillance.

Risk factors for TB

Several countries collected data on risk factors amongst those who had a positive symptom screen for TB, including smoking, alcohol use, HIV status, occupational history, history of diabetes, crowding, and indoor air pollution. Using these data, it was possible to compare the prevalence of these factors in symptomatic populations with and without confirmed TB. Some countries also collected data from routine program cases around selected cluster(s) to identify differences in key characteristics (e.g., socioeconomic status, age, gender, risk behavior: smoking, alcohol, etc.) between cases detected by the program routinely and those detected via the survey. Surveys that collected HIV data were able to develop a detailed picture of clinical and laboratory profiles of HIV+ and HIV- persons with TB. Unfortunately, however, not all countries which collected these data on symptomatic participants routinely included all results in the final report(s).

As will be discussed later in this report, few countries gathered this data from their non-symptomatic population. This would be a valid way of examining risk factors and would provide valuable prevalence information to the HIV and other non-communicable disease programs.

Stakeholder comments on data use

In those countries in which additional data have been collected, communication of results to partners and stakeholders has not always been complete and are not routinely included in the final report(s). Several stakeholders expressed the concern that prevalence surveys essentially provided a single number: TB prevalence. Some also commented that the data could be analyzed in innovative ways, both at national level but also by pooling or performing a meta-analysis of data from multiple countries. This work could be facilitated by the establishment of a global data repository open to researchers both within and outside countries. The following represents comments by stakeholders on these issues:

“We haven’t even optimized the results of the research—we are in essence changing one number—which doesn’t help in the country planning and doesn’t change the way they do things. In the countries that have done these surveys you rarely see it being used to improve the NTP since it doesn’t show them where to focus their resources... If we decide to do larger more expensive surveys, we need to optimize them not only for epidemiological purposes but also for planning and prioritizing interventions.” (A stakeholder)

“[These surveys can provide] a wealth of data in understanding clinical presentation and types of x ray findings. Follow on studies are possible to, for example, follow up persons with positive chest x rays and negative laboratory findings. You need to have an incentive in place, though, to get data analyzed.” (A stakeholder)

How did the countries use these data, and have changes in practice or policy resulted from the findings?

All of the NTP managers interviewed indicated that they routinely and actively used data from the prevalence survey(s) to make decisions about the implementation and design of their national TB programs. Although several of the proposed changes have yet to result in actual policy changes due to a variety of factors (e.g. timing, funding, political leverage), programs are

implementing, or are planning on implementing the following modifications to their TB programs:

- General updates to national strategic plans, goals, targets, and priorities that form the basis for the Global Fund New Funding Model (NFM) application
- Focus on newly identified population groups or geographic areas at higher risk
- Increase in emphasis on and activities related to active case finding and case detection
- Increased focus on the private sector and its role in TB case detection and treatment
- Modifications to screening criteria and algorithms (especially in response to identification of cases who were symptom-screen negative, as well as smear negative, culture positive cases)
- Implementation of GeneXpert (Xpert® MTB/RIF)
- Increased use of digital X-rays

“We found that the prevalence rate is higher in urban, but the rural population is greater. We are now trying to address the disease burden (not rate) so we are trying to boost our coverage of the rural areas. We are also increasing focus on private sector. We are changing our diagnostic algorithms to include chest X-ray and have put efforts into active case-finding, especially among our higher risk groups (for example, we are doing contact tracing). We use [GeneXpert, but primarily for those who have risk for drug-resistant TB. We also expanded community involvement to increase engagement of stakeholders.” (NTP manager)

In addition, in many cases, NTP managers commented that the data from the surveys gave them the power to influence change for TB priorities, strategies, etc. within their countries. Finally, the data are being used to secure additional resources and funds for TB activities.

“We are preparing some specific activities to improve screening – using CXR and new active case-finding and [Gene]Xpert machines. We are looking to use Global Fund money to push case-detection, especially in the higher burden groups – the elderly, but also children. We are using this data to convince partners and stakeholders to shift to case-finding and to provide the needed funding” (NTP manager)

For some countries, the asynchrony between the completion of survey analysis and the timing of Global Fund cycles has proven challenging as countries move to implement changes in their TB programs. There were examples of countries that either found a higher than expected number of cases and/or identified a need to intensify case finding (both resulting in increased programmatic costs) and have had to wait up to three years for the next funding cycle. These missed opportunities for funding impacted countries’ ability to implement identified programmatic and operational changes. To optimize the utility of survey results, we recommend that countries work to align the timing of survey result availability with the next National Strategic Plan.

What additional benefits did the NTP managers report from participation in the survey?

The ten NTP managers interviewed cited a number of additional benefits that accrued from in the surveys. These included the following:

- Capacity building, specifically for NTP, radiology, and laboratory staff

- Durable goods, which were then recycled for program purposes (e.g. vehicles, mobile CXRs, GeneXpert machines and microscopes), although in some countries, lack of ongoing maintenance contracts and supplies remain obstacles to their practical use after the survey.
- Teams, equipment, and technical capacity for active case finding. For example, Rwanda and Malawi have used the mobile X-ray van and the survey staff to systematically screen prison populations.
- Teams and technical capacity for further population-based surveys or national research efforts. Zambia, for example, absorbed the survey data management team into the monitoring and evaluation division of the Ministry of Health, thus increasing future survey capacity.
- Improved collaboration and communication amongst in-country divisions and institutes.

The following quotes summarize the experience of two of the NTP managers:

“Apart from the results, [the survey] offered the opportunity to test the capacity of the program to its limits. NTPs should take advantage of this—it discloses program weaknesses, it exposes your laboratory, it lets you see your program staff capacity, your resource mobilization capacity, and tests timeliness of procurement. It has developed our capacities in operations research and has given confidence do to research... [It has also] strengthened our laboratory systems—build QA capacity, GeneXpert, lab management. [We made] linkages with other partners, which has intangible benefits that can’t be quantified by way of costs. It helped in logistic management and also strengthened role of leadership in health sector. The benefits, other than the [prevalence] figure given, were great.”

“The biggest benefit is the knowledge we gained – which we can use to revise our plan and apply for additional Global Fund and support from Global Drug Facility (GDF)...[The survey] allows us to plan and realistically forecast and mobilize the funding. Also we built capacity, especially for case-finding. And we are using the portable CXR machines to accelerate case finding activities (using mobile teams equipped with portable digital CXR to go to hard to reach rural areas and the urban poor)”

How useful were the surveys to correctly assess under-diagnosis and under-reporting of cases in the program context?

Commonly, the criteria used to identify cases in prevalence surveys do not match those used for routine programmatic purposes. Cases currently on TB treatment are only taken into account in the prevalence estimation if they are bacteriologically positive at the time of the survey. The survey prevalence figures include patients with negative symptom screen but positive CXR who would not normally come to medical attention in the absence of screening programs, as well as individuals with a shorter duration of cough than is normally used to trigger TB evaluation. Additionally, the use of centrifuged smears and/or light-emitting diode (LED) fluorescence microscopy in countries that routinely use direct smears and light microscopy can also impact the survey’s ability to reflect the country program’s performance in case detection.

The majority of prevalence surveys used a cough duration of greater than two weeks in the screening algorithm, in alignment with NTP policy. However, some surveys used different cough durations (e.g. cough for one week in keeping with their algorithms for diagnosis among HIV patients, whereas some countries used three or more weeks); these misalignments with routine

NTP definitions limits comparability and sensitivity of the screening algorithm. A similar pattern was seen with sputum samples. Whereas most surveys used two sputum samples, in keeping with national policy, some countries routinely collect three sputum samples. Additionally, while the majority of countries used direct smears in keeping with local practices, some used centrifugation, which may increase sensitivity. Lastly, several countries used fluorescent/LED microscopy for their surveys, which were not used universally in routine work in these countries; both of these approaches have a higher sensitivity than does conventional microscopy.

[Were the surveys leveraged for other purposes?](#)

These surveys represent what are probably the largest and highest quality adult health surveys in the countries in which they have been conducted, and typically exclusively focus on TB. Concurrently, we are witnessing an increased interest in non-communicable diseases but a continued lack of recent population-based data on the prevalence of these conditions and associated risk factors. While several prevalence surveys have collected information on a limited number of health behaviors and HIV status (typically only for individuals with positive TB symptom screen), these data are of limited value and do not assess prevalence. For example, few countries have collected non-TB data from the full survey population or a sub-sample thereof. The additional data that have been collected in prevalence surveys, including the sub-populations on which they were collected, is presented in Table 1.

Table 1. Additional data collected on all or a sample of symptomatic and non-symptomatic participants:

Country	HIV status	Wealth/equity indicators	Health behaviors	Other diseases/ conditions
Africa				
Ethiopia				
Gambia				
Ghana				
Malawi	By history		Smoking	
Nigeria			Smoking	
Rwanda			Smoking, alcohol (sample)	
Sudan				
Tanzania				
Zambia	Opt-out testing			
Asia				
Myanmar	By history		Smoking, alcohol	BMI+history of diabetes, hypertension
China				
Cambodia				
Lao PDR				
Pakistan				
Thailand				
Indonesia			Smoking	Diabetes

Because this additional data collection and analysis were often secondary survey objectives, the approach was commonly not systematic or routinized. As a result, the data were rarely reported in the final report, and it is difficult to assess how the results were used.

Seven of the 10 NTP managers felt that it is feasible and useful to include other diseases or conditions in future surveys, although four expressed concerns about adding HIV testing. For example:

“The prevalence survey is very expensive, and it is a shame that we cannot use that same avenue to gather information that can help with other disease. With proper planning, I think we could include other aspects.”

“We think that is important and feasible. We were worried that HIV screening would jeopardize participation, but we learned that the stigma is reduced, and people were open to the idea of testing... We found that people often came to the survey sites with other problems. They thought we were a hospital or mobile clinic and they came with other conditions – we think that people would report their other conditions and be open to testing.”

What are the staffing needs to conduct a quality survey that is completed in a reasonable time and on budget, without disrupting routine NTP activities?

TB prevalence surveys are labor intensive. In general, each survey generally required the following:

- An executive or steering committee consisting of about 10-20 experts
- A technical committee/technical advisory group of 20-30 persons (representing the various competencies such as census, radiology, and bacteriology, and data management)
- Several fixed survey teams consisting of 10-15 staff
- A local support team with an additional 10-15 staff

For the three countries visited, the fixed field teams ranged in size from three teams of 15 in Cambodia to four teams of 10 in Ghana and five teams of 12 in Ethiopia.

A few countries noted that inadequate staffing caused delays in field implantation; the major rate-limiting component was often the lack of physicians on the field teams to read CXRs and/or serve as team leaders. The field team coordinator role is a full-time task; lack of qualified people can become a rate-limiting step in the survey implementation. As a result, we recommend that this role not be combined with other demanding roles, such as field CXR reading.

Because of the limited number of radiologists in many contexts, as well as their significant routine commitments, many countries found it challenging to identify and retain staff to perform central quality control of CXR reading. In some cases, these limitations necessitated the use of external radiologists or those from private facilities to complete the final readings and conduct quality assurance. Laboratories can also create a critical bottleneck, as the volume of survey specimens far exceeds the routine burden of the TB programs. Prior to survey implementation, experience in managing large numbers of cultures may be limited. Many countries trained or hired additional laboratory staff for the duration of the survey.

A few Asian countries conducted the surveys using existing NTP staff, but in other settings, the staff commonly came from the research institutes implementing the survey or were hired by the NTP. Some degree of NTP program disruption occurred in most countries—especially in the laboratory—but the level of disruption varied widely. In at least one country that used its own

NTP staff, routine case finding was impacted during the survey period, and in some countries the disruption was more complete:

“Everything was impacted, almost coming to a standstill. Most activities were disrupted. The survey came at a point when we had funding hiccups, so it made the problem worse. We used the NTRL, which was overwhelmed. The CXR reading took the attention of the clinicians. The disruption was very significant – most of the key [survey] activities were performed by key NTP staff.” (An NTP manager)

What measures were put in place to monitor quality?

All countries included extensive descriptions of quality control measures in their protocol. However, it was difficult to assess in most instances the extent to which the quality measures had been fully implemented during field operation since results for these measures were not presented in the final survey report. During the field work, quality control of CXR readings in near real-time is essential to carry out while it is still possible to collect sputum from missed CXR-positive participants before the survey team moves on. Correct reading of sputum smears, and examination of contamination rates and inconsistencies between smear and culture results are also essential ongoing quality control activities. Finally, data entry and cleaning must be done with care and all records successfully linked.

Adequate training is a critical driver of survey quality and appears to have been conducted well in most countries, often with assistance from the lead TA partner or WHO. Although most protocols mentioned repeat symptom screening and interviews of those with positive symptom screens, the reports include little information about if and how these QA elements were conducted. When this information was reported, discrepancies were sometimes observed. CXRs were routinely reread for QA; the typical approach was to reread all abnormal and a sample of normal images ranging from 10% to 100%, often by a joint team, but sometimes by single radiologists with a 3rd radiologist as tiebreaker. In some situations where digital CXRs were used, re-reading was conducted in near-real-time, and persons with initially false-negative readings were located and sputum specimens obtained before the team left the cluster. However, several countries faced technical challenges in transmitting digital images for remote re-reading. Zambia solved this issue by obtaining temporary extra bandwidth in each cluster during the team’s visit. In some countries, re-reading of the CXR represented a major rate-limiting step in the data finalization and analyses, especially in cases for which a high percentage of images required re-reading.

According to most protocols, both internal and external microscopy quality control was conducted. Internal control involved re-reading of all positive and a sample of negative slides by the national reference laboratory. External quality assurance consisted of proficiency and panel testing, and was completed with support provided by the Supranational Reference Laboratories. Quality control of culture procedures generally used standard operating procedures including the use of positive and negative controls and assessment of contamination rates. In addition, the surveys assessed the proportion of culture-positive among the smear-positive patients. However, the extent to which QA measures were conducted such that the outcomes could inform operational changes is not clear from most reports. Finally, though not intended for these purposes, GeneXpert provided a useful point of comparison for smear and culture results and, in

cases of culture contamination or strong decontamination, identified cases that may have been missed using traditional methods.

Most protocols included double data entry, but the extent to which this was conducted in the field, and the discrepancies observed, were not routinely reported. As discussed, some countries used bar-coding and electronic data entry as a means to improve linkage of records and reducing error. These techniques appeared to be successful in the countries in which they were used, although they did increase survey costs.

What were the primary issues encountered in processing the laboratory specimens?

As shown in Table 2, laboratory procedures were highly variable from country to country, making cross-country comparisons challenging and also potentially affecting the prevalence estimates obtained. The number of sputum specimens tested ranged from 1-3, some surveys used centrifuged smears, while most used direct, and slides were examined using fluorescent and LED microscopy, light microscopy, or a combination of the two. Culture techniques also varied, with some countries inoculating single samples. Eight of the sixteen surveys used LJ media, 5 used Ogawa, and three used MGIT. Furthermore, they various surveys employed different methods and products to identify MTB. GeneXpert was introduced in the more recent surveys, generally to confirm smear-positive sputum and/or assess MTB status when cultures were contaminated or indeterminate. Drug susceptibility testing, which was done in 10 countries primarily in Asia, was also conducted using a variety of different techniques.

Table 2. Overview of laboratory testing approach by country

Country	Year	Smear	Culture	GeneXpert	DST performed
Myanmar	2009	2 FM/ZN	2 Ogawa	No	No
China	2010	3 ZN	2 LJ	No	Yes
Cambodia	2011	2 FM/ZN	2 Ogawa	No	Yes
Ethiopia	2011	2 FM	1 LJ	No	No
Lao PDR	2011	2 ZN	2 Ogawa	No	Yes
Pakistan	2011	2 ZN	2 LJ	No	Yes
Nigeria	2012	2 ZN	2 LJ	No	No
Rwanda	2012	2 FM	2 LJ	No	Yes
Tanzania	2012	3 FM	1 LJ	S+ (retrospective)	No
Thailand	2012	2 ZN	2 Ogawa	No	No
The Gambia	2012	2 FM	2 MGIT	No	No
Ghana	2013	2 ZN	2 MGIT	S+ or contaminated cultures	No
Indonesia	2013	2 ZN	1/2 LJ	S+ or indeterminate cultures	No
Malawi	2013	2 FM	2 LJ	S+ or contaminated cultures	No
Sudan	2013	2 FM	2 Ogawa	No	No
Zambia	2014	2 FM	2 MGIT	S+ or contaminated cultures	No

FM = fluorescent microscopy; ZN = Ziehl-Neelsen; LJ = Lowenstein-Jensen; S+ = smear-positive DST = drug susceptibility testing

In addition to issues with standardization, many of the NTP managers reported that handling the large volume of specimens presented a major challenge for ongoing laboratory activities. Maintenance of field laboratory equipment (safety cabinet, etc.) and a consistent electrical supply, transporting specimens, and maintaining the cold chain of samples from the field to specialized laboratories was also challenging in many contexts. Finally, culture contamination rates varied widely, but in general, the highest rates were seen with liquid culture (MGIT).

What issues were encountered in data entry, management, and analysis?

In the countries for which data were available on actual survey time lines, the time between completion of field data collection and presentation of results to the Ministry ranged from 3-20 months. The fastest turn-around time was in Zambia, which implemented a fully digital survey; in this context, it took just 3 months to present the preliminary results to the MOH and key stakeholders and an additional 3 months to write the final report, although it took an additional 7 months for the report to be formally released. It is worth noting that not all countries that used bar coding and electronic data entry had equally rapid data turnaround times. Countries that seem to have fared the best gave considerable thought to the design and flow of questionnaires and numeric coding of data responses and used bar coding and electronic data entry.

Several countries struggled to create a final cleaned and validated data set; some countries saw delays of up to 24 months before analysis could begin. In the country with one of the longest delays, problems with patient identifier numbers, introduction of new forms during the survey, listing of non-presumptive cases in the presumptive case register, missing presumptive cases, and problems with data mergers all represented challenges in creating a final analyzable data set. Some of these problems were the result of a security situation which prevented good field monitoring and thus timely identification of challenges.

In several countries, the validation of lab results and/or CXR readings delayed the availability of the final database. In one country, a backlog occurred in data entry, the data on laboratory findings and central CXR reading results were not checked and cleaned regularly, and inconsistencies and duplicates in both databases were identified. The problem was further compounded by the need to transfer all laboratory data to a new register mostly due to very poor printing quality of the lab registry with a subsequent risk of transcription errors.

Seven of the 16 countries used MS Access for data entry, while the remaining countries used a variety of other software programs ranging from Epi Info, to SPSS, Stata, and in some cases, multiple systems. Most countries performed their analyses in STATA using a standardized STATA program provided by the WHO-led task force. Data analysis in most countries depended heavily on external TA by WHO staff and others as well as the analysis workshops held in Geneva. Most countries could have not completed the data analytics without these external resources. In this context, it is important that the country teams should be heavily involved in the

process to maximize their ability to use, disseminate, and make decisions based on survey results.

With few exceptions, analyses were limited to overall adult TB prevalence estimates, as well as sub-groups and health-seeking behaviors. In a limited number of countries, other secondary variables were adequately analyzed and commented upon in the reports. More detailed and thorough analytics were most successful when a PhD candidate or postdoctoral fellow was given the opportunity to do further analyses as part of their thesis or as publications for the literature.

How was the actual quality of the surveys?

Overall data quality is reliant on a number of different drivers, including response rates, accuracy of data collection, rate of false-negative CXR, consistent specimens from patients with positive symptom screens or positive CXR, high quality smear microscopy, careful culture procedures, and meticulous data entry and management. As mentioned previously, it was not always possible to examine each of these factors based on the final reports. A number of countries experienced low response rates, especially in some key age groups. Major laboratory issues, including missing specimens, over-decontamination, and lost or contaminated cultures also occurred. Most of these situations would have resulted in under-estimation of TB prevalence rates. By contrast, the extensive imputation that was needed in a few countries with lower response rates may have led to an over- or under-estimation of the TB rates, as detailed in the following section.

Most countries underwent a formal midterm review of the survey initiated by WHO and designed to identify potential quality issues. For some countries, the external monitoring team was independent of the technical agency providing the survey TA, but in many cases, teams also included members from the involved technical agency, bringing the independence of these reviews into question.

As previously discussed, there may be a greater role for an independent monitoring group that could assist in identifying problems and following through on their resolution, as well as in evaluating survey quality. This would place the burden of dealing with politically sensitive issues of data acceptance on a broader group rather than on WHO alone. It could also increase the probability that recommendations are fully implemented.

To what extent did the surveys produce reliable and credible data?

With some exceptions, the surveys had overall response rates greater than 80%, although rates as low as 57% were recorded. No response rate threshold appears to have been established by the WHO for acceptance of data; this would seem to be of particular importance as estimates of TB prevalence from Nigeria, a large country with low response rates had a major impact on the global TB burden estimates.

Even those surveys with high overall response rates saw very low participation in certain subgroups and clusters. Urban areas tended to have lower response rates than rural areas, and young males were less likely to participate. Imputation has been used to correct for poor response, but there is some debate over the validity of the methods since the imputation generally assumes a random distribution of missing outcome information. In reality, respondents and non-respondents differed in key ways, and if these differences are also associated with the risk of TB

(e.g., socio-economic status, gender, certain age groups), imputation may produce over- or under-estimates. Even in the three countries with a participation rate exceeding 90%, the imputation increased the prevalence rate of smear-positive TB by 6-13%. In cases where there may be concerns over the non-random distribution of outcome information, sensitivity analyses may be of use, although they do not appear to have been applied based on the final reports.

Other issues affecting validity include the rate of false-negative x-ray readings, the number of specimens obtained from each suspect case, contamination rates, and overly aggressive decontamination. Because one of the two criteria for initiating sputum collection is a positive CXR, false negative field readings may also affect reliability. Real-time quality control mechanisms would help identify these challenges and associated solutions over the course of the survey. Prevalence estimates can be affected by the number of sputum specimens collected across surveys and populations (e.g. two samples increase the likelihood of finding disease), contamination of sputum specimens in the absence of GeneXpert backup, and/or excessive decontamination, although it was not possible to quantify the effects of such factors based on the available data.

To what extent are the data comparable between countries?

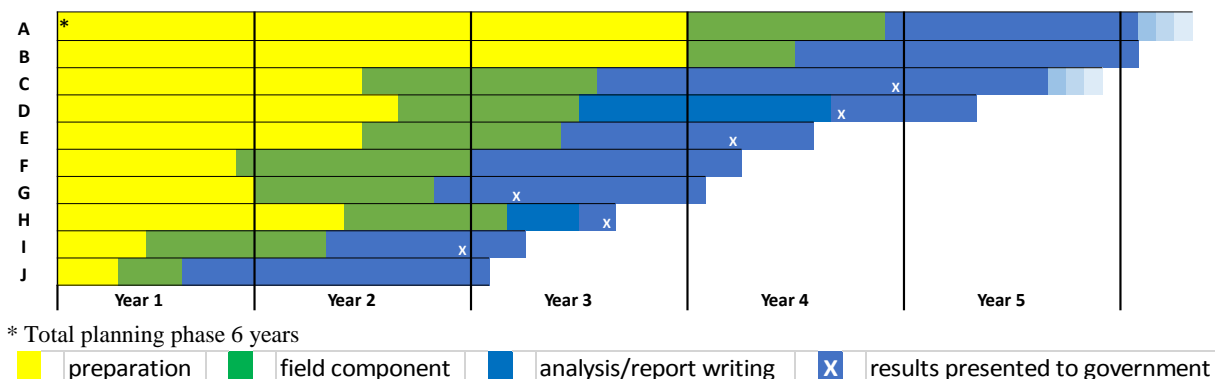
The development of an international database that included primary data from prevalence surveys that would allow groups to examine larger issues in TB epidemiology and the effects of programs on TB rates would be of great value. WHO is currently in the process of setting up a data repository. However, it is important to note that CXR readings and laboratory results are highly dependent on local techniques and skills, as well as other factors such as decontamination practices and media content. At present, there is a move toward a more standard questionnaire and consistent variable names and coding which would also facilitate analysis, taking into consideration local needs and definitions. In the future, automated chest radiograph readings and GeneXpert may also provide a path toward greater standardization.

A standard data set and centralized data repository would also encourage proper archiving of results and, more importantly, greater use of the data. The DHS surveys as well as a variety of US national surveys such as the National Health and Nutrition Examination Survey (NHANES), the National Health Interview Survey (NHIS), and the Behavioral Risk Factor Surveillance System make their data available at no cost to researchers, resulting in a rich body of research.

Were there time overruns?

The surveys took a minimum of two years to complete, with an upper limit of 10 years from protocol development to report publication. The time lines for 10 countries for which data are available are shown in Figure 4:

Figure 4. Time elapsed for preparation, the field component, analysis and report writing, and where available, when results were formally presented for 10 countries for which data were available.



The preparation time ranged from 5 months – 6 years, while the duration of the field component in the 10 surveys was 3-17 months. Analysis and reported varied widely, from 5 months to more than 2.5 years, with total timelines ranging between 25 months to nearly 10 years.

The time from protocol approval to beginning the survey was often affected by difficulties in obtaining funding and in acquiring/importing equipment. The time in the field was fairly standard, although weather, difficulties in reaching remote areas, equipment breakdown, and lack of qualified staff contributed to longer durations.

The time from survey completion to final report was of concern; written reports are not yet available for five surveys that began in 2013 or earlier (though in one case there is an English-language scientific journal article reporting the primary survey results). The reasons behind these delays varied but include time for completion of quality control activities and resolution of discrepancies, delays in data cleaning and analysis, and finally factors such as political considerations, concerns over data quality, lack of funding for writing and printing, staff turnover, lack of skilled epidemiologist(s) and/or statistician(s), and low priority for busy NTP managers.

Were there cost overruns?

While some countries included initial itemized budgets in the protocols, virtually none of the reports contained the final expenditures and it was thus difficult to assess overruns. Some donors reported being approached for additional funds to complete the surveys and at least one country experienced an estimated \$1M USD overrun. Initial budgets ranged from 0.9 million to over 5 million USD. The lowest costs were generally in those Asian countries that were able to leverage their NTP staff to conduct most of the survey. These surveys were primarily paper-based and used conventional radiography. Surveys with complex geographic challenges tended to be more expensive. The most expensive survey among the 16 was also the most fully electronic (bar coding + field data entry), although other surveys that used bar coding and electronic data entry and transmission for at least some aspects of the survey were less costly. Estimated costs and cost per survey participant are shown in Table 2.

Table 2: Number of participants, survey cost, and cost per participant enrolled for selected countries for which data were available.

Country	Number of participants	Cost, USD	Cost per participant (USD)
Myanmar	44,690	\$ 877,000	\$20
Pakistan	131,329	\$3,200,000	\$24
Lao	39,212	\$1,111,000	\$28
Ghana	61,726	\$3,000,000	\$49
Gambia	43,100	\$2,281,121	\$53
Rwanda	43,128	\$2,350,060	\$54
Indonesia	67,944	\$3,942,343	\$58
Ethiopia	41,667	\$2,832,420	\$68
Nigeria	44,186	\$3,067,804	\$69
Zambia	46,099	\$5,375,678	\$117

Not included in the costs were the technical assistance visits, which, as noted earlier, can exceed \$100,000 USD.

For those countries for which detailed budget information was available either from the protocol or the final report, the fieldwork was the most costly element, followed by acquisition of radiological equipment and mobile vans.

What were the major bottlenecks as reported by the NTP managers?

The most common bottlenecks resulted from chest radiograph readings and laboratory overload issues that led to delays in study completion, as well as the previously discussed challenges with data entry and analysis and report writing. When NTP managers were asked to list the major bottlenecks they encountered, the most common were difficulties in obtaining funding to conduct the surveys (cited by 5/10), procurement and equipment issues (8/10), laboratory issues (5/10), and logistical difficulties (6/10) in conducting the surveys. Concerns expressed by single NTP managers included low participation rates and acceptance of results.

To what extent did the data reach the countries' health leadership?

In virtually all the countries for which information on the methods used for disseminating survey results was available, briefings of government officials and of the NTP program at various levels were performed, and workshops involving donors, NGO, and the press were common. In some instances, these were conducted at the time of the release of the official survey report. In one case, a special briefing was held for parliamentarians, although outreach to political leadership did not appear to be common. Some also made efforts to disseminate the information to the broader public in the form of radio broadcasts or press releases. Of note, few if any of the programs appeared to have specifically developed a communication plan for the survey identifying the groups with which they would communicate, the message, the timing, and the modalities of communication, nor did they reserve funding for these activities.

What considerations should be taken into account in future activities?

There is a willingness and interest on the part of most stakeholders to identify and implement better approaches to prevalence surveys, including standardizing data entry and processing, using innovative methods such as automated x-ray readings, GeneXpert Ultra for those with positive symptom screens or CXR, bar coding, and moving to continuous surveys rather than periodic. Additional funding or piloting innovative strategies may be available through Global Fund monitoring and evaluation initiatives and/or other organizations such as the Bill & Melinda Gates Foundation.

“[We have] seen the usefulness of collecting and analyzing data appropriately, but we need to find a way to simplify the surveys. What technology is out there? Reading algorithms [for CXR], better CXR machines... GeneXpert Omni could be used—maybe not so far in the distant future—as a triage test with high sensitivity.”

Many countries, including several that are not on the list of high-impact countries, have expressed interest in doing surveys, which is likely to put a major strain on available technical resources and have serious financial implications. Care needs to be taken, however, to ensure that the in-country capacity as well as technical support is available to produce high-quality data:

“New countries should consider undertaking a survey if there is strong support from the Government/MOH/NTP, there is evidence to suggest that current burden of disease estimates may not be accurate based upon a weak surveillance system, and the country has a significant proportion of the world’s prevalent TB cases.... It has been recommended that non-global focus countries [that wish to do a survey] start with a small scale pilot exercise in known hotspots...; this will assist with capacity development and commitment prior to the real survey implementation.”

Countries have also expressed an interest in conducting repeat surveys, although a number of technical and financial concerns have been raised:

“WHO is willing to support repeat surveys. A willing commitment from the government/MOH/NTP along with the donors is paramount. The challenge in some countries is that as income status has improved since the last survey... countries may need to be co-funders... Technically assuming that the burden of disease is declining, more time is now required between surveys in order to detect a statistically significant change in prevalence e.g. 7-10 years”

“[In some situations, repeat surveys may be] worth doing to learn about dynamics of TB transmission, but in others they may not be necessary.”

The need also remains to improve surveillance so these surveys become unnecessary. Consideration can be given to establishing sentinel surveillance as a possible alternative to monitor trends and to re-visit tuberculin test surveys, especially given the new, more MTB-specific tuberculin products under development.

“Everybody has to have surveillance—we need to be able to count the cases—that’s the first thing we have to know. It’s one of the targets of the Sustainable Development Goals. It’s not easy, that’s for sure, but that doesn’t mean we shouldn’t do anything.... When the surveys are over] the countries still don’t have surveillance. [The money spent on the surveys] should be spent on surveillance.”

Conclusions and recommendations

TB prevalence surveys represent the most ambitious and complex health surveys in the world. WHO and its technical partners in the Global Task Force as well as the Global Fund have played a critical role in spearheading and funding these efforts, and countries have been highly committed to successfully completing them. The surveys have provided vital information and are universally valued in the TB world. At the same time, TB prevalence surveys are highly complex, expensive, require massive external technical assistance, and are subject to challenges related to radiography, laboratory testing, data management, and analysis. There are ways in which these surveys can be further improved to both increase their quality as well as their value for money. Going forward, the assessment team identified the following key issues:

1) The surveys should be simplified through greater standardization. New technical developments such as the use of GeneXpert should be incorporated to simplify and streamline the surveys.

At the Cape Town 2015 IUATLD meeting, Dr. Frank Cobelens of KNCV/AIGHD outlined a strategy that deserves serious consideration for future surveys. The approach aims to increase comparability between countries and reduce bias in prevalence estimates as well as reduce the need for the highly intensive technical assistance currently required for successful survey execution. Using this approach, CXR would be done using direct digital equipment and computer assisted diagnosis (CAD) reading in the field, with central re-reading for special purposes via a cloud connection. Those with CAD scores above a certain threshold would undergo a single GeneXpert test of a spot sample, and only invalid tests would be repeated. Those with positive GeneXpert tests would be asked to provide a second sample for smear and culture. Smear results would be used to compare with routine data and culture to confirm the presence of live TB bacilli and obtain isolates for future drug resistance or whole genome sequencing.

In this proposed revision, data from the CAD and GeneXpert would be linked to the field data using a single software package and transmitted for real-time survey monitoring. Prevalence estimates would then be based on GeneXpert and smear results. For comparison purposes, the GeneXpert findings could be used to provide rates of culture positivity based on known sensitivity and specificity data. Eliminating the use of smear and culture as the primary approach would reduce laboratory burden and costs substantially (despite the relatively high per-unit cost of GeneXpert). Additionally, this approach would provide an indication of MDR prevalence since GeneXpert also measures rifampin resistance, although its use would not replace the need for dedicated drug resistance surveillance with individual drug testing. Further efforts are needed to evaluate the advantages and potential disadvantages and to examine the feasibility of wide-scale field implementation of this diagnostic approach.

The assessment team recommends that electronic data capture should be routine; bar coding of questionnaires, CXR images, and laboratory specimens and results should be used to reduce error. Several countries now have models of bar-coding based systems that can be used to develop a more universal tool. Although room should be left for countries to individualize their surveys according to local needs, the survey design, variables, and coding should be standardized as much as possible, and analysis programs should be provided to support rapid data analysis. This will not only permit the development of a larger international data set that would prove invaluable for TB research purposes, but will also expedite analysis and reporting. Such an approach has been used in the DHS surveys with considerable success.

The Global Taskforce on impact measurement should take the lead for investigating the feasibility of a more standardized approach and seek the necessary resources to pilot these changes. Key evidence for such a survey should be provided by the current ongoing surveys in Bangladesh and Kenya that are using GeneXpert, culture and smear for all sputum eligible participants.

2) The Global Task Force should lead efforts to obtain external input from groups conducting other such large surveys to explore innovations in sampling and analysis that could improve quality and increase efficiency.

Experts from outside the TB world, including from the Demographic and Health Survey, groups such as the World Bank who have conducted large economic surveys, and other demographers, statisticians, and modelers with expertise in innovative survey and sampling techniques should be convened on an ad hoc basis. Their mission would be to examine alternatives to current survey design and sampling and to determine if prevalence surveys can be done more efficiently and using smaller sample sizes. This group could also address sample size issues involved in repeat surveys.

3) Prevalence surveys are expensive with important consequences for policy and funding, and therefore should adhere to Good Clinical Practice (GCP) principles.

The elements included under GCP principles include steering committees with independent members, continuous and protocol-defined quality monitoring, a data quality monitoring board that can make recommendations to the steering committee and sponsor, and protocol defined data analysis and endpoints. Implementing such an approach would not only lead to better quality surveys but would largely eliminate difficult dual role of WHO in monitoring the studies and ensuring that recommendations are followed.

4) TB prevalence survey data needs to be used more broadly to provide a better understanding of TB epidemiology and strengthen national and international TB control efforts.

Prevalence surveys provide a rich source of data that can be used to understand the dynamics of the TB epidemic and improve TB control efforts, both nationally and internationally.

Within countries, data is not always systematically analyzed, and secondary survey objectives/results are often left out of the final reports. Furthermore, critical TB control questions could be answered by embedding specific modular studies into the main survey. Creative means should be developed to identify persons who can conduct such analyses (as an example, the PhD program at the University of Amsterdam, which is willing to have these in-depth analyses serve as thesis projects for students who are accepted to their program). This would also serve to build in-country research capacity. Making the data sets widely available to researchers will also increase the use of these valuable data and increase global TB research capacity as well as increasing the knowledge base about TB.

5) Opportunities for synergies with HIV and non-communicable disease programs should be sought to take advantage of the quality sampling and to provide political and financial support for the surveys.

These surveys, which are of high quality and represent one of the few surveys done on adults of both genders over the ages of 15, provide a unique opportunity to obtain additional vital prevalence data that could be invaluable for other country-level disease control programs. HIV testing of a sample of the entire population has been shown to be feasible, and does not result in excessively high refusal rates. DHS surveys have also demonstrated response rates in excess of 90% when HIV testing has been added. Following the global ratification of the intention to treat policy, serious efforts should be made to, at a minimum, integrate HIV testing in the surveys and possibly integrate the current parallel HIV and TB prevalence surveys conducted in many African countries. Synergies with chronic disease programs and the WHO-sponsored STEPS surveys to measure the prevalence of diabetes, hypertension, obesity, and relevant health behaviors such as smoking should be actively encouraged and explored. These synergies may result not only in increased funding and staff for the surveys, but also could increase the local advocacy base for their performance. In an era of electronic data collection, sharing of data with other programs should be technically feasible and straightforward. Finally, consideration should be given to creating a biobank of dried blood spots for testing of new TB diagnostics.

10) The 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, and funds should be provided to facilitate more rapid generation of reports and greater dissemination of results to a broader audience.

At present, most surveys lack a communication plan and many experienced delays in publishing the final reports, which may lead to missed opportunities for advocacy, dissemination, and use of findings by the broader TB community. Furthermore, these reports provide an important permanent record of key survey methods and findings. The use of a more standardized survey format could contribute to more rapid generation of reports, as is done with the DHS surveys, where publication of comprehensive final reports typically occurs within 8-12 months of completion of data collection. As part of the survey process, a detailed plan should be developed that includes details of the key recipients of the findings,

the key messages conveyed to each group, and when, where, and how such communication should be operationalized. The plan should be completed jointly with local stakeholders and advocacy groups, with expert consultation, as needed, from the STOP TB partnership and others. The initial budget should include adequate funds to ensure that the communication plans are developed and executed, including the writing of the final reports.

- 6) Funding for the surveys must be closely coordinated to avoid delays, and the timing of surveys should be better synchronized with the Global Fund application process so that funding can be obtained in a timely way to make TB program changes based on survey results.**

While it is neither expected nor feasible to conduct surveys aligned with Global Fund funding cycles, the surveys nonetheless serve to re-set the base estimates upon which future projections can be made. When surveys are completed shortly after a new application and funding cycle begins, this opportunity to initiate new strategies and provide care identified cases may be lost. The planning of the surveys should take into account these deadlines, with the idea of completing critical analyses in time for new funding cycles. If possible, building in some flexibility in funding deadlines, would also be useful.

- 7) Serial surveys may provide highly useful data to monitor trends and evaluate program activities, but guidelines should be developed outlining under what conditions, and with which frequency, they should be considered.**

Countries that have conducted a TB prevalence survey should seriously consider conducting a repeat survey to monitor the trend of TB prevalence in cases where 1) a large enough impact can be expected to measure a difference of public health importance, 2) the current surveillance system does not provide accurate enough data to support measuring impact, 3) the burden has not dropped to below 100/100,000 and/or the sample size for a repeat measure will not increase above a logistically-feasible sample size. Such surveys should be undertaken at intervals of about 10 years (with a range of 8-12 years) depending on the expected magnitude of the effect to be observed; smaller effects may require sample sizes beyond what is practically and financially feasible.

A challenge of repeat surveys will be achieving comparability, especially as methods evolve. Sampling strategies will need to be devised to use both the older and new methods so that results of the repeat survey can be appropriately calibrated.

At the same time, countries should continue their efforts to optimize their surveillance systems to reliably monitor trends.

- 8) Continued investments should be made in surveillance, and efforts explored to examine sentinel surveillance as an alternative to periodic surveys.**

Although the surveys provide valuable information, they are ultimately not a substitute for the development of quality surveillance systems. The Global Task Force on Impact Measurement should explore the possibility of using sentinel surveillance, for example, as an alternative to surveys, and should identify countries which have managed to establish quality surveillance systems and distill and apply the lessons to other countries.

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ANNEXES

Annex 1: Terms of Reference

INDEPENDENT ASSESSMENT OF NATIONAL TB PREVALENCE SURVEYS CONDUCTED 2009–2015

TERMS OF REFERENCE

Background

Since 2009, there has been a substantial increase in the number of national TB prevalence surveys being implemented in high TB burden countries. In the 1990s and most of the 2000s, there was typically 0–1 survey each year; between 2009 and 2015/16, it is expected that a total of about 25 countries will implement surveys; this includes 17 that were already completed by early 2015. Many countries are conducting surveys for the first time, or for the first time according to recommended WHO methods. For this reason, there are only three countries with repeat survey data that provide a robust measure assess of trends (Cambodia, China, the Philippines).

This increase in national TB prevalence surveys has required a substantial increase in investment. Each survey usually costs about US\$2–4 million. For surveys conducted since 2009, most of the funding has been provided through Global Fund grants. Contributions have also been provided from domestic sources (e.g. China, Nigeria, Malawi) and from USAID (e.g. Bangladesh, Pakistan and Zambia as part of the TB CARE project). Most of the funding for technical assistance to countries has been provided by USAID (via PEPFAR grants, the TB CAP and TB CARE projects and an umbrella grant to WHO), by the government of Japan and the Global Fund. USAID projects (e.g. DELIVER and TO 2015) have also provided procurement and logistical support (e.g. Indonesia).

The WHO Global Task Force on TB Impact Measurement was established in 2006 with a mandate to ensure the best possible assessment of whether 2015 global targets for reductions in disease burden are achieved (for fuller details, see www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en/). At the end of 2007, the Task Force agreed on three major strategic areas of work, one of which was national TB prevalence surveys in 22 global focus countries.⁸ A subgroup of the Task Force, with membership from countries and their technical and financial partners, has been extremely active in providing global guidance and coordination of technical support to global focus countries (support has also been provided to other countries, such as the Gambia, Laos PDR, Mongolia, Sudan and Zimbabwe, but with lower priority). This includes the production of a handbook on national TB prevalence surveys in 2010, which includes comprehensive guidance on design, implementation, analysis and reporting,⁹ and subsequent updates to this guidance in web appendices, papers or informal communications; global, regional and national workshops and training opportunities; peer-review of survey protocols; mid-term survey reviews; exchange visits; and country missions related to all aspects of surveys,

⁸ These are: Bangladesh, Burma, Cambodia, China, Indonesia, Pakistan, Philippines, Thailand, Viet Nam (Asia) Ethiopia, Ghana, Kenya, Malawi, Mali, Mozambique, Nigeria, Rwanda, Tanzania, Uganda, Sierra Leone, South Africa, Zambia (Africa). The criteria used to select these countries are explained in the WHO handbook on national TB prevalence surveys.

⁹ Tuberculosis prevalence surveys: a handbook. World Health Organization, 2010 (WHO/HTM/TB/2010.17). Available at: www.who.int/tb/advisory_bodies/impact_measurement_taskforce/resources/documents/thelimebook

conducted by experts from technical agencies, national experts who have played a lead or key role in previous surveys and independent consultants.

To date, surveys have yielded extremely valuable data on the burden of TB in high burden settings (including trends when repeat surveys have been done) as well as insights about the limitations of current NTP screening algorithms and health seeking behavior. Further details are available in survey reports, in published papers, in papers that are in press or in preparation,¹⁰ and on the Task Force website. Examples have also been highlighted in the annual WHO global TB report (see Chapter 2 of the 2010–2014 editions of this report). In 2012/2013, several high burden countries completed surveys (for example Tanzania and Nigeria) and in 2014/2015, an unprecedented number of countries will launch prevalence surveys, including countries conducting a survey for the first time and repeat surveys. In the near future and coming years, international donors will need to make strategic decisions about the level of investment in surveys and ensure accountability for recent investments.

As the global TB community and individual NTPs gain more experience with these surveys, it becomes crucial to identify and share lessons learned to inform, streamline and facilitate future surveys. For example, the surveys require a high level of commitment from NTP managers and/or their delegated survey manager, as well as significant support from the existing laboratory network. Some stakeholders remain concerned that surveys have been too disruptive to the routine operations of the NTP and laboratory network. The collection, transport, handling and timely testing of sputum specimens, which produce a unique body of samples that could be used beyond the immediate need of prevalence surveys to evaluate or validate promising biomarkers or surrogate markers of disease progression, has been challenging in some surveys. Data management is also a key challenge, given the need for different forms linked to clinical and survey data. In terms of findings and results, there is also concern that there are sometimes lengthy delays between the completion of field operations and the completion of data analysis so that results can be used to inform policy and program decisions, and that there are opportunities to improve communication of findings for key stakeholders. There are also specific aspects of the survey design and methods that could benefit from independent review, for example, the sampling methodology for repeat surveys to ensure comparability of results over time.

At the same time, new technologies and innovative ways to collect and analyze data (particularly those related to analysis of specimens) for population based surveys are or will be available in the near future, and stakeholders can benefit from an in depth exploration of how TB prevalence surveys could incorporate new methods to address ongoing challenges. In addition to the use of improved diagnostic technologies such as GeneXpert MTB/RIF, there are opportunities to consistently collect improved data on co-morbidities such as diabetes and HIV (including viral load testing, which will be increasingly important) and second line drug resistance (in selected settings). There may also be opportunities to improve data management to help address concerns about the timeliness and use of survey results. For example, other professional disciplines have used new technologies to collect, analyze and publish data quickly (e.g. rapid mobile phone based surveys for malaria).

For these reasons, USAID and the Bill and Melinda Gates Foundation will support an independent assessment of surveys from 2008 to the present.

¹⁰ For a full list, see the latest quarterly update on prevalence surveys issued by the Task Force subgroup. For Asian surveys implemented 1990–2012, see “National TB prevalence surveys in Asia 1990–2012: An overview of results and lessons learned” (in press, available from WHO Global TB Programme on request).

Objectives

7. To review survey design in recent (since 2008) national TB prevalence surveys, including the processes used to develop and finalize survey design, and their main strengths and weaknesses.
8. To review experience with survey preparations and actual implementation (including but not limited to procurement, survey management and staffing, the clinical and laboratory aspects of field and central survey operations, data management) in recent (since 2009) prevalence surveys, and identify the main strengths, challenges faced and how they were addressed, and lessons learned.
9. To review experience with analysis of data and reporting of results in recent (since 2009) prevalence surveys, including the processes used to produce final results and disseminate/use these results, and identify the main strengths, challenges faced and how they were addressed, and lessons learned.
10. To produce three in-depth country case studies that highlight key aspects of survey design, preparations, implementation, analysis and reporting of results.
11. To consider how surveys could be modified in future to make processes (from design to reporting) more effective and efficient, including via the use of new technologies.
12. To consider the future role of prevalence surveys in efforts to improve measurement of the absolute burden of TB disease and trends in this burden.

Expected Outcomes/Deliverables

A report that includes:

1. A clear assessment of whether the design of surveys and the processes used to develop and finalize survey design since 2009 have been appropriate, and associated recommendations for improvement in future surveys if applicable.
2. A clear assessment of the main strengths of and challenges faced during survey preparations and implementation in surveys planned or implemented since 2009, how challenges were addressed and the main lessons learned, and associated recommendations for improvement in future surveys if applicable.
3. A clear assessment of the main strengths and challenges faced during data analysis and reporting of results for surveys implemented since 2009, how challenges were addressed and lessons learned, and associated recommendations for improvements in future surveys if applicable.
4. Three country case studies from USAID TB priority countries that clearly illustrate experience in survey design/implementation/analysis and reporting.
5. Clear recommendations for how surveys could be made more effective and efficient in future, with specific attention to the role of new technologies.
6. Clear recommendations regarding the role of prevalence surveys in future efforts to measure the burden of TB disease and trends in this burden.

Methods

The assessment should include interviews with key stakeholders, including:

- Staff with a key role in leading and managing surveys. For example, this includes survey principal investigators, survey coordinators, national TB program managers, survey data managers and laboratory staff;
- Senior officials of Ministries of Health;

- International experts that have provided guidance and support to surveys (including those from technical agencies and independent consultants);
- WHO staff that have played a lead role in providing global guidance and coordination of technical support to countries implementing national TB prevalence surveys;
- Staff from international donor agencies that have supported national TB prevalence surveys, in particular the Global Fund and USAID (including staff from headquarters and country missions).

It should also include desk review of key documents such as survey protocols; reports from missions by technical advisors; reports from mid-term survey reviews and other relevant/informative trip reports; workshop agendas, background documents and presentations; quarterly survey progress updates issued by the WHO Global Task Force on TB Impact Measurement; and final survey reports.

The assessment should include site visits to three USAID TB priority countries that are in one of the three phases of prevalence surveys: planning, implementation and analysis. Criteria to be used for country selection include:

- Baseline vs. repeat surveys – ideally the visits should include countries implementing surveys for the first time (likely in Africa) and countries conducting a repeat survey (Philippines, Myanmar and Viet Nam).
- Regional variation: Given the differences in regional capacity and experience, the evaluation should include surveys from Asia and Africa. A number of Asian countries have already completed surveys and are preparing for a repeat survey and in Africa, countries are implementing surveys for the first time.
- Level of USG investment in the survey: This would include countries where the USAID mission has provided survey support through an implementing mechanism.
- Country contribution to global uncertainty in estimates of TB disease burden.

Profile of evaluation team required

A multidisciplinary team is required. This should include experts in the following technical areas related to the design, planning, implementation, analysis and reporting of national TB prevalence surveys, as well as individuals with expertise and experience in related concepts, such as the design and implementation of population based surveys:

- Methodology: Population based surveys, use of census data to inform sampling, sampling procedures
- Logistics: specimen collection at field level and transportation of specimens; survey logistics at field level
- Laboratory networks: specimen transport, smear/culture/DST, quality assurance, data analysis and management
- Data management and analysis: data collection/entry/cleaning/quality assurance, database development and management, data analysis
- Planning and logistics: complex population based surveys, timely procurement and management of specialized equipment and supplies (lab reagents & equipment, digital X-ray machines, etc)
- Clinical aspects: implementation of TB screening algorithms at field level, chest X-ray, referral for follow up care and treatment
- Finance: assistance to work within budgets, monitor costs; think sustainably about how to maintain or use equipment/commodities and expertise long term

The team should also include experts with general knowledge of TB programs.

The team should also include senior experts in population based surveys that do not necessarily include TB specific data: for example, experts who are familiar with Demographic and Health Surveys (DHS), Multiple Indicator Cluster Surveys (MICS), and other standardized surveys, preferably those that include collection, transport and analysis of biological specimens.

Annex 2: Agenda of Paris Meeting and Assessment Timeline

TB Prevalence Survey Assessment Team Meeting 21-23 July 2015 Paris, France

Meeting Objectives

- Orient prevalence survey assessment team members to TB prevalence survey planning, implementation and analysis
- Identify three countries for site visits and initiate
- Draft survey review tools and desk review protocol
- Determine roles and responsibilities of all team members

Tuesday, 21 July

Time	Topic	Presenter/Chairperson
8:30-9:30	Welcome and Introductions	Karen Stanecki
9:30-10:15	Purpose of assessment: What do we hope to gain from this activity?	Ken Castro and Charlotte Colvin
10:15-10:30	WHO Task Force on Impact Measurement: Background and Achievements to date	Katherine Floyd
10:30-10:45	Coffee Break	
10:45-12:00	Overview of TB prevalence surveys	Ikushi Onozaki
12:00-12:30	Introduction to the Lime Book and structure of short discussions for afternoon/tomorrow morning	Babis Sismanidis
12:30-1:30	Lunch	
1:30-3:30	Lime Book <ul style="list-style-type: none"> • Protocol development and Standard operating procedures • Case definitions and screening strategies • Sampling design • Interviews, data collection tools and informed consent • Chest radiography 	WHO team, TBD
3:30-3:45	Coffee Break	
3:45-5:15	Lime Book <ul style="list-style-type: none"> • Bacteriology • Repeat surveys 	WHO team, TBD

	<ul style="list-style-type: none"> • Ethical considerations • TB treatment, HIV testing and other critical interventions 	
5:15-5:30	Wrap up and preparation for tomorrow	Karen Stanecki

Wednesday, July 22

Time	Topic	Presenter/Chairperson
8:30-10:30	Lime Book <ul style="list-style-type: none"> • Budgeting and financing • Survey organization and training (Hoa) • Field operations (Hoa) • Documents and data management (Eveline) • Analysis and reporting (Eveline) 	WHO team, TBD
10:30-10:45	Coffee Break	
10:45-12:30	Panel discussion on TB prevalence survey planning, implementation and analysis: Perspective of external technical assistance providers	Emily Bloss, Sean Cavanaugh, Nguyen Binh Hoa, Eveline Klinkenberg
12:30-1:30	Lunch	
1:30-3:30	Site visits – What, where and why?	Charlotte Colvin
3:30-3:45	Coffee break	
3:45-5:00	Planning for site visits - Identifying local stakeholders, local protocols and other practical issues	Charlotte Colvin and Babis Sismanidis
5:15-5:30	Wrap up and preparation for tomorrow	Karen Stanecki

Thursday, July 23

Time	Topic	Presenter/Chairperson
8:30-9:00	Summary of main outcomes, Days 1 and 2	Eveline Klinkenberg
9:00-10:30	Development of protocol and standardized tool(s) for desk review of TB prevalence surveys	TBD
10:30-10:45	Coffee Break	
10:45-11:30	<i>Tentative: Overview of laboratory needs for prevalence surveys and integration of innovative TB diagnosis tools</i>	TBD

11:30-12:30	<i>Tentative: What innovative data collection, management and analysis tools can be used to improve prevalence survey data?</i>	TBD
12:30-1:30	Lunch	
1:30-2:30	Structure of report: What are the key elements and how will we get to Capetown?	Eveline Klinkenberg
2:30-3:15	Roles and responsibilities: Who will cover key topics during site visits and in writing report?	Kendall Krause
3:30-4:30	Until we meet again: Discussion on routine communications and interim progress reports from Paris to Capetown	Karen Stanecki
4:30-5:30	Wrap up and summary	

Timeline developed during Paris Meeting:

Activity	Timeline
Initial team meeting in Paris	July 2015
Develop tools	August 2015
Conduct desk reviews	September 2015
Conduct key informant interviews	September/October 2015
Perform site visits	October 2015
Present preliminary results at Cape Town IUATLD symposium	December 2015
Finalize report	January 2016

Annex 3. Analytic plan

1. Was the survey justified based on what was, and was not, known about TB in the country? Was the primary impetus to do the study from the country itself, its TB partners, or from external groups such as the WHO?

Data items and sources:

1. *Abstraction of justification from protocol and/or final report (though language in most seems a bit boilerplate)*
 2. *Interviews with WHO TB Monitoring and Evaluation Group*
 3. *NTP director questionnaire (for those who were directors when survey was done)*
 4. *Queries or interviews with other sources (TB partners, former NTP directors)*
 5. *And, for a broader view, different voices from TB world about scientific need for a survey and relative importance for advocacy and other purposes of the survey results.*
2. Were appropriate local and international institutions involved? What role did they play in protocol development, training, implementation, data analysis, and dissemination? If the NTP was not the lead implementation agency, what role did they play? Was technical support from WHO and the Technical advisory group adequate?

Data items and sources:

1. *Names of implementation agency and technical partners (from final report)*
 2. *Roles played by institutions, including the NTP, from NTP director questionnaire, WHO TB Monitoring and Evaluation Group, partners if needed*
 3. *Interviews re: assessment of adequacy from WHO TB Monitoring and Evaluation Group or interviews with other sources (TB partners, former NTP directors)*
3. Was the sample size adequate and the sampling plan appropriate to answer the study objectives? (includes appropriateness of initial sample size assumptions and how they differed from what was really found, meaningful strata for programmatic purposes)

Data items and sources:

1. *Initial sample size assumptions and calculations from protocol the actual response rates, prevalence, kappa and DEFF from 4 pagers, final report, or Asia/Africa papers. The questions we would specifically seek to answer is whether there was an adequate level of precision attained in the end? Wasted resources because of too large a sample? Ultimately, a broader look at the relationship between prevalence and sample size across the countries and when it becomes prohibitive in terms of resources and costs to undertake these surveys)*
 2. *Overall, age-specific, sex-specific, and stratum-specific response rates from final report to evaluate representativeness.*
 3. *Use of stratum specific data for programmatic purposes (from questionnaires with NTP or former NTP program directors.*
4. Was the staffing adequate (person power and competence) to conduct the survey in a timely way and within budget? To what extent did the survey disrupt routine TB program and laboratory activities?
 1. *Adequate numbers of staff is a function of sample size and the time allocated to do the survey. There is information in the final reports on staffing that might be used,*

but we can probably get a qualitative assessment much more readily from WHO TB Monitoring and Evaluation group and from the technical partners (e.g., in their opinion was the staffing adequate/inadequate to conduct the survey within the timeline and budget, with an open ended comment option).

2. *Competency is dependent on training and supervision, the latter of which is addressed below with quality control. As with the numbers of staff, this probably is easiest to address by speaking with WHO TB Monitoring and Evaluation group and technical partners as well as the survey coordinators; critical areas probably are radiography and lab, as well as field managers.*
 3. *Assessment of disruption from NTP director questionnaire (for those who were directors when survey was done; otherwise may need to contact former director. Technical partners also likely to have opinion.*
5. Were the methods of case-finding appropriate to both reliably assess TB prevalence in the country for national and international purposes and also to determine how well the NTP is doing with case finding? (For the latter, need to be able to compare like - uncentrifuged or centrifuged smears, type of microscopy, case definition, role of X-ray etc)

Data items and sources:

1. *Assessment of the reliability of the case-finding methods/algorithm to accurately assess TB prevalence by speaking with WHO TB Monitoring and Evaluation group, assessing the algorithm used from survey report*
 2. *Symptom checklist for NTP and for survey purposes (from NTP manual and protocol)*
 3. *Chest radiograph type and where readings initially performed (from protocol); speaks also to efficiency of survey and quality control below)*
 4. *Number and type (centrifuged/uncentrifuged) of smears and type of microscope used (NTP manual or NTP manager questionnaire; protocol)*
 5. *Number and type of cultures or other diagnostic methods such as Gene XPert, LPA etc (from protocol)*
 6. *Ability to use survey to accurately examine under-ascertainment using same criteria as NTP diagnostic algorithm (compare NTP and survey criteria; examine findings in final report examining under-ascertainment).*
6. Were other data collected such as health seeking behaviors that could be useful for targeting their program or providing information for other programs within the MOH? (SES/equity, HIV, diabetes, smoking, etc)

Data items and sources:

1. *Examine protocol and study questionnaire for additional content*
2. *Assess whether data analyzed and used (final report)*
3. *Assess whether other programs were approached and/or consideration given to collecting additional information, and if not, why it was decided not to collect additional data (NTP questionnaire of current/former NTP directors; explore in-country with non-communicable disease program/MOH interviews)*
4. *For countries collecting additional data, questionnaire or interview with current or former NTP director regarding pros and cons of inclusion of additional data items*

7. Was data entry, management, and analysis efficient?

Data items and sources:

1. *Type and location of data entry; eg paper forms with in field entry, PDAs, etc (from protocol)*
2. *Time required to complete data entry, if centrally performed (from final report, midterm reports, interviews with NTP director/former director, interviews with WHO Monitoring and Evaluation staff)*
3. *Software used to construct relational data base and to analyze data (from final report)*
4. *Reasons for delays, if any, in data entry, and issues in data management (questionnaires of NTP current and former NTP managers, WHO Monitoring and Evaluation staff interviews)*
5. *Time to produce a usable data set (from interviews with NTP director/former director).*
6. *Time from having a usable data set to completing the analysis (from interviews with NTP director/former director)*

8. Were quality control measures in place, executed, and the results used?

Data items and sources:

1. *Quality control measures for radiography, smear, culture, and data entry (from protocol)*
2. *Quality control findings for each from midterm or final report (CXR initially mis-read by field readers, data entry errors requiring review of records, percent false-positive and false-negative smears on re-reading, % smear positive but culture negative, % of contaminated cultures, etc (Kendra to help decide best lab measures); may need to triangulate with partners, WHO Monitoring and Evaluation staff)*
3. *Evidence that actions taken based on quality control results from midterm reports or from current/former NTP program manager questionnaire, partners, WHO Monitoring and Evaluation staff interviews)*

9. Was the survey done in a way that produced reliable and credible data?

Data items and sources:

1. *Response rate overall and in strata of programmatic importance such as urban/rural, gender, age groups (from final report)*
2. *Acceptable levels of errors for items outlined in 8.2 above (WHO Monitoring and Evaluation staff)*
3. *Credibility of results based on interviews with WHO Monitoring and Evaluation staff and others as needed*

10. Did the survey stay within the recommended time line? If not, why not?

Data items and sources:

1. *Compare timeline and actual dates of completion for key events including protocol completion, data collection, data analysis, dissemination, and reporting (from protocol and final report, other project documents, WHO Monitoring and Evaluation staff and others as needed)*

2. *Reasons for delays and how many of these issues could have been prevented (NTP current/former program manager questionnaire, donors, WHO Monitoring and Evaluation staff interviews)*
11. Was the survey completed within the budget outlined in the protocol? If not, why not? How were shortfalls met? (the latter two would need to be done via questionnaires or interviews)
- Data items and sources:*
1. *Compare budget and actual expenditures (from protocol and final report, other project documents, WHO Monitoring and Evaluation staff and others as needed)*
 2. *Reasons for budget discrepancies and how many of these issues could have been anticipated (NTP current/former program manager questionnaire, donors, WHO Monitoring and Evaluation staff interviews)*
12. What were considered the main bottlenecks and difficulties during preparations, field operations and data analysis and reporting? (may be partly captured with the schedule and budget issues)
- Data items and sources:*
1. *Reported issues in midterm and final reports*
 2. *Elicited from NTP current/former program manager questionnaire, technical partners, WHO Monitoring and Evaluation staff interviews*
13. How were the findings disseminated, and to whom?
- Data items and sources:*
1. *From NTP current/former program manager questionnaire, technical partners, WHO Monitoring and Evaluation staff interviews, MOH, other programs*
14. Were feasible and actionable recommendations made?
- Data items and sources:*
1. *Final reports; also elicited from WHO Monitoring and Evaluation staff interviews, country stakeholders*
15. Were these recommendations acted on in the form of program or policy changes?
- Data items and sources:*
1. *Elicited from NTP current/former program manager questionnaire, technical partners, WHO Monitoring and Evaluation staff interviews*
16. What additional benefits resulted from the survey? (e.g., training, equipment being repurposed, use of human resources, etc)
- Data items and sources:*
1. *Elicited from NTP current/former program manager questionnaire, technical partners, WHO Monitoring and Evaluation staff interviews*
17. How were the findings used at country level and by WHO and by donors, and were there any caveats around their use?
- Data items and sources:*
1. *Elicited from WHO Monitoring and Evaluation staff, IUAT, WHO program staff, donors interviews*

Variable	Data source				Additional notes	Correspondence with item in Analysis Plan
	Desk review	NTP program manager questionnaire	WHO/other stakeholders (specify)	Case study (3 countries only)		
Study team members	x					
Name of country	x					
Year survey completed	x					
Data sources used (protocols, reports, presentations, publications; provide references and links if available)	x					
Contacts interviewed to obtain additional information (name, title, relationship to survey)		x	x	x		
Planning and Timeline						
Justification for undertaking survey, including, where relevant, issues with reliability of surveillance data	x	x	x		Protocol and final report, but eventually triangulated with other sources (SBB checklist report as part of epi assessment)	1
Dates of previous survey(s), if any	x					
Who decided to do survey	x	x	x		May be in final report, but most likely interviews; WHO	1
Implementation agency	x	(x)	x		Quarterly report, final reports; Ikushi et al	2
Technical partners/roles	x		(x)		ditto	2
Coordination between implementation agency and NTP, where relevant		x	x			2
Adequacy of technical support			x		Interviews with WHO, key stakeholders	2
TAG or advisory group constituted/met		x	x		Questionnaire NTP director/former director; mid-term reports, WHO	2

Year survey planned	x	(x)	(x)	Information on timeline often found in protocol or listed as protocol annex /actual sometimes in final report, but otherwise interviews, WHO	10
Date protocol writing began	x	(x)	(x)	planned: actual:	10
Date survey began	x	(x)	(x)	planned: actual:	10
Date data collection completed	x	(x)	(x)	planned: actual:	10
Date clean data set available for analysis	x	(x)	(x)	planned: actual:	10
Date analysis completed	x	(x)	(x)	planned: actual:	10
Date results presented to Ministry of Health	x	(x)	(x)	planned: actual:	10
Date final report published	x	(x)	(x)	planned: actual:	10
For discrepancies between initial plan and actual date accomplished, describe main bottlenecks		x	x	midterm reports; final reports but will probably also need Interviews; WHO	4
Methods					
Eligibility					
Age/residence eligibility requirements	x			Table 2 Asian prevalence surveys; table in Africa draft; where needed protocol, survey report	3
Geographical areas excluded	x			Table 2 Asian prevalence surveys; table in Africa draft	3
Sample size and strategy					
Targeted sample size	x			Table 2 Asian prevalence surveys; table in Africa draft	3
Assumption regarding sm+ prevalence	x			survey protocol; not sure it is in the draft prev survey tables;	3
Total number of clusters & cluster size (target)	x			Table 2 Asian prevalence surveys; table in Africa draft: final report or protocol	3

Stratification details (e.g., was sampling done by rural/urban etc; targeted sample size in each strata)	x	Table 2 Asian prevalence surveys; table in Africa draft	3
Precision	x	Individual protocols; sample size section	3
Expected design effect	x	Individual protocols; sample size section	3
Expected kappa	x	Individual protocols; sample size section	3
Expected response rate	x	Individual protocols; sample size section	3
Comparison with previous survey or planned future surveys taken into account?	x		3
Screening strategy			
Symptoms at interview	x	Table 2 Asian prevalence surveys; table in Africa draft	5
Type of X ray	x	Protocols to get sufficient level of detail	5
CXR criteria	x	Table 2 Asian prevalence surveys; table in Africa draft	5
NTP symptom screen for TB workup	x	NTP manual	5
NTP strategy for HIV+ patients	x	NTP manual	5
Laboratory methods			
Type (centrifuged/uncentrifuged) and number of smears	x	Table 2 Asian prevalence surveys; table in Africa draft	5
Type of microscopy	x	Protocol, in lab section	5
Where smears performed	x		5
Same procedures as used for routine smear exam in NTP?	x	NTP manual	5
Type and number of cultures	x	Table 2 Asian prevalence surveys; table in Africa draft	5
Where cultures performed	x		5

Gene Xpert used? If so, for which specimens?	x				Protocols; in lab section	5
Resistance testing	x				Table 4 Asian prevalence surveys; table in Africa draft	5
Additional survey elements (e.g., health seeking behaviors, HIV, smoking, SES, diabetes screen)	x				Protocol or final reports	6
Data collection and processing						
Method of collection (paper/electronic)	x				Protocols, data entry and management	7
Site of data entry	x				Protocols, data entry and management	7
Type of data base	x				Protocols, data entry and management	7
Staffing						
Where did staff come from to conduct the survey: field staff, radiologists, laboratory (NTP, implementing agency, external hires etc)	(x)	x			Questionnaire NTP director/former director; protocol, final report	4
Adequacy of field staff (numbers, training)	x		x	x	Information on numbers from protocol, final report; subjective input on adequacy from WHO, partners based on interviews; additional information from case studies	4
Adequacy of radiologists (numbers, training)	x		x	x	"	4
Adequacy of laboratory staff (numbers, training)	x		x	x	"	4
If NTP staff used, extent to which disrupted routine activities of case finding, supervision, and lab		(x)	x	x	Probably would require interview to obtain information from all NTP directors; may need to rely on WHO and stakeholders _ case studies	4

Description of quality control measures (who, when, where, how)

CXR	x	Protocols; for findings, final reports	8
Smear	x	Protocols; for findings, final reports	8
Culture	x	Protocols; for findings, final reports	8
Data collection (e.g. spot checks of interviews conducted)	x		8
Data entry	x	Protocols; for findings, final reports	8
Models used to calculate rate + which model finally used	x		

Results

Actual sample size	x	Table 3 Asian prevalence surveys; table in Africa draft	3
Overall response rate	x	Table 3 Asian prevalence surveys; table in Africa draft	9
Response rates by gender and age	x	Final reports	9
Response rates by stratum	x	Final reports	3
Actual sm+ prevalence (with 95% CI)	x	Table 3 Asian prevalence surveys; table in Africa draft	3
Actual BACT+ prevalence (with 95% CI)	x		
Results obtained with different models (asterisk one that was used in final report)	x		9
Actual design effect	x	Table 3 Asian prevalence surveys; table in Africa draft	3
Actual Kappa	x	Table 3 Asian prevalence surveys; table in Africa draft	3

Reasons for discrepancies, if any, between observed and expected values for sm+ prevalence, DEFF, kappa	x	x	x		May be in discussions of final reports, but more likely Interviews with WHO	9
Quality control results						
False + and false - CXR results on re-reading, %	x				Final reports and/or mid-term reports	8
False+ and false- smear on re-reading, %	x				Final reports and/or mid-term reports	8
Culture contamination, %	x				Final reports and/or mid-term reports	8
Other measures TBA	x				Final reports and/or mid-term reports	8
Evidence that quality control results used to improve study execution		(x)	x	x	may require interviews rather than questionnaires with NTP directors; WHO and case studies will provide additional info	8
Data interpretation and dissemination						
Recommendations made in report/briefings for actionable changes/improvements to TB program	x	x	x		Final report	14
Methods used for dissemination (publications, meetings, briefings, etc. and target audiences		x			May be in final reports, but more likely Interviews with WHO and others	13
Policy or other changes attributable to findings, including changes in surveillance resulting from survey		x	x		May be in NTP plans formulated after study, but more likely questionnaires with NTP managers, WHO and others	15

Did obtained estimate differ significantly from the previous estimate and what were consequences of this for the country?	x	x	x	NTP directors, but probably would need to do interview; otherwise WHO and other stakeholders, case studies	14	
Use of data by WHO and donors			x	x	Interviews with WHO and donors; case studies	17
Caveats around use of data by WHO/donors			x	x	Interviews with WHO and donors; case studies	17
Budget						
Projected/actual total	x				Projected often can be found in protocol; final sometimes in report; need to consult Ikushi re: where this information can be found.	11
Sources	x		x		Amounts if possible; in some final reports but may need to come from other sources	11
MOH						
USAID						
Global fund						
Other bilat/multilateral (specify)						
WHO						
Other						
Projected/actual by category*:	x	x	x		*Detail level differs from project to project, and so do categories. However, the main comparison is expected and actual rather than a cross country comparison	11
For any of the above where there is a >xx% discrepancy, describe:						
Reasons for discrepancy		x		x	Might be in final report but most likely will come from interviews, WHO	11

Source of supplemental funds	x	x	x		Might be in final report but most likely will come from interviews, WHO	11
Challenges/bottlenecks	x	x	x		mid-term reports and presentations, final reports, WHO, NTP, survey coordinator, technical advisors	12
Other advantages accrued by survey (resources, equipment, training HR)	(x)	x	x	x	NTP director/former director survey, WHO, case studies; may find some info in final reports	16

Annex 5. Data Abstraction Tool

NAME OF COUNTRY			
Variable	Data	Notes/Suggestions	Correspondence with item in Analysis Plan
Study team members completing form			
Year survey completed			
Data sources used (protocols, reports, presentations, publications; provide references and links if available)			
Planning and timeline			
Justification for undertaking survey, including, where relevant, issues with reliability of surveillance data		Protocol and final report, (SBB checklist report as part of epi assessment)	1
Dates of previous survey(s), if any			
Who decided to do survey		May be in final report	1
Implementation agency		Quarterly report, final reports	2
Technical partners/roles		ditto	2
Year survey planned		Try protocol or listed as protocol annex /actual sometimes in final report	10
Date protocol writing began	planned: actual:		10

Date survey began	planned:	actual:		10
Date data collection completed	planned:	actual:		10
Date clean data set available for analysis	planned:	actual:		10
Date analysis completed	planned:	actual:		10
Date results presented to Ministry of Health	planned:	actual:		10
Date final report published	planned:	actual:		10
Methods				
Eligibility				
Age/residence eligibility requirements			Table 2 Asian prevalence surveys; table in Africa draft; where needed protocol, survey report	3
Geographical areas excluded			ditto	3
Sample size and sampling strategy				
Targeted sample size			ditto	3
Assumption regarding sm+ prevalence			ditto	3
Total number of clusters & cluster size (target)			ditto	3
Stratification details (e.g., was sampling done by rural/urban etc; targeted sample size in each strata)			ditto	3
Precision			Individual protocols; sample size section	3

Expected design effect		ditto	3
Expected kappa		ditto	3
Expected response rate		ditto	3
Comparison with previous survey or planned future surveys taken into account?			3
Screening strategies			
Symptoms at interview		Table 2 Asian prevalence surveys; table in Africa draft	5
Type of X ray		Protocols to get sufficient level of detail	5
CXR criteria		Table 2 Asian prevalence surveys; table in Africa draft	5
NTP symptom screen for TB workup		NTP manual	5
NTP strategy for HIV+ patients		NTP manual	5
Laboratory methods			
Type (centrifuged/uncentrifuged) and number of smears		Table 2 Asian prevalence surveys; table in Africa draft	5
Type of microscopy		Protocol, in lab section	5
Where smears performed			5
Same procedures as used for routine smear exam in NTP?		NTP manual	5
Type and number of cultures		Table 2 Asian prevalence	5

		surveys; table in Africa draft	
Where cultures performed			5
Gene Xpert used? If so, for which specimens?		Protocols; in lab section	5
Resistance testing		Table 4 Asian prevalence surveys; table in Africa draft	5
Additional survey elements (e.g., health seeking behaviors, HIV, smoking, SES, diabetes screen)		Protocol or final reports	6
Data collection and processing			
Method of collection (paper/electronic)		Protocols, data entry and management	7
Site of data entry		Protocols, data entry and management	7
Type of data base		Protocols, data entry and management	7
Staffing			
Where did staff come from to conduct the survey: field staff, radiologists, laboratory (NTP, implementing agency, external hires etc.)		Check protocol, final report but may require interviews	4

Adequacy of field staff (numbers, training)		Information on numbers and training from protocol, final report	4
Adequacy of radiologists (numbers, training)		ditto	4
Adequacy of laboratory staff (numbers, training)		ditto	4
Description of quality control measures (who, when, where, how)			
CXR		Protocols; for findings, final reports	8
Smear		Protocols; for findings, final reports	8
Culture		Protocols; for findings, final reports	8
Data collection (e.g. spot checks of interviews conducted)			8
Data entry		Protocols; for findings, final reports	8
Models used to calculate rate + which model finally used			
Results			
Actual sample size		Table 3 Asian prevalence	3

		surveys; table in Africa draft	
Overall response rate		ditto	9
Response rates by gender and age		Final reports	9
Response rates by stratum		Table 3 Asian prevalence surveys; table in Africa draft	3
Actual sm+ prevalence (with 95% CI)		ditto	3
Actual BACT+ prevalence (with 95% CI)			
Results obtained with different models (asterisk one that was used in final report)		Final report	9
Actual design effect		Table 3 Asian prevalence surveys; table in Africa draft	3
Actual Kappa		ditto	3
Reasons for discrepancies, if any, between observed and expected values for sm+ prevalence, DEFF, kappa		May be in discussions of final reports	9
Quality control results			
False + and false - CXR results on re-reading, %		Final reports and/or mid-term reports	8
False+ and false- smear on re-reading, %		ditto	8
Culture contamination, %		ditto	8

Recommendations made in report/briefings for actionable changes/improvements to TB program		Final report	14
Budget			
Projected/actual total budget		Projected often can be found in protocol; final sometimes in report	11
Sources		Amounts if possible; in some final reports	11
MOH			
USAID			
Global fund			
Other bilat/multilateral (specify)			
WHO			
Other			
Projected/actual by category*:		*Detail level differs from project to project, and so do categories. However, the main comparison is expected and actual rather than a cross country comparison	11
Source of supplemental funds		Might be in final report	11

Challenges/bottlenecks		mid-term reports and presentations, final reports	12
Other advantages accrued by survey (resources, equipment, training HR)-- may be in final report		may find some info in final reports	16

Annex 6. Interview guides

Senior partners at WHO, the Global Fund, USAID, KNCV, CDC, and STOPTB

1. What has been your organization's role in the TB prevalence surveys?
2. Some consider the TB prevalence surveys to be costly, not only in financial terms but also in terms of the human resources they require. In your opinion, has the information they have produced justified the money and effort? If not, how do you believe these resources could be better spent?
3. In your opinion, what have been the biggest obstacles to the implementation and completion of these surveys? What could be done in the future by your organization or others to decrease or eliminate these problems?
4. Many of these surveys have a complex network of in-country partners, donors, and technical advisors. Did your organization encounter any problems in the coordination among these partners? In communication with these partners?
5. Based on the experience to date with these surveys, under what circumstances would you recommend that other countries take them on? Should all countries undertake such surveys?
6. Would you be willing to support repeat surveys in the countries which you have already supported or in other countries? Under what circumstances?

Country support staff

1. What was the justification for doing the survey?
2. Why did your organization decide to support the prevalence survey?
3. What was your experience with preparation and implementation of the survey, and can you describe the main challenges in such areas as:
 - a. (co)-funding
 - b. adequacy of technical support
 - c. coordination between the WHO, Global Fund, STOP TB, other partners, and the NTP
 - d. procurement
 - e. identifying adequate staff with appropriate skills
 - f. communication
 - g. staying with the initially planned schedule
 - h. receiving regular updates
 - i. staying within budget
 - j. obtaining additional funding where necessary
 - k. analyzing the data
 - l. developing a final report
 - m. other
4. Overall, what were the most important bottlenecks that were encountered in planning, implementing, and analyzing data? What were the primary causes of any delays or bottlenecks?
5. To what extent do you feel the survey interrupted normal TB program activities?
6. To what extent were the quality control measures that were in place adequate to ensure good quality data?
7. How have the results been used, and how useful do you think the prevalence survey results have been for the national TB program? Did policy change as a result of these findings? Did the visibility of the TB program change?
8. How have the results been used by your program?

9. Have results been used to re-align current interventions and activities funded or supported by your program?
10. Given other TB program needs, do you think the money spent on the prevalence survey could have been used for other activities that were of higher priority and had potentially greater impact?
11. If you could change one thing, what would you have done differently with regards to the PS implementation?
12. Have the material and human resources invested in the survey have been integrated in the country health system afterwards- have they contribute to building capacities, strengthen laboratory and diagnostic capacities, improve surveillance system and the overall HSS ?

NTP Managers

Survey of TB Program Directors

Subject: Prevalence Survey

- 1) Why did your country decide to do a prevalence survey?
 - a. Who was involved in the decision-making process?
- 2) Was the NTP the lead implementing agency?
 - a. If not, who was it and what role did the NTP have in the survey?
 - b. Would you rather the NTP had a different role? If yes, why?
- 3) Where did the funds for the prevalence survey come from? (please list all the sources of funding)
- 4) How were the results of the prevalence survey disseminated? (for example: publications, meetings, briefings etc)
 - a. What were the target audiences?
- 5) What were the greatest challenges you faced in conducting the prevalence survey? (think in terms of funding, procurement of supplies, field operations, data management analyzing the data, use of results, etc)
- 6) What do you think were the biggest benefits (positive outcomes) from the prevalence survey?
- 7) If you were going to repeat the prevalence survey, would you do anything differently? If so, please describe.
- 8) Did the prevalence survey cause any disruptions to the routine activities of the NTP (in regards to programmatic activity, laboratory functioning, etc)? If yes, please describe.
- 9) What was your initial reaction to the prevalence survey results?
 - a. Were the prevalence estimates higher or lower than you expected them to be?
- 10) If the findings from the prevalence survey are different from what you expected, what do you think are the reasons for that?
- 11) Do you think the findings of the prevalence survey are reliable? Why or why not?
- 12) What did you learn about the TB situation in your country and about your program from the prevalence survey?
- 13) Have you made any changes to the TB control program as a result of the prevalence survey? (In terms of laboratory and diagnostic capacities, surveillance systems, case finding strategy, etc)
 - a. Have you used the data to update your targets or your strategic planning?

- 14) Other than the findings, were there any benefits for the National TB Program as a result of doing the prevalence survey? (things like capacity-building, or equipment that is now being used for other purposes, etc)
- 15) Will you plan a repeat prevalence survey? Why or why not? When would you do a repeat survey?
- 16) Can you think of alternatives to a prevalence survey that would provide good epidemiologic data?
- 17) What other sources of information (other than the prevalence survey) do you use to make policy decisions on TB control in your country?
- 18) Do you think it is advisable or feasible to widen the scope of a TB prevalence survey in order to get more info about other disease programs? (For example, do you think it wise to do a joint TB-HIV survey, or to add data collection about diabetes or other diseases?)

Annex 7. List of Key Informants

Global Fund

- *Eliud Wandwalo (Senior Disease Coordinator, TB)*
- *Nathalie Zorzi (Senior manager M and E)*
- *Ezra Tessera (M and E staff member)*
- *Sai Pothepegada (country support, now Ethiopia coordinator)*
- *Saman Zamani (country support)*
- *Mark Saalfield (country support)*
- *Nibretie Workneh (country support)*
- *Tsvetana Yakimova (country support; interviewed 9/28)*

STOP TB

- *Lucica Ditiu*
- *Andrew Codlin*
- *Jacob Creswell*

WHO

- *Mario Raviglione*
- *Ikushi Onozaki*
- *Irwin Law*
- *Christian Gunnenberg*
- *Malgorzata Grzemska*

Gates Foundation

- *Daniel Chin*

USAID

- *Amy Bloom*
- *Cheri Vincent*

KNCV/University of Amsterdam

- *Frank Cobelens*

Consultant

- *Hans Reider, ex IUATLD*

Annex 8. NTP Managers Interviewed

- Dr. Philip Patrobas (WHO country officer from Nigeria)
- Dr. Beatrice Mutayoba (current NTP Director from Tanzania)
- Dr. Thandar Lwinn (current NTP Director for Myanmar; Dr Aung [past NTP Director] was also present at the time)
- Dr. Nathan Kapata (current NTP Director for Zambia)
- Dr. Rhoda Banda (TB Prev Survey Coordinator for Malawi)
- Dr. Dyah Mustikawati (former NTP Director for Indonesia)
- Dr. Chawetsan Namwat (current NTP Director for Thailand)
- Dr. Andargachew Kumsa (former NTP Director for Ethiopia); Dr. Zeleke Alebachew, Dr. Fasil Tsegaye (Prevalence Survey Coordinators)
- Dr. Mao Tan Eang (Cambodia)
- Dr. Frank Bonsu (Ghana)

Annex 9. Summary of Interviews of Key Informants (Senior Partners)

Qualitative interviews conducted 9/21-10/22/2015

Nancy Binkin, MD, MPH (Assessment team member)

Primary take-home messages:

TB is perceived to have much less reliable data on the current burden of disease than other conditions such as HIV and malaria, which makes planning and funding problematic. For this reason, doing these surveys remains essential, especially given the status of surveillance efforts. To date, the surveys have been done in 15 of the 22 global focus countries as well as three additional countries.

“We want the best estimate as possible—[now there are] no better options since other estimates come from modeling. We need these numbers to assess impact, justify investment.”

“[We] still need the prevalence surveys to happen, we need to find money for them, but we need to be smart about doing them and they should be done in parallel with strengthening surveillance.”

“[A] TB prevalence survey is a good return for investments – if implemented well.”

“Because the results to date have changed how we think about things, we should be doing more.”

“[The surveys] are essential to our work, especially as we talk about getting more and more grounded in facts rather than estimates based on estimates based on estimates.”

Stakeholders believe these studies are providing highly useful information in giving a realistic picture of the TB situation in the countries and provided information for the development of concept notes for Global Fund applications. In some, it has been a real game changer, with the realization that there are far more TB cases out there than previously estimated. Such findings have important financial implications since the burden is one of the important components in deciding levels of TB funding. It has also been useful for advocacy purposes. Furthermore, if they were not done, there would be no guarantee that the money used to fund them would be used for TB programs or improving TB surveillance.

“Numbers have become critical for funding allocations but also for advocacy. When you estimate mortality [using the new prevalence estimates], you get many more cases and deaths. TB and HIV both [were] killing the same number of people, but in reality TB probably killed more than HIV worldwide [in the past decade].”

“You recuperate [survey costs] rapidly in terms of efficiencies in how you run your program. [There’s a] much more focused program and better use of resources if data are accurate and there’s not a more cost-effective alternative... Nice to come into a portfolio where people are saying you have an accurate picture of what’s happening. It’s reassuring to start from good numbers.”

“For some countries, when they were doing strategic plan, they basically putting in a wish list of all the things that are in the WHO strategy... For me, I see [these surveys] as a way you build program interventions based on evidence. One of core baseline points in the TB strategy is to know your problem and then know how to address it. [These surveys allow you to] prioritize which interventions of the WHO strategy you need to implement to improve your program.”

“When I look at recent results of prevalence surveys from Nigeria, Indonesia and Ghana, they have been critical. The lack of these data has kept us from spending money as efficiently as they might. These surveys are really critical to estimating our disease burden at country level but also within country, [where they help identify] areas or populations that need more focus ...if we are to make an impact.”

While more than half of the studies have shown that the prevalence was within the range estimated via other means, the confidence intervals with the surveys are far tighter. In four cases, Lao, Indonesia, Malawi, and Ghana, the prevalence was much higher than expected, and in Nigeria, it was at the upper range of the expected limit; the only country with a far lower than expected value was Gambia. These new higher estimates have resulted in an increase in the projected number of TB cases worldwide, from 8.5 million to 9 million this past year after the Nigeria survey and will be 9.5-9.6 million this year with the Indonesian results now in.

“Without these exercises would not be able to say these things”

“You get more data –we thought we were fighting a little snake, but we are really fighting Godzilla.”

“[We] got a big shock when the numbers came out—[they are] worth it at any price.”

“Indonesia is an example—[finding a high rate]was really painful and caused turmoil at government level, but it has given visibility to TB and [the government knows] the world is looking at them.”

The surveys have also increased knowledge about TB programs and local TB epidemiology, although it has not always been possible to change practice and policy because of limitations in financial and other resources. These include the need to perform active case finding in higher risk populations and change the screening algorithms from two weeks of cough to a more sensitive definition (e.g., cough + one other symptom), screening of outpatients with pulmonary symptoms, and greater use of x-rays and culture/GeneXpert for TB diagnosis. Serial surveys have been of particular use in evaluating the DOTS strategy. The repeated surveys in Cambodia have demonstrated the success of the DOTS strategy in preventing MDR-TB development and in improving access through the decentralization of the TB program. The three most recent surveys from China have also suggested the ability of DOTS implementation to contribute to a decline in TB cases.

“In [country X], for example, the primary health care system doesn’t work well. It was important to know that people are going to primary care and are not being evaluated for TB. In [Country Y], the survey showed they were doing excellent job of identifying smear-positive TB and [overall] the rate was going down, but there are various groups in population with little access. Everybody knew, but you saw it in a way that [it was clear that in these groups] you needed a totally different approach.

“Because the prevalence survey showed lots of missed cases, [Ghana] plans on moving to GeneXpert and CXR as screening tool...and more sensitive screening in outpatient care—persons with cough + one more symptom get an evaluation. These changes have been included in National Strategic Plan.”

“The [Cambodia] TB prevalence survey identified key programmatic gaps, especially in relationship to the rolling out of DOTS and de-centralization. The findings were used in two main ways: first they were used in the 2012 program review and drafting the national strategic plan [that included] strengthening community service delivery.. in a more consistent and organized way rather than [the previous]project... [The second was] implementation of new technologies on the ground, like the decision to scale up GeneXpert testing. [These were included] in the Concept Note submitted and approved 2015-17.”

“The three most recent China surveys, 1990, 2000, and 2010, coincided with pre-DOTs, halfway through moderate quality DOTs in half the country, and full scaleup with good coverage by 2010. .. You can clearly and convincingly see that the data are really strongly supportive of changes that have occurred in TB control.”

“[These surveys can provide] a wealth of data in understanding clinical presentation and types of x ray findings and [follow on studies are possible to, for example, follow up persons with positive chest x rays and negative laboratory findings. You need to have an incentive in place, though, to get data analyzed.”

“The surveys show age groups at risk, the percentage of asymptomatic disease, that the guidelines of 3 weeks of chronic cough is not sensitive enough, that better education of population and HCW to identify cough—for example with smokers. These aspects would never had been discussed had the surveys not been done.”

The surveys usually do have other positive consequences, especially in terms of building skills in the laboratory and in X-ray reading that have had positive consequences, both nationally and internationally. In some cases, the equipment has been put to good use after the end of the survey, but this is by no means universal. In addition, some have helped build partnerships with research institutions in countries. An additional method of building research capacity has been to identify an NTP team member who can use the survey as the basis of a PhD through various universities in the Netherlands.

“[The survey] developed the capacity of national research institute in Ethiopia. [The survey team] went on to provide south-south collaboration and TA”

“In Malawi had prevalence teams and equipment and they now have done screening of prisons.”

“We were always complaining that there wasn’t research capacity in country and that the researchers were doing less relevant work for the NTP, but now they have been contracted by the NTP [to conduct the surveys] and they are establishing a working relationship for the future.”

At the same time, however, there were several areas where the surveys fall short:

There is concern that after spending up to 4 million dollars, the product is largely a single number, with minimal additional information of use to countries in targeting their programs and that it would be useful to have more information for funding purposes. The value of identifying cases who are not highly smear-positive has also been questioned, as has the potential diversion from the longer-term solution of improved surveillance. These feelings were not universal, however, and many countries used data on rural and urban differences and age- and gender-specific rates to identify targets for additional interventions or targeting. It was also pointed out that by using bacteriologically positive cases rather than smear-positive cases, there are larger numbers available to conduct additional sub-national analysis.

“We want more data—the current investment model driven by data. One number alone is not adequate for this...you spend 2-3 million just to get one figure that doesn’t really allow you to target your investment.”

“The amount of money generally produces a number used at global level for estimates and the like, but .. most prevalence surveys have only one level of stratification. This is less useful for countries themselves because the level of detail is not there for programmatic interventions.”

“We haven’t even optimized the results of the research—we are in essence changing one number—[which] doesn’t help in the country planning based on looking at concept notes, doesn’t change the way they do things. The countries that have done these surveys you rarely see it being used to [improve] the NTP [since it] doesn’t show them where to focus their resources. In terms of the investment have seen very little... If we decide to do larger more expensive surveys, need to optimize them not only for epi purposes but also for planning and prioritizing interventions.”

“Additional analyses need to be planned ahead and planned smartly.”

“The [surveys have] only used a few pieces of the data...[For example,] you can at least look for previously treated cases at the time of survey and why they have failed to be cured [and who represent] system failures. Not enough surveys are actually looking at those cases, [and knowing about them is something we can act on now...[Surveys] also provide information about new cases. China right now has really low prevalence of old cases. Now they need to start reducing transmission by finding cases earlier. We haven’t done enough to look at the data to help figure out who these people are.”

“Industrialized countries have never done [these surveys], but we are now telling low income countries to do them. They cost lots of money take people out of national programs... Everyone was talking about smear positive highly infectious cases they were missing in [Country X]...but 30% were scanty positive...but they are not disseminating and spreading. This is not the reason TB control fails. [Furthermore, when the surveys are over] the countries still don’t have surveillance. [The money] should be spent on surveillance.”

Delays in the release of survey results and in WHO approval of the results were also cited as an issue affecting survey credibility and creating ill-will.

“[WHO has been} too technical in past to work with donors and partners—[they] now have created more trust, but it’s hard to keep if we can’t be in front of the wave—makes us seem late and wobbly. It took 2 years to get out Nigeria report—affects credibility of advocacy and to [efforts] to put a target and measure a target.”

“The [lack of] timeliness leads to mistrust—[as occurred in] Ethiopia, Pakistan, and Nigeria-- creates mistrust about the quality of data. [It can] look like they are playing around with data to try to get “better” numbers.”

“In countries with limitations of survey procedures – there needs to be some consensus on agreeing on results – this led to loss of political capital for surveys; as well perception that it is a wasted exercise which yields inconclusive results that can be contested. After investing 3-5 million \$, such a conclusion is extremely damaging.”

The surveys are highly labor intense, requiring multiple visits by the WHO teams as well as by partners. In addition, there are many more countries that could benefit from doing them, but given the current methods and availability of technical assistance, this seems difficult. An alternative in some situations would be to make better use of the data from nearby countries which have done surveys to estimate the prevalence in smaller countries.

“[We] need to come up with simpler methods; we can do better than what we are currently doing. We are doing things as they were done in the 40s.”

“Can the surveys be done in a better way? [There are issues with] logistics, and these surveys engage a team for an entire year. [They are] limited to a few countries-- 22 high burden. [We] want to know what is happening in other countries as well. Few technical experts that can assist.”

“It’s very complicated methodology and countries could probably not conduct them without highly specialized technical assistance. If methodologies are simpler, more practical, this would be to the benefit of countries. Coupled with building more capacity at country level would create even more value for money.”

“The more countries possible, the better you can understand the situation..Early 2016 there will be a prioritization exercise to identify 20+10 top countries in terms of TB burden + top TB HIV + Top MDR TB. However, there is likely to be a slowdown in surveys after MDGs unless there is a breakthrough in technology or methods.”

“WHO is not making adjustment to other countries that share a common pattern—eg revising Cameroun based on Nigeria—so some things could actually be done [to get estimates for other countries].”

In some cases, there has not been enough emphasis on preparing the countries to deal with the political consequences of finding higher than expected rates, or in developing strategies to avoid complacency when rates are lower than expected. The emphasis seems more on technical issues than on political implications in some cases, and generally communication plans for the results have not been formally developed.

“Where results estimated higher burden – programs, TA and WHO were not well prepared to manage the political fall-out and did not plan the messaging/ communication. This has led to rejection of results, questioning the validity of survey, and in consequence the current study.”

“[The results in Ethiopia] gave reassurance to planners and political leadership – however, over years it set complacency...A box was checked and priorities moved on to other things.”

“[The surveys] Have been left to a very small group of people and in the midst of rigor the big picture is lost.”

The timing of studies also is important. If the study results are released after the submission of the concept note for the next Global Fund cycle of funding, they may have less impact:

“ [The usefulness] depended on the timing of results – unfortunately for several countries with higher burden results came after allocations were confirmed, for some they benefited from incentive funding and for some it came in too late after Global Fund grant approval – leading to confusion.”

Good management is one of the major obstacles to conducting a good survey and remaining within budget. Coordination and cooperation between survey management and laboratory management is essential for survey success and lack thereof can seriously jeopardize this.

“Ensuring the right person for the job with requisite skills to manage logistical, technical, political, and financial aspects of the survey is paramount...A dedicated team with a full complement of survey staff is vital..High turnover impedes survey quality. Unforeseen delays [result in] high financial burn rates.”

Laboratory issues are a critical weakness in the surveys. Most countries have experienced problems of various types, from lack of skilled technicians to contamination to poor labeling of specimens that has complicated analysis and, in some cases, raised issues about survey credibility, especially regarding bacteriologically positive case rates. Furthermore, it may divert laboratory resources away from critical diagnostic and quality control functions of the routine program.

“If the quality of culture testing is low, results cannot necessarily be relied upon. The Use of GeneXPert in recent surveys has offered a method to potentially ameliorate this,. It would be well advised that laboratories and related services are improved (and approved) before surveys begin.”

Although most studies had laboratory and radiological quality control in place, there have been major issues with the management of data, with delays in data entry, incorrect labeling of X-rays and laboratory specimens that jeopardize study reliability. In addition, low response rates, especially in younger men leave uncertainties in the overall estimate that cannot be fully overcome with imputation. Although the surveys are monitored, there is not always the leverage needed to correct the problems when they are detected.

“[It is] critical to verify data quality and lab quality measures during pilot. This is rarely given attention. Should lead to GO or no-Go.

“We need to look at prevalence surveys as serious research projects. [They need] a steering committee with independent members, and a data monitoring group, as is done in clinical trials. Someone also needs to have political leverage to solve problems in the field. [In some surveys, they have] noticed problems right from the start. The way the monitoring was set up was that WHO was overseeing, and teams visited and recommendations were made, but the recommendations are not acted upon because no pressure placed on the country. Should have advisory group reporting to the donors to make sure things are happening... WHO doing a great

job and is technically proficient, but they are under fire because they are always put in a monitoring position. Having a strong independent advisory group could help protect them. “

There is a general belief that when the NTP runs the surveys, they are of higher quality and the results are more likely to be used, although this was not a universal sentiment and that having the NTP involved rather than directly running the surveys has also resulted in quality results. In addition, in countries with limited TB staff, the surveys may be a distraction from conducting critical TB activities, especially when they offer the incentive of per diem for field work. While in several cases, partnerships with universities and research institutes has improved the quality of the surveys and decreased the burden on the NTPs, an area of concern is that they may view the data as “theirs” and may be reluctant to release data until publication has occurred.

“Having a strong in-country survey team..assists with the final dissemination of the results and their implications to Ministers and Directors of Health, and other partners. Generally, higher quality surveys and greater acceptance of results/implications have been met if NTPs have been directly involved from the outset.”

“NTP managers should have a strong position in steering committee, but this doesn’t mean having the program running the survey—they not generally good at doing it and they have other jobs.”

“Just like DHS – it should be considered as a national survey where all partners work together and contribute. It should not be an academic exercise by few vested investigators who are more interested in the publications. Prevalence survey results should be published by national investigators- and not by WHO or other TA providers”

“[A country] asked to publish the results on the SES—the university said no, not until their student finished his PhD.

Future directions

There is a willingness and interest in looking at better ways of doing the surveys, including means of standardizing data entry and processing, using innovative methods such as automated x-ray readings, the use of GeneXPert Ultra, bar coding, and moving to continuous surveys rather than periodic. In some instances, such as improving the data processing and analysis, additional funding or piloting innovative strategies may be available through Global Fund M and E initiatives or potentially through other organizations such as the Gates Foundation.

“The surveys have two methodological issues. First, there is the whole problem of verification bias. Both chest x rays and symptoms have insufficient sensitivity, but we don’t know the extent to which they underestimate cases. Problem two is the assumptions we make about non participation—especially for places like Nigeria. In other countries TB male problem and seen very commonly in young men, but these are the highest non-respondents, and any bias you have in that estimate affects total estimate. We need to rethink our algorithms, lab simplification, and smarter sample sizes, [especially for repeat surveys]. All this requires some simulation work—someone has to invest in this.”

“It might be possible to outsource a team to speed up analysis at the country level for analysis. We have a special initiative budget that might be used for that.”

“[We have] seen the usefulness of collecting and analyzing data appropriately, but we need to find a way to simplify the surveys. What technology is out there? Reading algorithms [for CXR], better CXR machines...GeneXPert Ultra could be used—maybe not so far in the distant future—as a triage test with high sensitivity.”

New surveys:

“New countries should consider undertaking a survey if there is strong support from the Government/MOH/NTP, there is evidence to suggest that current burden of disease estimates may not be accurate based upon a weak surveillance system, and the country has a significant proportion of the world’s prevalent TB cases....It has been recommended that non-global focus countries [that wish to do a survey] start with a small scale pilot exercise in known hotspots.; this will assist with capacity development and commitment prior to the real survey implementation.”

And in terms of repeat surveys:

“WHO is willing to support repeat surveys. A willing commitment from the government/MOH/NTP along with the donors is paramount. The challenge in some countries is that as income status has improved since the last survey...countries may need to be co-funders...Technically assuming that the burden of disease is declining, more time is now required between surveys in order to detect a statistically significant change in prevalence e.g. 7-10 years”

“[In some situations, repeat surveys may be] worth doing to learn about dynamics of TB transmission, but in others they may not be necessary.”

The need also remains, though to improve surveillance so these surveys become unnecessary. Consideration can also be given to establishing sentinel surveillance as a possible alternative to monitor trend and to re-visiting tuberculin test surveys, especially given the new, more MTB-specific tuberculin products under development.

“Everybody has to have surveillance—we need to be able to count the cases—that’s the first thing we have to know. It’s one of the targets of the Sustainable Development Goals. It’s not easy, that’s for sure, but that doesn’t mean we shouldn’t do anything.”

Annex 10. Interviews with NTP Managers

Q1. Why did your country decide to do a prevalence survey?

Cambodia: The initial goal was to help develop regional guidelines using survey data. However, detail by province wasn't available due to sample size, so we did a nationally representative sample. We wanted a more accurate burden estimate.

Ethiopia: In 2007 the WHO TB impact measurement Task Force Group did not designate Ethiopia as prevalence country. TB control efforts had been scaled up to reach 100% geographical coverage and 92% of public health facilities, and health extension workers were deployed at community level, contributed in giving health information and screening for TB during their routine home visit activities but little improvement in TB case detection rate. Despite these efforts, the estimated case rates were stagnant and between 2007 and 2008, it actually increased. WHO organized a workshop in 2009 to inform the estimates ("onion skin" approach), suddenly our case detection was high and disease burden low. NTP expressed doubt and championed the cause to do a National Prevalence survey.

Indonesia: Indonesia is a high prevalence country, and the last survey was conducted in 2004, so the timing was right to repeat. The support was available and it was important to learn about the impact of the significant investment in the years since the past survey. The decision makers decided that it was important to do something as precise as a survey to really determine the impact. It was also decided that we needed to establish a baseline for future efforts.

Malawi: We did not have a baseline information in terms of TB Prevalence. We were largely dependent on WHO estimates. So as a country, we thought it important to check to learn the actual numbers.

Myanmar: We did not know the epi situation in our country, and the Myanmar NTP attended a workshop on the topic held in India, with experts from WHO HQ. We discussed the trend of TB in Myanmar, but we could not guess the direction and real size of burden. We realized that we needed to know our disease burden based on scientifically sound studies/surveys. At that workshop, the WHO expert presented different ways of doing epidemiological assessment, including TB prevalence surveys. The last TB prevalence survey done in Myanmar was in 1994, and the method used was not strong enough (identifying only sputum smear positive). Therefore, NTP decided to do another survey with stronger methodology and sought technical assistance and funding.

Nigeria: The main reason was that knowledge about the burden of TB was based primarily on WHO estimates, and the country was not comfortable with those estimates. The motivations was to clarify the burden of TB in Nigeria – to assist with policy and planning Tanzania: To establish a close, realistic estimate of TB prevalence, which would allow us to determine the effect of the program activities. This was the first TB prevalence survey – and it was important to do.

Thailand: In the past we had some data from WHO, but some questions from different audiences led to some skepticism. And the previous one was over 15 yrs in the past – so when the opportunity from GF came, we thought it important to take it to get a better idea of the true TB burden

Zambia: The TB Control Program nearly collapsed in Zambia in the late 1990's and there was a period where there is no data, hence we always felt that the TB prevalence estimates for Zambia by WHO may not be accurate as they are based on historic data; also from the notification data that we were having we felt that the actual prevalence would probably be higher than what was being estimated, therefore conducting a national TB prevalence survey would provide the best estimates. Also, Zambia was among the 21 Countries that the WHO task force on impact evaluation had identified as a priority country to conduct a prevalence survey.

SUMMARY: 9 countries (all but one) mentioned the need to get precise estimates; 6 countries mentioned skepticism about WHO estimates; 1 country (Indonesia) mainly wanted to follow-up from last survey in 2004

Q1A. Who was involved in the decision-making process?

SUMMARY: Of the 10 countries, 9 mentioned NTP as the primary decision maker. 6 mentioned the WHO (1 country, Malawi, mentioned the MoH and WHO and USAID, but not NTP).

Q2. Was the NTP the lead implementing agency?

SUMMARY: Of the 10 countries, 6 said the NTP led the survey. The 4 others (Indonesia, Ethiopia, Zambia and Malawi) had other in-country partners lead.

Q3. Where did the funds for the prevalence survey come from?

SUMMARY: GF mentioned by 9 of the 10 (excluding Zambia); USAID mentioned by 9 (excluding Thailand); JICA mentioned by 2; MoH was mentioned as a source of funding by 4 countries (albeit in varying amounts; Ghana, Indonesia, Malawi, Thailand, and Indonesia).

Q4. How were the results of the prevalence survey disseminated?

Cambodia: Initial internal discussions of findings, then moved to larger forum and final report. Dissemination workshops (supported by JICA): included MoH, partners, funders, NTP staff. Dissemination of results to typical and atypical partners, including public via newspaper and media coverage. Results used for advocacy opportunities. Presented in media. Shared successes and advocated for additional work. Director put emphasis on dissemination and use of data. Used opportunity to showcase program, demonstrate successes. Int'l observers came to learn from survey, including survey coordinators from countries planning prevalence surveys. JICA supported staff to present results at UNION mtg

Ethiopia: There was one national, full-day workshop attended by all national stakeholders, including WHO (local and Geneva), USAID, CDC, GF. That was followed by international publications and presentations at the Union conference. We also did a media brief (local and international media). We tried to release the results on many levels.

Ghana: Results of prevalence survey dissemination are continuous and systematic. It has currently been disseminated through presentations at various fora and is currently being prepared for publications in peer review journal. Order of dissemination: NTP (advisory board and weekly meetings); MoH/Ghana Health Svc; Parliamentary subcommittee on Health; Academia; Nation (world TB Day and media); International Conferences (Union).

Indonesia: The results were principally reported at a national symposium last March (by MoH on National TB Day) and during the National Health Research Institute parade. The NTP, research team, TORG and WHO-HQ Impact team are discussing some manuscripts for journal publications – it is in discussion/development

Malawi: *We are delayed a bit, because we have not yet disseminated the finalized results. We are dependent on technical help to finalize the analysis. We are just updating the final report now. We learned a lot from the Union conference in Barcelona and made a preliminary oral presentation there of the results; the senior officers in the MoH are aware of the results, but not formally. We plan to make a presentation in Cape Town if we can arrange to attend. In country, we plan to make a final formal announcement with all involved stakeholders. This is planned before end of the year.*

Myanmar: *We had internal consultation meetings, then a broader dissemination (first within the Ministry of Health and then with the partners, donors and UN agencies and civil society. We did not write up a publication for a journal – just distributed the report to Ministry of Health. We did have a media campaign in two big cities, Yangon and Mandalay, to share the results and reveal the true disease burden and to ask their help to educate the community about TB disease (the symptoms and when/how they could get TB diagnosis and treatment) but the media were not mature enough to capture the main messages.*

Nigeria: *First in a meeting by TA providers (WHO and CDC) with the NTP and the main TB technical and implementing partners in the country. Second with a large stakeholder group of including anti-leprosy organizations, USAID, CDC, WHO, MSF, PRs and SRs of the Global Fund. Results were presented and discussed/commented upon. Results were presented to higher up in the government (Director Public Health and the Permanent Secretary) in the Ministry of Health. Report was finalized and printed. The results officially launched by the Minister for Health in a large ceremony which included the launching of the TB Strategic plan 2016-2020. In attendance during the launching was WHO-HQ, WR Nigeria, members of parliament, State TB programme managers, NGOs, civil society agencies TB program implementing partners, etc.*

Tanzania: *There was a dissemination meeting with the MoH, stakeholders from different academic and research institutions and local government authorities. There was a write-up that was published led by NIMR (very recently). The members of Parliament were made aware and the results were included in budget planning.*

Thailand: *We received support from WHO for analysis and data presentation as well as from the Dept of Disease Control. Meetings were held within the Dept and within the Ministry (direct meetings with the Minister). The data was released to the WHO. After these internal meetings, we are in the process of finalizing the manuscript for a peer-reviewed journals*

Zambia: *The results were disseminated through dissemination meetings and publications (The Final TB Prevalence Survey Report was posted on the Ministry Of Health Website and can still be accessed there).*

SUMMARY: Most (8/10) describe a deliberate pattern of local (NTP/MoH) to wider audiences. Only 4 spontaneously mentioned plans for publication in journals.

Q5. What were the greatest challenges you faced in conducting the prevalence survey?

Cambodia: *There were no real stumbling blocks that delayed the survey or its implementation, some minor operational challenges were identified and solved over the course of the survey. This was most likely as a result of experiences with the first survey, including strong planning and anticipation of what the survey would entail. Both a 2-3 month initial and follow-up mid-term evaluation were useful, and were as a mechanism to check progress.*

Ethiopia: *Procurement, but we were lucky to be able to outsource. We were in a hurry to start and convinced MOH to hire a procurement agent. Hired UNOPS, but even then there was a delay of about 6 months. It didn't affect performance because it was election time anyway and they didn't want to do during that period. Laboratory management—managing*

huge sample number—accumulating specimens—even storage became a problem. At the beginning, there was a high contamination rate, in part because they are field specimens with long transport times. Also, we used only one lab, and only one specimen for culture (morning sputum); smears done on both spot and morning and thus may have underestimated the rate. Tracing the x rays during panel review was also an issue; more than 40,000 images (we used X ray film) and then we had to find the x-rays. Tracing patients afterward who were positive on culture was also a problem—info sent out, but not clear how many really end up on treatment.

Ghana: How do you organize a study of this scale when you have no experience and the last study on this was in 1957? Procurement, etc they knew they could do, but organizing and moving logistics was the greatest challenge. Massive, impressive WHO support. Never regretted asking them to be partners—came down several times to guide and coach.

Indonesia: Geographical challenges were the biggest. And the logistical issues. The response rates were problematic, especially during the pilot. We worked hard to increase the response rate and had to launch a big campaign – which was effective. Procurement was very complicated – especially the XRay machines weren't made in Indonesia, so importing and getting the permits was very complicated (very complicated clearance regulations). Worked hard with the Ministry of Finance (with GF and the implementing partners assistance and facilitation) – this required a lot of meetings with multiple stakeholders. We almost failed because of this. The lab was also difficult, but it was manageable. We used the prevalence survey to really accelerate the capacity building of the lab – it was a deliberate decision to leverage the survey to boost the lab capacity. I think the investment of WHO-HQ to provide really good consultants to assist the implementation of TB prevalence survey at the country level is very important - countries need good TA especially with the more complicated aspects of the surveys (in Indonesia – that was mostly geography).

Malawi: Funding in itself was a problem. We wanted to do the survey in 2011, but there was not sufficient funding. There were also delays in procurement and procuring faulty or incorrect equipment. We also have poor infrastructure in Malawi, and the roads were a big problem. We had to replace some clusters because the original ones were not reachable. We also had problems with equipment: we used the conventional, analog XRay and that was cumbersome (the machines are heavy and hard to transport, we needed dark rooms for developing films and we difficulty finding suitable spaces because of these requirements). Many things required repeated repairs. Also, we captured everything on paper, and it was difficult to keep track of everything.

Myanmar: The procurement of parts – especially Xray machines. And new parts for when the machines broke down. We also had problems with electricity and generators. The field operations worked well and we were able to manage and trouble-shoot well, but we did have a lot of problems with equipment. We started slow and built our capacity gradually. The field ops and data collection took 9 months. Establishing the cold chain and guaranteeing electricity in the lab were also challenges, we had to procure a big generator – which we did just set up before the prevalence survey with the support of Expand TB Project.

Nigeria: The biggest challenges were material procurement and the lab. We had to use mobile digital X-rays, and the process of ordering was difficult – this required clearance, importation licenses, etc - all of which took a long time. Once we got them, the machines worked quite well (Mini-Xray was the company – and we were pleased with them). There were power issues, and we relied on generators – and this was at times a problematic. Also the lab issues were huge. The available labs were not sufficient to keep up with the amount work. We had to develop partnerships with private labs to assist. Also transportation of sputum from the field was very challenging (large distances), cool chain challenges during transportation of specimens.

Tanzania: *Implementation was delayed – planning started in 2007, and the study was implemented in 2011. GF came in with support, but the planned survey was very expensive. There were issues with lack of human resources – specifically in the lab. Processing of specimens was done in the field, so lab staff from the reference laboratory did the training and provided technical support to the field teams (the lab staff was stretched very thin). Transportation of sputum specimens around the country was very difficult. There were also breakdowns of the Xray machines – and we didn't have the technical capacity in the country to repair, so that further delayed activities. Had the external technical support for conducting the study been provided by WHO – it would have been easier for WHO to approve the analysis and results. Acceptability of the results was an issue – and this is likely because tech support was provided by another agency.*

Thailand: *Low participation rates were a big problem with any national survey, especially in urban settings – that was a big struggle for us. The second main problem was trouble coordinating sufficient funding. The last main struggle was the sample size – it was a very large undertaking. 90,000 is a very large number.*

Zambia: *Procurement issues – some items were procured late, while sometimes the wrong items were procured. The Cluster size that we used was big (census supervisory areas) instead of the standard enumeration areas. This entailed participants travelling long distances. Funding was not adequate initially, however, the GRZ was always ready to fill-in the funding gaps.*

Summary: 8/10 countries mentioned procurement and equipment issues; 5 mentioned funding as an issue; 6 mentioned roads/geography; and 5 mentioned lab issues. Participation rate and acceptability of results were each mentioned by one country.

Q6. What do you think were the biggest benefits (positive outcomes) from the prevalence survey?

Cambodia: *Concrete data, which are more useful than extrapolation/modeling for decision making*

Ethiopia: *The biggest benefit for the program was the understanding of the real prevalence of TB in the country. We were also able to identify specific high and low prevalence areas – which helped us revise our strategy and focus our efforts. We also learned about high burden populations. It also helped us to re-prioritize our interventions. We put much emphasis on community-based interventions as a result of the findings. Also the capacity-building was very important. Learning to manage a task so large was very beneficial to the country (the NTP and the Ministry as a whole). We learned how to conduct surveys of this scope and to gain confidence in our ability to do so*

Ghana *Apart from the results, it offered us the opportunity to test the capacity of the program to its limits. NTPs should take advantage of this—it discloses program weaknesses—it exposes your laboratory, lets you see your program staff capacity, your resource mobilization capacity, tests timeliness of procurement. Has developed capacities in operations research—has given confidence do to research. Strengthened laboratory systems—build QA capacity, GeneXpert, lab management. Linkages with other partners—intangible benefits—can't quantify by way of costs. Helped in logistic management. Strengthened role of leadership in health sector. The benefits, other than the figure given, were great.*

Indonesia: *Improvements in the lab capacity. We had lab consultants (Sandeep was from India and was hired under the USAID program and he resided in Indonesia throughout the survey), IVMS (supra-national lab); and WHO-HQ consultants. The network allowed us to increase effective communication. Getting the National Health Research Institute involved in a project like this was very important. We were worried about the Institute – at first we were not sure if they were capable to do the project. The survey improved the capacity of the Institute by bringing in these consultants. So the technical*

capacity increased substantially and gave them confidence to do projects at international standard. And we are proud that TB prevalence survey in Indonesia was considered among the highest standard one.

Malawi: We went into hard to reach areas, we learned a lot about the TB problem first hand. There are issues with access in Malawi, and we have a new appreciation of the difficulties with case-finding. We learned a lot about our case-detection (the data itself was very important and informative) but we also learned the reasons for the high prevalence. Access to care is quite an issue here. And there are capacity limitations – many of our health workers are missing the diagnosis. So we learned a lot about why the prevalence is so high.

Myanmar: The biggest benefit is the knowledge we gained – which we can use to revise our plan and apply for additional GF (Round 9) and support from Global Drug Facility (GDF). We have received first line anti-TB drugs from GDF for up to 7 years. This allows us to plan and realistically forecast and mobilize the funding. Also we built capacity, especially for case-finding. And we are using the portable Xray machines to accelerate case finding activities (using mobile teams equipped with portable digital Xray to go to hard to reach rural areas and the urban poor).

Nigeria: The biggest benefit is the establishment of a good reliable baseline estimate of TB prevalence. The DOTS program will benefit from incorporating the results into their programming. We learned that the knowledge about TB general in the community remains low, and we have realized the importance of focusing on public education. So the Strategic Plan is now focused on community-based education and outreach for case detection, using existing community structures and organizations (pulled from Q 13: The survey itself was an important capacity builder for many people – we learned how to conduct surveys such as this one).

Tanzania: Knowing the actual estimates of the TB burden. It was important for us to find how much TB we were missing, and this will allow us to follow the impact of our efforts.

Thailand: We have accurate estimates of TB burden (40-50% higher than previously expected). This survey used very good technology, and was able to diagnose a lot of people and refer them to care. It was a more sensitive approach, with more definite findings. Also the survey contributed to improvements in capacity (lab, skills, experience, etc). Also this survey was able to document characteristics of the TB burden (the epidemiology – age and gender and location). We also learned what proportion of them had symptoms.

Zambia: The understanding of the actual disease burden in the country; capacity building in the staff who worked on the survey; coordination and involvement of various government departments and stakeholders and general health systems strengthening.

SUMMARY: All countries mentioned the actual knowledge/data; 6 countries mentioned capacity-building (blue).

Q7. If you were going to repeat the prevalence survey, would you do anything differently? If so, please describe.

Cambodia: Move to digital Xray, Move to liquid culture, possibly use GeneXpert, increase sample size (increased population, decreased prevalence), Not very excited about electronic data capture “might take focus off site work”, Not interested in other disease states “would take focus off of TB”, HIV testing could be considered for TB cases and possibly presumptive cases, would include SES.

Ethiopia: I think we want to understand the prevalence better among different populations – so we might design the survey differently. We need to look into the prevalence in populations living in a congregated setting. The next survey

should be able to better characterize the prevalence by region as well (so we would design the survey with a tighter focus on groups and by regions). We also want to plan to do data-entry in real time – so we would want to do a more digital survey. Would do two specimens for culture; would use digital Xray both for management purposes and ease of re-reading; electronic bar coding to avoid human errors (they didn't use double data entry); GeneXpert.

Ghana: Would take advantage of new technology that would be available, and include GeneXpert in the initial design. Would obtain backup parts for lab.

Indonesia: I think we would secure other (different) technical equipment (like different Xrays) – and secure them well in advance. I would start with the equipment and make sure we had enough. The delays and lack almost held us up. Delays were 6 months – which was very costly, we had to extend contracts for the investigators and team. So I would secure the equipment even before I started the contracts with the staff (staff were idle while waiting for equipment).

Malawi: The survey was so hectic – but I am not sure. I would make sure that we had a system that was electronic. We would like to have a system to digitalize the data and the Xrays. We think that electronic data capture is much better and easier.

Myanmar: We are planning a repeat survey in 2017. We want to learn from the African experience – they use portable digital Xray, Xpert and have electronic data collection, a fully digital survey. We want to enhance our mobile technology.

Nigeria: If the survey was repeated now, we would ensure that all the issues with the labs are fixed in advance and the procurement is started well in advance of the survey and is sufficient for the survey needs. I would ensure that all the materials are on the ground first.

Tanzania: We would opt to use the zonal culture labs (4 or 5) – to improve turn-around time and quality of results. Also maybe outsource lab techs (microscopists) to expand staff capacity. We would work more directly with WHO for technical support.

Zambia: We would ensure that there is enough time to prepare and adequate funding available before starting the whole process.

SUMMARY: 5/9 respondents mentioned changing equipment (mostly to do a digital survey; 4 mentioned revised lab equipment or protocols (liquid culture, GenXpert); 2 mentioned a change in protocol.

Q8. Did the prevalence survey cause any disruptions to the routine activities of the NTP

SUMMARY: 5/10 countries mentioned lab being overwhelmed; 4 countries denied any disruptions. See report for specific quotes on laboratory disruption.

Q9. What was your initial reaction to the prevalence survey results?

Cambodia: All knew that burden had decreased, but didn't know how much. This was the value of conducting a second survey...could quantify this. Allowed NTP to evaluate impact of DOTS, compare Cambodia with global trends/data. NTP had done a lot, but didn't know what kind of impact they were having.

Ethiopia: *We had been following WHO estimates for years, so our expectation was that the results would be similar. But the results were much lower. For the program managers, the reaction was like “at last!” The data showed that the program seemed to be functioning better than expected, overall, and there was some celebration. But on closer inspection of the data, we learned that more than 60% of the cases detected by the survey were not (yet) picked up by the routine program – so we realized that we have work to do to on case detection (there were some delays in our routine case detection).*

Ghana: *Our initial reaction was that of relief, excitement that we have much more reliable knowledge of TB burden, which planning can be done and against which any progress can be measured.*

Indonesia: *Actually I already saw the results from the other countries, and we knew about the increases in those surveys. We knew that we were using more sensitive screenings, so I myself anticipated an increase – and I communicated that to my supervisors in the Ministry. When the results came out I explained the results to my supervisors, but there was denial from the perspective of my bosses – because they didn’t think there was sufficient explanation of what was going on. It seemed from their perspective that the NTP was worsening and that the TB in Indonesia was worsening. There should be appropriate sensitization process for high level authorities to understand the situation and assisting them to respond appropriately particularly to the media. And now we feel we have a better understanding of how to fix the problem. But it was a process to come to that...Now TB is becoming one of the national development indicators (2015-2019). It is one of the more important indicators (one of the 4 main priority indicators for the MoH: reducing maternal and infant mortality, reducing nutritional deficits, reducing accelerating AIDS TB Malaria and the 4th is chronic, non-communicable disease)/*

Malawi: *It was quite a shock to see that the numbers of TB cases were much higher than we thought. We had used WHO estimates for prevalence, but the survey showed that the actual prevalence was much higher. At certain populations are even higher than the national average. This was a surprise. When we looked at the trend, we were able to see that the program was going down, so we were able to see that this was not a total surprise.*

Myanmar: *It was definitely higher than we expected – but was not shocking. We were able to accept and we think the results are valid and more precise. We are happy with the results. There were no political problems or tensions caused by the results. The advantage of having NTP lead the survey is that since we did it on our own, we observed the real situation in the field during the data collection period. That allowed us to more easily accept our real findings, that is results of the survey.*

Nigeria: *It was something of surprise - but not really. The process was a good one and the results were very reliable. I would have been more surprised if I was not a part of the process. We learned the TB is more prevalent than we thought, and the fact that I was part of the survey made that easier to accept and understand.*

Tanzania: *The results were higher than expected – more than twice as high. We were surprised. But because the NTP was directly involved in the whole process, the results were accepted by the health officials in the country.*

Thailand: *I anticipated a higher prevalence than was previously estimated. I learned that the prevalence surveys in Asian countries often reveal higher numbers. So I accepted these results. We had to work with the Ministry to convince them of the results. We worked with the WHO country office to explain the results and to make them acceptable (they explained that the survey was well done and reliable).*

Zambia: *The survey results were not very different from what we anticipated they would be.*

SUMMARY: 6/10 countries reported that the results were higher, and some had issues because of this.

Q10. If the findings from the prevalence survey are different from what you expected, what do you think are the reasons for that?

SUMMARY: No countries fault the survey. All accepted the results - although one country, Ethiopia, mentioned perhaps insensitive testing since cultures were done only on morning specimens

Q11. Do you think the findings of the prevalence survey are reliable? Why or why not?

SUMMARY: All countries think the results are reliable, although Ethiopia mentioned the caveat that results were reliable for smear positive cases.

Q12. What did you learn about the TB situation in your country and about your program from the prevalence survey?

Cambodia: Variation on geographic level, High rate in elderly, High rate of asymptomatic and smear negative, Current algorithm was unable to capture all cases.

Ethiopia: Overall the TB program is functioning well and the estimates of TB prevalence are lower than expected, but there are some issues with the timing of case detection, and there are regions and populations where TB is concentrated – and we need to address those. There was a fair amount of TB in young people—this was new and meant that TB circulating in the community. Found routine program can't reach many of the cases because they are asymptomatic, but it's impractical to use X-ray. Less than 50% of cases had symptoms.

Ghana: Two things have been learnt about TB situation and the program in Ghana. TB is endemic and can be described as a generalized epidemic and not concentrated epidemic. The burden is now pronounced with bacteriologically positive TB cases much higher than smear positive cases. There are missing TB cases in the community that the program has not reached. Persons with cough usually take action on their cough situation. The program itself is efficient and it performs very well what it was been designed to do. That is detection of smear positive cases.

Indonesia: We learned that there was more TB than we thought, and more in the private sector. We also are learning that drug resistance is more of an issue than we thought. We are concerned about that – which is why we are initiating the DRS.

Malawi We learned that the prevalence is much higher, and that we are missing cases. Especially in special populations. And we learned about the issues with access to care and case-finding

Myanmar: The program coverage is good but is geared toward smear-positive cases. So to that extent, the program is effective. But we are missing smear negative, culture positive cases. Most asymptomatic TB patients were also detected in this survey. And we are missing cases from the private sector. We learned this from the DRS as well – where cases are often treated in the private sector. Only about 20% of private patients are under the PPM scheme – the majority are not reporting to us.

Nigeria: We learned that the TB surveillance system is very weak. Routine surveillance data was previously by the country to measure performance of the programme but the surveillance itself is weak, so now we know we cannot rely on surveillance data. And in general, the health system in Nigeria is very weak, and in need of a lot of improvement. The

survey also gave us some insight about the health-seeking behavior in the community. The informal sector is actually getting stronger because the formal sector is not available to the people. It also informed the programme on the need to address laboratory issues.

Tanzania: We learned that the burden is much higher than estimated, and that we are missing cases.

Thailand: We learned that we have a low case detection rate (the burden of disease is much higher) – and we now have a much better characterization of the TB epidemic in the country. We have focused on treatment success in the past – and we need to focus on case detection.

Zambia: There are more cases that are being missed through routine TB services; Use of a combination of diagnostic tools improved the detection of cases; There are certain areas that could be considered as “hot spots” for TB in Zambia; Non-tuberculous mycobacteria (NTM) may be an issue that should be addressed; The health centers and clinics is also failing to timely diagnose TB; TB/HIV co-infection is important, however, there are still quite a lot of people with TB who do not have HIV.

SUMMARY: All countries mentioned learning about TB epidemiology and/or the strengths and weaknesses of their TB programs.

Q13. Have you made any changes to the TB control program as a result of the prevalence survey?

Cambodia: Goal of performing survey was to inform TB control program. The survey results were supplemented and triangulated by other types of data. The body of data was used to inform priorities and operations plans. “A survey is just a survey...it’s not necessarily representative of reality”. Need to supplement with site visits, triangulate with day-to-day data. Survey results were used to set new goals, create more ambitious targets. Saw high prevalence in elderly; and decided to increase focus on this population. Emphasizing treatment of asymptomatic cases. Introduced new diagnostic screening algorithm (any symptom > 2 weeks). This was implemented based on survey results. “Information for action.”

Ethiopia: Yes – we learned that the TB in Ethiopia is concentrated in the pastoral or nomadic groups, so we have developed our strategy to focus on these groups and to devote more resources. And also we learned that our routine case detection was not sufficient, so there was a major shift to community-based interventions – we shifted from passive, facility-based case detection to active case-finding in the communities. These changes were written into our strategic plan, and are implementing these key changes. Culture facilities have been scaled up at regional and reference lab levels. Expansion of X ray has been recommended but hasn’t happened yet.

Ghana: The prevalence survey results and lessons have informed and culminated with development of new National Health Sector Strategic Plan. The plan completely addresses the gaps identified through the prev survey. It also employs the use of the tools used in the prevalence survey, such as digital Xrays GeneXpert, and MGIT as part of routine diagnosis. The case definition and screening strategy have been revised and new diagnostic algorithm have been introduced. All targets set in the NSP are based on prevalence survey results.

Indonesia: The DRS for one. We are also moving to more active case-finding strategies – looking more actively at all pregnant women (all will be screened for TB) as well as persons with HIV and with the Indonesia workers who work outside Indonesia (migrant workers), we are also stepping up TB/diabetes activity and increasing our involvement with

PPM. The prevalence survey has given us the power to put these things on the agenda. We realized that the potential for transmission in the clinics was high – so we are moving some of efforts are going out to the house (community work).

Malawi: Yes- we are focusing on case-finding and more active ways of case-finding in special populations. We have been doing this first in the special populations, now we want scale this up to the nation. We have talked about capacity building (improving clinician diagnostic ability), and the programmatic issues involved. I think people need this kind of capacity building. We are still planning to formal changes to the TB strategy, but these are the things we are talking about

Myanmar: We found that the prevalence rate is higher in urban, but the rural population is greater. We are now trying to address the disease burden (not rate) so we are trying to boost our coverage of the rural areas. We are also increasing focus on private sector. We are changing our diagnostic algorithms to include chest Xray and have put efforts into active case-finding, especially among our higher risk groups (for example, we are doing contact tracing). We use Xpert, but primarily for those who have risk for drug-resistant TB. We also expanded community involvement to increase engagement of stakeholders.

Nigeria: The results have already informed the TB Strategic Plan - we are now focused on a community based approach to increase cases: leveraging existing community-based structures to educate and serve the public. Targets for the TB control were also revised. The prevalence survey also established the initial capacity for electronic data capture. The TB program itself is moving from paper-based to electronic.

Tanzania: We are putting more effort into case-finding, especially in rural areas. We are making deliberate efforts to increase case detection: intensive and focused trainings for staff and community interventions. We have seen an increase in cases where we have made those efforts – which supports the findings from the prevalence survey (that the cases are out there, and were being missed). The National Strategic Plan was informed by the prevalence survey – we are implementing that now with a focus on case-finding in specific communities.

Thailand: We are preparing some specific activities to improve screening – using XRays and new active case-finding and GenXpert machines. We are looking to use GF money to push case-detection, especially in the higher burden groups – the elderly, but also children. We are using this data to convince partners and stakeholders to shift to case-finding and to provide the needed funding.

Zambia: Yes, there has been some improvement in terms of laboratory capacity and we have made some changes in strategies whereby more resources are being put in areas where the burden seems to be much higher.

SUMMARY: 7/10 mentioned an increase in case-finding, 3 of whom mention rural areas; 3 others mentioned other special populations that they are focusing on as a result of the survey.

Q14. Other than the findings, were there any benefits for the National TB Program as a result of doing the prevalence survey?

Cambodia: Capacity for ongoing operations (e.g. active case finding and other surveys). Experience and expertise for other TB surveys, as well as surveys for other disease states

Ethiopia: Huge national capacity-building for research was a major benefit. The mobile Xray machines are continuously being used and the lab equipment and capacity is still being used widely (the LED microscopes are now being used throughout the country – so there was the equipment, but also an increase in technical capacity as our staff were trained

in the use of these machines). LED Microscopes were first used in the NTRL for this particular survey and the same staffs who used the microscope have able train more laboratory personnel on LED Microscopy. The service was subsequently decentralized. Capacity for research in the research institute increased—the magnitude of the survey as well as the population-based village level data collection has led them to do more field surveys. Good capacity building in data management and analysis, and in the lab as well. First exposure of lab to huge burden. They improved their performance that fed into the drug resistance surveillance activities.

Ghana: The organization and planning of the survey itself brought added benefit to the program. First, it strengthened program management and coordination. The survey was highly intensive and complicated in management working with other sectors such as Statistical Svc and Universities and private sector. The skill set learnt from supra-national reference lab are available in the program and are currently being used. Data management and skills provided through technical assistance from WHO is available to the program management unit of M&E unit. The available mobile digital Xray is an essential component of the program outreach screening strategy. The study itself built operations research capacity confidence for the program and follow-up studies have been planned as a result.

Indonesia: The lab and technical capacity of research group.

Malawi: There was a lot of capacity building – especially for specific people (in the lab for example). This was the first population-based survey that we (the NTP) has done, and that taught us a lot. WE also learned population problems: we saw the over-crowding. We learned the issues and reasons for the high TB prevalence. We also got a deeper understanding of the cultural beliefs that inhibit people from coming to care. So in addition to the actual numbers of TB, we learned a lot about the issues that contribute to the problem. We have yet to really analyze these other aspects (like the impact of SES on TB), but we plan to analyze that data.

Myanmar: Other benefits include Xray machines; capacity of staff improved and can be used for active case-finding; the confidence of NTP staff that we can do this kind of work/research. The lab was already well-suited. The lab is still strained with PMDT, but they benefitted from doing the survey.

Nigeria: The capacity-building is an important one. Human capacity and equipment. We learned a lot from this survey, and expanded our abilities. The Xray machines were distributed to HIV clinics and are in use. The establishment of reliable baseline estimates, which will help in planning (setting realistic targets). It was also important for the govt to realize that this is a priority issue, and requires funding. It showed the weakness of the culture laboratories which required further support.

Thailand: We developed the capacity to conduct a survey of this size. We learned a lot – how to do the survey and how to interpret the results. Having the mobile Xray units will help with regional work and case-finding (we are using them in elderly shelters), we also can use the equipment for general lung health programs.

Zambia: Yes, there were other benefits in terms of capacity building, trainings and new equipment, especially in the laboratories, that were procured for the survey is now being used in routine services.

SUMMARY: 8/9 mentioned capacity building; 5 mentioned new equipment. Nigeria mentioned that the findings would help prioritize TB and prompt funding

Q15. Will you plan a repeat prevalence survey? Why or why not? When?

SUMMARY: all 10 said yes (or probably).

Q16. Can you think of alternatives to a prevalence survey that would provide good epidemiologic data?

Cambodia: Didn't ID any. Would prefer primary data over extrapolated or modeled data

Ethiopia: If we are having case-based electronic reporting system throughout the country, that could replace the prevalence survey (if there is good QA of the system), but we do not have that now. That could be an alternative: strengthening the routine surveillance by developing electronic case-based reporting. It would be nice to do a program review and look at routine reporting + survey data to get some idea of this

Ghana: If the routine surveillance system is comprehensive, and able to capture all diagnosed cases, and assuming all those with history of cough will utilize our health system for screening - that will be a good alternative. We are not yet there, so we may need to fall on prevalence surveys for now.

Indonesia: Enhancing the TB surveillance system – to push to more routinely collected data. Linking all the GeneXpert machines (using FIND) to develop the surveillance system and the information systems. Ideally we get to the point of continuous surveillance using this network (also mentioned the use of inventory studies to measure the unreachable population and follow the reporting).

Malawi: I don't know. If we can have very good and straightforward monitoring of the problem at the healthcare facility level, with feedback to the central level, then maybe that would be cheaper than the survey. If we could have district hospitals being able to do random and repeated screenings, then I think we could get good data and not need to conduct a big national survey.

Myanmar: Not really... We have a better understanding of morbidity with these surveys, but we do not have a good idea of how to get good mortality data (this is important as the WHO is focusing on mortality).

Nigeria: For Nigeria, I am not sure of any alternative for now. The routine surveillance system is weak and not reliable.

Thailand: We have an idea to improve surveillance in the country, so one day we can rely on that without having to do a survey. The idea of inventory study would help us to learn more about our surveillance, and would help us to improve so that one day we can rely on our own routine surveillance.

Zambia: The alternative that would provide good epidemiological data would be routine notification data, however, for this to be reliable it will require that there is adequate coverage of service including good reliable and accurate diagnostic tools

SUMMARY: 7 of the 9 respondents reported that ideally, reporting could be used, but all of these felt that their countries were not to the stage of having fully reliable surveillance data at present.

Q18. Do you think it is advisable or feasible to widen the scope of a TB prevalence survey in order to get more info about other disease programs?

Cambodia: In general, the NTP director was of the impression that adding information about other disease programs would not be advisable, as it would take focus off of TB and possibly negatively impact the quality of the survey. It is worth noting, however, that other NTP staff and partners in the survey were interested in learning more about how the survey scope could be widened.

Ethiopia: I think it is feasible. The interaction between HIV and TB and the emerging interaction a between non-communicable diseases and TB are very important. Adjusting to learn about these diseases is valuable and very feasible during the prevalence survey. This is something we need to look into. This would allow us to pool resources from different programs/agencies. As a downside, it might introduce some difficulties in maintaining confidentiality and there is the question about peoples' willingness to be tested for HIV. TB is less stigmatizing than HIV, so the concern would be about the effect on participation rates.

Ghana: The countries with experience is doing prevalence surveys can easily widen the scope. We attempted to collect information on diabetes and NHIS, smoking that did not require lab work, even at our first attempt rather successfully.

Indonesia: Yes – I think the TB problem is a larger one. The prevalence of a disease has more impacts than just the disease. We need to understand the interplay between the diseases. These diseases are significant to each other. However, I am not sure about diseases that are not very prevalent – like HIV. That would be difficult to be integrated in TB prevalence survey in Indonesia. So I think it depends on the country. In Indonesia, I would focus on working with diabetes and with maternal health program – these are the most impactful and important interactions with TB.

Malawi: We think that is important and feasible. We were worried that HIV screening would jeopardize participation, but we learned that the stigma is reduced, and people were open to the idea of testing. We think we would widen the scope to include these other issues. We think that it is feasible and we would be interested in doing that. It would make sense. We found that people often came to the survey sites with other problems. They thought we were a hospital or mobile clinic and they came with other conditions – we think that people would report their other conditions and be open to testing.

Myanmar: It is possible. The survey is really expensive, and if we can harness the efforts and expense to learn about other diseases, it is possible. Now that we are doing mandatory HIV testing for TB patients, we can leave that out. The problem to include HIV or other diseases is to be considered that the prevalence is not the same, so the sampling would be different. But the idea is feasible.

Nigeria: Yes – we initially wanted to include HIV testing, but we decided (after discussion) that the sample size would be different – and would be much larger if we included HIV. So to include other diseases, the sample size would have to be re-adjusted. This can have huge cost implications

Tanzania: I think with proper planning, it could be done. The prevalence survey is very expensive, and it is a shame that we cannot use that same avenue to gather information that can help with other disease. With proper planning, I think we could include other aspects. If it is not properly planned, then it would become a problem. Also combining the prevalence survey with a DRS might also be feasible.

Thailand: I worry that the sensitivity and stigma issues around HIV might be a problem – people might not want to come. I think the idea of looking at diabetes is a good idea. So I think that we need to be aware of the sensitive issues when considering other diseases

Zambia: *It is feasible to collect more information during the TB surveys and combining with HIV surveys may be possible. In our Survey HIV testing was also included. However, collecting a lot of info may be tedious and might be costly.*

SUMMARY: 7/10 thought it would be feasible. However, 6 expressed particular concern about HIV testing (4 for stigma related issues, 2 for epi related issues). Malawi and Zambia have some experience with HIV testing in their surveys - and Malawi said they learned that stigma had decreased.

Annex 11: Country Visits

Ethiopia Site Visit: September 29-October 2, 2015

Chiang Chen-Yuan, The Union Against Tuberculosis and Lung Disease

Karen Stanecki, Team Leader, Independent Assessment

1. Was the survey justified based on what was, and was not, known about TB in the country? Was the primary impetus to do the study from the country itself, its TB partners, or from external groups such as the WHO?

One of the most important reasons that the government of Ethiopia decided to conduct a TB prevalence survey was that the estimated case detection rate of TB remained unsatisfactorily low, despite that substantial efforts have been invested on strengthening TB cases finding in Ethiopia in past decade. The statement of State Minister clearly reflected why Ethiopia decided to conduct a TB prevalence survey:

“As Ethiopia is one of the 22 Highest TB burden countries in the world, Federal Ministry of Health of Ethiopia is implementing TB Prevention and control program at all level of the health facility. The implementation of TB prevention and control interventions is guided by the five year TB Strategic plan, The recent scale up of community TB Care by health extension workers ensured access of DOTS at grass root level in the community. However compared to the previous estimation of TB burden for the country, the program achieved TB case detection rate **less than 36%** which is much lower than the minimum target (70%). **The steady progress in case detection rate raised a question whether the previous estimate was reliable or not.**”

The uncertainty of estimated case detection rate resulted in difficulty in planning for intervention on case finding, thus justified the decision to conduct a TB prevalence survey. Ethiopia was encouraged by WHO to conduct a TB prevalence survey and the decision was made by MoH.

2. Were appropriate local and international institutions involved? What role did each play in protocol development, training, implementation, data analysis, and dissemination? What was the role of the NTP? If the NTP was not the lead implementation agency, what role did they play, and what issues arose in coordinating activities between the lead agency and the NTP? Was there a TAG or a steering committee, and if so, what was its role in preparations for the survey, in data collection and in analysis? Was technical support from external institutions adequate?

The TB prevalence survey was initially led by the NTP under Ministry of Health. However, the NTP at that time had limited capacity in conducting the survey. Consequently, the Ethiopian Ministry of Health delegated the Ethiopian Health and Nutrition Research Institute (EHNRI, recently renamed as Ethiopia Public Health Institute) to undertake this survey. The EHNRI as a health research arm of Ethiopia MoH has several years of research experience on the national priority health research agendas including on infectious and non infectious diseases, nutritional problems, and modern and traditional drugs.”(report, p iv) The PI was Dr Amha Kebede, who was acting Director General of EHNRI. NTP sent two individuals, Zeleke Alebachew and Fasil Tsegaye, to EHNRI to function as Survey Coordinator and deputy Survey Coordinator, respectively. The TB prevalence survey was mainly designed and implemented by the EHNRI (including protocol development, training, implementation,

data analysis, and dissemination) in collaboration with The Federal Ministry of Health of Ethiopia and with the technical support from the World Health Organization. In addition, Global Fund, TBCARE Ethiopia, USAID Ethiopia, GLRA Ethiopia, and Italian Cooperation have supported the study in various ways (Pii). A Steering Committee, a Survey Coordinating Team, a Technical Advisory Group, and a Medical/Diagnostic Panel were established.

“The **Steering Committee** (SC) composed of the FMoH State minister, NTP manager, Ethiopian Health and Nutrition Director, survey coordinator, representatives of national and international institutions (Addis Ababa University medical faculty, Ethiopian Radiation control Authority, Ethiopian Central statistics Authority, Armauer Hansen Research Institute and international organizations: WHO, TBCARE, USAID, GLRA, Italian Cooperation, and CDC) was formed. The steering committee had the primary responsibility for selecting the survey implementing organization and the principal investigator, designing the study, eliciting funding, and ensuring the quality of survey implementation.” Members of the SC participated in monitoring and supervisory activities directly both in the field and at the central level. (p11)

“The **Survey Coordinating Team (SCT)** composed of chiefs for the Lab, Radiography, Statistics and Logistic teams as well as the leaders of field teams. The SCT was responsible for carrying out the survey and reporting to the SC. A Survey Coordinator was nominated December of 2008. The Survey Coordinator chaired the SCT and also served as secretary of SC. The Survey Coordinator was an NTP staff member engaged full-time for the whole duration of the survey. He had responsibility for day-to-day survey preparation and management, organization and coordination of training, piloting, field work, survey implementation, data management, monitoring of progress, and data quality. He reported to the Steering Committee on progress and general monitoring issues.” (p12)

“The **Technical Advisory Group (TAG)** consisted of national TB experts as well as international experts in survey, lab, radiology, and epidemiology. The aim of TAG was to timely provide technical advice to the Survey Coordinator and central units.” (p13)

“The **Medical/Diagnostic Panel** made medical decisions during the survey. The panel reviewed documents, X-rays, and lab results for all suspected TB cases and reached consensus on definite, probable, and possible study cases according to the study case definitions.” (p13)

Substantial technical support was provided by WHO TB Monitoring and Evaluation Group, which was critical in ensuring proper implementation and data analysis of the TB prevalence survey.

3. Was the sample size adequate and the sampling plan appropriate to answer the study objectives? (includes appropriateness of initial sample size assumptions and how they differed from what was really found, meaningful strata for programmatic purposes and also whether the sample size was adequate to examine changes in prevalence, if repeat surveys conducted)

The target sample size was 46514, and the actual sample size was 46,697. The assumption was that the prevalence of smear positive pulmonary TB among adult age 15 y/o or elder was 364 per 100,000 and the design effect was 1.5; but the observed prevalence was 108 (72-138) per 100,000 and actual designed effect was 1.26. The sample size and sampling frame appeared to be appropriate.

4. Was the staffing adequate (person power and competence) to conduct the survey in a timely way and within budget? To what extent did the survey disrupt routine TB program and laboratory activities, including supervision?

The survey did not cause significant disruption of routine TB program and laboratory activities because the majority of individuals participated in the survey were newly and specifically recruited for the survey.

“Survey operations were carried out by five teams, specifically recruited for the prevalence survey. Each team consisted of fixed and flexible components. The fixed part consisted of one team leader (physician or senior health professional), one receptionist, three census takers/interviewers, two X-ray technicians, one radiologist or physician as CXR reader, one lab assistant, and three drivers. The flexible part of the team included local staff from the region, zone, woreda, kebele, local health workers including HEWs and community assistants/volunteers.” (p13)

Visitors interviewed Mr. Zelalem Yaregal, Manager, National TB Reference Lab; Mr. Abebaw Kebede, Former Manager, National TB Reference Lab and Ms. Muluwork Getahun, Researcher, National TB Reference Lab and was informed that laboratory work was managed smoothly without much disruption of routine laboratory activities. At the time when the survey was conducted, there were 13 lab staff working in the national reference lab (NRL). All sputum specimens were sent to the NRL for smear and culture examinations. On average there were 50 sputum samples per day thus was manageable by the NRL team. Overtime of lab staff due to high workload was paid.

The survey did not progress smoothly initially due to limited capacity of the NTP; it proceeded much smoothly after the EHNRI took over the responsibility of the prevalence survey

The team has difficulty in obtaining details of expenditure of the survey and only has information of budget. The total budget was USD\$ 2,832,420, in which 2,625,520 (92.7%) came from Global Fund (Procurement, training, salary and field operation), 106,900 (3.8%) from WHO (TA), and 100,000 (3.5%) from TB CARE/USAID (salary).

5. Were the methods of case-finding appropriate to both reliably assess TB prevalence in the country for national and international purposes and also to determine how well the NTP is doing with case finding? (For the latter, need to be able to compare like - uncentrifuged or centrifuged smears, type of microscopy, symptoms, , use of X-ray etc)

Methods of cases finding followed WHO recommendations and were appropriate. Case detection in the prevalence survey was not directly comparable with case finding under programme condition. For example, two sputum specimens were collected among symptomatics or CXR positive in the prevalence survey, while three were collected among presumptive TB cases in national TB programme. The majority of microscopy centers used light microscopes and a minority use LED microscopes under programme condition; in the prevalence survey, LED microscope was used.

“All sputum samples received at the national reference laboratory, both spot and morning, were examined with fluorescence microscopy: one slide from each sample was air dried, fixed and stained with auramine” (p26)

6. Were other data collected that could be useful for targeting their program (e.g., health-seeking behavior for TB symptoms) or providing information for other programs within the MOH? (SES/equity, HIV, diabetes, smoking, etc)

The Primary objectives of the survey were

1. To determine the prevalence of smear positive TB
2. To determine the prevalence of culture positive TB
3. To determine the prevalence of symptoms suggestive of TB
4. To determine the prevalence of radiological abnormalities suggestive of TB

The Secondary objectives were

1. To measure the prevalence of cervical lymphadenitis among study participants;
2. To assess knowledge, attitudes, and practices of the population concerning TB
3. To assess health seeking behavior among participants with TB symptoms

It did not collect independent information for other programs (SES/equity, HIV, diabetes and smoking) within the MOH, but had collected information on smoking in re-interview of symptomatic individuals.

Analysis of data related to primary objective was completed but that for secondary objectives was incomplete. There was no reported information on the prevalence of cervical lymphadenitis among study participants, despite that this information was captured in symptoms questionnaire (p87).

Those who were on anti-TB treatment or have been treated for anti-TB drugs in past 5 years were re-interviewed. Unfortunately, analysis on health seeking behavior was not presented in the final report.

There were findings related to anti-TB treatment. “Out of the 75 people on anti-TB treatment, information on where treatment was received was collected from 64 participants, in whom 54 (84.4%) report that they were receiving treatment at a government or public health facility and 10 (15.6%) at private sector (p38)...Of those who had Anti-TB treatment history in the last 5 years, 15.9% had received treatment at non-public or non-government health facilities. The proportion treated at non public or non government facilities is high than the ratio of PPM DOTS sites registered by FMOH over the total number of DOTS clinics in the country (<10%). This high proportion may suggest that some private health facilities are treating TB without any agreement with FMOM.”

Visitors were informed that there were preliminary results of the KAP study, but final results were not available to date; the KAP study drew attention to the need of increased activities on ACSM. A good example is World TB day, which became a big event after the survey.

7. Were data entry, management, and analysis efficient?

The team of data entry and data management was recruited for the survey as was reported in the final report. “The survey coordinating unit appointed a central data management unit, composed of a qualified data manager and two data entry clerks. The central data management unit was responsible for entry of field and central data entry using (CSPro) as database. Data entry was done concurrently and continuously as data were collected.”

Data entry appeared to be efficient. However, data analysis for secondary objectives was incomplete.

8. Were quality control measures in place, executed, and the results used?

Several quality control measures were implemented as reported in the final report, including training, development of SOP, piloting, timely transportation of sputum, rechecking of slides, and re-reading of CXR, monitoring, and technical assistance.

“Training workshops were held for regional and woreda staff. Health centre staff and health workers received a brief training during the preparation visit by the central team approximately one month before the start of field data collection. Community volunteers received instructions during the preparation visit and on the arrival of the survey team.” (p13)

“In order to prepare the survey activities, extensive training of staff was conducted. The training was organized in different steps and included in house training as well as field visit experience.” (p15)

“Standard operating procedures (SOPs) were prepared and laid out in the field manual for each field activity (team leadership, census, interviews, X-ray, lab). They described in detail the tasks and responsibilities of each field team members.” (p14)

“After the training, a pilot test was conducted in a rural cluster before the launch of the survey in order to familiarize the trained staff to survey operations, field test the forms and registers, and finalize the SOPs.” (p32)

“Collected specimens were stored in ice boxes at four degrees and then transported to the National Reference Laboratory(EHNRI) in Addis Ababa within three days (at most five days) for bacteriological examination” (P25)

“All positive slides and 10% of negative slides were double checked by a second reader/supervisor for quality control purpose.” (p26)

“At the central level, all abnormal CXR films and approximately 15% of normal films have been reviewed by senior radiologists in Addis Ababa (St Paul Hospital, Radiology Department) for internal quality control and further classification.” (P26)

Monitoring (p31), QC (p32)

9. Was the survey done in a way that produced reliable and credible data?

WHO provided technical assistance on data management and Statistical analysis was done in collaboration with WHO” (p30) The finding that the observed prevalence was 2-3 times lower than WHO’s previous estimate was generally well accepted and it seems that no major concern was raised on reliability and credibility of the data in part because data analysis was closely supervised by WHO HG

10. Was the survey completed in the outlined timeframe? If not, why not?

Data items and sources: Protocol, Final Report, interviews with EPHI

1. *The survey was completed very close to scheduled timeline once the protocol was finalized. However, there was some delay from the time the decision was made to conduct a national prevalence survey, 2008, until the*

protocol was produced mid 2009. NTP capacity was weak, not enough resources. It was decided that EPHI would conduct the survey since they had capacity to conduct National household surveys.

11. Was the survey completed within the budget outlined in the protocol? If not, why not? How were shortfalls met (the latter two would need to be done via questionnaires or interviews)

Data items and sources: Protocol, final report, interviews with USAID, NTP

- 1. Only the budget was available from the protocol and final report. Expenditures were not published.*
- 2. From the interviews, additional funding was obtained from partners to cover additional expenses, for example, from TB Care*

12. What were considered the main bottlenecks and difficulties during preparations, field operations and data analysis and reporting? (may be partly captured with the schedule and budget issues)

Data items and sources: Final Report, interview with USAID and NTP

- 3. Lack of experience in prevalence survey required technical assistance and capacity building*
- 4. As regional culture labs were not available during the survey, all sputum specimens needed to be sent to NRL, which was costly and time consuming; delay in transportation might have resulted in false negative of culture, especially in specimen with low bacillary load.*
- 5. Relatively high contamination in the beginning of the survey and the use of only one culture (usually in the morning) Reported issues in midterm and final reports*
- 6. NTP initially very weak. Decision finally made from MOH to move Survey work to EPHI. NTP provided 2 staff members to EPHI with funding from Global Fund and WHO*
- 7. Capacity in data analysis was weak, required travel to Geneva to seek assistance of data analysis; analysis of data related to the prevalence of lymphadenopathy, KAP study, and health seeking behavior remained unavailable to date.*

13. How were the findings disseminated, and to whom?

Data items and sources: Interviews with WHO/Ethiopia, NTP,

- 2. Large national dissemination workshop including program TB managers, researchers, university staff. Results presented at The Union meeting, Ethiopia TB Research Annual meeting, used as input for WHO global estimates*
- 3. Published on the international Journal of Tuberculosis and Lung Disease (Int J Tuberc Lung Dis 2014;18(6):635–639)*

14. Were feasible and actionable recommendations made to improve the TB program and to improve national surveillance (e.g., targeting of at-risk groups and enhanced case finding for groups with active TB who had not sought care or been diagnosed by NTP)?

Data items and sources: Final report, interviews with WHO/Ethiopia, EPHI, USAID, CDC, NTP

- 1. Although the observed prevalence was 2-3 times lower than WHO's estimates, it was clear that the burden of TB in Ethiopia remained high, and intensified efforts were needed.*

2. *As the survey revealed that TB cases were not detected before the prevalence survey, Efforts have begun to strengthen community screening for early detection and treatment of cases to limit transmission of TB in the community.*
3. *As a relatively high proportion of cases were smear negative culture positive (50%) or symptom screening negative (50%), the role of sputum culture and chest X-ray in the diagnosis of TB were raised in the report. Although sputum culture has not yet been fully utilized in the diagnosis of TB, Culture diagnostic services have been expanded from NRL to regional laboratories. The utility of Xpert tests was not mentioned because Xpert was not yet available when the report was prepared. However, application of Xpert test for the diagnosis of TB has been expanded gradually.*
4. *Since prevalence was unexpectedly higher among Pastoralist, programs are being developed to reach this at-risk group*
5. *A high proportion of cases (55%) were among those aged <35 years-old. Interventions targeting young age groups (especially schools and work places) have been identified as an important component in the fight against TB in Ethiopia.*

15. Were these recommendations acted on in the form of program or policy changes?

Data items and sources: interviews with WHO/ Ethiopia, EPHI, USAID, CDC, NTP

1. *Yes, programs and policies were modified as a result of the survey.*
2. *Improvements have been made in case finding. More confidence in pursuing case detection, contact tracing by the NTP. NTP realizes it still needs to advocate for resources. Majority of cases detected in the survey were new cases, so still an issue. Have started community based efforts training extension workers. Expanded community based TB care. In order to reach younger population a strategy is being devised to focus programs at universities, workplace areas, prisons.*

16. What additional benefits resulted from the survey? (e.g., training, equipment being repurposed, use of HR etc)

Data items and sources:

The Ethiopia Public Health Institute has gained substantial experience in conducting a TB prevalence survey, and is well positioned to conduct a repeat survey.

17. How were the findings used by WHO and by donors at local level and at international level, and were there any caveats around their use?

Data items and sources: interviews with USAID, CDC

1. *Programs re-focused to address high prevalence among pastoralists, increased community outreach to expand knowledge.*
2. *WHO has used findings of the TB prevalence survey to revise estimated TB incidence and estimated TB prevalence in Ethiopia.*
3. *Results used for Global TB estimates*

Annex 1 Itinerary of the visit (a meeting with AHRI and MoH was cancelled)

DAY		ORGANIZATION
SEPT 29	MORNING	EPHI(PI/co-PI (Local research institute)/ Survey coordinator)
	AFTERNOON	Laboratory teams (EPHI)
SEPT 30	MORNING	WHO Country office and
	AFTERNOON	USAID Mission
OCTOBER 1	MORNING	AHRI
	AFTERNOON	CDC
OCTOBER 2	MORNING	NTP Manager
	AFTERNOON	MOH (HIV, NCD program directors, HSS)

Annex 2 Persons met in the visit

Ethiopian Public Health Institute

Dr Desta Kassa

Mr. Zelalem Yaregal

Mr. Abebaw Kebede

Ms. Muluwork Getahun

Director, HIV/AIDS and TB Research Directorate

Manager, National TB Reference Lab

Former Manager, National TB Reference Lab

Researcher, National TB Reference Lab

WHO Ethiopia

Dr Esther Mary Aceng

Dr Kassa Hailu

Team leader of communicable diseases

TB medical officer

USAID Ethiopia

Yared Kebede Haile

Helina Worku

Senior Infectious Disease Officer

Health system strengthening specialist

NTP

Lelisa

Endale

Manager

WHO supported Officer for PPM, prison

CDC Ethiopia

Beniam Feleke

Kussito Kursha

Cambodia Country report

Visit 4-10 Oct 2015

Team: Kendall Krause (BMGF), Binh Hoa (NTP Vietnam), Eveline Klinkenberg (KNCV)

8. Was the survey justified based on what was, and was not, known about TB in the country? Was the primary impetus to do the study from the country itself, its TB partners, or from external groups such as the WHO?

Based upon our desk reviews and interviews, the consensus is that Cambodia's 2011 prevalence survey was justified for a number of reasons.

Cambodia completed its first survey in 2002 and wanted to measure if its subsequent modifications to the TB control programme had made an impact on TB control 8-10 years later. The timing in 2011 of the survey was catalyzed by the ending of the JICA country support and a proposition of Dr Onozaki (WHO Geneva, previously WHO medical officer in Cambodia) to JICA to support in its final 3 years a 2nd TB prevalence survey. Cambodia's completion of two surveys resulted in a positive national and global case study.

This justification for the survey is outlined on page 1 of the protocol: "a reduction in TB prevalence is one of the Millenium Development Goals (MDGs) and an indicator within the Global Stop TB Plan. TB prevalence surveys are an effective tool to monitor the impact of the program. The results of a series of high quality prevalence surveys may show the impact of national and international investments in TB control in Cambodia. The first national prevalence survey was carried out in 2002. After 8 years, the second survey is planned to measure both the current prevalence and any change in prevalence since the previous survey. The first survey suggested an impact of DOTS since 1994. The second survey is expected to show stronger evidence of a downward trend in TB prevalence in Cambodia due to DOTS expansion since 2001. TB data in Cambodia are primarily based on case notification and WHO estimation efforts. As such, there are limited data with which to make assumptions about the true, current underlying TB epidemiology. While every effort is made by WHO expert groups to develop accurate estimates, there is a considerable range of uncertainty around these figures. There was a large discrepancy between WHO estimates and prevalence as measured by the 2002 prevalence survey. Therefore, the national TB program will conduct this second national TB prevalence survey in order to provide the program with updated and more accurate information on the current tuberculosis burden which can also serve as baseline information for future planning within the National Tuberculosis Control Program in the Kingdom of Cambodia."

Cambodia's sequential surveys played a global advocacy role for the value of prevalence surveys (see also page 28 of the Global TB report 2012 Box 2.7 Reducing the burden of TB disease: a success story from Cambodia) is clearly illustrated: "Cambodia is unique among developing countries in having two national prevalence surveys carried out using comparable methods. The first was just after DOTS had been established in all referral hospitals and the program started introducing HC-DOTC in some health center; and the second in 2011 after HC-DOTS covered 100 % of HCs and C-DOTS had covered most of the country. Therefore, the two surveys provide an accurate assessment of the health impact of TB control by the widespread availability of HC-DOTS and C-DOTS in the community in the nine years from 2002 to 2011"

9. Were appropriate local and international institutions involved? What role did each play in protocol development, training, implementation, data analysis, and dissemination? What was the role of the NTP? If the NTP was not the lead implementation agency, what role did they play, and what issues arose in

coordinating activities between the lead agency and the NTP? Was there a TAG or a steering committee, and if so, what was its role in preparations for the survey, in data collection and in analysis? Was technical support from external institutions adequate?

Yes, CENAT/NTP was the lead agency for both Cambodian TB prevalence surveys. The majority of the survey team was involved in both surveys, resulting in good local capacity. CENAT staff was involved in all steps of the survey and its laboratory was one of the two involved labs. Central X-ray reading and data management were completed at CENAT. Furthermore, CENAT staff acted as team leaders and was actively involved in supervision and monitoring of survey activities. Although data analysis itself was mainly conducted by a RIT/JICA expert, interpretation of findings was a joint effort.

The survey was heavily supported in all aspects by JICA through JATA/RIT (Dr Okada, Dr Yamada and others see list Annex 5 page 87 of the final survey report). JICA and JATA both maintain a local office within CENAT. A consultant of RIT developed the first draft of the protocol based on the 2002 survey protocol (which was also heavily supported by JICA). This draft was then discussed at country level with CENAT and other stakeholders. During the survey, 3 full time RIT staff members (a project leader, a project coordinator and a laboratory expert) were supported by the JICA project and engaged in every step of the survey and ensured quality throughout, from protocol, SOP development, training with certification for quality to monitor of field and central level activities and data management up to analysis and report writing. The survey budget was managed by the JICA project leader. In addition, regular TA visits were made by a Japanese expert to ensure quality of X-ray reading. The analysis was conducted mainly by JICA/RIT experts. Other partners (WHO, TB CARE I/USAID) were also involved in field monitoring visits. Besides the JICA support in country and through regular TA visits, an external review mission of the survey was done by WHO and CDC staff during country visit while the survey field activities were in operation. During field operation in Aug 2011, Cambodia served as a demonstration site to train survey coordinators from other countries on how to perform a good quality survey.

A survey executive committee was chaired by the CENAT/NTP director, and had overall responsibility for the implementation and monitoring of the survey. The team also included JICA staff and the WHO medical officer.

10. Was the sample size adequate and the sampling plan appropriate to answer the study objectives? (includes appropriateness of initial sample size assumptions and how they differed from what was really found, meaningful strata for programmatic purposes and also whether the sample size was adequate to examine changes in prevalence, if repeat surveys conducted)

The sample size was adequate to achieve the main aim of the survey, which was to detect a difference from the first survey. To calculate sample size, it was assumed that prevalence fell by 42% over the 9 year period since the 2002 survey, in line with the Western Pacific regional Target of 50% reduction in 10 years (with power of 80% and 95% confidence). Precision of at least 25% was sought, in line with the lime book. Based on the 2002 survey, a participation rate of at least 90% was assumed. The DEFF was carefully considered based on the cluster size of the first survey and the expected intra-cluster correlation coefficient (ICC) and expected geographical variation in decline across the country (page 5 protocol), and was conservatively assumed to be double that of the first survey. The assumptions seem appropriate and therefore the sample size can be considered adequate.

The results of the survey show that the assumptions were reasonable as a 38% reduction was observed and participation was 92.6%. Final DEFF is not stated in the report.

A total of 314 TB cases were detected (103 SM+ and 211 SM-) which provided sufficient power for further analysis. Stratum specific analysis was conducted to obtain estimates for urban, rural and 'other' (the areas excluded in the first survey (stratum 3), which were kept separate for reasons of comparability)

The three models provided similar estimates; model 1 was adopted because of comparability with the 2002 survey. This seems reasonable although the 2002 survey data could maybe have been reanalyzed and comparisons made between the surveys based on the recommended model 3. Page 68 of the survey report explains: "Several analytical methods were conducted, however the same analytical method as in the first survey was adopted for the primary estimation of prevalence rate in order to make the results between the first and the second survey comparable: design-based analysis restricted to survey participants who received CXR screening and/or symptom screening without imputation (model 1). Stratification, PSU level clustering effect and weights adjusting for sampling probability were taken into account. Other analytical methods with imputation showed only from -1.4% to 6.2% difference in smear-positive prevalence rates from the primary estimate." Full details on all models with assumptions and outcome are presented in annex 10 of the survey report.

In the extrapolation to all ages to compare with the 2002 survey it was assumed that there were no smear positive cases in children aged <15 years. In 2011 Cambodia reported 34 new smear positive cases in children aged <15 years (Global TB database) resulting in a CNR of 2.4 per 100,000 population. This would not have altered the smear positive prevalence estimate of 183 per 100,000 for all forms. However, overall in 2013, a total of 6,412 childhood TB cases were notified across the country, which accounted for about 16% of total TB cases. Assuming a population of 2,399,593 children <15 years (2013 population data lineary extrapolated based on 2014 and 2015 estimates CIA factbook) results in a case notification rate for children (all forms) of 267 per 100,000 population <15 years. If this is used for extrapolation with an assumed 38% EPTB cases the overall estimate for all forms of TB would be slightly higher at 856 compared to the estimated prevalence rate of 715 (604–834) for all forms and all ages (2013 estimates WHO).

Although there are uncertainties in the reported childhood TB data as stated in the 2012 Program Review report indicating that the number of children with TB is overestimated; it is unlikely to be zero which was assumed to estimate TB among all ages in the survey report.

Overall response rate was high at 92.6%, 90.9% in males and 94.0% in females. Although increasing by age, it was > 88% in all age groups, with the lowest at 88.8% in males 15-24 years and the highest in women 45-54 years at 97.2%. The lowest participation was observed in the urban strata at 84.6% overall participation rate for this strata. There were six clusters with a participation rate below 85% with the lowest at 53.5% in one cluster in Phnom Penh (other rates below 85% were 79.2%, 83.8%, 70.7% and 83.4% and 79.9%).

Stratum specific data were used to illustrate the higher prevalence in the rural areas and advocate for more activities these areas.

11. Was the staffing adequate (person power and competence) to conduct the survey in a timely way and within budget? To what extent did the survey disrupt routine TB program and laboratory activities, including supervision?

Interviews revealed that partners felt that overall staffing was adequate. For future surveys, additional field laboratory staff, population listing, and census work would be useful. The number of team leaders was expanded from four to six during the survey to ensure quality work and allow for sharing of duties of more senior staff to avoid disruption of routine activities.

It was noted by one of the interviewed that people were very busy and quarterly case notification data decreased during the prevalence survey, potentially suggesting a decline in case finding capacity due to survey activities.

Additional staff was hired to support the survey:

- Radiology: CENAT had 3 radiologists available, and hired 3 consultant staff through the private sector.
- Laboratory: no additional staff was hired and the full laboratory team worked in rotation schedule. The majority of the staff involved in the first survey were also involved in the second survey.

CENAT staff involved in the survey indicated routine activities were not disrupted as others in the organization took over duties from those involved in the survey and survey and other work was divided. Besides additional evening and weekend time was used for example by the radiologist to perform chest X-ray readings.

Training took about 1 month and staff was trained by JICA. Certification was done before staff was considered 'ready' for the prevalence survey. Training was done for the team in full as well as separate specialized training for each technical team (lab, CXR, interview). Both radiology readers and technicians were trained for 5 days and were certified at the end of training. All (20) lab technicians at central level were involved in the prevalence survey and were trained during one week and after that followed up for assessment till they passed the exam on culture techniques. Which all technicians had to pass to participate in the survey.

Besides that 10 JICA experts were involved, of which 3 fulltime staff in Cambodia provided constant on the job training. On the job training was done continuously during monitoring visits. At month 2/3 and midterm (month 6), meetings with all survey staff were held to discuss results and any issues experiences during the field work to ensure all involved remained on the same page.

12. Were the methods of case-finding appropriate to both reliably assess TB prevalence in the country for national and international purposes and also to determine how well the NTP is doing with case finding? (For the latter, need to be able to compare like - uncentrifuged or centrifuged smears, type of microscopy, symptoms, , use of X-ray etc)

There were few differences between routine and survey case finding. The survey used solid culture while routinely liquid culture was used. Solid culture was chosen to ensure comparability with the 2002 survey that used solid culture. The downside of this was that many of the lab equipment procured for the survey could not be used routinely afterwards as for routine services they were performing liquid culture.

Although comparison with case notification with routine is important for Cambodia this seems less relevant. First of all routine surveillance data are considered to have data quality issues and secondly a large proportion of the population is seeking care in the private sector who does not notify case leading to substantial underreporting. The country completed 2 national TB prevalence survey and can therefore directly measure impact through comparison of the two surveys. Comparability between the first and second survey was high and deliberately pursued to ensure comparability of results. It should be noted that a difference between the two surveys was that the definition of a TB case was 2 positive smears among 3 specimens in the first survey while this was adopted to 1 positive smear among 2 specimens in the second survey. In routine work 3 specimens are still being used.

Although the diagnostic algorithm was very similar more cases were put on treatment programmatically then counted as survey cases.

The routine smear procedure was the same as in the prevalence survey: Direct sputum smear by fluorescence microscope /centrifuged. The difference between routine and survey is in the number of smears, in the routine work 3 specimens are requested while the prevalence survey used 2 specimens. When discussing this difference

with the chief of LAB he indicated that the NTP prefers to keep 3 specimens in the routine work to increase (if even just by a few) the case detection. Only policy change regarding to the lab: in the prior prevalence survey, the definition of TB cases is 2 smear positives among 3 specimens; changed to 1 smear positive among 2 specimens.

13. Were other data collected that could be useful for targeting their program (e.g., health-seeking behavior for TB symptoms) or providing information for other programs within the MOH? (SES/equity, HIV, diabetes, smoking, etc)

Yes, other data collected were useful for targeting TB program activities. Additional survey elements collected included: i) age, sex, and occupation; ii) past and current history of TB treatment; iii) presence of symptoms (cough, sputum, haemoptysis, chest pain, loss of weight, fatigue, fever, night sweat and other TB related symptoms); iv) health-seeking behavior (e.g. visit to hospitals, health centers, private clinics, pharmacies, traditional healers) for those with symptoms.

However, other programs were not approached during survey design. For example, the HIV program did not participate in the planning and development of the survey protocol. The expressed reasons for not collecting HIV data or performing HIV tests were due to stigma, capacity and anticipated acceptability by the survey participants.

Although other information was collected, the focus was on detecting TB cases, as the goal of performing the survey was to inform the TB control program. The survey results were supplemented and triangulated using other types of data. The body of data was used to inform priorities and operations plans. Survey results were used to set new goals and create more ambitious targets.

Future surveys should consider including HIV and/or diabetes. Low in-country HIV prevalence (current 0.7% but could be as low as 0.2% by 2020) may result in challenges related to necessary sample size. On the other hand, DM prevalence is 7% among TB patients, while it is estimated at 2.9% (in 25-40yr olds population in Cambodia).

14. Were data entry, management, and analysis efficient?

Yes. Data entry, management, and analysis were efficient.

- Data was collected based paper forms and was entered at the central level. As a result, data was not available in real-time for monitoring of field operation. However, at the end of each site in the field, the team summarized the data for report to local authority and monitoring purpose. The final validated data set was available about 6 months after completion of the survey. All data were entered into EpiInfo 3.5 (Centers for Disease Control and Prevention, Atlanta, United States of America). Some key data were double-entered for quality control; discrepancies were resolved by checking against the raw data. Prevalence rates, odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated by using logistic regression models incorporating sampling designs (stratification, clusters and weights) in STATA version 12 (StataCorp LP, College Station, USA).

In general, data quality is considered as good, data management unit in central have 4-5 staff, data entry took around 5-6 months.

For the data entry: During the field operation, all individual survey forms were to be checked every evening by the team leader to avoid missing information. Electronic databases on household registry, individual survey form, CXR register, and laboratory register were developed.

Data management & analysis: The analysis was carried out by JICA experts in consultation with CENAT staff and Several analytical methods were conducted, however the same analytical method as in the first survey was adopted for the primary estimation of prevalence rate in order to make the results between the first and the second survey comparable: design-based analysis restricted to survey participants who received CXR screening and/or symptom screening without imputation (model 1). Stratification, PSU level clustering effect and weights adjusting for sampling probability were taken into account. Other analytical methods with imputation showed only from -1.4% to 6.2% difference in smear-positive prevalence rates from the primary estimate.

15. Were quality control measures in place, executed, and the results used?

Yes. The quality control measures were in place, executed and the results used.

The quality was perceived as good, highly standardized with high quality output; quality checks were rigorous, Likewise, the quality of lab and CXR were considered to be acceptable. All the lab technicians have been trained and have passed the skill for culture.

Quality control measures for radiography, smear, culture, and data entry:

- **CXR:** Japanese experts attended some of the field operations and checked the quality of CXR films and CXR screening results. All films including normal CXRs were re-interpreted by them and the results of the reading from field screening and central reading were compared with those by the Japanese experts. CXR screening 2 steps, 1) screening; 2) central full reading; QA screening there were about 20 person missed by the field with abnormal CXRs who should have submitted sputum. About 10 were still traced back in the field. Reading was done by CENAT staff and JICA staff as 1st and 2nd reader and where needed a 3rd reader was used to make the case.
- **Smear:** Direct sputum smears were observed by fluorescence microscope. 40 visual fields (1line) are observed; Positive slides were confirmed by other laboratory staff; Smear negative culture positive cases were rechecked by re-examined with ZN microscopy by a senior technician. Slides were selected by OMC lab supervisor; All any positive slides (FM+ and C+) and same number of negative slides are collected by cluster; If there is no positive cases in one cluster, ten negative slides are collected; Ten slides are minimum per one cluster. All selected slides were restrained by ZN. OMC cross checker read without knowing the results of BTB or CENAT. If there is a discordant for positive slides, OMC lab supervisor rechecked.

Culture: contamination rates and recovery rates were carefully monitored. If C+ found they would look back at the smear. They monitored contamination carefully. Culture recovery was 85% much better than many of the African surveys.

Contamination rate by tubes was 4% in total (CENAT 4%; BTB 3.8%). In the final report (Table 3.19, page 46 final survey report) the culture contamination was only 0.9%

Data entry: All the variables were entered using double entry except for the variables from two sources. After matching the databases by survey ID, inconsistent values were detected by comparing values between the databases or between the double entered data. The original forms and two computers protected by specific

password for the survey were kept in a locked room accessible only to persons designated by the executive committee.

16. Was the survey done in a way that produced reliable and credible data?

Yes, survey done in a way that produced reliable and credible data

Overall response rate: 92.6%. Response rates by gender and age: Male 90.9%, female 94.0%; by age group: 15-24yrs 89.6%; 25-34 yrs 91.3%; 35-44yrs 93.7%; 45-54yrs 95.3%; 55-64 yrs 96.0% and 65+ yrs 96.6%. Response rates by stratum: urban 84.6%; rural 94.8%

The contamination rate was 4% in total. In the final report (Table 3.19, page 46 final survey report) the culture contamination was only 0.9%

A total of 314 TB cases were detected (103 SM+ and 211 SM-). As presented in the page 56 survey report, the actual SM + prevalence was 271 (95% CI: 212-348); the actual bacteriologically confirmed prevalence was 831 (95% CI: 707-977).

Actual design effect: SM+ 1.57; BACT+ 2.47 (Table 3 Asian prevalence)

Actual Kappa: SM+ 0.59; BACT+ 0.54 (Table 3 Asian prevalence)

The four models provided similar estimates as below (Annex 10 – final survey report):

Model-1: Survey Analysis based on participants without imputation

Unknown status of TB was categorized as negative. Analysis was limited to participants who received CXR screening and/or symptom screening. Stratification and PSU level clustering effect were taken into account. Weights proportional to inverse of the number of participants in each cluster was given to the participants in each cluster.

Using model 1, the SM+ prevalence was 271 (212-348); the bacteriologically confirmed prevalence was 831 (95% CI: 707-977).

Model-2: Survey Analysis based on eligible population with IPW adjusting for non-participants

Weights proportional to inverse of (1/the total number of eligible in each cluster) x (1/participation rate for age/sex subgroup of eligible population in each cluster) was given. Other specification was the same as the Model-1

Using model 2, the SM+ prevalence was 268 (209-342); the bacteriologically confirmed prevalence was 822 (95% CI: 699-966).

Model-3: Survey Analysis based on participants with imputation

Imputation model for the missed TB status among the eligible for sputum examination: MI (20sets) was carried out for imputing missing data of TB status among participants eligible for sputum examination which had non-conclusive results of bacteriological examination. MI was carried out separately for smear-positive TB and bacteriologically positive TB.

Estimation model: Analysis for MI data sets incorporating the same specification for survey analysis as mentioned in the Model-1 was applied.

Using model 3, the SM+ prevalence was 288 (222-373); the bacteriologically confirmed prevalence was 863 (95% CI: 751-1036).

Model-4: Survey Analysis based on eligible population with imputation (MI and IPW)

Imputation model for the missed TB status among the eligible for sputum examination: the same method as the above 3) was applied.

IPW for adjusting for non-participation: IPW was incorporated in the estimation model as mentioned in the Model-2.

Estimation model: Analysis for MI data sets incorporating the same specification for survey analysis as mentioned in the Model-2 was applied.

Using model 4, the SM+ prevalence was 284; the bacteriologically confirmed prevalence was 873 (95% CI: 743-1025).

For both smear-positive TB and bacteriologically-positive TB, the estimates from the above models were close to each other. The difference from Model-1 was less than 10%. In the models adjusting for non-participation, estimates tended to be lower than in non-adjusting models because participation rates were lower among young age groups, which had lower prevalence.

At conclusion, the result of Model 1 was used, with the the SM+ prevalence was 271 (212-348); the bacteriologically confirmed prevalence was 831 (95% CI: 707-977).

In the page 68 of the final report mentioned “Other analytical methods with imputation showed only from -1.4% to 6.2% difference in smear-positive prevalence rates from the primary estimate.”

All the reviewers, from CENAT staff; JICA; JITA; WHO and others, are confident and said that the results are credible.

17. Was the survey completed in the outlined timeframe? If not, why not?

In general, the survey was completed in the outline timeframe. Only 2 months delayed due to a slight delay in release of Global Fund monies.

Preliminary preparation started in 2009, but major preparation were started in 2010. Protocol development took approximately one year before conducting the survey; a pilot was done in late 2010.

The 4th version of draft protocol was as of 12 May 2010. The date survey began was planned in October 2010 and actual in December 2010 (02 months delayed). The date data collection completed was planned in July 2011 and actual in September 2011 (02 months delayed, due to 02 months delay in began the survey). The results were presented to Ministry of Health in February 2012 and final report published in December 2012.

18. Was the survey completed within the budget outlined in the protocol? If not, why not? How were shortfalls met (the latter two would need to be done via questionnaires or interviews)

The protocol outlines funding sources and cost breakdown as follows:

Funding sources:

Ministry of Health/Global Fund	Human resources, operational costs	\$203,650
JICA	TA, equipment, field operations, printing, data management, dissemination workshop	\$760,300
USAID (through TBCAP)	TA, training, workshop, printing	\$53,600
		\$1,017,550

For the costs (excluding technical assistance), procurement represented 48%, training and workshops 5%, survey activities (operational costs) 41%, and printing 6%.

We were unable to obtain a list of final expenditures to evaluate discrepancies between the budget and actual expenditures but our interviews indicated that any discrepancies that existed were minimal. Furthermore, the CENAT Director indicated that he was generous in his initial budgeting to ensure that all costs would be covered. In fact, the only budget issue mentioned was a small budget shortfall due to a delay in disbursement of funds by one partner; this delay would have threatened to delay initiation of field operations for 2-3 months, but the funds in question were covered quickly using a small loan facilitated by existing relationships.

The funding from this survey was provided by multiple sources, which was associated with both benefits and challenges. JICA mentioned that they saw the pooled funding as a success story although the project leader indicated that complying with the various financial reporting timelines, requirements and disbursement timings was challenging and time-intensive. Also, other funders felt that they may not have been adequately informed of the pooled funding, and, in retrospect, were concerned that this approach could have resulted in duplication of funding.

19. What were considered the main bottlenecks and difficulties during preparations, field operations and data analysis and reporting? (may be partly captured with the schedule and budget issues)

Our interviews with a variety of partners involved in the survey did not uncover any significant bottlenecks or difficulties during preparations, field operations, analysis, or reporting. The delay in funding disbursement threatened to delay the project by some months, but was dealt with expediently. The proposed timeline, as put forth in the protocol was as follows:

- 1st quarter 2010:
 - Complete draft protocol
 - Submit budget
 - Develop draft SOPs
 - Nominate team leader and technical team
 - Establish executive committee and technical committee
- 2nd & 3rd quarter 2010:
 - Sample sites
 - Visit sites to assess feasibility etc
 - Conduct workshop
 - Conduct training
 - Conduct field test and pilot study
 - Modify protocol and SOPs based on pilot
- Oct 2010-July 2011: Field operations
- Nov 2011: Assess preliminary results

The actual timeline was as follows:

- Date protocol writing began: TA began drafting protocol last quarter 2009, draft completed first quarter 2010, **protocol approved August 2010**
- Date survey began: **Dec 2010**
- Date data collection completed: **Sept 2011**
- Final lab tests run: **December 2011**
- Date initial results presented for internal discussion: **February 2012**
- Date final report published: **December 2012**
- Data full-scale dissemination meeting **December 2012**

A comparison of the proposed and actual timelines shows a delay of only 2-3 months for completion of field activities and initial data analysis.

The time from the beginning of the protocol writing to beginning the survey was ~1 year, which appears to be quite reasonable for prevalence surveys (as this time also included IRB approval and procurement). Field operations took approximately 9 months, and initial data analysis was presented only 5 months later. The time between the presentation of initial results and the release of the final report was approximately 10 months.

The relative timeliness and lack of significant bottlenecks/difficulties can likely be attributed to the following:

- Strong ongoing relationship with JICA/JATA (funding and TA) and other technical and operational partners
- Experience with previous prevalence survey

- Low staff turn-over rate between first and second survey, resulting in significant technical and operational expertise within CENAT.
- Rapid and smooth procurement by JICA, as well as relationship between CENAT director and customs (thereby limiting any hold-ups due to customs)
- Strategic up-front that accounted for foreseeable delays and needs for backup resources (e.g. trained additional human resources, serviced back-up portable CXR)
- Implementation of interim assessments (one at 2 months, one at mid-term), and incorporation of findings in iterative quality improvement

The team did note that central data abstraction and management took 5-6 months, which contributed to the overall length of the survey which likely could be reduced with the implementation of electronic data capture.

20. How were the findings disseminated, and to whom?

The findings were actively disseminated to internal and external partners.

Data was first discussed internally, then shared with external partners. The timeline is as follows:

- Data collection completed: Sept 2011
- February 2012: provisional data was formally disseminated to partners, dissemination workshop supported by JICA was conducted and was attended by multiple national partners, including CENAT, HIV/AIDS programme staff, Ministry of Health staff, WHO, and other partners.
- Preliminary data was used in the WHO Workshop on repeat survey design and analysis on Feb 8 2012
- Data was presented at the TSRU on 19 April and at the TF meeting on 9 May 2012
- Final analysis was completed Sept 2012
- Data was highlighted in 2012 Global TB report
- Final report was published December 2012
- Paper was published in the Bulletin of the WHO in June 2014 (submitted October 2013)
- Presented at UNION conference Nov 2012

The programme also presented additional findings from the 2012 prevalence survey at the 2012 UNION meeting including:

- A comparison of the use of fluorescent microscopy and ZN staining for prevalence surveys (abstract #PC-213-15)
- Epidemiological impact of mass TB screening: a two-year follow-up after a national tuberculosis prevalence survey (abstract #PC-441-16)
- TB in less symptomatic and elderly cases (abstract #PC-443-16)

21. Were feasible and actionable recommendations made to improve the TB program and to improve national surveillance (e.g., targeting of at-risk groups and enhanced case finding for groups with active TB who had not sought care or been diagnosed by NTP)?

The recommendations that came out of the final prevalence survey report included the following:

- 1) The NTP in Cambodia should maintain the facility DOTS at hospitals and health centers as a core of TB control, combining other types of DOTS like community DOTS and public-private mix DOTS;
- 2) There are other factors that are possibly associated with the reduction in TB prevalence in the country: the decline of HIV sero-prevalence rates among TB patients and doubling of GDP per capita in the last nine years, which should last long in the future for continuous reduction of TB prevalence;
- 3) Limitations DOTS strategy due to focus on passive case detection & symptomatic patients;

- 4) The NTP should consider two things for further reduction in TB: a) strengthening the diagnostic capacity for OPD patients with respiratory symptoms. The current diagnostic procedures which entirely depend on smear microscopy should be thoroughly reviewed: active use of CXR for any respiratory symptom cases; referral system for smear-negative suspects to facility equipped with CXR; or introduction of more sensitive diagnostics including WHO-approved diagnostics such as Xpert MTP/RIF than smear microscopy.; and b) expansion of active case detection to highly prevalent groups such as the elderly, household contacts with smear-positive TB and those co-infected with HIV; Interventions such as INH preventive therapy or full TB treatment might need to be considered for those with CXR suggestive of active TB but negative bacteriological-test results. Another option is performing active case finding for the middle-aged and the elderly

One of the major successes of the Cambodia survey was the translation of data into policies and other actions to improve national surveillance. These include:

- Clarified notification rate trend: the programme had previously noted that their notification rate was decreasing, and didn't have sufficient evidence to demonstrate why that might be the case. The survey provided insight into the existence of a large portion of smear negative and asymptomatic patients, which clearly explained the trend that had been identified. It also revealed that although TB control program had made impact in substantially reducing SM+ prevalence this was less so for smear negative.
- Data revealed previously unknown epidemiological patterns
 - Smear negative cases (resulted in adoption of GeneXpert)
 - Asymptomatic patients (resulted in change in symptom screening algorithm)
 - Identification of additional high risk groups (e.g. elderly) (resulted in change in approach to active case finding)
- These two pieces of data resulted in in adaptation of the case finding strategy, including:
 - Implementation of a 4-symptom screening algorithm (Any of cough, fever, weight loss, and/or night sweats for > 2 weeks; the programme was moving from a single symptom "cough > 2 weeks" screening approach), though it took 2-3 years to move from suggested policy change to full-scale implementation of the new approach; during this time, the majority of healthcare workers continued to focus on cough as primary screening mechanism.
 - Increased focus on high risk groups. This includes the use of GeneXpert in these groups, as well as a modified symptom screening. If a member of a high-risk group (HIV, DM, contacts over the last 2 years, elderly) exhibits any of the 4 symptoms for >2 weeks, they are tested. Within the Challenge TB programme, they are evaluating a multi-symptom, multi-risk factor approach. The identification of these high risk groups also informed increased population targeting of active screening (for example, now screening at pagodas and other locations where elderly congregate).
 - Implementation of GenXpert at multiple regional hospitals. This technology continues to be scaled up across the country. Furthermore, through the enhanced case finding approach, any member of a high-risk group displaying one of the 4 symptoms for >2 weeks will be directed straight to GeneXpert without first obtaining a sputum sample.
- Expansion of active case finding (ACF)

The prevalence survey also indicated that 47% of patients were seeking treatment at private providers. This has resulted in multiple interventions and policies, including banning TB drugs from the private sector, referral mechanism, and the development of a community sputum transport approach (the latter to address access issues).

The survey data was also a central input to the NSP and NFM strategic planning process.

The push to use data to inform policies was strongly supported by the local WHO TB Medical Officer. He did note that it took almost three years for the Cambodian government to change the screening algorithm following the initial data analysis that revealed this deficiency in screening. TB programme staff were trained on the new algorithm in 2013. It should be noted, however, that this official modification of the screening criteria has not yet resulted in a significant increase in case finding.

22. Were these recommendations acted on in the form of program or policy changes?

Please see response to Q 14.

23. What additional benefits resulted from the survey? (e.g., training, equipment being repurposed, use of HR etc)

The interviews indicated that the survey resulted in multiple benefits to the TB program in addition to the resulting data. These included:

- Increased capacity: because the team at CENAT is stable (a significant portion of the team had been involved in both prevalence surveys, even more were involved in the 2011 survey), the skills and knowledge gained as a result of planning and conducting the survey have been maintained within the division. This resulted in improved laboratory and radiology capacity for routine surveillance activities. Furthermore, as the organization ramped up active case finding (ACF) activities, they very quickly learned that the skillsets for prevalence surveys and ACF were almost interchangeable. This resulted in a highly skilled and efficient ACF-ready team.
- Durable equipment (lab & CXR): the NTP benefitted from 3 new portable x-rays, 4 film processers, and a variety of supporting X-ray equipment, including 2 portable dark rooms. Furthermore, they benefitted from lab equipment, including a 3 incubators, 3 fluorescence microscopes, and 1 ultra-low freezer.
- External recognition: as a result of its survey, Cambodia was recognized as a positive example for other countries. This was demonstrated by presentations
- Technical expertise supporting capacity in other countries
- Cambodia's work directly contributing to global policy and guidelines

24. How were the findings used by WHO and by donors at local level and at international level, and were there any caveats around their use?

Data items and sources:

Many of the policies described above, including the move to a multi-symptom, multi-risk factor approach, scaling up of enhanced active case finding, banning of TB drugs from the private sector, and development of the community sputum transport mechanism were driven by the national WHO office.

The Cambodian NTP programme has also been an innovator in relation to case detection. As described by the local WHO MO, "Cambodia is a gold mine of innovative approaches". One such approach was the early initiation of active case finding. Cambodia instituted this approach in 2005, prior to WHO endorsement. Local operational research indicated that the approach was effective and cost-effective, which influenced WHO's overall recommendations around the approach (Eang et al. BMC Public Health 2012, 12:469). This study found that community-based ACF was cost-effective (\$108/case), and likely contributes to early case finding and detection of patients from vulnerable age groups, and may reduce secondary cases in the community. This evidence was instrumental in the development of the current WHO ACF policy.

Visit itinerary

Date/time	Activities	With	Venue
Mon, 5 Oct 2015			
8:30 am	Arrive in office	FHI 360 car pick up from hotel	FHI Cambodia office
9:00 – 09:30	Orientation on logistic arrangement	Ngak and Dr Vanna	CENAT office
10:00 – 11:00	Courtesy call and interview with Getting inputs from CENAT director	Dr Mao Tan Eang	CENAT office
11:00-12:00	Meet with GF's PR	Dr Mao Tan Eang, Dr Sivanna and other PR-CENAT team	CENAT office
12:00 – 13:30	Lunch		
14:30 – 15:30	Meeting with JICA	TBD (The person who knows about the survey is not in the office).	JICA
16:00 – 17:30	Meeting with JATA	Mr. Seak Kunrath	JATA office
Tue, 6 Oct 2015			
8:00 – 8:30	Meet with WHO representatives	Dr. Dong Il Anh	WHO office
8:30 – 10:00	Meeting with WHO	Dr Rajendra Yadarw, Medical Officer	WHO office
11:00 – 12:00			
12:00 – 13:30	Lunch		
14:00 – 15:30	Meet with study coordinator	Dr Peou Setha—	CENAT
15:30 – 17:30	Meet with Advisory group members	Dr Tieng Sivanna, Dr. Saint Saly, and Dr Koeut Pichenda	CENAT
Wed, 7 Oct 2015			
8:30 – 09:30	Meeting with NCHADS (HIV/AIDS)	Dr Ly Penhsun, director of NCHADS	NCHADS
10:30 – 12:00	Data use for planning --- Meeting with Department of Planning and health information(HSS and Vital registration)	Dr. Lo Veasna Kiri Director of Department of Planning and Health Information	MOH
10:30 – 12:00	Explore collaboration and integration among departments-- NCD program	Dr Piseth Raingsey Director of Department of NCD	MOH
12:00 – 1:00	Lunch		
14:00- 15:00	Meeting with TB prevalence coordinator	Dr OKADA, JATA	Skype call at FHI office
15:00-15:30	Meeting with TBCARE I (now Challenge TB) team		
14:00- 15:00	Meeting with JICA – donor of TB prevalence survey	Ms Mizusawa	JICA
14:30 – 15:30	Laboratory team	Dr Heng and Boy Sambo	CENAT

Thur, 8 Oct 2015			
07:30 - 9:00	Travel to province		
9:00 - 10:30	HC and Chief of village	Health Center: Ang Rokar. Provincial & OD (Ang Rokar) TB Supervisor Dr. Saly & Dr. Sothin from CENAT.	Health Center: Ang Rokar
10:30 - 12:00	Courtesy visit to Provincial Health Department	PHD Director, Provincial & OD (Ang Rokar) TB Supervisor Dr. Saly & Dr. Sothin from CENAT.	Takeo Provincial Health Department
12:00 - 14:00	Travel back to Phnom Penh		
Frid, 9 Oct 2015			
09:00 - 10:00	Debriefing with CENAT's director	Dr Mao Tan Eang	CENAT
14:30 - 15:15	USAID debriefing	Ms Christina Lau	USAID
15:30	Meet with LFA	Jan de Jong	Price Waterhouse

Prevalence survey report- GHANA field visit 18-24 October

Authors: Nancy Binkin, MD, MPH and Alaine Umubyeyi Nyaruhirira, MPH, PhD

1. *Was the survey justified based on what was, and was not, known about TB in the country? Was the primary impetus to do the study from the country itself, its TB partners, or from external groups such as the WHO?*

The last prevalence survey in Ghana had been done pre-independence in 1957, and since that point, all estimates were based on mathematical modeling of program data. Although the program had improved over time, with creative involvement of the private sector in treatment and reporting, rising cure rates, and decreased default and transfer out rates, the death rate remained unchanged over time. In 2009, following a WHO workshop, Ghana's case detection, which had previously relatively low, was estimated at 80% and the prevalence rate at 71/100,000. The belief was that Ghana had transitioned to a concentrated epidemic, but this did not track with the unchanged death rate and the widespread geographic distribution of cases. For this reason, the NTP director was highly insistent that a survey be done, even though Ghana was not on the original list of 21 high-burden countries. Thus the impetus was from the country itself in this case, though WHO was then convinced to support the study.

2. *Were appropriate local and international institutions involved? What role did each play in protocol development, training, implementation, data analysis, and dissemination? What was the role of the NTP? If the NTP was not the lead implementation agency, what role did they play, and what issues arose in coordinating activities between the lead agency and the NTP? Was there a TAG or a steering committee, and if so, what was its role in preparations for the survey, in data collection and in analysis? Was technical support from external institutions adequate?*

WHO provided considerable technical support for the protocol development, training, implementation, and analysis and made multiple support visits (Ikushi, Marina) and team visits to Ethiopia and Cambodia were also helpful, but the NTP had full ownership of the survey, turning down additional offers of technical support and use of existing training manuals in favor of finding their own path. They wrote protocol, designed the study, and made their own assumptions so they could appropriately power study. A pilot, done in the prisons, disclosed numerous problems, which they were able to correct with guidance from WHO. Laboratory quality support was provided by the Supranational Reference Laboratory (SRL) Borstel in Germany, and assistance in writing up the findings is being provided by Mr. Zeleke Alebachew, who was the survey coordinator in Ethiopia and is being funded by USAID.

The NTP did seek laboratory support from the Noguchi Research Institute and from the Chest Clinic Reference Laboratory at the University Teaching Hospital at Korle Bu, both located in Accra, and involved the university's radiology staff in the reading of X rays. Importantly, they also hired an outstanding information technology group which helped them design the entire data management system. There was a TAG that was kept informed of developments frequently throughout the survey, but their role in the decision-making process does not appear to have been major.

There was a steering committee consisting of participating agencies and stakeholders which was kept informed on a frequent basis of survey activities but did not appear to have played an important role in decision-making.

The technical support supplied by WHO was judged to be an essential and much-appreciated component of the success of the survey and was appropriate given the experience and background of the NTP manager.

3. *Was the sample size adequate and the sampling plan appropriate to answer the study objectives? (includes appropriateness of initial sample size assumptions and how they differed from what was really found, meaningful strata for programmatic purposes and also whether the sample size was adequate to examine changes in prevalence, if repeat surveys conducted)*

The sample size of around 60,000 was fortunately based on an expected rate of 105/100,000 for smear + cases, which was about 1.5 times the estimated WHO value. The actual value was remarkably close at 111/100,000 (95% CI 78-140/100,000). The design effect was slightly higher than expected (1.55 versus 1.4). Rural and urban strata were used and data analyzed for the strata, although the definition of urban consisted of any agglomeration with a population >5000. A repeat survey is planned, but the sample size did not take this into account.

4. *Was the staffing adequate (person power and competence) to conduct the survey in a timely way and within budget? To what extent did the survey disrupt routine TB program and laboratory activities, including supervision?*

The survey was conducted within the budget, although there were some delays in completing the study as a result of a large backlog of X-rays when the decision was made to re-read all X rays rather than the originally intended 10% for quality control purposes. The field staffing was adequate for survey purposes. The laboratory was stressed, although they did hire additional staff in both of the laboratories to deal with the increased burden. The two initially identified radiologists were unable to keep up with the large burden of work, resulting in a backlog of 20,000 X-rays. Radiology residents were paid to work extra hours to catch up on the backlog.

Because the four survey teams consisted of persons hired from outside the NTP, NTP activities were essentially unchanged. Although the program director was spending 80% of his time on the survey, his deputy was able to assume his activities. The study coordinator was from the NTP's M & E unit, which was sufficiently staffed. At each cluster site, the local TB district coordinator staff assisted in mobilization, but their involvement was brief. While NTP staff was encouraged to keep abreast of developments with the survey, TB program supervision was not affected.

5. *Were the methods of case-finding appropriate to both reliably assess TB prevalence in the country for national and international purposes and also to determine how well the NTP is doing with case finding? (For the latter, need to be able to compare like - uncentrifuged or centrifuged smears, type of microscopy, symptoms, use of X-ray ,etc.).*

The methods of case finding were those recommended by WHO, but the program does not routinely use chest radiographs, nor does it routinely use centrifuged specimens. Thus the data are not strictly comparable, even when only those cases who were symptom-positive and had a positive smear are considered, and the rate obtained even for symptomatic cases is higher than what would be expected under program conditions.

6. *Were other data collected that could be useful for targeting their program (e.g., health-seeking behavior for TB symptoms) or providing information for other programs within the MOH? (SES/equity, HIV, diabetes, smoking, etc)*

Data were collected on health-seeking behavior, on known diabetes, and on smoking, though these were collected only on the TB suspects interviewed with a second questionnaire. SES data consisted of age, gender, and occupation. The health seeking behavior data, which provided highly useful information, showed that a third of participants with symptoms of cough were self-medicating, and that patients were coming into facilities but their diagnoses apparently were being missed. The smoking and diabetes data have not yet been fully analyzed, but may be of limited usefulness since they are limited to those on whom sputum specimens were obtained. The original protocol called for HIV testing, but because of the program's concern about lowering response rate, it was not included in the survey (although the 2014 DHS survey obtained a 90%+ response rate even with routine HIV testing).

7. *Were data entry, management, and analysis efficient?*

The data entry, management, and analysis were exemplary. Unique features included the design of the questionnaires, in which all responses were given numeric codes placed in the right margin to facilitate data entry and the use of a clever system of bar codes and filing codes to track each participant and label and link together the various forms, X-rays, and laboratory specimens. This allowed for real-time tracking, the data were clean and ready for analysis after the last bit of data was collected.

Unfortunately, the laboratory portion of the tracking system, which performed very well during the survey, has been abandoned even though with some minor programming modifications, it could be adopted for routine use.

18. *Were quality control measures in place, executed, and the results used?*

The X-rays were all re-read, but not in real time, with 20,000 read after the end of the survey. Data management had an excellent series of quality control checks built in that permitted errors and problems to be identified and corrected in real time.

With respect to the laboratory, two approaches were used by the laboratory staff at both the Chest Clinic and the Noguchi TB lab. All smear-positive slides were sent to The Chest Clinic for review by a senior technician as second reader. Additionally, an external quality assessment was performed by the Kumasi Center for Collaborative Research, which did blinded rechecking of all positive and 15% of negative slides.

MGTT cultures were used in the survey analysis (although LJ was also performed). For culture, the manufacturer's SOP was used for MGIT culture and drug susceptibility testing (DST). If the inoculated MGIT tube was positive, material from the tube was used to perform another smear and was inoculated into blood agar. If AFB were found and the blood agar culture was negative, a TB identification test was performed. Additionally, H37RV strains were used as internal positive controls for new batches of MGTT for internal quality control (QC) purposes. For external QC, the laboratory continued to participate during the prevalence survey period in the NHLS South Africa quality control panel program. With respect to DST, the Chest Clinic is part of the network that receives panels twice yearly for testing from the SRL in Borstel, Germany. For GeneXpert, the laboratory participated quarterly at the NHLS South Africa external quality assessment program using dried culture spot (DCS) panel. All 42 strains that were culture-positive but smear

negative or had discrepant culture results or discrepancies between GeneXpert and other tests were sent to the Borstel SRL: Three were MTB and 39 were confirmed to be MOTT or NTM. The quality control process detected a problem with contamination of MGTT specimens due to problems with the biosafety cabinet, but fortunately it was possible to run GeneXpert on all those found to be contaminated, and the GeneXpert results were used for these particular specimens.

19. Was the survey done in a way that produced reliable and credible data?

Participation in the survey was over 90% and was relatively high even in urban areas as a result of the high motivation of the staff. An informal competition to achieve higher enrollment was set up between the teams based on the real-time monitoring of the number of daily interviews. Despite some of the issues encountered in laboratory contamination, the data produced appears to be reliable and realistic. Fortunately, it was possible to run GeneXpert on the contaminated cultures that occurred as a result of problems with the biosafety cabinet to obtain an accurate estimate of the bacteriologically positive cases. The data management system contributed to the quality of the data by ensuring that each participant's x-ray and laboratory findings were truly theirs and that the information entered into the data base were accurate.

20. Was the survey completed in the outlined timeframe? If not, why not?

The survey started later than hoped because of the time required to obtain the necessary funds and because of practical considerations such as the 2012 elections and the Christmas holidays, but once it was under way, the field data collection was done in a timely way. The rate limiting step was the re-reading of the X-rays, which took several additional months of work by radiology residents and others. Although dissemination took place earlier this year, the final report has not been released, though a draft has been produced by Mr. Alebachew that does not contain the final recommendations, which are to be written by Dr. Bonsu.

21. Was the survey completed within the budget outlined in the protocol? If not, why not? How were shortfalls met (the latter two would need to be done via questionnaires or interviews)

The project essentially stayed within budget, in part because of the many years of pre-planning in which equipment and supplies were gradually purchased. Italian funds were used to fund the pilot, and the Global Fund paid for most of the actual survey, with additional contributions from USAID to support technical assistance.

22. What were considered the main bottlenecks and difficulties during preparations, field operations and data analysis and reporting? (may be partly captured with the schedule and budget issues)

The challenges and bottlenecks stemmed largely from the lack of experience in performing such a large-scale study, which was more than four times as large as the recent Ghana Demographic and Health Survey (DHS). Problems did occur with procurement, funding, laboratory management, and the readings of the X-rays, but all were overcome in the end with technical input from WHO and the Supranational Reference Laboratory and some creative solutions such as planning the procurement of equipment and supplies well ahead of time.

23. How were the findings disseminated, and to whom?

The findings were widely disseminated through a variety of mechanisms. During the survey, there were periodic updates to the National TB Advisory Board and meetings with NTP staff. Results were presented at the Ghana Health Service Council's annual stakeholders meeting, to the Parliamentary Subcommittee on Health, and to the University of Ghana School of Public Health, Nursing College, and the College of Physicians and Surgeons. They were presented to the press and other stakeholders at World TB Day, presented at the IUATLD conference, at an international dissemination workshop with WHO, USAID, STOP TB, academia, the London School of Tropical Medicine and Hygiene, and others. TB has been the subject of national radio programs. Results were incorporated into the National Strategic Plan and NGO newsletters. Finally, the Director of Public Health has recently used the findings in a Sino-Ghanaian summit on potential health collaborations, although he believes that greater dissemination to the public and to providers is needed.

24. *Were feasible and actionable recommendations made to improve the TB program and to improve national surveillance (e.g., targeting of at-risk groups and enhanced case finding for groups with active TB who had not sought care or been diagnosed by NTP)?*

Yes. Several major findings came out of the survey. First, TB is endemic and the epidemic is generalized rather than concentrated. Second, the number of bacteriologically positive cases is much higher than smear positive cases. Third, that people do take action when they have cough and they are missing TB cases in the community that the program has not reached or has not recognized when they are seen in facilities. Fourth, the program itself is efficient and performs very well at what it has been designed to do, namely the detection of smear positive cases, but a different approach is now needed to further reduce the TB burden

25. *Were these recommendations acted on in the form of program or policy changes?*

The results and lessons learned have informed and culminated in the development of a new National Health sector strategic plan, which addresses many of the gaps identified through the prevalence survey. Digital X-rays have now been introduced for screening certain populations, and GeneXpert and MGIT are to be used more routinely in diagnosis, with a total of 90 GeneXpert machines to be rolled out for use throughout the country. The case definition and screening strategy have been revised and a new diagnostic algorithm has been developed. All targets set in the national plan are based on the prevalence results.

26. *What additional benefits resulted from the survey? (e.g., training, equipment being repurposed, use of HR etc)*

In the words of the NTP director Dr. Bonsu, *“Apart from the results, [the survey] offered the opportunity to test the capacity of the program to its limits. NTPs should take advantage of this—it discloses program weaknesses, it exposes your laboratory, it lets you see your program staff capacity, your resource mobilization capacity, and tests timeliness of procurement. It has developed our capacities in operations research and has given confidence do to research... [It has also] strengthened our laboratory systems—build QA capacity, GeneXpert, lab management. [We made] linkages with other partners, which has intangible benefits that can't be quantified by way of costs. It helped in logistic management and also strengthened role of leadership in health sector. The benefits, other than the [prevalence] figure given, were great.”*

The available mobile digital X ray machines are now being used as part of the program's outreach strategy and the GeneXpert machines have also been put to use. Vehicles used in the project are now being used by the NTP.

27. How were the findings used by WHO and by donors at local level and at international level, and were there any caveats around their use?

As stated above, the Director of Public Health has used the data in a recent presentation to the Chinese delegation, which has a multi-billion dollar budget for bilateral activities with Africa. With respect to USAID, funding for TB was eliminated in 2013 when Ghana was considered a low-burden country. The survey has provided evidence that this is not the case and interest in TB has been rekindled. Although large-scale funding has not been provided, the funds to support Dr. Zeleke's presence to assist in the completion of the report and assist in other research and planning activities was obtained through USAID. WHO has used the Ghana case as evidence of the importance of truly understanding TB burden through the use of prevalence surveys.

Annex 1 Itinerary of the visit

Monday 18 October	<ul style="list-style-type: none"> Meeting with CTU Prevalence survey team, IT consultants, and data management team.
Tuesday 19 October	<ul style="list-style-type: none"> Meeting with radiologist Meeting with lab staff from Chest Clinic and Noguchi Laboratory
Wednesday 20 October	<ul style="list-style-type: none"> Meeting with Director of Public Health, Ghana Health Service Meeting at USAID (TB focal program officer)
Thursday 21 October	<ul style="list-style-type: none"> Debriefing with NTP team Meeting with Chest Clinic Laboratory team Meet the Non-Communicable Disease Program Director
Friday 22 October	<ul style="list-style-type: none"> Visit the renovated NTRL TB lab (Dr. Nyaruhirira)
Departure of consultants	Dr. Binkin departed on Thursday night and Dr. Nyaruhirira on Saturday.

Annex 2 Persons met in the visit

NTP	
Dr. Frank Bonsu	NTP Program Director
Mr. Raymond Gocah	NTP Survey Coordinator (now M and E officer)
Mrs. Francesca Dzatar	NTP Laboratory Focal Person
Mr. Zeleke Alebachew	Technical Advisor to the National TB Control Programme of Ghana
Stanley Mangortey, Michael Asare Baah, Hilda Smith, Mabel Tetteh, Samuel Apau-Danso, and Cynthia Owase	NTP Program Officers attended the debriefing
Health Research Unit, Ghana Health Service	
Mrs. Jane Amponsah	Data manager
Information technology consultants	
Mr. Prince Boni	Department of Health Policy, Planning, and Management, School of Public Health University of Ghana, Legon
Mr. Herve Awako	TABS (consultation company)
Noguchi Research Institute, University of Ghana	
Samuel Ofori Addo	Senior research assistant, Bacteriology department
Christian Bonsu	Research assistant, Bacteriology department
Central Chest Clinic Laboratory	

Samuel Kumah Atiadeve	Technical officer , National TB control Program (Chest Clinic, Korle Bu)
Michael Amo Omari	Principal Biomedical Scientist, Supervisor at Cheet clinic
Radiology Department, Korle-Bu Teaching Hospital	
Dr. Jimah Bashiru Batunde	Chief resident
Ghana Health Service- Ministry of Health	
Dr. Badu Sarkodie	Director of Public Health, MOH
USAID	
Dr. Felix Osei-Sarpong	Public Health Specialist, Office of Health, Population, and Nutrition
Non-communicable Disease Program, Ghana Health Service	
Dr. Kofi Nyarko	Program manager