STOP TB

policy paper

No. 2

TB Impact Measurement

Policy and recommendations for how to assess the epidemiological burden of TB and the impact of TB control

World Health Organization

TB Impact Measurement

Policy and recommendations for how to assess the epidemiological burden of TB and the impact of TB control

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Contents

Contributors

Ana Bierrenbach and Katherine Floyd wrote this policy paper, with input from Jaap Broekmans, Philippe Glaziou, Ikushi Onozaki and Brian Williams. It was prepared based on recommendations agreed by the WHO Global Task Force on TB Impact Measurement, a paper published by members of the Task Force in *Lancet Infectious Diseases* in January 2008 *(5)* and comments from WHO's Strategic and Technical Advisory Group for TB.

Abbreviations

DOTS
The basic package that underpins the Stop TB Strategy

G8
Group of Eight industrialized countries

HIV
Human Immunodeficiency Virus

ICD
International Statistical Classification of Diseases

MDG
Millennium Development Goal

STAG-TB
WHO's Strategic and Technical Advisory Group for TB

TB
Tuberculosis

WHA
World Health Assembly

WHO
World Health Organization

Executive summary

Global targets for reducing the epidemiological burden of tuberculosis (TB) – measured as incidence, prevalence and mortality – have been set for 2015 within the context of the Millennium Development Goals (MDGs) and by the Stop TB Partnership. The targets are that the TB incidence rate should be falling globally by 2015 and that TB prevalence and death rates should be halved by 2015 compared with their levels in 1990. Achieving these impact targets is the focus of national and international efforts to control TB, and demonstrating whether or not they are achieved is of major importance for individual countries, the United Nations, the Stop TB Partnership and a variety of technical, financial and development agencies.

A Global Task Force on TB Impact Measurement was established in June 2006. The Task Force is convened by the Stop TB Department of the World Health Organization (WHO), and includes international experts in TB epidemiology, representatives from countries with a high burden of TB, and representatives from a range of technical and financial agencies. The Task Force has a three-fold mandate:

- To produce a robust, rigorous and widely-endorsed assessment of whether the 2015 impact targets are achieved at global level, for each WHO region and in individual countries;
- To regularly report on progress towards the 2015 impact targets in the years leading up to 2015; and
- To strengthen national capacity in monitoring and evaluation of TB control.

This policy paper sets out WHO policies and recommendations for how TB incidence, prevalence and mortality should be measured in the years up to 2015. Many of these policies and recommendations will apply after 2015. The paper is based on policies and recommendations agreed by the WHO Global Task Force on TB Impact Measurement, which have also been endorsed by WHO's Strategic and Technical Advisory Group for TB (STAG-TB).

The major policies and related recommendations are as follows:

- Measuring TB incidence and TB mortality requires periodic analysis of the reliability and coverage of TB notification and vital registration data. The Task Force has developed a standard framework and related analyses and tools for this purpose. The framework has three major components: 1) assessment of data quality; 2) assessment of the extent to which time-series of notification and vital registration data provide a good proxy for trends in TB incidence and mortality, respectively; and 3) assessment of the fraction of all incident cases and deaths from TB that are recorded in surveillance data. Application of this framework should also be used to define recommendations for how national surveillance systems need to be strengthened, to progress towards the ultimate goal of measuring TB burden directly from notification and vital registration data, and to update estimates of disease burden;

- Surveys of the prevalence of TB disease should be implemented in at least 21 global focus countries. At least one survey should be implemented in these countries before 2015, and the Task Force will make special efforts to provide the necessary technical guidance and support. There are a further 32 countries that meet Task Force criteria for implementing a prevalence survey, but in most cases it will not be possible for the Task Force to provide intensive guidance and support. All surveys should follow WHO guidelines published in 2007 and related Task Force recommendations. For countries where surveys are not implemented, TB prevalence will need to be measured indirectly from estimates of TB incidence and the average duration of disease;

- Surveys of the annual risk of infection, which have been used in the past to estimate TB incidence, are no longer recommended;

- The Task Force will periodically review and update the data, assumptions and analytical methods used to translate surveillance and survey data into the estimates of TB incidence, prevalence and mortality that are published annually by WHO;

- The impact of TB control on changes in TB incidence, prevalence and mortality needs to be evaluated in more countries.

Introduction

The World Health Organization (WHO) declared tuberculosis (TB) a global public health emergency in 1993. In that year, there were an estimated 7.0 million new TB cases and 1.6 million deaths from TB, compared with an estimated 9.3 million cases and 1.8 million deaths in 2007. With the introduction of the DOTS strategy in the mid-1990s, WHO began to systematically monitor progress in TB control using the two global indicators and related targets for TB control that were established by the World Health Assembly (WHA) in 1991 *(1)*. The indicators were 1) the percentage of estimated new (incident) cases of smear-positive TB detected in DOTS programmes (the case detection rate) and 2) the percentage of detected cases successfully treated (the treatment success rate). The targets were to reach a 70% case detection rate and an 85% treatment success rate by 2000, a target year that was later reset to 2005. In 2005, the global case detection rate under DOTS reached 57% and the treatment success rate was 85% *(2)*.

The WHA targets have proved very useful for stimulating greater efforts to control TB in endemic countries, and case detection and treatment success rates are well-established and widely used indicators of the performance of national TB control programmes at global, regional and country levels. Their limitation is that they do not directly measure whether the epidemiological burden of TB – measured in terms of cases and deaths – is being reduced. They measure the outcomes, but not the impact, of TB control.

Starting in 2000, global targets for TB control were extended to include targets for reducing cases and deaths. These newer impact targets were set as part of the Millennium Development Goals (MDGs) and by the Stop TB Partnership, with target years of 2015 and 2050 *(3)*. The main targets are to halt and reverse incidence by 2015, and to halve prevalence and death rates by 2015 compared with their levels in 1990.

Achieving the impact targets set for 2015 is now the focus of national and international efforts to control TB, and demonstrating whether or not they are achieved is of major importance for individual countries, the United Nations, the Stop TB Partnership and a variety of technical, financial and development agencies. Measuring changes in TB incidence, prevalence and deaths is challenging, however, and countries with a high burden of TB and their technical, financial and development partners are seeking clear guidance about how it should be done.

To respond to the need to measure progress towards the 2015 targets for reductions in TB incidence, prevalence and mortality, WHO established a Global Task Force on TB Impact Measurement in June 2006. The Task Force includes experts in TB epidemiology, representatives from major technical and financial agencies and representatives from countries with a high burden of TB (Annex 1). The Task Force has a three-fold mandate:

- To produce a robust, rigorous and widely-endorsed assessment of whether the 2015 impact targets are achieved at global level, for each WHO region and in individual countries;

- To regularly report on progress towards the 2015 impact targets in the years leading up to 2015; and

- To strengthen national capacity in monitoring and evaluation of TB control.

The importance of this work is reflected in a WHA resolution passed in 2007 (WHA60.19), in which WHO is requested to report on whether the 2015 global targets for TB control are achieved and to report on progress in the interim, and all Member States are urged to accelerate the improvement of health-information systems (Annex 2).

This policy paper, which is part of a series being produced by the Stop TB Department, sets out WHO policies and recommendations for how TB incidence, prevalence and mortality should be measured in the years up to 2015, as agreed by the Task Force and as endorsed by WHO's Strategic and Technical Advisory Group on TB (STAG-TB). Many of the policies and recommendations will apply after 2015 as well.

The document is structured in eight major sections:

1. **Global targets for TB control.** This section defines the global targets that have been set for 2015 and 2050 within the framework of the MDGs and by the Stop TB Partnership.

2. **Measuring TB incidence, prevalence and mortality: evidence for WHO policy and recommendations.** This section explains how the work of the Task Force from 2006 to 2008 underpins the policy and recommendations included in this policy paper.

3. **WHO policy package for measuring TB incidence, prevalence and mortality.** This section summarizes the major WHO policies and recommendations for measuring TB incidence, prevalence and mortality. Sections 4–8 then provide more explanation and details.

4. **Measuring TB incidence.** This section describes the six methods available to measure TB incidence and the number of countries for which these methods were used to produce WHO estimates of TB incidence as of mid-2008. It then provides WHO policy and recommendations for how to measure TB incidence from 2009 onwards. Guidance material and tools and sources of technical and financial support are identified.

5. **Measuring TB prevalence.** This section describes the two major methods available to measure TB prevalence and the number of countries for which these methods were used to produce WHO estimates of TB prevalence as of mid-2008. It then provides WHO policy and recommendations for how to measure TB prevalence from 2009 onwards, emphasizing the importance of national surveys of the prevalence of TB disease in 21 global focus countries. Guidance material and tools and sources of technical and financial support are identified.

6. **Measuring TB mortality.** This section summarizes the three major methods available to measure TB mortality and explains the number of countries for which these methods were used to produce the WHO estimates of TB mortality as of mid-2008. It then provides WHO policy and recommendations for how to measure TB mortality from 2009 onwards. Guidance material and sources of technical and financial support are identified.

7. **Producing estimates of TB incidence, prevalence and mortality, 1990–2015.** The recommendations in Sections 3–6 focus on strengthening surveillance and use of surveillance data in all countries, combined with surveys of the prevalence of TB disease in 21 global focus countries. To assess whether the global targets of halving TB prevalence and death rates by 2015 compared with 1990 are achieved, estimates are needed from 1990 to 2015. This section explains how WHO, together with other members of the Task Force, proposes to produce such estimates.

8. **Evaluating the impact of TB control.** Besides measuring changes in TB incidence, prevalence and mortality, evaluating the extent to which these changes are due to TB control and the extent to which they are due to other factors is important. This section provides guidance on such evaluation.

The policy paper also includes a list of references and five annexes. Annex 1 lists the members (institutions and/or individuals) of the WHO Global Task Force on TB Impact Measurement. Annex 2 provides extracts from the WHA resolution on TB passed in 2007. Annex 3 and Annex 4 provide further details on surveys of the prevalence of TB infection and disease, respectively. Annex 5 lists countries that met Task Force criteria for implementing surveys of the prevalence of TB disease but that are not among the 21 global focus countries selected by the Task Force.

1 Global targets for TB control

Global targets and indicators for TB control have been developed within the framework of the MDGs and by the Stop TB Partnership and the WHA *(2-5)*. Although the targets are global, WHO regions and individual countries commonly use them. Box 1 summarizes the main and most widely-quoted targets and indicators.

The impact targets are to halt and reverse the incidence of TB by 2015 and to halve TB prevalence and death rates by 2015 compared with a baseline of 1990. The incidence target is MDG Target 6.c, which the Stop TB Partnership has adopted. The MDG framework also includes indicators, but not targets, for TB prevalence and death rates. The Stop TB Partnership set the targets of halving TB prevalence and death rates by 2015 compared with 1990 based on a resolution of the 2000 meeting of the Group of Eight (G8) industrialized countries in Okinawa, Japan. Achieving these targets is much more challenging than the target of ensuring that incidence is declining by 2015.

As explained in the introduction, the WHA established outcome targets in 1991. The targets were to detect 70% of new smear-positive cases, and to successfully treat 85% of those cases detected, by 2000. The target year was later reset to 2005. Although 2005 has now passed, the indicators of case detection and treatment success remain part of the MDGs and continue to be used by WHO and the Stop TB Partnership to measure progress in TB control.

Box 1

Goals, targets and indicators for global TB control

United Nations MDGs

Goal 6: Combat HIV/AIDS, malaria and other diseases

Target 6.c: To halt and begin to reverse the incidence of malaria and other major diseases

Indicator 6.9: Incidence, prevalence and death rates associated with TB

Indicator 6.10: Proportion of TB cases detected and cured under DOTS

Stop TB Partnership targets

By 2005: At least 70% of people with sputum smear-positive TB will be diagnosed (under the DOTS strategy) and at least 85% successfully treated. The WHA first set these targets in 1991.

By 2015: The global burden of TB (per capita prevalence and death rates) will be reduced by 50% compared with 1990 levels. This means reducing prevalence to about 150 cases per 100 000 population or lower and deaths to about 15 deaths per 100 000 population or lower per year by 2015 (including TB cases co-infected with HIV)[1]. The number of people dying from TB in 2015 should be less than 1 million, including those co-infected with HIV.

By 2050: The global incidence of active TB will be less than 1 case per million population per year (the criterion for elimination adopted within the United States of America).

[1] To avoid double-counting of deaths from AIDS and TB, WHO world health statistics on TB deaths exclude TB deaths among people coinfected with HIV. However, the aim of TB control is to eliminate the disease from whole populations. In the annual report on global TB control, WHO therefore publishes TB statistics both overall and for the HIV-positive and HIV-negative subpopulations separately.

The Stop TB Partnership has also set the goal of eliminating TB by 2050. The target for elimination is to have less than 1 case per million population per year.[1]

Besides outcome and impact targets, other kinds of targets can be set for TB control (input, process and output targets) (7). For example, the Stop TB Partnership's Global Plan to Stop TB for the period 2006 to 2015 includes financial (input), process (such as the percentage of the population for whom community-based TB care is available) and output (such as the number of cases treated in DOTS programmes or the number of HIV-positive TB patients who are enrolled on antiretroviral therapy) targets. These targets are not the subject of this policy paper, and so are not discussed further here.

[1] The criterion for elimination presented in Box 1 is that defined by the United States Centers for Disease Control and Prevention. It differs from a European recommendation (3) that elimination be defined as less than one smear-positive case per million population per year.

2 Measuring TB incidence, prevalence and mortality: Evidence for WHO policy and recommendations

The WHO policies and recommendations included in this document are based on four building blocks:

- A systematic review of the methods available to measure TB incidence, prevalence and mortality, which was published in a peer-reviewed journal in January 2008;
- Discussions and related recommendations of the WHO Global Task Force on TB Impact Measurement, from three meetings held between June 2006 and September 2008;
- Recommendations and advice provided by the WHO Strategic and Technical Advisory Group on TB (STAG-TB), including review of a draft version of this policy paper in June 2008; and
- The wider literature on monitoring and evaluation.

The full Task Force has endorsed all policies and recommendations included in this publication.

Members of the Task Force co-authored a systematic review of the methods available to measure TB incidence, prevalence and mortality, based on discussions at the first meeting of the Task Force in June 2006. The paper was endorsed by the full Task Force in December 2007 and published in *Lancet Infectious Diseases* in January 2008 *(5)*. Box 2 summarizes the methods used in the systematic review. This policy paper cites a few of the 137 references included in the journal article, where this is considered particularly useful. Otherwise, readers should consult the original article for the full set of references.

Box 2

Methods used to systematically review the evidence about how TB incidence, prevalence and mortality can be measured

The search strategy and selection criteria for the Lancet Infectious Diseases article included searches of Medline, ISI Web of Science and the libraries of all authors. Search terms used in the online databases were, in various combinations, "tuberculosis", "environmental mycobacteria", "incidence", "prevalence", "mortality", "infection", "annual risk of infection", "tuberculin skin test", "mixture method", "mirror-image method", "survey" and "surveillance". Among many thousands of papers on this topic, only the key papers in English that are relevant to the methods were selected.

The Task Force met in June 2006, December 2007 and September 2008. The 2006 meeting covered general recommendations about how TB incidence, prevalence and mortality should be measured. The 2007 meeting discussed the three major strategic tracks of work to be pursued by the Task Force (assessment and use of routine surveillance data and related strengthening of surveillance systems; implementation of surveys of the prevalence of TB disease; and methods to translate surveillance and survey data into estimates of TB incidence, prevalence and mortality from 1990 to 2015) and how these would be organized. This meeting gave particular

attention to assessment of which countries should implement surveys of the prevalence of TB disease and the methods to be used in such surveys. The 2008 meeting focused on the direct and indirect measurement of TB incidence (its absolute value and trends) using routine surveillance data.

Details of Task Force meeting discussions and recommendations are available in meeting reports, a series of background papers and peer-reviewed articles *(5,8–12)*, and on the Task Force's web site (http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en).

WHO's STAG-TB reviewed a draft version of this policy paper at its June 2008 meeting. The advice and recommendations provided, which focused on surveys of the prevalence of TB disease, were addressed when the paper was finalized.

3 WHO policy package for measuring TB incidence, prevalence and mortality

Box 3 shows the WHO policy package for measuring TB incidence, prevalence and mortality. Sections 4–8 explain this package in more detail.

Box 3

WHO policy package for measuring TB incidence, prevalence and mortality up to 2015 and beyond

General

1. Improvement of surveillance systems towards the ultimate goal of measuring TB incidence directly from TB notifications and measuring TB mortality directly from vital registration systems i.e. TB case notification data include all (or almost all) incident TB cases and vital registration systems record all (or almost all) TB deaths
2. Strengthening of national capacity to monitor and evaluate the TB epidemic and to measure progress in global TB control
3. Periodic updating of methods used to translate surveillance and survey data into WHO estimates of TB incidence, prevalence and mortality
4. Report (by the Task Force) on whether global targets for TB control set for 2015 within the MDGs and by the Stop TB Partnership are achieved, shortly after 2015

Measuring TB incidence

5. Periodic assessment of the quality and coverage of TB case notification data using the framework developed by the Task Force, with results used to produce updated estimates of disease burden and recommendations for how surveillance needs to be strengthened
6. Certification that TB notification data provide a direct measure of TB incidence for countries whose surveillance data meet the required standards

Measuring TB prevalence

7. Surveys of the prevalence of TB disease in at least 21 global focus countries, according to WHO guidelines and Task Force recommendations

Measuring TB mortality

8. Periodic assessment of the quality and coverage of TB mortality data recorded in vital registration systems using the framework developed by the Task Force, with results used to produce updated estimates of disease burden and recommendations for how surveillance needs to be strengthened
9. Develop national vital registration systems to reliably record all TB deaths, using sample vital registration combined with verbal autopsy if national vital registration systems are not yet available

Evaluation of the impact of TB control

10. Studies to evaluate how TB control activities affect rates of TB incidence, prevalence and mortality

4 Measuring TB incidence

4.1 Definition of TB incidence

The incidence of TB is the number of new cases of TB that arise in a given time period. It is usually reported as the total number of incident cases per year or as the number of cases for a given unit of population per year (such as the number of incident cases per 100 000 population or per million population). TB incidence changes relatively slowly. Even high-quality control programmes are expected to reduce the incidence rate by only 5–10% per year (in the absence of HIV coinfection).

4.2 Methods for measuring TB incidence

Six methods are available to measure TB incidence in a given year (1).

1. Direct measurement from TB notification data i.e TB notifications are assumed to be equal to (or be a very close proxy of) TB incidence. This method is only valid if there is strong evidence that all TB cases are diagnosed and that all diagnosed TB cases are notified.

2. Direct measurement from prospective cohort studies. This method requires that a large population cohort is followed for one year and that the number of TB cases that occur within this cohort is counted. The cohort size would need to be around 400 000 people if TB incidence is around the global average of 100 per 100 000 population. Existing examples of such studies are limited to a specific population group in the Republic of Korea and to a limited geographical area in southern India *(13,14)*.

3. Indirect estimation using surveys of the annual risk of TB infection. Here, incidence is estimated as the annual risk of infection multiplied by 50, based on the Styblo assumption or "rule-of-thumb" that an annual risk of infection of 1% is equivalent to about 50 smear-positive cases per 100 000 population.

4. Indirect estimation using studies of the prevalence of TB disease. Here, incidence is estimated as the prevalence of TB disease divided by the estimated average duration of disease in years.

5. Indirect estimation using mortality data recorded in vital registration systems. TB incidence is estimated as the number of TB deaths divided by the estimated case-fatality rate.

6. Indirect estimation based on an assessment of the completeness of TB notification data. For example, if TB notifications are estimated to include 60% of incident cases (60% case detection rate), then TB incidence is estimated as the number of TB notifications divided by 0.6.

To estimate trends in TB incidence, these six methods can be used every year or at regular intervals.

- **Method 1** (direct measurement from TB notification data) can be used every year if the necessary data exist.
- **Method 2** (prospective cohort study) could theoretically be used at regular intervals.
- **Methods 3 and 4** can be used at periodic intervals, provided that surveys use consistent methods.

- **Method 5** can be used every year provided that both 1) mortality data are timely, of high quality and complete, and/or are timely and of consistent quality and completeness and 2) the case-fatality rate is constant.

- **Method 6** can be used to measure trends in TB incidence in one of two major ways: 1) it can be used at regular intervals or 2) a one-time estimate can be combined with an estimate of trends in TB incidence. Trends in TB incidence can be estimated from TB notification data, a series of annual risk of infection surveys, a series of surveys of the prevalence of TB disease, a series of TB mortality data or (in theory but never in practice) a series of prospective cohort studies. For TB notifications to be considered a direct proxy of trends in TB incidence, programmatic or health system efforts to find and treat TB cases must remain constant during the years for which TB notification data are used as a direct proxy for trends in TB incidence (and probably for 1–2 years before the start of the series of notification data).[1] If programmatic or health system efforts are not constant – for example, the quality and coverage of TB diagnostic and treatment services change (either positively or negatively) and/or the range of interventions being used to find and treat cases changes (either positively or negatively) – then changes in TB notifications may not correspond well to changes in TB incidence.

Table 1 shows the number of countries for which each of these methods was used to produce WHO estimates of TB incidence, as of mid-2008. For most countries, estimates of TB incidence (as of mid-2008) were based on indirect estimates of the completeness of TB notification data (method 6), usually for 1997, combined with estimates of trends in TB incidence using trends in TB notifications for years before and after 1997.[2]

4.3 WHO policies and recommendations for measuring TB incidence

Box 4 (see box on page 12) summarizes the main WHO policies and related recommendations about how TB incidence should be measured (both its absolute value and trends). Subsections 4.3.1–4.3.5 explain these in more detail.

4.3.1 Strengthening routine TB surveillance

The best method for measuring TB incidence is through a routine surveillance system that captures reliable and comprehensive data about new cases of TB (defined above as method 1). All countries should strengthen their surveillance systems (TB-specific recording and reporting systems and/or general health information systems) until TB notifications can be considered to be a direct measure (or close proxy) of TB incidence.

Strong foundations for effective TB surveillance already exist. Standard WHO recording and reporting forms are available and are widely used *(15)*. For most national TB control programmes, data collection, management and reporting form a core part of their activities. The United Nations Statistical Division and agencies such as the Global Fund to Fight AIDS, Tuberculosis and Malaria have developed (and continue to improve and update) methods for assessing the quality of data. The Health Metrics Network, a partnership housed by WHO, is aiming to increase the availability and use of timely and accurate health information by catalysing the joint funding and development of core country health information systems. This offers an opportunity to improve TB surveillance in the context of more general strengthening of health information systems.

Training courses on TB surveillance and epidemiology have been developed and are regularly organized by WHO and its collaborating centres and by the International Union against Tuberculosis and Lung Disease, the United States Agency for International Development, the United States Centers for Disease Control and Prevention, MEASURE Evaluation and the Research Institute of Tuberculosis – Japan Anti-Tuberculosis Association.

Case-based national TB information systems allow much more precise analysis of TB data than is possible with aggregated data that are compiled on a quarterly basis. For this reason, countries should develop case-based recording and reporting systems using flexible computer

[1] This is because case-finding efforts can affect incident cases from previous years (that are now part of a backlog of prevalent cases).

[2] Methods were updated for some countries in late 2008. Updates for other countries, based on the methods described in subsection 4.3, began in April 2009. For further details of these updates, see the update to the 2009 Global TB Control Report published in December 2009 *(3)*.

solutions. Ideally, these systems should be web-based to allow remote data entry and real-time data management and reporting. They should also be designed with flexibility and safety in mind, so that systems can be readily adapted when information needs change. If general health information systems provide an adequate platform for case-based reporting of TB cases (reports are timely, reliable and complete), then countries are encouraged to integrate case-based TB reporting into these existing systems.

Box 4

WHO policies and recommendations for measuring TB incidence

Policy 1. WHO will promote the strengthening of routine TB surveillance (of cases and deaths) in all countries as the major mechanism for measuring progress in TB control.

Policy 2. WHO, together with other members of the Task Force, will use a standardized framework and related tools for producing and documenting estimates of TB incidence (both its absolute value and trends). The framework focuses on analysing the quality and coverage of TB notification data and includes benchmarks that need to be met for TB notification data to be considered a direct measure (or close proxy) of TB incidence.

Policy 3. WHO, together with other members of the Task Force, will support countries to systematically assess the quality and coverage of their TB notification data using the framework and tools developed by the Task Force, with results used to produce updated estimates of TB incidence (its absolute value and trend) and the case detection rate. WHO estimates of TB incidence will be reviewed and updated in close collaboration with national TB control programmes and WHO's country and regional offices. If appropriate, countries will be invited to request the Task Force to certify their data as providing a direct measure of TB incidence, or to self-certify their own data if there is local capacity to do so, using the methods developed by the Task Force.

Policy 4. WHO will promote the development of vital registration systems and will support countries to use the mortality data from these systems to help cross-validate estimates of TB incidence, particularly in countries in which 1) the quality and coverage of vital registration data is considered to be higher than TB notification data and 2) the necessary links between TB mortality and notification data can be made.

Policy 5. WHO will not encourage the use of surveys of the annual risk of infection to measure TB incidence.

Recommendation 1. All countries should strengthen their surveillance systems until TB notifications provide a direct measure (or close proxy) of TB incidence.

Recommendation 2. All countries should conduct periodic assessments of the quality and coverage of surveillance data, using the standard framework and related tools developed by the Task Force for this purpose. Findings should be used to improve estimates of TB incidence (its absolute value and trends) and the case detection rate, to define recommendations for how surveillance needs to be improved, and to identify interventions that could help to improve TB control.

Recommendation 3. Countries that would like the Task Force to certify their TB notification data as providing a direct measure of TB incidence should approach the Task Force so that a formal evaluation can be undertaken.

Recommendation 4. Countries with reliable and complete mortality data from vital registration systems should consider using these data to cross-validate estimates of TB incidence, especially if these data are likely to be more reliable and complete than TB notification data.

Recommendation 5. Surveys of the annual risk of infection should not be used to measure TB incidence in most countries. Their use should be limited to a few countries where there is good reason to believe that data on the annual risk of infection can be interpreted reliably and where there is no feasible alternative approach to estimating TB incidence.

4.3.2 Standardized and systematic assessment of TB incidence via evaluation of the reliability and coverage of TB notification data

For most countries, estimates of TB incidence published up to 2008 were based on two things (see Table 1 on page 14):

- An estimate of the case detection rate in 1997. The absolute number of incident cases of TB in 1997 was estimated as the number of notified TB cases in 1997 divided by the estimated proportion of TB incident cases that were notified in 1997 (method 6); and

- An assumption that trends in TB notifications (of all forms of case) since 1997 were a direct proxy for trends in TB incidence. In other words, trends in TB incidence after 1997 were assumed to be the same as trends in TB notifications.

From 2009 onwards, an updated approach to measuring TB incidence (both its absolute value and trends) is needed.

- It is more than 10 years since the original estimates of TB incidence were made.

- The assumption that trends in TB notifications reflect trends in TB incidence is increasingly problematic, given programmatic efforts to increase case-finding.

- There are now more data and more experience with analysing TB surveillance data that can be drawn upon to produce updated estimates.

From 2009, two approaches to measurement of TB incidence (both its absolute value and trends) need to be emphasized. These are:

- Direct measurement of TB incidence (both its absolute value and trends) from TB notification data (defined above as method 1). This is likely to be feasible in a relatively small number of countries before 2015, but it will set a standard which other countries should aim to reach as well.

- A more systematic, standardized and well-documented approach to indirect measurement of TB incidence, combining periodic assessments of the case detection rate (the proportion of incident TB cases accounted for in TB notification data, defined as method 6 above) with analysis of the extent to which trends in TB notifications are a proxy of trends in TB incidence.[1]

[1] It is important to note that attempting to estimate case detection rates at the subnational level using WHO national estimates is methodologically wrong and should not be attempted. Assessing case detection rates at the subnational level requires subnational (rather than national) estimates of TB incidence.

Table 1. Number of countries for which the six major methods available to measure TB incidence (its absolute value and trend) were used to produce WHO estimates, as of mid-2008

Method for estimating TB incidence in absolute terms in one particular year	Method for estimating trends in TB incidence							
	1. Directly from trends in TB notifications	2. Series of prospective cohort studies	3. Series of surveys of the annual risk of infection	4. Method for estimating trends in TB incidence	5. Series of TB mortality data	6. Trends in TB notifications (country-specific or regional),[b] with assumption trend in TB notifications = trend in TB incidence, or trend in TB notifications adjusted to remove the influence of factors besides TB incidence	No attempt to estimate trend: incidence rate assumed to be stable	Total
1. Direct measurement from TB notification data (mostly in 1997)[a]	20	–	–	–	–	–	–	20
2. Prospective cohort study (direct method)	–	–	–	–	–	–	–	–
3. Annual risk of infection (tuberculin) survey (indirect method)	–	–	India Somalia	–	–	15	Myanmar Democratic People's Republic of Korea	19
4. Disease prevalence survey (indirect method)	–	–	Bangladesh Indonesia	China	–	9	Pakistan	13
5. Estimates or counts of TB deaths from vital registration data (indirect method)	–	–	–	–	Brazil South Africa Mexico	–	–	3
6. Assessment of the completeness of TB notification data in a specific year, mostly in 1997 (indirect method)	–	–	–	–	–	151	6[c]	157
Total	20	–	4	1	3	175	9	212

[a] Considered here as direct measurement from TB notification data because the case detection rate was estimated to be ≥ 90%.

[b] Country's own notification data for 97 countries, regional trend for 98 countries. For almost all countries, trends in TB notifications (all forms of case) were assumed to be the same as trends in TB incidence.

[c] Belize, Iraq, Papua New Guinea, Sri Lanka, Thailand and Timor-Leste.

Example of how to read the table: There are two countries for which **1)** TB incidence was estimated in absolute terms in 1997 from survey data of the annual risk of infection and **2)** trends in TB incidence have been estimated from a series of surveys of the annual risk of infection (India and Somalia). There are 151 countries for which **1)** TB incidence in absolute terms was estimated from an assessment of the completeness of TB notification data in 1997 and **2)** trends in TB incidence in the years before and after 1997 have been estimated from TB notification data, mostly using the assumption that trends in TB notifications (of all forms of case) are the same as trends in TB incidence.

The Task Force has developed a conceptual framework for both approaches (see Figure 1 below and Table 2 on page 16). The framework has three major and interrelated components. These are:

1. Assessment of the quality and completeness of notification data for TB cases (in the TB routine notification system) and deaths (in the vital registration system);

2. Assessment of the extent to which notification and vital registration data reflect trends in TB incidence and mortality; and

3. Assessment of the number of incident TB cases and deaths that are "missing" from surveillance data ("undetected" cases and deaths).

These components are explained in more detail below.

Figure 1. Framework for assessment of TB surveillance data

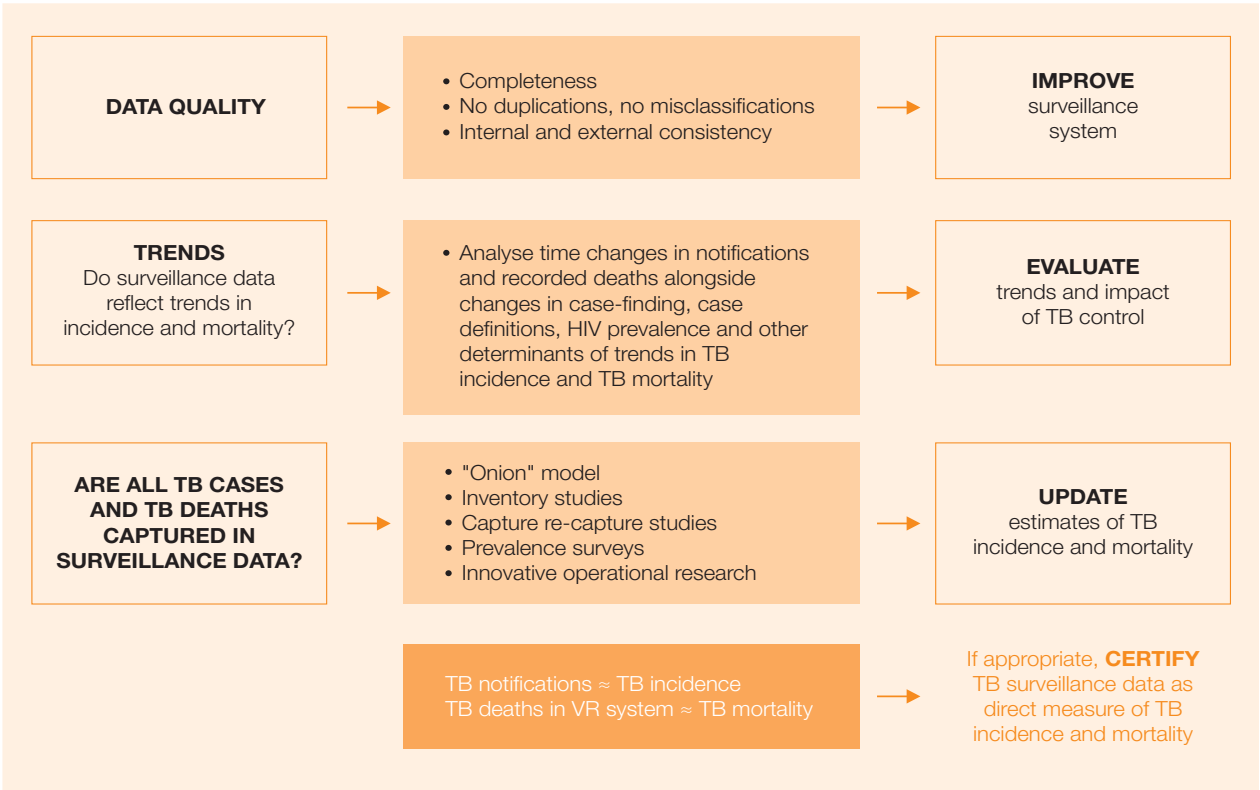


Table 2. Framework for assessing the absolute value of and trends in TB incidence

Step	Standard or benchmark	Outcomes or action
Part 1: Standardized analysis of available TB notification data		
1. Assess the completeness of reporting from the lowest administrative level to the national level	All reports available at national level	1. Data confirmed as complete *or* 2. Data assessed as incomplete (i) missing data retrieved and included *or* (ii) missing data not available, notifications adjusted by imputing for missing data *and* (iii) corrective measures to ensure complete reporting
2. Check for duplications and misclassifications	No duplications or misclassifications	1. Data confirmed as not including any duplications or misclassifications *or* 2. Data assessed as including duplications and misclassifications (i) Duplications and misclassifications removed *and* (ii) Corrective measures put in place to avoid duplications and misclassifications in the future
3. Compare standard indicators across geographical areas (subnational analysis) and over time and compare standard of indicators with commonly-observed or expected values in TB epidemiology *Examples of indicators*: % of cases with pulmonary or extrapulmonary TB, % of pulmonary cases that are smear-positive, age and sex distribution, % change in notifications per year	Limited variability over time and space unless this can be justified Indicators are consistent with expected or commonly observed values in TB epidemiology	1. Notification data are confirmed as showing limited variability over time and space and being consistent with commonly observed or expected values *or* 2. Notification data show considerable variability over time and space, which can be explained, and consistent with commonly observed or expected values *or* 3. Notification data show considerable variability, some or none of which can be explained, and/or considerable deviation from commonly observed or expected values. Further investigation of the reasons for variability and deviations from the expected values is needed
Part 2: Standardized analysis of whether trends in TB notifications are a good proxy of trends in TB incidence		
4. Compare trends in TB notifications with trends in variables that can influence TB incidence and TB notifications *Examples of variables*: HIV prevalence in the general population, number of health units providing TB diagnostic and treatment services, funding and staffing levels in the national TB control programme, number of smears and cultures examined per diagnosed TB case, prevalence of risk factors for TB	Trends in TB notifications consistent with trends in variables known to influence TB incidence and not associated with other factors that can influence TB notifications	1. Trends in TB notifications considered a good proxy of trends in TB incidence 2. Trends in TB notifications strongly associated with non-epidemiological and epidemiological factors known to be capable of influencing TB notifications (i) Trends in TB notifications adjusted, adjusted trend considered good proxy for trend in TB incidence 3. Trends in TB notifications assessed as too unreliable to be used to assess trends in TB incidence (i) Corrective measures to ensure more reliable data
Part 3: Standardized assessment of the fraction of cases missing from routine TB notification data		
4. Compile and assess evidence about whether TB cases are being diagnosed (but not treated or notified) by national TB control programme laboratories or other laboratories	No cases being diagnosed but not treated or notified	1. No un-notified cases found in laboratory registers *or* 2. The number of un-notified cases found in registers is estimated and measures are put in place to ensure that all cases diagnosed by laboratories are correctly registered and enrolled on treatment
5. Compile and assess evidence about whether TB cases are being treated (but not notified) by national TB control programme laboratories or other laboratories	No cases being treated but not notified	1. No cases treated by providers not linked to the national TB control programme *or* 2. The number of cases treated by national TB control programme providers or other providers are estimated and measures are put in place to ensure that all care providers notify cases
6. Compile and assess evidence about whether cases are presenting but not being diagnosed at health-care facilities	No cases for whom diagnosis was missed at health-care facilities	1. No or a negligible number of TB cases are missed at health-care facilities *or* 2. The number of cases missed at health-care facilities is estimated and measures to improve diagnosis are implemented
7. Compile and assess evidence about whether cases are not going to health facilities despite having access to them	No cases that fail to go to health-care facilities	1. No or a negligible number of TB cases with access to health-care facilities are not seeking care *or* 2. The number of cases with access to but not seeking health care is estimated and measures to address this are identified
8. Compile and assess evidence about whether there are cases without access to health facilities	No cases without access to health-care facilities	1. No or a negligible number of TB cases are without access to health-care facilities *or* 2. The number of cases without access is estimated and measures to improve access are identified

1. Assessment of data quality

Using notification data to measure the incidence of TB and trends in TB incidence requires that certain standards of data quality are met. Assessment of data quality should include:

- Analysis of the completeness and timeliness of reporting. For example, the number of expected reports submitted by reporting units can be compared with the number of reports actually received from those units during a given period;
- Analysis of whether there are duplicate or misclassified records;
- Exploration of variability in notification patterns geographically and over time (to check for internal consistency);[1]
- Comparison of observed values of certain variables with the values that would be expected according to existing knowledge of TB epidemiology (for example, the fraction of pulmonary cases that are sputum smear-positive).

This assessment should be used as the basis for removing duplications and misclassifications, imputing for missing data, identifying where and how surveillance needs to be strengthened, and an initial assessment of the extent to which TB notifications account for all incident TB cases.

To facilitate this analysis, TB notification data should be available in electronic format (either as aggregated data or, ideally, as data for individual people) and disaggregated by 1) time period (such as quarters), 2) geographical or administrative unit, 3) case type, 4) smear results and 5) age and sex. Indeed, for some analyses (for example, whether there are duplicate records), it is essential that data are available in electronic format. Countries need to implement electronic recording and recording systems to make this feasible.

2. Are surveillance data a good proxy for trends in TB incidence?

Distinguishing changes in notifications that are due to real changes in TB incidence from changes that are due to other factors is crucial when using notification data to estimate trends in TB incidence (and trends in case detection).

TB notification data can be used as a direct proxy for trends in TB incidence if TB notification data are both reliable and account for all (or almost all) incident cases over the time period being considered. They may also be a good proxy for trends in TB incidence even when incident cases are missing from routine TB notification data, provided that the proportion of incident TB cases being notified (the case detection rate) remains constant (or relatively constant) over time.

Certain conditions must apply for the proportion of incident TB cases being notified to remain constant over time. These include consistency in the completeness of reporting (for example, all districts have reported TB notifications in all quarters of all of the years for which trends are being estimated) and consistency in programmatic efforts to diagnose and treat TB during the years being considered (for example, the number of diagnostic and treatment units, funding and staffing of the national TB programme, and the number of sputum smears being examined per TB case diagnosed has remained relatively stable). If any of these indicators change, however, trends in TB notification data may not be a good proxy for trends in TB incidence (Box 5 on page 18 provides an example to illustrate this point). Analysis of which of these indicators have changed and whether these changes are related to trends in TB notifications is therefore important. If a relationship exists, trends in TB notifications need to be adjusted to allow for the influence of these factors, before using them to estimate trends in TB incidence.

In addition to data on changes in case-finding efforts, analysis of changes in the prevalence of important risk factors for TB is necessary. For example, the HIV epidemic has had a major impact on TB incidence in Africa. Changes in immigration patterns and polices, TB outbreaks and TB in prisons can have a major influence on TB notifications in middle- and high-income countries with a low incidence of TB. Screening practices for TB disease and infection, as well

[1] TB cases develop from a large and widely distributed reservoir of latent infection, such that the true incidence of TB does not usually vary greatly across small areas or short time periods (less than 5 years). Large geographical variation as well as large changes in notifications over short time periods may indicate that cases are being over- or underreported in some places and time periods.

as patterns of drug resistance, are particularly relevant for several countries in eastern Europe. Changes in these variables need to be accounted for when assessing the extent to which changes in TB notifications are due to case-finding efforts and/or real changes in the underlying incidence of TB.

Box 5

Revision of estimates of TB incidence in Kenya following in-depth analysis of surveillance and programmatic data for the period 1996–2006

The incidence of TB in Kenya was indirectly estimated from TB notification data in 1997 as part of a global effort to estimate the global epidemiological burden of TB (16). The estimate was based on an expert assessment that the percentage of incident smear-positive cases being notified was 57% (i.e. the case detection rate was estimated as 57%). Until 2006, the trend in TB incidence before and after 1997 was assumed to be the same as the trend in TB notifications (of all forms of TB cases).

Kenya has experienced a generalized HIV epidemic since the early 1980s, and substantial efforts to improve the quality and coverage of TB diagnosis and treatment services were made from 2001 onwards. This created difficulty in disentangling the effect of HIV (which affects TB incidence) from the effect of programme performance on TB notifications, which in turn created difficulty in estimating the trend in TB incidence. Between September 2006 and December 2007, WHO and the national TB control programme jointly reviewed estimates of the absolute value of TB incidence and the trend in TB incidence in the context of new evidence and new analysis. The major new sources of evidence were: 1) data on trends in HIV-positive and HIV-negative TB notifications separately; 2) a direct measure of the prevalence of HIV among people with TB; 3) a recent survey of the prevalence of HIV in the general population; and 4) evidence about how programme performance had changed during the period 1996–2006. Both 1) and 2) became available following the introduction of provider-initiated HIV testing for people with TB in 2005.

Evidence about programme performance during the period 1996–2006 was compiled during 2007. The four main indicators used were: the number of health units at which TB diagnosis was available; the number of health units at which TB treatment was available; the number of national TB control programme staff at the national, provincial and district levels; and national TB control programme funding. All four of these indicators were clearly related to trends in TB notifications from 2001 to 2006, while HIV-related data suggested that the epidemic peaked around 2000 and had not caused any increase in TB incidence from 2001 to 2006. In combination, these new data provided strong evidence that the increase in TB notifications after 2001 was due to programmatic improvements and not increases in TB incidence. This led to a downward revision in the estimate of TB incidence in 2006, an adjustment of the estimated trend in TB incidence and an upward revision in the estimated case detection rate (to 70%). The original estimate of TB incidence (and case detection) in 1997 was left unchanged.

Reliable measurement of trends in TB incidence from 2007 onwards requires maintaining high rates of HIV testing for people with TB. This will allow trends in HIV-positive and HIV-negative TB notifications to be separated. Trends in HIV-negative TB notifications can be used to measure changes in case-finding. Comparison of trends in HIV-positive and HIV-negative TB notifications can be used to assess the impact of HIV on TB incidence.

The national TB control programme has not yet thoroughly investigated the reliability and coverage of its TB notification data, but this could be used to further improve estimates of TB incidence (in absolute terms). Efforts to strengthen the routine surveillance system, including introducing new recording and reporting forms and expanding the use of electronic recording and reporting systems, have begun. A survey of the prevalence of TB disease is also planned.

Source: Mansoer et al. (17).

As part of the standardized approach to implementing the framework shown in Figure 1, WHO and other members of the Task Force are developing a minimum or essential set of analyses of patterns and trends in TB notifications. This includes analysis of changes in the reporting of TB cases (including drug-resistant cases), changes in a core set of indicators of programme performance (such as the number of diagnostic and treatment units, the number of staff employed in the national TB programme, and the number of smears and cultures examined per TB case diagnosed and funding), and changes in important risk factors for TB and their association with changes in TB notifications. Results can be used to assess whether TB notifications can be used to reliably measure trends in TB incidence, whether they can be used to measure trends in TB incidence after adjustment for factors besides TB incidence that affect TB notifications, or whether they are too unreliable to assess trends in TB incidence at all.

Box 5 provides an example of what the recommendations mean in practice, based on an analysis of the absolute value of and trend in TB incidence in Kenya.

3. What fraction of cases are missed in TB notification data? The onion model

Analysis of available TB notification data is an essential component of any assessment of TB incidence (its absolute value and trend). However, on its own it is not sufficient to estimate the TB incidence in absolute terms, because it will not identify how many TB cases exist but are not accounted for in TB notification data.

Figure 2 (page 20) shows a model that can be used to understand why TB cases might be missing from TB notification data, to investigate and quantify the proportion of incident TB cases that are missing from TB notification data and to identify the programmatic or health system interventions that might be required to increase the fraction of incident TB cases being recorded in TB notification data. This framework was first presented to the international TB community in 2002 and has been termed the "onion" model.

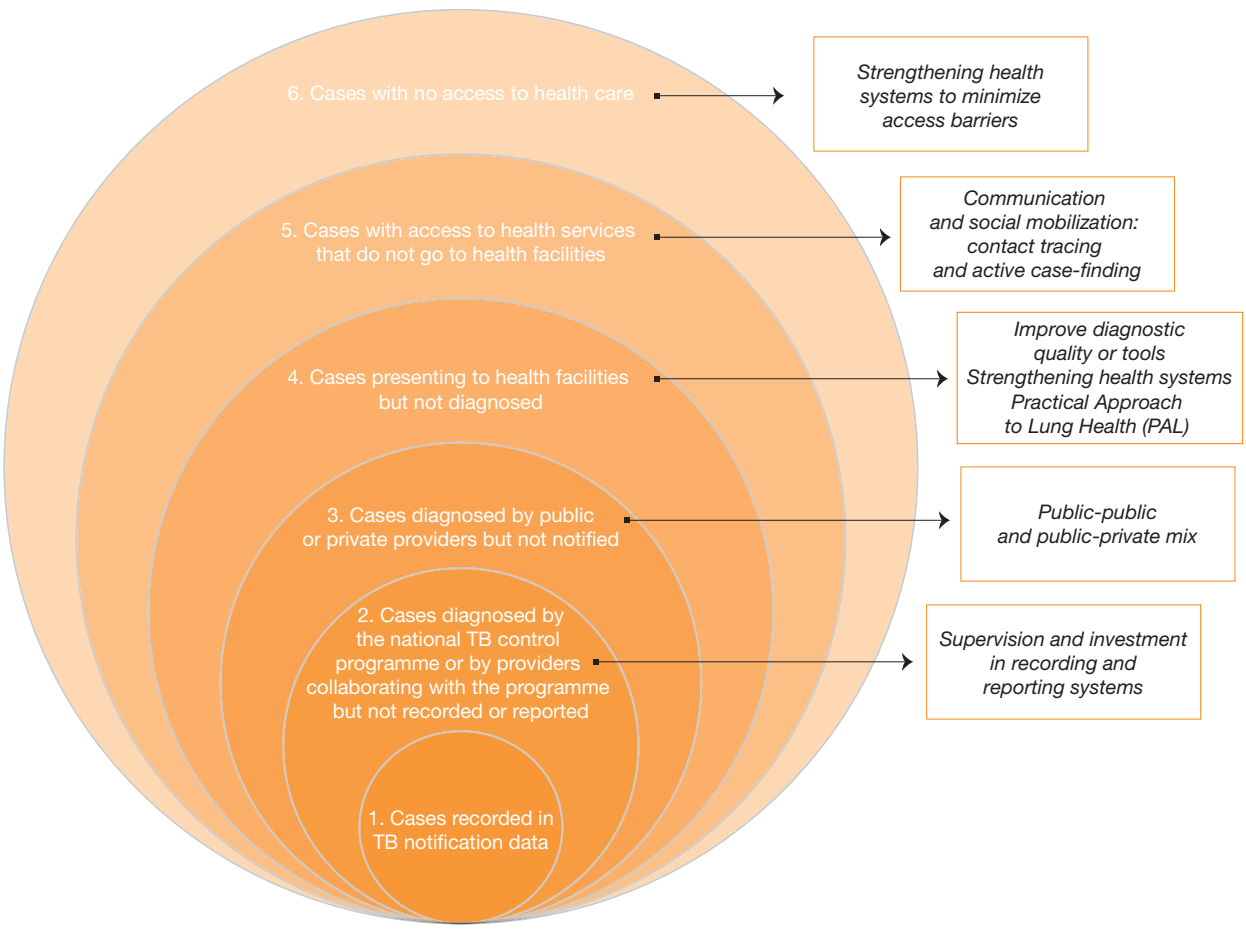
In the onion model, only TB cases in the first (innermost) ring are found in TB notification data. The relative size of rings 2 to 6 determines the proportion of TB incident cases being accounted for in TB notification data. The major reasons why cases are missed from official notification data include laboratory errors, lack of notification of cases by public and private providers, failure of cases accessing health services to be identified as people suspected of having TB and lack of access to health services.

Although conceptually simple, quantifying the fraction of TB cases that are missing from TB notification data (rings 2 to 6) is challenging. Table 3 (page 21) provides examples of methods that can be used to assess how many cases exist in rings 2 to 6. Box 6 provides a practical example of a revision of WHO TB estimates based on a capture-recapture study.

To assess the number of cases that are being correctly diagnosed but not notified (rings 2 and 3), a common approach is to perform an "inventory" study. These studies compare lists in which people suspected of having TB, TB cases and TB deaths are recorded with lists of notified cases. Where lists are not readily available (typical sources include hospital registers, HIV notification records with information on TB comorbidity, mycobacterial laboratory registers and prescriptions in pharmacies), study registers may have to be introduced in a sample of health facilities (including laboratories and non–national TB control programme facilities). If three or more lists can be generated (see Box 6 on page 22 for an example), capture-recapture methods may be used *(18–21)* to estimate total incident cases. These methods allow estimation not only of the number of cases that are missing from notifications, but also the number of cases missing from all lists (i.e. cases that are not in contact with health facilities at all, such as those in ring 6).

Other types of data may also provide indirect evidence of the magnitude of the number of TB cases in rings 2 and 3. Examples include drug sales in the private sector, health expenditures in the private and/or nongovernmental organization sectors, out-of-pocket expenditures, the number and proportion of health facilities and private practitioners that are not collaborating with the national TB control programme, the number and value of TB prescriptions in pharmacies, regulations on prescribing and availability of drugs and their application in practice, and knowledge and use of the international standards for TB care.

Figure 2. The onion model: a framework for assessing the fraction of TB cases accounted for in TB notification data and how to increase it



Assessment of the number of cases in rings 4 and 5 is more challenging. Evidence that could be used to understand the reasons why TB cases are being missed at health care facilities and why cases are experiencing symptoms but not seeking care include data on population access to health care, data from surveys of the knowledge, attitudes and practices of staff and the general population, practices for managing people suspected of having TB (including the number of slides that are examined per person suspected of having TB or per case) and the performance of bacteriological laboratories.

Table 3. Examples of methods that could be used to assess how many TB cases are missing from TB notification data

Possible reason for cases to be missing from TB notification data	Examples of published studies	Examples of supporting evidence that could be used
Cases diagnosed by national TB control programme but not recorded in notification data (Ring 2) Cases diagnosed by providers not linked to the national TB control programme that are not notified (Ring 3)	Botha et al. (South Africa) *(22)* Migliori et al. (Italy) *(23)* Maung et al. (Myanmar) *(24)* Lonnröth (Viet Nam) *(25,26)* Ambe et al. (India) *(27)* Arora et al. (India) *(28)* Dewan (India) *(29)*	Drug sales in the private sector Health expenditure in the private or nongovernmental organization sectors, out-of-pocket expenditure Number of health facilities or private practitioners and proportion that are not collaborating with the national TB control programme Prescriptions in pharmacies Regulations regarding prescription and availability of drugs and their application in practice Knowledge and use of the international standards for TB care
Cases presenting to health facilities that are not diagnosed (Ring 4) Cases that have access to health services but do not seek care (Ring 5)	Gasana et al. (Rwanda) *(30)* Espinal et al. (Dominican Republic) *(31)* Lee et al. (Hong Kong SAR) *(32)*	Knowledge, attitudes and practices of health staff Practices in managing people suspected of having TB Slides examined per person suspected of having TB Percentage of laboratories with satisfactory performance (based on external quality assessment) Data on population knowledge, attitudes and practices from TB-related surveys
Cases that do not have access to health services (Ring 6)	van Hest et al (Netherlands) *(18,20)* Baussano et al. (United Kingdom) *(19)* Crofts et al. (United Kingdom) *(21)*	Population access to health services, such as the percentage of the population living within a certain distance of a health facility Number of laboratories performing smear microscopy per 100 000 population Number of nurses and doctors per 100 000 population compared with international norms of what is required Data from major household and demographic surveys Vital registration data showing what proportion of people who died from TB never accessed TB diagnosis and treatment
All reasons listed above	Prevalence survey from Myanmar	Survey on the prevalence of TB disease in which questions about health-seeking behaviour and contact with health services are asked. See also Section 5.

Box 6

Revision of estimates of TB incidence using capture-recapture methods: an example from Egypt

The national TB control programme in Egypt compiled evidence that most TB cases have access to health care services provided by public or private facilities as part of a multi-country operational research project in the Eastern Mediterranean. The number of TB cases experiencing symptoms and seeking care but not being diagnosed is therefore expected to be low. Nevertheless, TB cases diagnosed by providers that are not linked to the national TB control programme are unlikely to be recorded in official notification data. Quantifying the proportion of cases diagnosed by non–national TB control programme providers (the extent to which there is undernotification) may therefore allow a more accurate estimate of the total number of cases in the country as well as the proportion detected by the national TB control programme (the case detection rate).

To assess the extent to which cases were being missed in official notification data and in turn to update estimates of TB incidence and the case detection rate, the Ministry of Health in Egypt together with the WHO Regional Office for the Eastern Mediterranean implemented a capture-recapture study in 2008. Study registers for listing TB cases were introduced in a nationally representative sample of non-national TB control programme health facilities in the private and public sectors. The list of cases in these registers was then compared with the list of notified cases for the same period. Using capture-recapture log-linear models, the number of cases missed by all sources was estimated by comparing 1) the number of cases observed in each source of data independently with 2) the number of common cases among all sources (that is, the overlap in cases). Analyses were undertaken for the whole sample and for sputum smear-positive cases only (Table 4).

For capture-recapture estimates to be considered valid, certain conditions must be met. In particular, three or more sources of data should be available to allow adjustment for dependence among the sources of data. This was the case in Egypt: the three available sources were the national TB control programme registry, the study registers of private providers outside the national TB control programme and the study registers of public providers outside the national TB control programme.

Based on the study results, the case detection rate for smear-positive cases was revised slightly upwards to 66% (from 62%). The case detection rate for all cases remained virtually the same. Similar studies in other countries where all (or almost all) cases have access to health services could also help to revise existing TB estimates.

Table 4. Revised estimates of TB incidence in Egypt based on capture-recapture analysis

	Notification data (2007)		Original WHO estimates (2007)		Revised WHO estimates (2007)	
	All cases	Sputum smear-positive cases	All cases	Sputum smear-positive cases	All cases	Sputum smear-positive cases
New TB cases	9 459	4 887	17 517	7 882	15 873	6 765
Rate per 100 000 population per year	13	6.5	24	10.5	21	9
Case detection rate (95% confidence interval) (%)[a]	–	–	54	62	55 (46–68)	66 (55–75)

[a]The original estimates were based on a WHO method that does not calculate confidence intervals.

Studies of the health-care seeking behaviour of notified cases can also be useful. Prevalence surveys (see Section 5) are an excellent opportunity to identify cases not yet known to notification systems and the reasons for this. Contact investigation studies, screening and other active case-finding practices, as well as studies of the number of TB cases found postmortem and/or exclusively recorded in vital registration systems can also help to identify the extent to which cases are not reaching health facilities. The yield of new cases found through contact investigations and the screening of high-risk populations may also help to estimate TB incidence in populations that share similar epidemiological characteristics and risks.

Box 7

Estimating TB incidence using mortality data from a vital registration system: an example from Brazil

WHO estimates of TB incidence are based on notification data, surveys of the annual risk of infection, surveys of the prevalence of TB disease combined with estimates of the average duration of disease and mortality data from vital registration systems combined with estimates of the case-fatality rate. Where several sources of evidence exist, greatest weight is attached to the most reliable data. For most countries, incidence is indirectly estimated from TB case notification data and an expert assessment of the percentage of incident TB cases being notified. When case-finding efforts do not change much over time, trends in TB incidence are often assumed to mirror trends in TB case notification rates. Until 2005, these methods were used to estimate TB incidence and its trend in Brazil.

By 2005, the Ministry of Health of Brazil had greatly improved the TB notification system and the death registration component of the vital registration system. This included extending coverage of both systems throughout the country, validating data and systematically linking records within and between the two databases. Records were linked within the TB notification database and procedures to distinguish between new and re-treatment or transfer-in records were implemented to identify duplicate records. This showed that notifications had been artificially inflated and that the cure rate had been underestimated (see Table 5 on next page). Removal of duplicate records increased the gap between the number of new TB cases notified and the number of new TB cases estimated by WHO, highlighting the need for a review of existing estimates.

Estimates of TB incidence in Brazil are now based on analysis of TB deaths recorded in the vital registration system. The case-fatality rate was calculated by cross-linking the case-based TB notification database and the mortality database. Incidence in 2005 was then estimated as the number of TB deaths in the mortality database divided by the case-fatality rate, estimated as the number of deaths in the mortality database divided by the number of cases in the notification database, with appropriate adjustments for the proportion of records in both systems that could be linked and a minor adjustment for the coverage of TB mortality records. Since the local authorities considered that the mortality information system had higher coverage than the TB notification system, and since the case-fatality rate had probably not changed markedly in recent years, the trend in incidence over time was estimated by assuming that the trend in the TB incidence rate was the same as the trend in the TB mortality rate from 2001 to 2005. This suggested that incidence was falling at a rate of 3.3% per year. Incidence in absolute terms for the years before 2005 was also based on this trend (see Table 6 on next page).

Table 5. The effect of removing duplicate records from the database of TB case notifications in Brazil, 2005

Duplicates removed	New notified cases		Notification rate (%)		Change (%)	Cured (%)		Change (%)
	Before	After	Before	After		Before	After	
19 064	81 330	74 113	44.2	40.2	–9.7	60.5	64.5	+6.7

Table 6. Original and revised WHO estimates of TB incidence in Brazil using TB mortality data, 2005

	Notifications	Original estimate of incidence	Revised estimate of incidence
New TB cases	74 113	111 050	95 408
Incidence or notification rate (per 100 000 population per year)	40	60	51
Case detection rate	–	69%	78%

Many countries collect data on chronic respiratory cases and people suspected of having TB who attend outpatient clinics and submit sputum samples. Where such records are available, it is usually possible to identify the proportion of people suspected of having TB that are new TB cases (laboratory-confirmed or clinically-diagnosed). Besides helping to understand practices for managing people suspected of having TB, such data can also be used to estimate TB incidence in populations that share similar epidemiological characteristics and risks.

Since not all health-care facilities can be studied, a critical design issue common to many of the studies identified above is how to sample facilities such that results are representative of the population as a whole. Convincing providers outside the national TB control programmes to participate in such studies may also be challenging.

4.3.3 Certification of TB notification data

Countries with TB notification data that can be shown to be of high quality and completeness using the framework described in subsection 4.3.2 (via self-assessment, and/or joint review by national staff together with external agencies, and/or an external independent review) will be encouraged to approach the Task Force so that their data can be formally certified or validated as a direct measure of TB incidence.

4.3.4 Vital registration data

In addition to analysis of TB notification data, another form of routine surveillance data – vital registration data that include data on deaths from TB – can help to cross-validate estimates of TB incidence and trends in TB incidence. Countries with vital registration systems that include mortality data of high reliability and coverage should consider using these data to cross-validate estimates of TB incidence (described as method 5 above). Brazil, Mexico and South Africa are three examples of countries for which this has already been done (Box 7 on page 23 explains the method used in Brazil). For other countries considering the use of vital registration data for this purpose, however, two points should be highlighted: 1) vital registration data should be considered more

timely, reliable and complete than TB notification data and 2) linking mortality records with TB notification records should be feasible.

4.3.5 Surveys of the annual risk of infection and the prevalence of TB disease

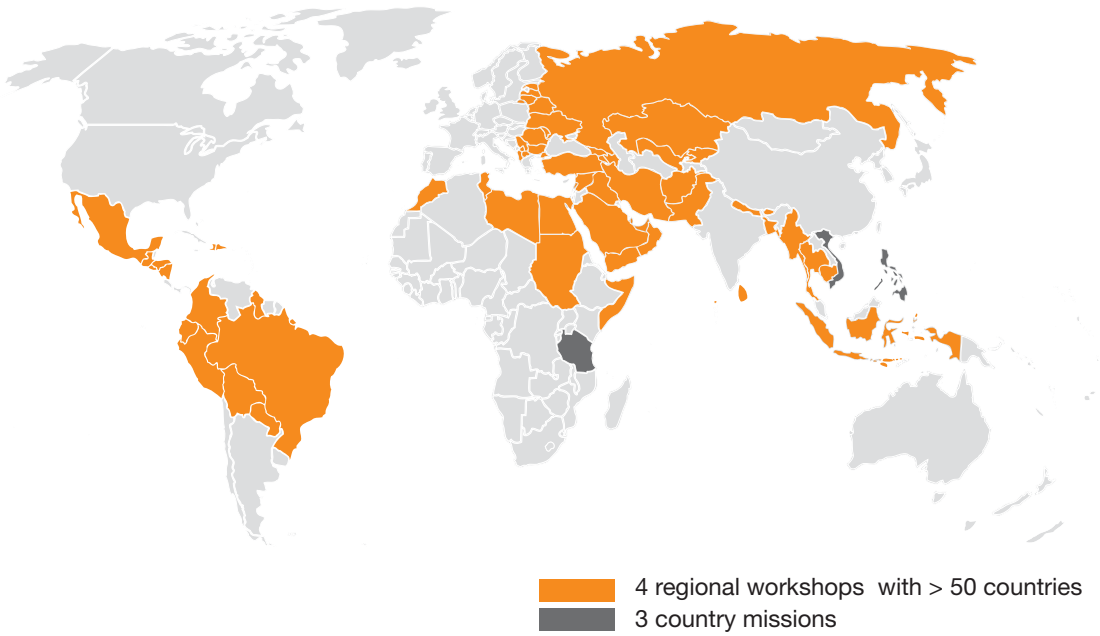
Surveys of the annual risk of infection to measure TB incidence are not recommended in most countries. This is because survey results are usually difficult or impossible to interpret. The use of surveys of the annual risk of infection should be limited to a few countries in which there is good reason to believe that data can be interpreted reliably and there is no feasible alternative approach to estimating TB incidence. Annex 3 provides further details about surveys of the annual risk of infection.

Surveys of the prevalence of TB disease are likely to provide an additional source of evidence about TB incidence. However, these surveys will probably be performed in a relatively small number of countries. Moreover, even when data on disease prevalence are available, there will be considerable uncertainty in any estimates of TB incidence, because of the wide confidence intervals on estimates of TB prevalence and uncertainty about the duration of TB disease. Section 5 provides further details.

4.4 Guidance material, tools and technical and financial support

Implementation of the framework illustrated in Figure 1 began in 2009, via regional workshops and country missions. This has been done by defining a standard dataset, questionnaire and set of analyses that allow the framework to be put into practice *(33)* and by working on compiling data, questionnaires and analyses with relevant staff at country level. Methods will continue to be refined, and workshops and missions will be extended to a wider range of countries. The Task Force web site provides further information *(34)*[1]. The map below shows in orange the countries that participated in WHO regional workshops held in 2009, and in dark grey the three countries in which country review missions were carried out in 2008 and 2009 (Figure 3).

Figure 3. Progress in applying the Task Force framework for assessing TB surveillance data, as of mid-2009



[1] http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en

Boxes 5–7 provide examples of how components of the framework can be implemented in practice.

Studies in Kenya, Morocco and Viet Nam provide three recent examples of in-depth studies of TB incidence. In Kenya (see Box 5 on page 18), data on HIV prevalence in the general population and TB patients, programmatic efforts to increase case-finding and a series of TB notification data were used to re-estimate TB incidence in absolute terms as well as its trend over time *(17)*. In Morocco, an analysis of trends in TB notifications from 1996 to 2005 indicated that TB incidence rates had fallen more slowly among men than among women and that TB incidence had fallen more slowly than expected *(35)*. In Viet Nam, the lack of any decline in TB notification rates could not be explained by increasing efforts to diagnose TB *(36)*. Such reductions in the TB incidence had been expected given that the World Health Assembly targets of a 70% case detection rate and an 85% treatment success rate had been assessed to have been achieved.[1]

Two published studies have measured TB incidence through a population cohort study: one from the Republic of Korea and one from southern India *(13,14)*. Neither study provides evidence of TB incidence at the national level.

The KNCV Tuberculosis Foundation and the National Tuberculosis Institute in Bangalore, India have produced guidelines on surveys of the annual risk of infection *(8,9)* based on previous guidelines and reviews *(37,38)*.

Technical support is available from a variety of agencies, including those that are represented on the Task Force. Sources of financial support include national or local budgets, the Global Fund (which recommends that 7% of a grant should be allocated for monitoring and evaluation) and other donors that are committed to supporting monitoring and evaluation.

[1] Subsequently, a survey of the prevalence of disease has suggested that TB incidence is higher than previously thought, and that the case detection rate is lower than previously estimated.

5 Measuring TB prevalence

5.1 Definition of TB prevalence

The prevalence of TB is the number of TB cases at a given point in time. It is usually reported as the total number of prevalent cases or as the number of prevalent cases for a given unit of population (such as the number of cases per 100 000 population). The prevalence of TB determines the risk of TB infection in a community (in other words, how much transmission is occurring). The prevalence of TB is (approximately) the incidence of TB multiplied by the average duration of disease. Improved case-finding and treatment both shorten the duration of disease, so prevalence responds more rapidly than incidence to changes in TB control. Periodic assessment of the prevalence of TB disease can therefore be more useful for measuring the short-term impact of TB control (such as within five years) than efforts to measure changes in TB incidence.

5.2 Methods for measuring TB prevalence

There are two methods for estimating the prevalence of TB (see Annex 4 for further details). The first is direct measurement using a cross-sectional population-based survey. Such surveys typically require sample sizes of around 50 000 to 100 000 people in high-burden countries, and implementation is expensive (typically in the range US$ 1–3 million per survey) and logistically challenging. The second is indirect measurement, with TB prevalence estimated as the incidence of TB multiplied by the average duration of disease (in years). In WHO estimates published up to 2008, estimates of TB prevalence in all but 13 countries were based on multiplying estimates of TB incidence by the estimated average duration of disease.

Changes in TB prevalence over time are best measured by implementing at least two (but preferably more) surveys at large enough intervals. Alternatively, changes in the prevalence of TB can be estimated from changes in TB incidence and the average duration of disease. Indirect measurement of the prevalence of TB and trends requires obtaining the best possible estimates of the incidence of TB and the average duration of disease. The duration of disease depends on several factors, and WHO estimates produced up to mid-2008 were based on three of these factors: 1) whether TB cases are HIV-positive or HIV-negative; 2) whether TB cases are treated in DOTS programmes, treated but outside DOTS programmes or untreated; and 3) whether TB cases are sputum smear-positive, sputum smear-negative or extrapulmonary. The Task Force is currently reviewing the literature on several of these issues, and the information gathered will be used to revise estimates of the duration of disease, if appropriate.

Besides the challenges of costs and logistics, Box 8 (page 28) highlights important basic facts and limitations about surveys of the prevalence of TB disease.

5.3 WHO policies and recommendations for measuring TB prevalence

Box 9 (page 29) summarizes WHO policies and recommendations for measuring TB prevalence. These are explained in the following two subsections. The report of the December 2007 meeting of the Task Force *(10)* provides further details.

Box 8

Surveys of the prevalence of TB disease: important facts and limitations

Extrapulmonary cases
Typically, surveys do not look for or identify extrapulmonary cases. The diagnostic methods needed to diagnose such cases are invasive and would be difficult to apply in the context of a population-based survey. For this reason, the WHO guidelines on surveys of the prevalence of TB disease *(11)* do not recommend investigations to diagnose extrapulmonary TB.

Children
Typically, surveys do not try to identify TB cases among children. This is because the current technology used for screening (such as venepuncture, radiation and gastric tubing) is too invasive for use in healthy children. Alternative ways to measure the epidemiological burden of TB in children are to strengthen surveillance and to systematically trace children who have been in contact with infectious adults. Better diagnostic tools are needed to measure the number of TB cases among children in population-based surveys.

Pulmonary cases not confirmed by bacteriology
A survey of the prevalence of TB disease will not identify cases of TB that are not confirmed by smear or culture. Diagnosing such cases requires patient follow-up that is not part of survey procedures.

Cases among people living with HIV
The recommended screening strategy includes culture examinations, so culture-positive (but smear-negative) TB among individuals living with HIV will be diagnosed.

Estimates of the total prevalence of TB disease in the community
Uncertainty about the proportion of TB cases accounted for by children and extrapulmonary TB in adults means that estimating the total prevalence of TB in the community can be difficult even with an (imprecise) estimate of the prevalence of smear- and/or culture-positive TB.

Adding TB prevalence surveys to existing surveys or survey platforms
This is difficult if not impossible. Surveys for other diseases are usually designed to estimate the prevalence of diseases and conditions for which the prevalence is much higher than the prevalence of TB. This means that the size of the population studied (required sample size) is much smaller than the 50 000 to 100 000 people who need to be included in a survey of the prevalence of TB disease. Adding a TB-prevalence component to an existing Demographic and Health Survey, for example, would overwhelm it. In addition, TB surveys depend on mobile X-rays, radiographers to read the X-rays, facilities for collecting and transporting sputum samples and laboratories to process the samples. In contrast, most surveys depend mainly (or solely) on the results of questionnaires. It is therefore more likely that surveys of other diseases and health conditions would be added to surveys of the prevalence of TB disease rather than the converse.

Using surveys to assess the coverage of routine TB notification data
Surveys can be useful for identifying how many cases of active TB have attended health-care facilities and how many cases are accounted for in TB notification data. This information will help to estimate the fraction of incident TB cases being missed from TB notification data, which in turn will help to produce better estimates of TB incidence and the case detection rate (see also Section 4).

5.3.1 Countries in which national population-based surveys of the prevalence of TB disease are recommended

The Task Force has identified 21 countries (termed global focus countries) in which surveys of the prevalence of TB disease are strongly recommended. These countries are shown in Figure 4 and in Table 7. The Task Force will give these countries particular attention and support, including providing training to the principal investigator of the survey and co-investigators,

and matching at least one technical partner to each country.

Table 8 (page 32) shows the criteria used to select these countries. To be selected, a country had to meet at least one of the four sets of criteria.

The additional 32 countries that met at least one of the four sets of criteria but were not included in the list of 21 global focus countries are shown in Figure 4 (page 30) and listed in Annex 5.[1] These countries may decide to implement surveys for the purpose of producing better national estimates of the epidemiological burden of TB but will not be the focus of Task Force efforts to support survey implementation.

The rationale for selection of the 21 countries shown in Table 7 (page 31) was as follows.

- Surveys of the prevalence of TB disease are expensive and logistically difficult to implement, and providing the necessary technical and financial support to all 53 countries that met at least one of the four sets of criteria for undertaking a survey would be very challenging if not impossible.

Box 9

WHO policies and recommendations for measuring TB prevalence

Policy 1. WHO will promote the implementation of national surveys of the prevalence of TB disease in 21 global focus countries identified by the Task Force and will assist these countries in accessing the necessary technical and financial support.

Policy 2. WHO will incorporate the findings of reviews of studies about the duration of TB disease among people in different settings and with different clinical conditions into revised indirect estimates of TB prevalence.

Recommendation 1. There are 21 countries that should implement at least one survey of the prevalence of TB disease between 2008 and 2015. Some of the countries without prior survey data should carry out two surveys during the period 2008–2015.

Recommendation 2. Surveys on the prevalence of TB disease should be implemented according to the WHO guidelines published in 2007 *(11)*.

Recommendation 3. In a survey of the prevalence of TB disease, the sampled population should at least be screened using both X-rays and a questionnaire about symptoms of TB. This is strategy 3 in the WHO guidelines *(11)*. The Task Force no longer recommends strategy 4 to perform sputum smear for all eligible individuals unless culture is done for all of them. All sampled individuals should be asked about their health-seeking behaviour.

Recommendation 4. Any TB cases identified during a survey of the prevalence of TB disease should be tested for HIV according to national policy and standard practice. Questions about other diseases and risk factors can be included if they do not compromise the TB component of the survey.

Recommendation 5. Drug susceptibility testing should be carried out for all diagnosed TB cases in those countries where appropriate treatment is available, to allow for an initial assessment of the prevalence of multidrug-resistant TB if a drug resistance survey has not yet been done and to ensure optimal treatment of the multidrug-resistant TB cases identified in a survey.

Recommendation 6. All countries that implement surveys of the prevalence of TB disease should also promote the strengthening of routine TB surveillance and should use surveys as an opportunity to strengthen national and local capacity in monitoring and evaluation.

Recommendation 7. For countries that do not implement surveys of the prevalence of TB disease, TB prevalence should be indirectly estimated using methods recommended by the Task Force.

[1] Of the 53 countries that met the criteria, 33 were in the WHO African Region, 7 in the Western Pacific Region, 5 in the South-East Asia Region, 4 in the Eastern Mediterranean Region, 3 in the European Region and 1 in the Region of the Americas.

- Taken together, the 53 countries represent about two-thirds of total TB cases globally. For certain regions, the countries that met the criteria accounted for a very high percentage of total TB cases: 98% of total cases in the African Region, 97% of total cases in the Western Pacific Region and 75% of total cases in the Eastern Mediterranean Region. Undertaking surveys in a smaller number of countries is sufficient to measure progress at the global and regional levels and represents a much more efficient use of available technical and financial resources.

- All 22 high-burden countries that met at least one of the four sets of criteria in Table 8 (page 32) were included.

- In combination, the 21 countries account for a substantial share of the regional number of TB cases in the four WHO regions in which routine surveillance systems are weakest: the African, Eastern Mediterranean, South-East Asia and Western Pacific regions.

- In the African Region, the selected countries represent central, western, eastern and southern Africa and include Anglophone, Francophone and Lusophone countries.

A single survey of the prevalence of TB disease in countries with no prior survey data will be useful for helping to improve current estimates of the epidemiological burden of TB as well as providing a baseline for any surveys conducted after 2015. However, assessing changes in the prevalence of TB requires surveys to be carried out on (at least) two separate occasions, several years apart. It is also necessary that the point estimates obtained have sufficient precision such that, if there is a difference between surveys, it can be observed. Finally, it is crucial that surveys of the prevalence of TB disease do not distract from the need to simultaneously establish mechanisms to strengthen the routine surveillance of TB cases and deaths.

Figure 4. The 21 global focus countries where at least one survey of the national prevalence of TB disease is recommended between 2008 and 2015

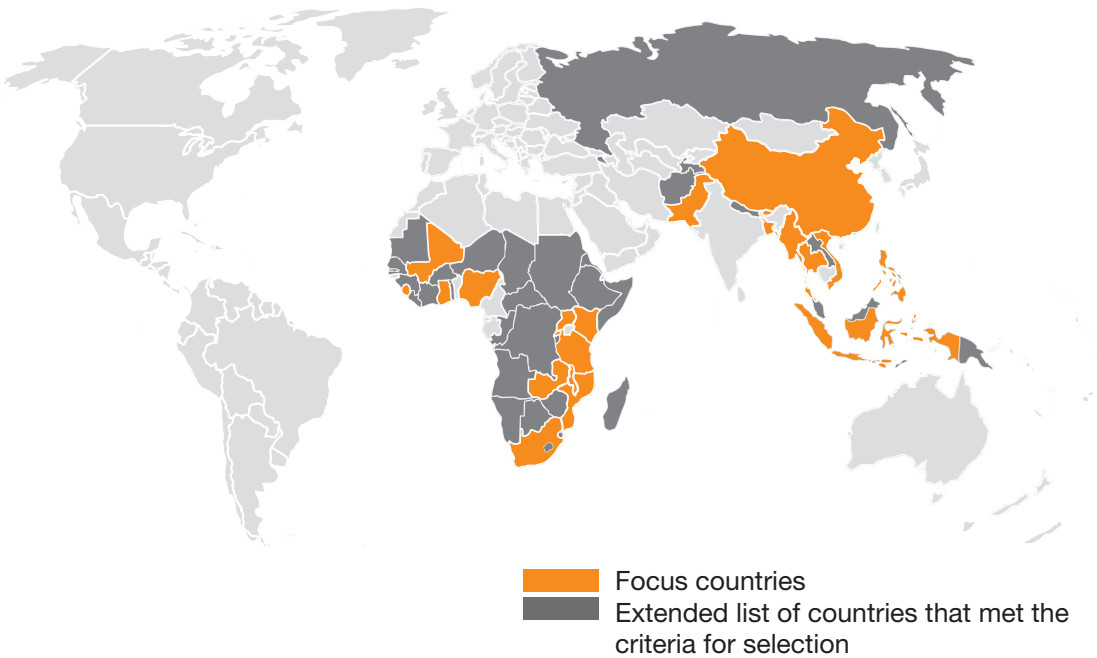


Table 7. WHO's 21 global focus countries in which the implementation of at least one survey of the prevalence of TB disease between 2008 and 2015 is recommended

Country	Criteria met	Region[a]	High-burden country	Estimated prevalence of sputum smear-positive TB in 2005, per 100 000 population	Survey data from 2008 or earlier exist
Kenya	2, 4	African Region, high HIV prevalence	Yes	154	No
Malawi	1–4	African Region, high HIV prevalence	No	239	No
Mozambique	1–3	African Region, high HIV prevalence	Yes	245	No
Nigeria	1–4	African Region, high HIV prevalence	Yes	226	No
South Africa	2, 3	African Region, high HIV prevalence	Yes	396	No
Uganda	1–4	African Region, high HIV prevalence	Yes	237	No
United Republic of Tanzania	1–4	African Region, high HIV prevalence	Yes	205	No
Zambia	2, 3	African Region, high HIV prevalence	No	291	No
Ghana	1, 2	African Region, low HIV prevalence	No	158	No
Mali	1–4	African Region, low HIV prevalence	No	243	No
Rwanda	1–3	African Region, low HIV prevalence	No	278	No
Sierra Leone	1–3	African Region, low HIV prevalence	No	416	No
Pakistan	1, 4	Eastern Mediterranean Region	Yes	132	Yes
Bangladesh	4	South-East Asia Region	Yes	142	Yes
Indonesia	4	South-East Asia Region	Yes	107	Yes
Myanmar	4	South-East Asia Region	Yes	76	Yes
Thailand	2,4	South-East Asia Region	Yes	84	Yes
Cambodia	2,3	Western Pacific Region	Yes	267	Yes
China	4	Western Pacific Region	Yes	89	Yes
Philippines	4	Western Pacific Region	Yes	166	Yes
Viet Nam	4	Western Pacific Region	Yes	90	Yes

[a] Regional analyses are generally undertaken for the six WHO regions. In the current analysis, nine epidemiological groups are used. The African Region is divided into countries with low and high rates of HIV infection (with "high" defined as an infection rate of ≥4% in adults aged 15–49 years in 2004, as estimated by UNAIDS); central and eastern Europe (countries of the former Soviet states plus Bulgaria and Romania) are also distinguished; and countries in western Europe are analysed together with other high income countries, as defined by the World Bank.

Table 8. Criteria used to select countries as candidates for implementing surveys of the prevalence of TB disease during the period up to 2015

Criteria	Explanation
Group 1	
1. Estimated smear-positive TB prevalence rate in 2006 ≥100 per 100 000 population *and* 2. Accounts for ≥1% of the estimated total number of smear-positive TB cases globally in 2006 *and* 3. Case detection rate in 2005 ≤50% or >100%	• Major contribution to the global burden of TB • Sample size small enough to make surveys feasible in terms of cost and logistics • Excludes countries whose contribution to the global burden of TB is insignificant for the purposes of global and regional assessment of burden and impact • A case detection rate ≤50% or >100% indicates weak reporting systems and problematic TB estimates, respectively
Group 2	
1. Estimated smear-positive TB prevalence rate in 2006 ≥70 per 100 000 population *and* 2. Accounts for ≥1% of the estimated total number of smear-positive TB cases globally in 2006 *and* 3. Estimated HIV prevalence rate in the adult population (15–49 years) ≥1% in 2005	• Less stringent criteria for the TB prevalence rate but incorporates countries with high HIV prevalence and therefore with potential for a rapid increase in TB incidence and prevalence rates
Group 3	
1. Estimated smear-positive TB prevalence rate in 2006 ≥200 per 100 000 population *and* 2. Accounts for ≥0.5% of the estimated total number of smear-positive TB cases globally in 2006	• Less stringent criteria for the country's contribution to the global burden of disease but incorporates countries with particularly high TB prevalence rates
Group 4	
1. Survey implemented between 2000 and 2007 *or* 2. Survey planned before 2010	• Prior survey data allow monitoring of trends • High motivation of national TB control programme to conduct a survey

Sources of data used to apply the criteria shown: 1) Global tuberculosis control: surveillance, planning, financing (39); 2) WHO TB data collection form for 2007 (39); 3) Report on the global AIDS epidemic (40).

5.3.2 Recommended methods for surveys of the prevalence of TB disease

Countries that implement surveys of the prevalence of TB disease should follow the guidelines published by WHO in 2007 *(11)*, which were universally endorsed by the Task Force *(10)*.

In some cases, the guidelines *(11)* present options rather than a strong recommendation about which of the available options should be implemented. The Task Force discussed these options and several other important issues during its December 2007 meeting. The following specific recommendations and advice were agreed upon.

1. Screening strategy. The minimum screening strategy that should be used in surveys of the prevalence of TB disease is strategy 3 in the WHO guidelines *(11)*. In this strategy, the sampled population is screened using X-rays and a questionnaire about TB symptoms. All people suspected of having TB are then asked to provide two sputum samples for smear microscopy and culture examination. Although screening all the sampled population with an X-ray considerably increases the cost of a survey, it reduces the workload of microscopy laboratories and is thought to provide the best possible estimates.

2. Subnational surveys and estimates. In general, countries should not attempt to estimate the prevalence of TB at the subnational level.

Producing estimates at the subnational level greatly increases the sample size required, which increases costs. Estimates obtained at the national level are satisfactory for the purposes of measuring progress towards the 2015 global targets. If countries have a particular interest in comparing specific groups of the population or geographical areas (such as urban versus rural or coast versus inland), then the strata should be clearly predefined and the sample size calculated accordingly. Stratification may also be useful for improving the precision of the national estimate of TB prevalence produced by a survey.

3. **HIV testing.** All TB cases identified in a survey should be offered HIV testing according to national policy and standard practice. Countries should only consider the possibility of offering HIV testing to all the sampled population if there is evidence that this will not compromise the survey participation rate, if funding is available or can be mobilized and if there are HIV treatment services to which those diagnosed with HIV can be referred *(41)*. In general, however, all the sampled population should not be HIV tested. The reasons include: 1) providing HIV screening for all the sampled population is logistically difficult; 2) obtaining informed consent from all participants may reduce the percentage of people willing to participate in the survey; and 3) ensuring that results are provided to everyone tested may be difficult.

4. **Combining surveys of the prevalence of TB disease with surveys for other diseases.** Adding surveys of the prevalence of TB disease to other surveys or survey platforms is difficult if not impossible (Box 8). Adding surveys of other diseases to surveys of the prevalence of TB disease is more feasible. However, although adding other surveys to surveys of the prevalence of TB disease allows additional data to be collected, the disadvantage is that it will increase the time required for interviews and the overall complexity of the survey (such as training needs, logistics, time required for data entry and validation). The diseases and conditions that it is most suitable to survey in combination with TB have the following characteristics: 1) they occur mostly among adults (≥15 years); 2) the prevalence is higher than the prevalence of TB; 3) screening methods do not diverge, or diverge only marginally, from those used for TB (not many questions would need to be added to the questionnaire and the main diagnostic tool required would be an X-ray machine); and 4) they help with the differential diagnosis of TB, such as chronic respiratory diseases. Collecting data beyond that needed for a survey of TB prevalence should only be attempted if it will not compromise the quality of the basic TB survey data.

5. **Collecting data on health-seeking behaviour.** Questions about health-seeking behaviour and the extent to which identified cases already had contact with health services are strongly recommended. The results can be used to assess how many cases have not had contact with health services, the number that had not been diagnosed despite visiting health services and the number of cases that had not been notified due to health care providers not being linked to the national TB control programme. Such findings will help to identify the fraction of cases likely to be included in TB notification data, reasons for lack of access to TB care and the absence of notification, and to develop interventions that will accelerate progress in TB control (see also section 4.3.2). Recent examples of surveys that have included the collection of such data are those undertaken in Myanmar and the Philippines.

6. **Collecting data on socioeconomic status and risk factors for TB.** Collecting data on socioeconomic status and risk factors for TB should be carefully considered. The time and effort required to collect such data must not compromise the quality of the basic survey data. Recent experience from a survey of the prevalence of TB disease in the Philippines will help to inform decisions about whether or not future surveys should collect similar information.

7. **Drug susceptibility testing.** Positive cultures from a survey of the prevalence of TB disease should be tested for drug susceptibility if the people who are found to be drug resistant can access appropriate treatment. Including drug susceptibility testing in a survey of the prevalence of TB disease is especially relevant for countries that have not yet implemented a representative drug resistance survey. However, collection of such data should not be a substitute for conducting a drug resistance

survey. The overall number of drug-resistant cases found in a survey of the prevalence of TB disease (which typically identifies about 100–300 TB cases) is likely to be too small to provide precise estimates of the prevalence of drug-resistant TB, although the data will help to calculate the sample size needed for a drug resistance survey and may provide an initial estimate of the prevalence of drug resistance. Annex 11 of the WHO guidelines *(11)* further discusses drug susceptibility testing in the context of surveys of the prevalence of TB disease.

8. Combining surveys of the prevalence of TB disease with surveys of the annual risk of infection. In the Model DOTS Project in south India, simultaneous surveys of disease and infection have allowed results to be calibrated and the national prevalence of TB disease to be estimated by extrapolation from subnational data. However, since the results of surveys of the annual risk of infection are usually difficult to interpret, combining such surveys with surveys of the prevalence of TB disease is not encouraged (see also Section 4).

Important lessons have also been learned from recently implemented surveys in Asia. Box 10 highlights key things to do and key things to avoid.

5.4 Guidance material, tools and technical and financial support

WHO published guidelines on the design, implementation and analysis of surveys of the prevalence of TB disease in 2007 *(11)*. They were developed over two years (2006 and 2007) as a collaborative effort by several technical agencies coordinated by the WHO Regional Office for the Western Pacific. Several people who contributed chapters are members of the Task Force.

Box 10

What to do and what to avoid when designing and implementing a disease prevalence survey

Do

1. Follow the WHO guidelines on disease prevalence surveys published in 2007 *(11)*.
2. Make sure that the sample size is calculated correctly, allowing for the design effect associated with cluster sampling and the likely survey participation rate.
3. In comparing surveys, balance the need for similarity in methods used in previous surveys with the value of using newer and better screening methods and diagnostic tools.
4. Remember to adjust survey design and sample size calculations if one of the survey objectives is to compare prevalence among different geographical areas and/or socioeconomic groups.
5. Consult recent survey protocols known to be of high quality as well as technical experts to ensure that the survey is designed correctly.
6. Pay attention to data management and analysis at the beginning rather than leaving them until the survey has been completed.
7. Use available budget templates to estimate the funding required.
8. Use the most recent population count or estimate available in the country to calculate sampling weights and prevalence rates.
9. Use appropriate statistical methods to analyse the data, accounting for sampling design and missing data, and seek appropriate statistical expertise from the outset.

Avoid

1. Do not underestimate the sample size required.
2. Do not underestimate the likely budget requirement.
3. Do not neglect the importance of strengthening the routine TB surveillance system just because a prevalence survey is being implemented.
4. Do not make the mistake of thinking that a prevalence survey will allow a straightforward re-estimation of the case detection rate. The denominator of the case detection rate is incidence, not prevalence. Converting prevalence estimates to estimates of incidence requires assumptions about the duration of disease; there will also be uncertainty about the true incidence rate because of uncertainty in the estimate of prevalence.

The guidelines have 18 chapters.

- Chapter 1 explains the purpose of surveys of the prevalence of TB disease, explains their role in the context of available methods for estimating the epidemiological burden of TB and progress towards the MDG and Stop TB Partnership targets, and summarizes the criteria that should be used to decide whether or not a survey should be implemented.

- Chapter 2 defines the objectives of a survey of the prevalence of TB disease.

- Chapters 3–7 describe the methods to be used, covering sampling methods, screening strategies, diagnostic methods and case definitions.

- Chapter 8 discusses what measures of socioeconomic status and exposure to risk factors could be included in a survey of the prevalence of TB disease. An annex provides specific advice on how to measure selected risk factors.

- Chapter 9 identifies the ethical issues that need to be considered when carrying out a survey.

- Chapters 10–14 cover the organizational aspects of survey implementation and highlight how quality assurance and safety practices need to be applied to every component of measurement.

- Chapters 15–17 explain the critical role of data management, data analysis and reporting of results and how their quality can be ensured.

- Chapter 18 briefly introduces budgeting for a survey of the prevalence of TB disease.

The guidelines on disease prevalence surveys are also available in the form of a series of articles published in a special issue of the International Journal of Tuberculosis and Lung Disease in 2008 *(42–48)*. These include some updates to the guidelines based on feedback and experience since the guidelines were published.

A second edition of the guidelines is due to be published in 2010.

Survey protocols from recent high-quality surveys also provide useful guidance material. A particularly good example is the protocol developed for the survey that was implemented in Cambodia in 2002 *(49)*.

Several published studies document the results of surveys of the prevalence of disease:

- National surveys implemented at five-year intervals from 1965 to 1995 in the Republic of Korea, which showed substantial reductions in parallel with improved treatment results and better case-management practices *(50)*;

- National surveys conducted in China and Indonesia (China in 1990 and 2000 and Indonesia in the early 1980s and 2004), both of which demonstrated large reductions in TB prevalence *(51,52)*;

- Studies undertaken in southern India over a study period of about 30 years *(53)*; and

- Surveys in the Philippines conducted in 1983 and 1997, which documented a negligible decline in bacillary disease that was attributed, at least in part, to an inconsistent supply of anti-TB drugs and low quality of treatment during this period *(54)*.

At the time of writing, the major source of financial support for the 21 global focus countries was the Global Fund. In 2008, the Tuberculosis Control Assistance Program funded by the United States Agency for International Development committed funding for the survey planned in Pakistan.

6 Measuring TB mortality

6.1 Definition of TB mortality

TB mortality is the number of deaths from TB that occur in a given year. It is usually reported as the total number of deaths from TB (such as millions of deaths) or as the number of deaths for a given unit of population (such as the number of deaths per 100 000 population). TB mortality can usually be reduced more quickly than TB incidence because drug treatment reduces not only transmission but also the case-fatality rate.

6.2 Methods for measuring TB mortality

There are three ways to measure TB mortality.

- **Direct measurement using vital registration data.** This is possible if the death registration data collected in vital registration systems are coded according to the International Statistical Classification of Diseases (preferably ICD-10; ICD-9 is not ideal) and the data are of proven completeness and accuracy.

- **Direct measurement using verbal autopsy studies**. In such studies, structured questions are asked of caregivers or family members of people who have died, with the aim of determining the cause of death *(55,56)*. Such studies can form part of a sample vital registration system or may be undertaken in conjunction with other studies. In a sample vital registration system, births and deaths are registered from a nationally representative sample of sites throughout the country. All deaths are followed up at the household level, where a verbal autopsy interview is conducted with the aim of determining the underlying cause of death. The results for the sample are then extrapolated to the national population.

- **Indirect measurement using estimates of case-fatality rates and TB incidence.** Here, TB mortality is estimated as TB incidence multiplied by the estimated case-fatality rate. The method is only as reliable as the underlying estimates of incidence and case fatality.

From a TB perspective, a general problem with death certification is that TB may be listed as one of the associated causes of deaths in vital registration systems but not recorded as the underlying cause of death. This is in contrast to HIV/AIDS, which is always recorded as the underlying cause of death. Since national statistics usually only consider the underlying cause of death, they may understate the number of deaths in which TB is a contributing factor.

The case-fatality rate is easiest to assess for people receiving treatment, especially in DOTS programmes. However, the fate of people who default or are transferred without follow-up is often unknown, and relatively large proportions of people in both categories die. Case-fatality rates outside DOTS programmes are much harder to estimate. Outcomes are not recorded, and while the risk of dying is likely to be higher it is difficult to quantify. This creates considerable uncertainty about the overall case-fatality rate among TB cases. A further problem is that, based on current guidelines, deaths recorded in DOTS cohorts may or may not be due to TB.

Estimating case-fatality rates accurately from the TB notification system requires:

- Detecting a high proportion of cases and knowing the treatment outcomes of all (or almost all) those treated for TB;
- Knowing the outcomes of re-treatment cases;
- Routinely checking the validity of outcome data; and
- Ensuring that recorded deaths are clearly attributed to TB or to other causes.

As DOTS cohorts account for an increasing share of total cases, cohort outcomes should converge more closely with national death registration.

6.3 WHO policy and recommendations for measuring TB mortality

Box 11 (page 38) summarizes the main policies and recommendations for how TB mortality should be measured.

The best way to measure the number of deaths from TB is via a national vital registration system. In the long term, all countries should be able to report TB deaths among routine death registrations (coded as in ICD-10) in systems that provide data of proven completeness and accuracy.

Currently, few countries with a high burden of TB have vital registration systems that can be used to directly measure TB deaths. A review published in 2003 found that vital registration systems reported only about one third of the 56 million deaths that occur each year (all causes) *(57)*. Among 115 countries that reported deaths and their causes, only 23 were assessed to have high-quality data (≥90% complete and ill-defined codes <10%). None of the 22 high-burden countries (the group of countries that collectively account for about 80% of the world's TB cases) were among this list of 23 countries, although three of the 22 high-burden countries (Brazil, the Philippines and the Russian Federation) were among 55 countries assessed to have data of medium quality (70–90% completeness). Of these three countries, the accuracy of the TB records, among all other causes of death, has been investigated only in Brazil. Two other high-burden countries (South Africa and Thailand) were assessed to provide death registration data of low quality. Most countries in the WHO African and South-East Asia regions did not have national systems for death registration. Although the classification of countries has been questioned, the review indicates the scale of the challenge involved in developing or strengthening vital registration systems.

Better systems for reporting and recording TB deaths within vital registration systems need to be developed as part of wider efforts to increase death registration and improve health information systems. The resources that are needed to establish and maintain a functional vital registration system are considerable, requiring maintaining the flow of information at the national and subnational levels (from data entry to analysis and dissemination of findings) and providing training to doctors to ensure that death certificates are completed correctly.

Where both vital registration and TB notification systems already exist, systematic assessment (as illustrated in Figure 1 on page 15) or cross-referencing of data should be used:

- To reduce the proportion of TB cases for whom no outcome data are available;
- To check the validity of the mortality data held in the TB notification system;
- To check the diagnosis of the cause of death that is stated in the vital registration system;
- To identify how many TB deaths occurred without health care being accessed (TB diagnosed close to or after death);
- To identify how many TB cases died without being notified; and
- To assess trends in TB mortality.

This assessment can be done at the national level using sophisticated record-linkage methods. It can also be done at the district level, at regular intervals, by manually comparing records. Some countries may have additional sources of data on deaths from TB that could be used for cross-referencing with vital registration or TB notification data *(21)*.

Besides cross-referencing, vital registration data should be used to better understand the epidemiology of TB and, in turn, to identify how deaths from TB could be reduced. The variables listed on death certificates (such as age, sex, residence, occupation and place of death) can be analysed to better understand the risk factors for TB deaths. In addition, although the ICD-10 system stipulates only one underlying cause of death, the multiple proximate or associated cause-of-death codes listed on the death certificates can be analysed to assess how many of the deaths attributed to other causes (notably HIV/AIDS) have TB as an associate cause, how many deaths are attributed to TB sequelae and the extent to which TB deaths attributed to different clinical types and the availability of microbiological confirmation vary spatially and over time.

Where vital registration systems are weak or not yet developed, sample vital registration represents the most promising interim solution for reliably measuring deaths (including deaths from TB) *(55)*. When applied together with validated verbal autopsy procedures and implemented in a nationally representative sample of population clusters, this represents an affordable, cost-effective and sustainable short- to medium-term alternative. As such, its use should be expanded. The major challenge for sample vital registration studies based on verbal autopsy is to prove the validity of the diagnosis of cause of death.

6.4 Guidance material

Published studies that have analysed TB deaths using data from vital registration systems are scarce. One example is a descriptive study in Brazil. Using data from 2004, this found that adding the number of deaths with TB as an underlying cause to the number of deaths with TB as an associated cause and with TB sequelae as an underlying cause would increase the total number of TB deaths as computed in the national statistics by 50% *(58)*. Another example is a capture-recapture study in England *(21)*. Using three sources of TB mortality data, this study found that national TB notification data underestimated the number of deaths among TB cases.

The use of verbal autopsy to estimate TB deaths has been described for China, India and the United Republic of Tanzania.

Box 11

WHO policy and recommendations for measuring TB mortality

Policy 1. WHO will promote the strengthening of vital registration systems in all countries as part of more general efforts to improve health information systems. Where reliable vital registration systems are not yet in place, the use of sample vital registration will be encouraged.

Recommendation 1. The best way to measure deaths from TB is through a national vital registration system in which the causes of death are coded using the ICD-10 system. All countries should strengthen their vital registration systems so that TB deaths and other causes of death can be reliably measured.

Recommendation 2. Where vital registration systems are weak or not yet developed, sample vital registration should be used as an interim solution for the reliable measurement of deaths, including deaths from TB.

Recommendation 3. Deaths recorded in DOTS cohorts should be attributed either to TB or to other causes. Ultimately, DOTS cohorts should adhere to ICD-10 coding.

In Chennai, India, verbal autopsy has been used to substantially reduce the number of deaths attributed to unspecified causes on death certificates. Some of these deaths were reclassified as TB deaths, although the accuracy of this reclassification is unknown *(59,60)*.

In China, verbal autopsy was found to frequently misclassify leading causes of death among adults, although for a given cause of death the number of false-positives and false-negatives tended to cancel out *(61)*.

A study in the United Republic of Tanzania found that verbal autopsy for TB deaths met validation criteria. For example, verbal autopsy corresponded with medical records *(62)*.

A recent review *(63)* summarizes the available data and methods used to measure and estimate TB mortality in adults, assesses the strengths and weaknesses of each and suggests ways to improve current mortality statistics.

7 Producing estimates of TB incidence, prevalence and mortality 1990–2015

The recommendations in Sections 4–6 focus on strengthening TB surveillance and implementing national population-based surveys of the prevalence of TB disease. To assess whether or not the targets of halving TB prevalence and death rates by 2015 compared with a baseline of 1990 have been achieved or not, estimates are needed for the period 1990 to 2015. Moreover, few countries will have routine surveillance systems that directly measure TB incidence and mortality by 2015; the quality and coverage of routine surveillance data cannot be assessed in depth every year; and relatively few countries will implement surveys of the prevalence of TB disease. This means that a set of methods is needed to:

- Produce country-specific estimates back to 1990;
- Produce estimates of the prevalence of TB disease for a) countries that do not implement surveys of the prevalence of TB disease and b) all countries for the years in which a prevalence survey was not undertaken; and
- Produce estimates of TB mortality for countries without vital registration or sample vital registration systems.

Sections 4–6 explain the range of available methods for doing each of these things. In each case there is more than one choice, and within each of the available methods there is room for judgement and interpretation of the available data.

To respond to the challenges that this presents and with a view to ensuring that estimates of TB incidence, prevalence and mortality are both credible and widely endorsed (a key component of the Task Force's mandate), one of the three subgroups of the Task Force will periodically review the data, assumptions and analytical methods that are used, with the first review conducted from 2008 to 2010.

Such reviews will contribute not only to the data, assumptions and analytical methods that WHO uses to produce the estimates included in the annual series of reports on global TB control, but will also be used to produce the estimates of disease burden associated with TB for the 2010 update of the Global Burden of Disease (with data for 2005).

8 Evaluating the impact of TB control

The previous four sections (Sections 4–7) have explained the variety of methods that can be used to measure TB incidence, prevalence and mortality and the methods that are recommended up to 2015. Such measurement is essential for determining whether the 2015 global targets for TB control have been achieved. It also prompts a further and more difficult question: to what extent are changes in TB incidence, prevalence and mortality attributable to interventions specifically designed to control TB and to what extent are they due to other factors? In other words, what is the impact of TB control?

There have been relatively few evaluations of the epidemiological impact of TB control. Examples include studies of the impact of DOTS on the prevalence of TB in China and the impact of DOTS on TB incidence and mortality in Peru. Most recently, the observation that there has been no obvious reduction in TB incidence in countries that have implemented DOTS programmes with high reported treatment success rates and estimated case detection rates for several years (such as India and Viet Nam) *(36)* has raised concerns about the impact of DOTS and whether the impact of chemotherapy on TB incidence that was observed in the mid-twentieth century in western Europe and North America can be reproduced *(64)*. More evidence about the impact of TB control on TB incidence, prevalence and mortality is needed.

This section starts by defining impact evaluation, followed by a brief discussion of the methods that can be used to assess the impact of any intervention or programme. It then discusses how these methods can be applied to evaluate the epidemiological impact of TB control, using recent examples.

8.1 Definition of impact evaluation

There is no single and universally used definition of impact evaluation. However, there is agreement that impact evaluations assess the broad, long-term effects or results of interventions and that they assess these long-term effects or results by comparing an intervention with at least one relevant alternative. The relevant alternative could include no intervention or an alternative intervention (or set of interventions). This emphasis on comparison with at least one alternative scenario allows analysis of the extent to which the intervention under evaluation caused changes in impact indicators or to what extent changes were due to other factors.

8.2 Methods for evaluating the impact of public health interventions

The gold standard for evaluating an intervention is a randomized controlled trial. In a randomized controlled trial, the intervention being evaluated is randomly applied to otherwise similar individuals or populations. Provided that the study design is robust enough (such as a large enough sample size and a long enough period of follow-up) to detect real differences between the populations under investigation, any observed differences between the intervention and control group in the outcomes of interest can be attributed to the intervention. Three well-known examples of randomized controlled trials for public health

interventions are: treatment for sexually-transmitted infections for preventing HIV transmission in Mwanza, United Republic of Tanzania; mass treatment for sexually-transmitted infections for preventing HIV transmission in Rakai, Uganda; and treatment of sexually-transmitted infections combined with behavioural intervention in Masaka, Uganda *(65–67)*.

Public health interventions can often not be evaluated through randomized controlled trials *(68)*. The reasons include the fact that interventions may already be widely implemented and removing them is neither feasible nor ethical; that randomization based on geographical areas can break down if people seek prevention or care services outside their place of residence; and that there is often international, national or local pressure to implement interventions universally rather than in selected areas. Moreover, even when an intervention has been shown to have an impact in the context of a trial, its impact under routine programmatic conditions still needs to be demonstrated *(69)*. In theory, step-wise implementation can overcome these problems for new interventions, provided that the individuals or geographical areas that receive the intervention in each phase are truly comparable. Natural experiments in which interventions are withdrawn for short periods for reasons beyond the control of a programme can also help to evaluate the effect of an intervention; the caveat is that, in such situations, it is rarely only the intervention that changes and the role of other factors has to be considered *(51)*.

Besides randomized controlled trials, impact assessment can be based on observation of what happened when an intervention or programme was implemented and comparisons with 1) otherwise similar areas during the same time period and/or 2) with the same area before a new intervention or programme was implemented and/or 3) with a hypothetical scenario for the same area during the same time period. In the literature on evaluation, such evidence is said to allow "plausibility" statements to be made, in contrast to the "probability" statements that can be made based on randomized controlled trials *(70)*.

A third approach to impact evaluation is to analyse trends in the impact indicators of interest in combination with trends in indicators that measure the implementation of the intervention or programme being evaluated. If changes in indicators of implementation of the programme or intervention can explain changes in impact indicators, this can be used as evidence of programmatic or intervention impact. Such evidence is said to allow "adequacy" statements to be made.

A checklist for the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) (the equivalent of the CONSORT statement developed for randomized clinical trials) has been developed and is useful when designing and reporting an impact evaluation *(71)*. Regardless of which of the three main approaches to impact evaluation is used, defining a causal framework is essential. This should show how a programme or intervention is expected to influence long-term results or impact in the context of other external and internal factors. It should also explain any underlying assumptions.

8.3 Impact evaluation in the context of TB control

Evaluation of the impact of TB control on TB incidence, prevalence and mortality at the population level has never been attempted using a randomized controlled trial. To date, randomized controlled trials related to TB interventions have mainly been used to assess the efficacy of alternative drug regimens and, more recently, the efficacy of alternative approaches to the supervision of treatment (comparing directly observed treatment (DOT) by different types of supervisor with unsupervised treatment) in cohorts of individual patients. In both cases, the cure rate was the main outcome indicator.

Using observational data combined with before-and-after comparisons and/or comparisons between similar areas with different approaches to TB control is more feasible. Even so, this has been done relatively rarely, but there are three examples.

- The impact of DOTS on the prevalence of TB disease in China *(51)*. This could be evaluated because, during the 1990s, the DOTS strategy was

implemented in half the country but not in the other half. The impact of DOTS on the prevalence of TB disease was then assessed by comparing reductions in the prevalence of TB in the two areas from 1990 to 2000. The prevalence of TB disease was similar in the two areas in 1990, but in 2000 the prevalence of TB in the DOTS areas was 32% lower than in non-DOTS areas.

- The impact of DOTS on TB mortality in India *(72,73)*. Here, a before-and-after comparison was used to evaluate how introducing the revised national TB control programme in the late 1990s had reduced the number of deaths from TB.

- The impact of DOTS on TB incidence and mortality in Peru *(74)*. Notification data for the years 1958 (32 years before DOTS was implemented) to 2000 (10 years after being introduced), data on registered deaths from TB for the period 1948–1998, treatment outcome data and assumptions about the fraction of cases that were untreated were used. TB incidence and mortality under DOTS (1991 to 2000) were estimated from these observed data and compared with hypothetical projections of TB incidence and mortality in the absence of DOTS. Evidence that was used to support the case that reductions in TB incidence and deaths were due to DOTS included trends in the number of health units providing TB diagnosis and treatment services and the number of sputum smears examined.

Although few impact evaluations have been based on observational data for TB, many countries have reported declining TB notifications over many years and reduced TB mortality rates in cohorts of people treated under DOTS. With such data, the impact of TB control programmes can be estimated as:

[total number of TB cases that would have occurred without DOTS × case-fatality rate prior to DOTS] – [total number of TB cases that occurred with DOTS × case-fatality rate under DOTS].

The evaluation of DOTS in Peru used this method. A more conservative approach would be to estimate the number of deaths averted by TB control as:

[number of people treated] × [reduction in the case-fatality rate under DOTS].

Although such indirect estimates of impact are inferior to direct measures of the number of deaths averted, they can be produced for most countries.

The impact of TB control can be evaluated by analysing trends in variables that are thought to influence TB incidence, mortality and prevalence, although this has not been done systematically. A recent example is an ecological analysis of the relationship between a variety of indicators and trends in TB incidence, with trends in notifications used as a proxy for incidence *(75)*. Another recent study based on analysis of trends in HIV prevalence, gross domestic product per capita, DOTS population coverage and treatment success rates also illustrates the use of trend data to explore the impact of TB control, although in this case the analysis focused on case detection and treatment success rates (outcome indicators) rather than incidence, prevalence or mortality *(76)*.

As noted in subsection 8.2, a causal framework should be defined when any of the above methods (randomized controlled trial; observational data that allow comparison with what would have occurred in the absence of TB control or a specific strategy for TB control; and analysis of trends) is used. A simple example based on the classification of indicators used in the TB compendium of indicators *(7)* is shown in Figure 5. In this causal framework, inputs (such as funding, staff and buildings) are transformed into processes (such as training, supervision, providing drugs to people with TB and laboratory tests), which are then transformed into outputs (such as the numbers of people treated for TB). Depending on the quantity and quality of treatment provided, this output is transformed into outcomes – the two major outcome indicators for TB control being the treatment success rate and the case detection rate. Increases in case detection and treatment success rates should reduce TB incidence, prevalence and mortality because 1) the average duration of infectiousness should fall and 2) the proportion of cases dying should decrease. The greater the effect on the duration of

Figure 5. An example of a causal framework

infectiousness and the greater the reduction in the risk of dying on treatment, the greater will be the combined effect on TB mortality. However, TB incidence can remain stable or even increase when case detection and successful treatment rates are rising if the risk of developing TB at the population level is increasing (such as when the prevalence of risk factors for TB is rising).

This type of causal framework places emphasis on measures of programme performance besides the traditional indicators of case detection and treatment success rates as well as factors that influence the epidemiology of TB besides TB control programmes. In particular, it shows the relevance of collecting data on a standard set of programmatic input, process and output indicators to track and evaluate progress in TB control over time. For example, linked to the measurement of trends in incidence discussed in Section 4, data on trends in programmatic inputs, processes and outputs can help to separate out the effect of programmatic changes on case notifications from the effect of underlying changes in incidence (Box 9 - page 29). This is particularly important where notification data are used to measure trends in incidence. Data on programmatic input, process and output indicators can also be used to evaluate the extent to which changes in TB control can explain changes in TB prevalence and mortality (Box 12).

Compiling data on inputs, process and outputs in addition to the standard monitoring of case notifications and treatment success rates can be difficult and time-consuming. However, if this is done routinely or at regular intervals, it will provide a much stronger basis for evaluating both progress in TB control and the impact of TB control than currently exists. The study from Kenya described in Box 5 (page 18, Section 4) and the study in Peru described in this section show that such data can be collected and analysed and that it can be used to draw important conclusions about the absolute level of TB incidence and mortality and their trends over time. The TB data collection form used by WHO to collect data from national TB control programmes has been revised with the aim of compiling and analysing such data more systematically and for more countries.

Box 12

WHO policy and recommendations for evaluating the impact of TB control on incidence, prevalence and mortality

Recommendation 1. The impact of TB control on TB incidence should be evaluated using trends in TB incidence combined with evidence about the extent to which changes in TB control can explain these trends.

Recommendation 2. The impact of TB control on TB prevalence should be evaluated using data from at least two population-based surveys of the prevalence of disease that used identical or similar methods, combined with evidence about the extent to which changes in TB control can explain trends in TB prevalence.

Recommendation 3. The impact of TB control on TB mortality should be evaluated using trends in TB deaths combined with evidence about the extent to which changes in TB control can explain trends in mortality, and/or estimation of averted TB deaths using data on trends in TB incidence, reductions in mortality rates observed in cohorts of people with TB and the share of TB incident cases being treated in these cohorts.

Recommendation 4. Indicators that could be used to understand the extent to which changes in TB control explain changes in TB incidence, prevalence and mortality include: treatment success and case detection rates (outcome indicators); the numbers of people receiving particular interventions (output indicators); the number of people trained and the number of sputum smears examined (process indicators); the number of health units at which TB diagnostic and treatment services are available; the number of staff working for the national TB control programme; and funding (input indicators).

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Annex 1
Membership of the WHO Global Task Force on TB Impact Measurement

TB-endemic countries. Representatives from countries with a high burden of TB. Task Force meetings to date have included representatives from India, Indonesia, Malawi, Nigeria, the Philippines, South Africa and the United Republic of Tanzania.
International technical agencies with expertise in TB epidemiology. United States Centers for Disease Control and Prevention, Atlanta, USA; European Centre for Disease Prevention and Control, Stockholm, Sweden; KNCV Tuberculosis Foundation, The Hague, The Netherlands; Research Institute of Tuberculosis – Japan Anti-Tuberculosis Association, Tokyo, Japan; International Union against Tuberculosis and Lung Disease, Paris, France; PATH, Washington, DC, USA; MEASURE Evaluation, ICF Macro, Fairfax, VA, USA; WHO (headquarters and regional offices).
Financial agencies. Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland; United States Agency for International Development, Washington, DC, USA; World Bank, Washington, DC, USA.
Task Force Chair: Jaap Broekmans, former Executive Director of the KNCV Tuberculosis Foundation and former Chair of the WHO Strategic and Technical Advisory Group on TB.

Three subgroups have been established for each of three major strategic tracks of work the Task Force will pursue. Membership is based on the areas of interest and expertise of Task Force members. Experts from outside the Task Force who have been nominated to each group and who have participated in at least one meeting of a subgroup are also listed.

Area 1 (Routine surveillance data)
Ana Bierrenbach (leader/coordinator, WHO headquarters), Ibrahim Abubakar (Health Protection Agency, UK), Amal Bassili (WHO Regional Office for the Eastern Mediterranean), Chen-Yuan Chiang (International Union against Tuberculosis and Lung Disease, France), Ted Cohen (Harvard University, USA), Charlotte Colvin (PATH, USA), Andrei Dadu (WHO Regional Office for Europe), Vahur Hollo (European Centre for Disease Prevention and Control, Sweden), Nico Kalisvaart (KNCV Tuberculosis Foundation, The Netherlands), Ryuichi Komatsu (Global Fund, Switzerland), Eugene McCray (United States Centers for Disease Control and Prevention, USA).

Area 2 (Prevalence surveys)
Ikushi Onozaki (leader/coordinator, WHO headquarters), Amal Bassili (WHO Regional Office for the Eastern Mediterranean), Ana Bierrenbach (WHO headquarters), Vineet K. Chadha (National Tuberculosis Institute, India), Daniel Chemtob (national TB control programme, Israel), Sian Floyd (London School of Hygiene and Tropical Medicine, UK), Punnathanathu Gopalan Gopi (formerly Tuberculosis Research Centre, India), Eveline Klinkenberg (KNCV Tuberculosis Foundation, The Netherlands), Eugene McCray (United States Centers for Disease Control and Prevention, USA), Philip Patrobás (WHO Country Office, Nigeria), Marieke van der Werf (KNCV Tuberculosis Foundation, The Netherlands), Frank van Leth (KNCV Tuberculosis Foundation, The Netherlands), Charalambos Sismanidis (WHO headquarters,

and formerly London School of Hygiene and Tropical Medicine, UK), Eliud Wandwalo (United Republic of Tanzania, Management Sciences for Health, United Republic of Tanzania and formerly national TB programme, United Republic of Tanzania), Norio Yamada (Research Institute of Tuberculosis – Japan Anti-Tuberculosis Association, Japan).

Area 3 (Production of epidemiological estimates and evaluation of trends)

Marieke van der Werf (co-leader/coordinator, KNCV Tuberculosis Foundation, The Netherlands), Philippe Glaziou (co-leader/coordinator, WHO headquarters), Ibrahim Abubakar (Health Protection Agency, UK), Amal Bassili (WHO Regional Office for the Eastern Mediterranean), Ana Bierrenbach (WHO headquarters), Vineet K. Chadha (National Tuberculosis Institute, India), Daniel Chemtob (national TB control programme, Israel), Ted Cohen (Harvard University, USA), Andrei Dadu (WHO Regional Office for Europe, Denmark), Katherine Fielding (London School of Hygiene and Tropical Medicine, UK), Punnathanathu Gopalan Gopi (formerly Tuberculosis Research Centre, India), Eline Korenromp (Global Fund, Switzerland), Davide Manissero (European Centre for Disease Prevention and Control, Sweden), Nico Nagelkerke, (United Arab Emirates University, United Arab Emirates), Ikushi Onozaki (WHO headquarters), John Stover (Futures Institute, USA), Masja Straetemans (KNCV Tuberculosis Foundation, The Netherlands), Andrew Thomson (independant statistical consultant, UK), Edine Tiemersma (KNCV Tuberculosis Foundation, The Netherlands), Eliud Wandwalo (United Republic of Tanzania, Management Sciences for Health, United Republic of Tanzania and formerly national TB programme, United Republic of Tanzania), Brian Williams (formerly WHO headquarters), Norio Yamada (Research Institute of Tuberculosis – Japan Anti-Tuberculosis Association, Japan).

Annex 2
Extracts from World Health Assembly resolution WHA60.19 (2007)

The World Health Assembly (WHA) urges member states:

"… (1) to develop and implement long-term plans for tuberculosis prevention and control in line with the Global Plan to Stop TB 2006–2015, in the context of overall health development plans, in collaboration with other programmes (including those on HIV/AIDS, child health and strengthening of health systems), and through national Stop TB partnerships where appropriate, with the aim of:

…(b) accelerating improvement of health-information systems, both in general and for tuberculosis in particular, in order to serve the assessment of national programme performance.

The WHA requests the Director-General:

"… (5) to strengthen mechanisms to review and monitor estimates of impact of control activities on the tuberculosis burden, including incidence, prevalence and mortality with specific attention to vulnerable groups highly at risk, such as poor people, migrants and ethnic minorities; …

… (8) to report to the Sixty-third World Health Assembly through the Executive Board on:

… (b) progress made in achieving the international targets for tuberculosis control by 2015, using the "proportion of tuberculosis cases detected and cured under DOTS" (Millennium Development Goal indicator 24) as a measure of the performance of national programmes, and tuberculosis incidence and "prevalence and death rates associated with tuberculosis" (Millennium Development Goal indicator 23) as a measure of the impact of control on the tuberculosis epidemic."

Annex 3
Surveys of the annual risk of infection

Tuberculin skin test surveys of the annual risk of infection are usually conducted with a sample of about 10 000 children aged 5–15 years old. Children infected with *Mycobacterium tuberculosis* are identified by the size of their skin-test reaction. The prevalence of infection combined with the mean age of sampled children (= average years of exposure) can then be used to estimate the annual risk of infection. The incidence of smear-positive TB is then estimated using the rule-of-thumb proposed by Styblo, which is that an annual risk of infection of 1% is equivalent to 50–60 smear-positive cases per 100 000 population per year (equation 1). The value is usually assumed to be 50.

incidence (smear-positive) = ***annual risk of infection*** × ***coefficient*** (usually 50) (Eq. 1)

Tuberculin skin test surveys have the advantage of being relatively cheap (about US$ 20 000 to US$ 50 000 each) and logistically straightforward to implement. However, the results can be difficult to interpret. The reasons for this include the following.

- Positive responses to ***M. tuberculosis*** infection can be obscured by unpredictable cross-reactions from BCG vaccination or environmental mycobacteria. In general, the lower the annual risk of infection, the harder it is to distinguish the population of true positives from the population of cross-reactors.

- In recent surveys, the distributions of true and false positives have often overlapped considerably. This means that a single cut-off point cannot be used to identify the number of children that are infected.

- Measuring the prevalence of infection requires rigorous application of standard methods.

- The Styblo rule-of-thumb, which is based on the assumption that each smear-positive case will infect 10 individuals in a year, that an untreated case remains smear-positive for two years and that the reproduction number equals one (the epidemic is in a stable state), does not necessarily apply. Two recent reviews found that the number of contacts that became infected was much less than 10 in most settings *(1,2)*. This implies that the ratio of the smear-positive incidence to the annual risk of infection exceeds 50.

The value of tuberculin skin test surveys can be improved if the data can be calibrated with results for people with active disease and if it can be assumed that tuberculin skin test indurations have the same distribution among people with TB (usually adults) and the infected individuals studied in a tuberculin skin test survey (usually children). The most commonly used tuberculin preparation appears to generate a plausible distribution of induration sizes for people with TB with a mode at around 18 mm but may not always do so.

A second approach is to calibrate tuberculin skin test survey data with highly specific, interferon-γ release assays. Examples including the enzyme-linked immunospot (ELISpot) and the enzyme-linked immunosorbent assay (ELISA). The drawback of interferon-γ release assays is that they are costly (>US$ 10 per assay) and require blood taken by venepuncture (not merely a finger-prick). They are also less sensitive than the tuberculin skin test for indicating whether a child or adult has ever been infected: in studies undertaken to date, a significant proportion of TB cases tested negative on the interferon-γ release assay.

References

1. van Leth F, Van der Werf MJ, Borgdorff MW. Prevalence of tuberculous infection and incidence of tuberculosis: a re-assessment of the Styblo rule. *Bulletin of the World Health Organization*, 2008, 86:20–26.

2. Dye C. Breaking a law: tuberculosis disobeys Styblo's rule. *Bulletin of the World Health Organization*, 2008, 86:4.

Annex 4
Surveys of the prevalence of TB disease

Population-based surveys of the prevalence of TB disease rely on cluster sampling: whole areas are selected, and then suitable numbers of individuals are selected from each of these areas. Cluster sampling is used to reduce survey time and costs. Six national surveys were implemented between 1995 and 2007: in China, Cambodia, Eritrea, Indonesia, the Philippines and the Republic of Korea. Further surveys are underway or planned.

Large sample sizes are needed to produce precise estimates of the national prevalence of TB (although not as large as the sample sizes needed to measure incidence). For example, if the prevalence of sputum smear-positive TB is 100 per 100 000 population, a random sample of 100 000 people can be expected to yield 100 cases with a 95% confidence interval of ±20%. To allow for incomplete data as well as the need to increase sample size when cluster rather than simple random sampling is used (the design effect), a good rule of thumb is to double the sample size compared with that needed for a simple random sample of individuals: in this example, to 200 000 people. In the six national surveys listed above, the prevalence of smear-positive TB was measured with an accuracy that varied from ±25% (China and the Republic of Korea) to ±60% (Eritrea).

Surveys can also be carried out to measure TB prevalence subnationally, such as in states or provinces. Recent examples include surveys in Bangladesh, Botswana, Cambodia, Ethiopia, India and Uganda. However, for a given level of precision, a much larger overall sample size is needed if the objectives of a national prevalence survey include subnational estimates of prevalence. If this is combined with data on the annual risk of infection, subnational data on the prevalence TB disease may be used to derive a national estimate of the prevalence of TB disease. For example, calibration of data on the annual risk of infection and prevalence of TB disease from the same site in south India have been combined with data on the annual risk of infection from four different regions to construct a national estimate of disease prevalence for India.

One critical methodological issue in any survey of the prevalence of TB disease is how to select which members of the survey sample should have sputum specimens taken for microscopy and culture examination. The major options are:

- Screening all sampled individuals with chest X-rays: few cases of active TB are missed when this approach is used;

- Screening all sampled individuals on the basis of the symptoms of chest illness (such as cough for two weeks), which tends to miss mildly symptomatic and asymptomatic cases;

- Screening using a combination of chest X-rays and symptoms, the most commonly used screening method in recent surveys; and

- Obtaining sputum from all sampled individuals, which is low-cost and requires minimal technology but requires consistent efforts in sputum collection and generates a large laboratory workload that must be accurately processed.

The third strategy is the one recommended by the Task Force.

Most surveys of the prevalence of TB disease have been based on TB survey-specific sampling frames. However, other possibilities exist. The 2004 survey in Indonesia took advantage of a sampling frame established for the National Household Health Survey.

Changes in prevalence over time are best measured by implementing at least two (but preferably more) surveys at large enough intervals. The sample sizes required to measure changes in prevalence are larger than those needed for a one-time measurement of the total (absolute) number of cases. For example, if two surveys are carried out five years apart with the aim of detecting a 30% reduction in prevalence (from 100 cases per 100 000 population to 70 cases per 100 000 population), about 400 000 people would need to be examined in each survey. The lower the initial estimate of prevalence and the smaller the expected change in prevalence, the larger the sample size needed to detect changes over time.

Besides the importance of large enough sample sizes, surveys to measure changes in TB prevalence over time need to be comparable in terms of study design, diagnostic protocols and case definitions. When new surveys are implemented, there can be a trade-off between maximizing the similarity of methods and making use of newer and better screening methods and diagnostic tools; if so, care is needed to ensure that the comparability of the surveys is not compromised.

Annex 5
Additional countries that met criteria for implementing a survey of the prevalence of TB disease

Table 1. Extended list of 32 countries that met one of the four sets of criteria for carrying out a survey of the prevalence of TB disease but that were not selected as global focus countries by the Task Force

Criteria met	Region	Country	High-burden
2, 3	African Region, high HIV prevalence	Botswana	No
1–3	African Region, high HIV prevalence	Burundi	No
1, 2	African Region, high HIV prevalence	Central African Republic	No
2, 3	African Region, high HIV prevalence	Congo	No
1–3	African Region, high HIV prevalence	Côte d'Ivoire	No
2	African Region, high HIV prevalence	Democratic Republic of the Congo	Yes
1, 3	African Region, high HIV prevalence	Ethiopia	Yes
2	African Region, high HIV prevalence	Lesotho	No
3	African Region, high HIV prevalence	Namibia	No
1–3	African Region, high HIV prevalence	Swaziland	No
1–3	African Region, high HIV prevalence	Zimbabwe	Yes
1, 2	African Region, high HIV prevalence	Angola	No
1–3	African Region, high HIV prevalence	Burkina Faso	No
1–3	African Region, high HIV prevalence	Chad	No
4	African Region, high HIV prevalence	Eritrea	No
4	African Region, high HIV prevalence	Gambia	No
2	African Region, high HIV prevalence	Guinea	No

1	African Region, low HIV prevalence	Liberia	No
1, 3	African Region, low HIV prevalence	Mauritania	No
1, 2	African Region, low HIV prevalence	Niger	No
1–3	African Region, low HIV prevalence	Togo	No
4	European Region	Armenia	No
2	European Region	Russian Federation	Yes
1	European Region	Tajikistan	No
1	Eastern Mediterranean Region	Afghanistan	Yes
3, 4	Eastern Mediterranean Region	Djibouti	No
1, 2	Eastern Mediterranean Region	Sudan	No
2	Latin America and the Caribbean	Haiti	No
3	South-East Asia Region	Timor-Leste	No
4	Western Pacific Region	Lao People's Democratic Republic	No
4	Western Pacific Region	Malaysia	No
1–3	Western Pacific Region	Papua New Guinea	No

[1] To avoid double-counting of deaths from AIDS and TB, WHO world health statistics on TB deaths exclude TB deaths among people coinfected with HIV. However, the aim of TB control is to eliminate the disease from whole populations. In the annual report on global TB control, WHO therefore publishes TB statistics both overall and for the HIV-positive and HIV-negative subpopulations separately.

Web site
www.who.int/tb/advisory_bodies/impact_measurement_taskforce/en

Framework for assessment of TB surveillance data
(notification and vital registration data)

DATA QUALITY	• Completeness • No duplications, no misclassifications • Internal and external consistency	**IMPROVE** surveillance system
TRENDS Do surveillance data reflect trends in TB incidence and mortality?	• Analyse time-changes in notifications and recorded deaths alongside changes in case-finding, case definitions, HIV prevalence and other determinants of changes in TB incidence and TB mortality	**EVALUATE** trends and impact of TB control
ARE ALL TB CASES AND DEATHS CAPTURED IN SURVEILLANCE DATA?	• "Onion" model • Inventory studies • Capture re-capture studies • Prevalence surveys • Innovative operational research	**UPDATE** estimates of TB incidence and mortality
	TB notifications ≈ TB incidence TB deaths in VR system ≈ TB mortality	If appropriate, **CERTIFY** TB surveillance data as direct measure of TB incidence and mortality

World Health Organization

WORLD HEALTH ORGANIZATION
STOP TB DEPARTMENT
20, AVENUE APPIA
1211 GENEVA 27, SWITZERLAND
Fax: +41 22 791 4285
Web site: www.who.int/tb
Information resource centre: tbdocs@who.int

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