A cured TB patient has a follow-up chest X-ray in Howrah, India

IMAGEBROKER / ALAMY STOCK PHOTO

CHAPTER 3.

TB disease burden

KEY FACTS AND MESSAGES

TB is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS. In 2016, there were an estimated 1.3 million TB deaths among HIV-negative people (down from 1.7 million in 2000) and an additional 374 000 deaths among HIV-positive people.[a]

An estimated 10.4 million people (90% adults; 65% male; 10% people living with HIV) fell ill with TB in 2016 (i.e. were incident cases).

Most of the estimated number of incident cases in 2016 occurred in the WHO South-East Asia Region (45%), the WHO African Region (25%) and the WHO Western Pacific Region (17%); smaller proportions of cases occurred in the WHO Eastern Mediterranean Region (7%), the WHO European Region (3%) and the WHO Region of the Americas (3%). The top five countries, with 56% of estimated cases, were (in descending order) India, Indonesia, China, the Philippines and Pakistan.

Globally, the TB mortality rate is falling at about 3% per year. TB incidence is falling at about 2% per year; this needs to improve to 4–5% per year by 2020 to reach the first milestones of the End TB Strategy.

Regionally, the fastest decline in TB incidence is in the WHO European Region (4.6% from 2015 to 2016). The decline since 2010 has exceeded 4% per year in several high TB burden countries, including Ethiopia, Kenya, Lesotho, Namibia, the Russian Federation, the United Republic of Tanzania, Zambia and Zimbabwe.

Regionally, the fastest declines in the TB mortality rate are in the WHO European Region and the WHO Western Pacific Region (6.0% and 4.6% per year, respectively, since 2010). High TB burden countries with rates of decline exceeding 6% per year since 2010 include Ethiopia, the Russian Federation, the United Republic of Tanzania, Viet Nam and Zimbabwe.

Globally, the proportion of people who develop TB and die from the disease (the case fatality ratio, or CFR) was 16% in 2016. This needs to fall to 10% by 2020 to reach the first milestones of the End TB Strategy.

There is considerable country variation in the CFR, from under 5% in a few countries to more than 20% in most countries in the WHO African Region. This shows considerable inequalities among countries in access to TB diagnosis and treatment that need to be addressed.

Between 2000 and 2016, TB treatment averted an estimated 44 million deaths among HIV-negative people. Among HIV-positive people, TB treatment supported by ART averted an additional 9 million deaths.

Drug-resistant TB is a persistent threat, with 490 000 million cases of multidrug-resistant TB (MDR-TB) emerging in 2016 and an additional 110 000 cases that were susceptible to isoniazid but resistant to rifampicin (RR-TB), the most effective first-line anti-TB drug. The countries with the largest numbers of MDR/RR-TB cases (47% of the global total) were China, India and the Russian Federation.

National notification and vital registrations systems need to be strengthened towards the goal of direct measurement of TB incidence and mortality in all countries. National TB prevalence surveys provide an interim approach to directly measuring the burden of TB disease in an important subset of high TB burden countries. Between 2007 and the end of 2016, a total of 25 surveys that used the screening and diagnostic methods recommended by WHO were implemented.

[a] When an HIV-positive person dies from TB disease, the underlying cause is classified as HIV in the international classification of diseases system (ICD-10).

The burden of tuberculosis (TB) disease can be measured in terms of:

- *incidence* – the number of new and relapse cases of TB arising in a given time period, usually 1 year;
- *prevalence* – the number of cases of TB at a given point in time; and
- *mortality* – the number of deaths caused by TB in a given time period, usually 1 year.

Global targets and milestones for reductions in the burden of TB disease have been set as part of the Sustainable Development Goals (SDGs) and WHO's End TB Strategy (**Chapter 2**).[1] SDG 3 includes a target to end the global TB epidemic by 2030, with TB incidence (per 100 000 population per year) defined as the indicator for measurement of progress. The 2030 targets set in the End TB Strategy are a 90% reduction in TB deaths and an 80% reduction in TB incidence, compared with levels in 2015. Targets for 2035 and milestones for 2020 and 2025 have also been defined (**Table 3.1**).

TABLE 3.1

Targets for percentage reductions in TB disease burden set in WHO's End TB Strategy

	MILESTONES		TARGETS	
INDICATORS	2020	2025	2030	2035
Percentage reduction in the absolute number of TB deaths *(compared with 2015 baseline)*	35	75	90	95
Percentage reduction in the TB incidence rate *(compared with 2015 baseline)*	20	50	80	90

This chapter has five major sections. **Section 3.1** and **Section 3.2** present the latest WHO estimates of TB incidence and mortality between 2000 and 2016, and highlight sources of data and actions needed to improve measurement of TB incidence and mortality. **Section 3.3** focuses on the burden of drug-resistant TB, including progress in global surveillance of resistance to anti-TB drugs, and estimates of the incidence of multidrug-resistant TB (MDR-TB) and rifampicin-resistant TB (RR-TB). **Section 3.4** discusses national TB prevalence surveys. TB prevalence is not an indicator for which a global target has been set during the period 2016–2035.[2] Nevertheless, in many countries, national TB prevalence surveys still provide the best method for estimating the burden of TB disease (including by age and sex) and for planning actions needed to reduce that burden. In addition, results from national TB prevalence surveys can inform estimates of TB incidence and mortality, and thus contribute to monitoring of progress towards SDG and End TB Strategy targets. Finally, **Section 3.5** covers estimates of TB incidence and mortality disaggregated by age and sex. This is in line with the increasing emphasis on the importance of within-country disaggregation of key indicators in the SDGs and the End TB Strategy (**Chapter 2**).

WHO updates its estimates of the burden of TB disease annually, using the latest available data and analytical methods.[3,4] Since 2006, concerted efforts have been made to improve the available data and methods used, under the umbrella of the WHO Global Task Force on TB Impact Measurement (**Box 3.1**). A summary of the main updates to available data and methods since the 2016 global TB report is provided in **Box 3.2**.

3.1 TB incidence

3.1.1 Methods to estimate TB incidence

TB incidence has never been measured at national level because this would require long-term studies among large cohorts (hundreds of thousands) of people, which would involve high costs and challenging logistics. However, notifications of TB cases provide a good proxy indication of TB incidence in countries that have high-performance surveillance systems (e.g. with little underreporting of diagnosed cases), and in which the quality of and access to health care means that few cases are not diagnosed. In the large number of countries that have not yet met these criteria, better estimates of TB incidence can be obtained from an inventory study (i.e. a survey to quantify the level of underreporting of detected TB cases); also, if certain conditions are met, results from an inventory study can be combined with capture–recapture methods to estimate TB incidence.[5] To date, such studies have been undertaken in only a few countries, but interest and implementation is growing (**Box 3.3**).

The ultimate goal is to directly measure TB incidence from TB notifications in all countries. This requires a combination of strengthened surveillance, better quantification of underreporting (i.e. the number of cases that are missed by surveillance systems) and universal health coverage. A TB surveillance checklist developed by the WHO Global Task Force on TB Impact Measurement (**Box 3.1**) defines the standards that need to be met for notification data to provide a direct measure of TB incidence.[6] By August 2017, a total of

[1] World Health Organization. WHO End TB Strategy: global strategy and targets for tuberculosis prevention, care and control after 2015. Geneva: WHO; 2015 (http://www.who.int/tb/post2015_strategy/en/, accessed 8 August 2016).

[2] This is in contrast to the period covered by the Stop TB Strategy (2006–2015), when a target of halving prevalence by 2015 compared with a baseline of 1990 was set.

[3] The **online technical appendix** is available at http://www.who.int/tb/publications/global_report/en/

[4] The updates can affect the entire time-series back to 2000. Therefore, estimates presented in this chapter for 2000–2015 supersede those of previous reports, and direct comparisons (e.g. between the 2015 estimates in this report and the 2015 estimates in the previous report) are not appropriate.

[5] Inventory studies can be used to measure the number of cases that are diagnosed but not reported. For a guide to inventory studies, see World Health Organization. Assessing tuberculosis underreporting through inventory studies. Geneva: WHO; 2012 (http://www.who.int/tb/publications/inventory_studies/en/, accessed 15 August 2016).

[6] World Health Organization. Standards and benchmarks for tuberculosis surveillance and vital registration systems: checklist and user guide. Geneva: WHO; 2014 (http://www.who.int/tb/publications/standardsandbenchmarks/en/, accessed 24 August 2016). One of the standards is that levels of underreporting of detected TB cases should be minimal.

BOX 3.1

The WHO Global Task Force on TB Impact Measurement

Establishment and progress made, 2006–2015

The WHO Global Task Force on TB Impact Measurement (hereafter referred to as the Task Force) was established in 2006 and is convened by the TB Monitoring and Evaluation unit of WHO's Global TB Programme. Its original aim was to ensure that WHO's assessment of whether 2015 targets set in the context of the MDGs were achieved at global, regional and country levels was as rigorous, robust and consensus-based as possible. Three strategic areas of work were pursued:

- strengthening routine surveillance of TB cases (via national notification systems) and deaths (via national VR systems) in all countries;
- undertaking national TB prevalence surveys in 22 global focus countries; and
- periodically reviewing methods used to produce TB disease burden estimates.

Work on strengthened surveillance included the following:

- Development of a TB surveillance checklist of standards and benchmarks (with 10 core and three supplementary standards).[a] This checklist can be used to systematically assess the extent to which a surveillance system meets the standards required for notification and VR data, to provide a direct measurement of TB incidence and mortality, respectively. By the end of 2015, 38 countries including 16 high burden countries had used the checklist.
- Electronic recording and reporting. Case-based electronic databases are the reference standard for recording and reporting TB surveillance data. A guide was produced in 2012,[b] and efforts to introduce such systems were supported.
- Development of a guide on inventory studies to measure underreporting of detected TB cases,[c] and support such studies in priority countries. An inventory study can be used to quantify the number of cases that are detected but not reported to national surveillance systems, and can serve as a basis for improving estimates of TB incidence and addressing gaps in reporting.
- Expanded use of data from VR systems and mortality surveys to produce estimates of the number of TB deaths, and contributions to wider efforts to promote VR systems. By 2015, VR data were used to produce estimates of TB mortality in 127 countries, up from three in 2008.

There was substantial success in the implementation of national TB prevalence surveys 2007–2015, which has continued. Between 2007 and the end of 2015, a total of 23 countries completed a survey and a further two had done so by the end of 2016; this included 18 of the 22 global focus countries. A Task Force subgroup undertook a major review and update of methods between June 2008 and October 2009. A second thorough and comprehensive review was undertaken in 2015, with consensus reached on methods to be used for the 2015 targets assessment published in WHO's 2015 global TB report.[d]

Updated strategic areas of work, 2016–2020

In the context of a new era of SDGs and WHO's End TB Strategy, the Task Force met in April 2016 to review and reshape its mandate and strategic areas of work for the post-2015 era. An updated mandate and five strategic areas of work for the period 2016–2020 were agreed.[e]

The mandate was defined as follows:

- To ensure that assessments of progress towards End TB Strategy and SDG targets and milestones at global, regional and country levels are as rigorous, robust and consensus-based as possible.
- To guide, promote and support the analysis and use of TB data for policy, planning and programmatic action.

The five strategic areas of work are as follows:

1. Strengthening national notification systems for direct measurement of TB cases, including drug-resistant TB and HIV-associated TB specifically.
2. Strengthening national VR systems for direct measurement of TB deaths.
3. Priority studies to periodically measure TB disease burden, including:
    a. national TB prevalence surveys
    b. drug resistance surveys
    c. mortality surveys
    d. surveys of costs faced by TB patients and their households.
4. Periodic review of methods used by WHO to estimate the burden of TB disease and latent TB infection.
5. Analysis and use of TB data at country level, including:
    a. disaggregated analyses (e.g. by age, sex, location) to assess inequalities and equity;
    b. projections of disease burden; and
    c. guidance, tools and capacity building.

The SDG and End TB Strategy targets and milestones referred to in the mandate are the targets (2030, 2035) and milestones (2020, 2025) set for the three high-level indicators; that is, TB incidence, the number of TB deaths and the percentage of TB-affected households that face catastrophic costs as a result of TB disease (Chapter 2).

Strategic areas of work 1–3 are focused on direct measurement of TB disease burden (epidemiological and, in the case of cost surveys, economic). The underlying principle for the Task Force's work since 2006 has been that estimates of the level of and trends in disease burden should be based on direct measurements from routine surveillance and surveys as much as possible (as opposed to indirect estimates based on modelling and expert opinion). However, strategic area of work 4 remains necessary because indirect estimates will be required until all countries have the surveillance systems or the periodic studies required to provide direct measurements. Strategic area of work 5 recognizes the importance of analysing and using TB data at country level (as well as generating data, as in strategic areas of work 1–3), including the disaggregated analyses that are now given much greater attention in the SDGs and End TB Strategy. ➜

➜ In the years up to 2020, the top priorities for the Task Force are strengthening of national notification and VR systems as the basis for direct measurement of TB incidence and TB mortality.

Further details about the work of the Task Force are available online;[f] an up-to-date summary is provided in the latest brochure about its work.[g]

[a] World Health Organization. Standards and benchmarks for tuberculosis surveillance and vital registration systems: checklist and user guide. Geneva: WHO; 2014 (http://www.who.int/tb/publications/standardsandbenchmarks/en/, accessed 24 August 2017).

[b] World Health Organization. Electronic recording and reporting for tuberculosis care and control. Geneva: WHO; 2012 (http://www.who.int/tb/publications/electronic_recording_reporting/en/, accessed 11 September 2017).

[c] World Health Organization. Assessing tuberculosis underreporting through inventory studies. Geneva: WHO; 2012 (http://www.who.int/tb/publications/inventory_studies/en/, accessed 15 August 2017).

[d] World Health Organization Global Task Force on TB Impact Measurement. Third meeting of the TB estimates subgroup: methods to use for WHO's definitive assessment of whether 2015 global TB targets are met. Geneva: WHO; 2015 (http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/consultation_april_2015_tb_estimates_subgroup/en/, accessed 11 September 2017).

[e] World Health Organization Global Task Force on TB Impact Measurement. Report of the sixth meeting of the full Task Force; 19–21 April 2016, Glion-sur-Montreux, Switzerland. Geneva: WHO; 2015 (http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf6_report.pdf?ua=1, accessed 11 September 2017).

[f] Available at: http://www.who.int/tb/areas-of-work/monitoring-evaluation/impact_measurement_taskforce/en/

[g] Available at: http://www.who.int/tb/publications/factsheet_tb_impactmeasurement.pdf?ua=1

BOX 3.2 Updates to estimates of TB disease burden in this report and anticipated updates

Updates in this report

1. New data from national TB prevalence surveys

Between October 2016 and August 2017, final results from national TB prevalence surveys in Bangladesh, the Democratic People's Republic of Korea, Kenya and the Philippines became available.

The post-survey estimate of TB prevalence in the Philippines was significantly higher than anticipated from the results of previous national prevalence surveys, which had found a decline between 1997 (the second national survey) and 2007 (the third national survey). Between 2007 and 2016, there was no decline. Based on survey results, there were an estimated 1 million prevalent cases in 2016 (1 in 15 of the prevalent cases globally) and 570 000 incident cases. Broader social and economic influences on the TB epidemic are plausible reasons for the burden of TB disease being higher than expected. These influences include undernourishment, with a prevalence of 14% in 2015 and no improvement since 2008; a large proportion of the population living below the national poverty line (25% in 2012); and low coverage of health insurance and social protection (4% in the poorest quintile in 2013), resulting in financial barriers to accessing health services and high levels of out-of-pocket expenditures on health care (34% in 2014). The prevalence of HIV in the general population remains below 0.1% and has a limited impact on the size of the TB epidemic. Further details are provided in Box 3.6.

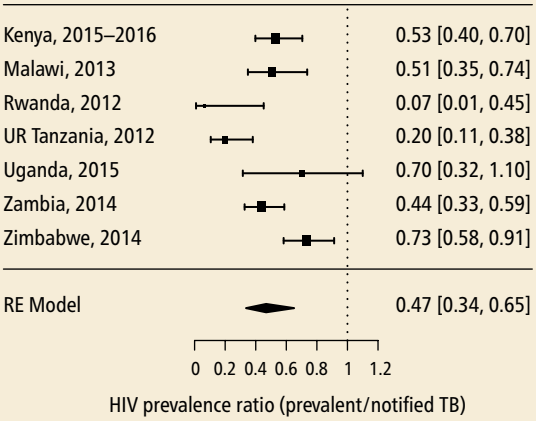
The best estimate of TB incidence in Kenya based on the prevalence survey was higher than the pre-survey estimate, but with overlapping uncertainty intervals. The post-survey estimate of TB incidence for Bangladesh was slightly lower, and for the Democratic Republic of Korea it was similar to the pre-survey estimate.

The survey in the Democratic Republic of Korea confirmed that the country has one of the highest burdens of TB disease among countries where the prevalence of HIV in the general population is under 1%. One factor contributing to the severity of the TB epidemic is high levels of undernourishment, which increases the risk of breakdown to TB disease among infected people (see also Chapter 2 and Chapter 7). The prevalence of undernourishment was 42% in 2015 (38% in 2000), and the percentage of TB cases attributable to undernourishment (population attributable fraction) was estimated at 48%. This demonstrated the need for a stronger intersectoral response to TB, addressing undernourishment and other social and economic determinants of the TB epidemic.

Data on the prevalence of HIV among prevalent TB cases identified during national prevalence surveys are now available from seven countries. These data were used to re-estimate TB incidence in Nigeria, accounting for the lower prevalence of HIV among survey cases compared with notified cases (Fig. B3.2.1). As a result of this adjustment, the updated incidence estimate was reduced by 32%. This can be explained by the fact that a lower HIV prevalence among prevalent TB cases increases the estimated average duration of disease. With incidence ➜

FIG B3.2.1

HIV prevalence ratio (survey/notified TB cases)



➜ estimated as prevalence divided by disease duration, this increase in estimated disease duration results in a reduction in estimated incidence.

2. Newly reported data and estimates from other agencies

New VR data were reported to WHO between mid-2016 and mid-2017. This included data from the Islamic Republic of Iran for 2013–2015 and updates by other countries to historical data. Updated estimates of the burden of disease caused by HIV were obtained from UNAIDS in mid-July 2017. In most instances, any resulting changes to TB burden estimates were well within the uncertainty intervals of previously published estimates, and trends were generally consistent.

For 18 countries (Fig. 3.10), estimates of TB mortality among HIV-negative people were based on estimates from the Institute of Health Metrics and Evaluation (IHME).[a] These are based on combining data from national VR systems, data from sample VR systems and data from verbal autopsy surveys in a Bayesian framework that includes predictors of mortality. For the 18 countries, the quantity of mortality data available to IHME is larger than the amount available to WHO. Estimates in South Africa are adjusted by IHME for miscoding of deaths caused by HIV and TB.[b,c] IHME estimates used in this report were adjusted to fit WHO estimates of the total number of deaths (referred to as the mortality envelope). The median country-year envelope ratio (WHO/IHME) was 1.03 (interquartile range, 0.92–1.05).

3. National TB epidemiological reviews

In-depth epidemiological reviews with an assessment of the performance of TB surveillance (Fig. 3.1) inform estimates of TB disease burden. The main update from such a review in this report is for the Russian Federation. During a review in February 2017, best estimates of TB incidence were revised downwards by 15%, with notifications assumed to be a good proxy for TB incidence (previously, a standard adjustment had been applied to notification data to allow for underreporting or underdiagnosis). This update was justified for four major reasons. First, there is an extensive and regular screening programme, with all adults screened every 1–2 years, all children and adolescents screened every year, and contact tracing undertaken for all TB cases. This makes underdiagnosis unlikely. Second, notification of cases is mandatory and the reporting system has complete national coverage, leaving little room for underreporting of detected TB cases. Third, culture or molecular testing (or both) are routinely used for diagnosis. Fourth, there have been no major changes in screening, diagnostic and reporting practices in recent years. In addition, there may be some over-diagnosis of people screening positive for TB but with no bacteriological confirmation using the most sensitive TB diagnostics, which would compensate for any underdiagnosis or underreporting. Further details are provided in Box 3.5.

4. Country-level estimates of TB incidence and mortality disaggregated by age and sex

Previous reports have included global, regional and country-specific estimates of TB incidence and TB mortality by age (adults and children) and sex. This report includes estimates for more age categories (0–4, 5–14, 15–24, 25–34, 35–44, 45–54, 55–64 and ≥65 years).

Updates anticipated in the near future

Updates to estimates of TB disease burden are expected in 2018 for Myanmar, Mozambique, Namibia, South Africa and Viet Nam, following the completion of national TB prevalence surveys. The surveys in Myanmar and Viet Nam are repeat surveys. A national TB prevalence survey in India is planned for 2018.

[a] Downloaded from http://ghdx.healthdata.org/gbd-results-tool, July 2017

[b] Murray CJ, Ortblad KF, Guinovart C, Lim SS, Wolock TM, Roberts DA et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9947):1005–1070 (http://www.sciencedirect.com/science/article/pii/S0140673614608448?via%3Dihub, accessed 24 August 2016).

[c] Groenewald P, Nannan N, Bourne D, Laubscher R, Bradshaw D. Identifying deaths from AIDS in South Africa. AIDS. 2005;19(2):193–201 (http://www.ncbi.nlm.nih.gov/pubmed/15668545, accessed 24 August 2016).

61 countries, including 23 of the 30 high TB burden countries (listed in Table 3.1) had completed the checklist, often in association with a TB epidemiological review or regional workshop focused on analysis of TB data (Fig. 3.1).

Methods currently used by WHO to estimate TB incidence can be grouped into four major categories, as follows (Fig. 3.2):

- **Results from TB prevalence surveys.** Incidence is estimated using prevalence survey results and estimates of the duration of disease, with the latter derived from a model that accounts for the impact of HIV coinfection on the distribution of disease duration. This method is used for 24 countries, of which 23 have national survey data and one – India – had a survey in one state. The 24 countries accounted for 68% of the estimated global number of incident cases in 2016.
- **Notifications in high-income countries adjusted by a standard factor to account for underreporting and underdiagnosis.** This method is used for 134 countries that comprise all high-income countries except the Netherlands and the United Kingdom, plus selected upper-middle-income countries with low levels of underreporting, including Brazil, China and the Russian Federation. For three countries (France, Republic of Korea and Turkey) the adjustment was country specific, based on results from studies of underreporting. These 134 countries accounted for 15% of the estimated global number of incident cases in 2016.

BOX 3.3

Inventory studies to measure the underreporting of detected TB cases: progress to date

In countries with state-of-the-art national surveillance systems, where most, if not all, new TB cases are diagnosed and registered, the number of notified TB cases provides a good proxy for TB incidence. In many countries, however, underreporting of detected cases as well as underdiagnosis mean that there are gaps between the number of notified TB cases and TB incidence. National TB inventory studies can be used to quantify one of these gaps – the level of underreporting – and in turn can inform better estimates of TB incidence as well as the actions needed to minimize levels of underreporting. If certain assumptions are met, results can also be used to estimate TB incidence using capture–recapture methods.[a]

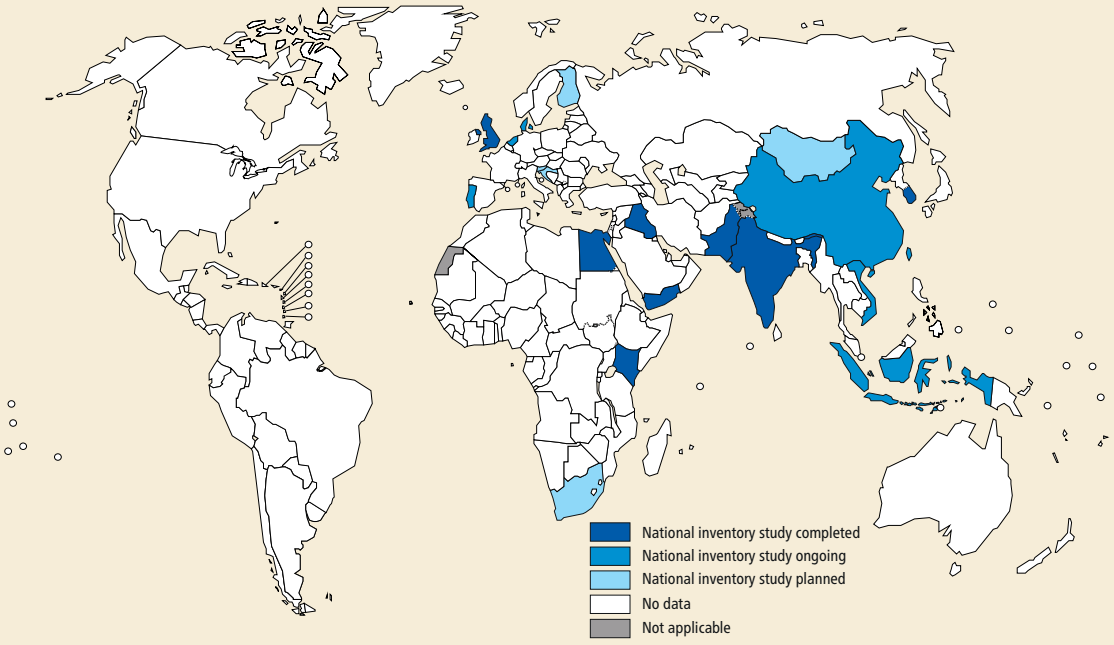
Countries in which a national inventory study has been implemented since 2000 are shown in Fig. B3.3.1. Progress in 2016–2017 includes the completion of a study focused on the underreporting of TB cases in children in Pakistan, and completion of fieldwork for the first-ever such studies (covering adults and children) in Indonesia and Viet Nam. Final results from these three studies are expected by early 2018. National studies in Denmark, the Netherlands and Portugal are also under way as part of a project funded by the European Centre for Disease Prevention and Control, and a study protocol is being developed for a study in South Africa.

As countries begin working towards the TB incidence targets set within the SDGs and the End TB Strategy, there is a need for increased commitment, from national TB programmes (NTPs) and funding agencies, to conduct and fund TB inventory studies.

[a] World Health Organization. Assessing tuberculosis underreporting through inventory studies. Geneva: WHO; 2012 (http://www.who.int/tb/publications/inventory_studies/en/, accessed 15 August 2017).

FIG. B3.3.1

Countries in which national inventory studies of the underreporting of detected TB cases have been implemented since 2000 (status in August 2017)[a]

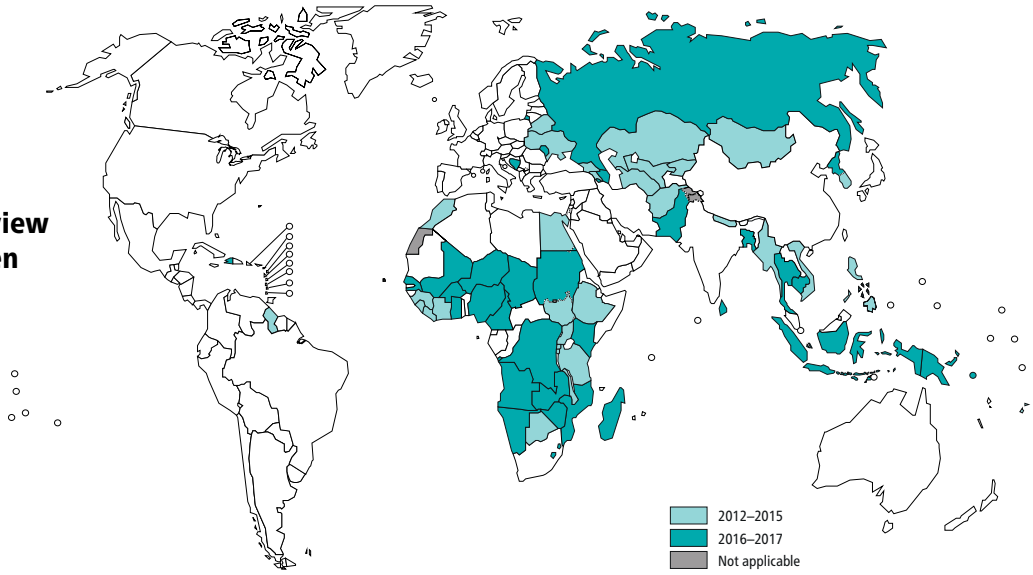


[a] Pakistan has completed a second inventory study focusing on children with TB. Nigeria is planning to undertake a subnational level study (in metropolitan Lagos). The Netherlands is carrying out a repeat of the inventory study conducted in 2006.

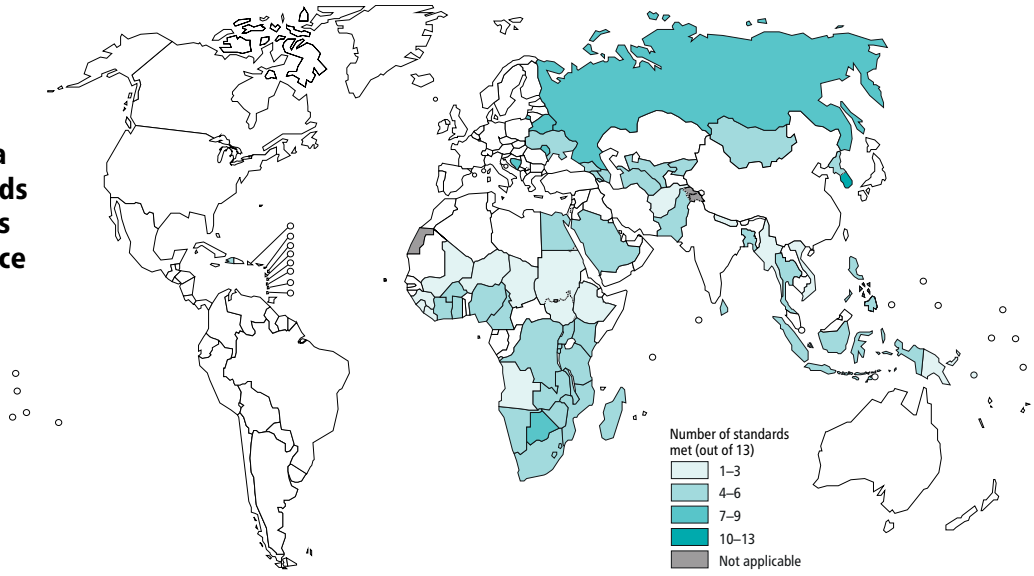
FIG. 3.1

Strengthening national TB surveillance (status in August 2017)

Countries in which a national TB epidemiological review has been undertaken since July 2012



Countries in which a checklist of standards and benchmarks has been completed since January 2013



Countries covered by a regional or country-specific workshop focused on TB data analysis and use for action since October 2015

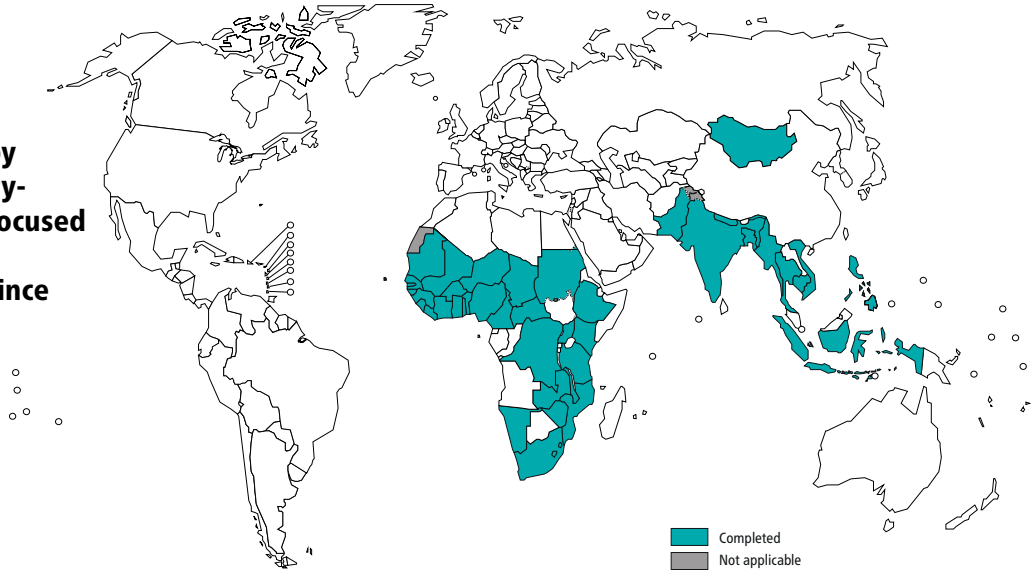
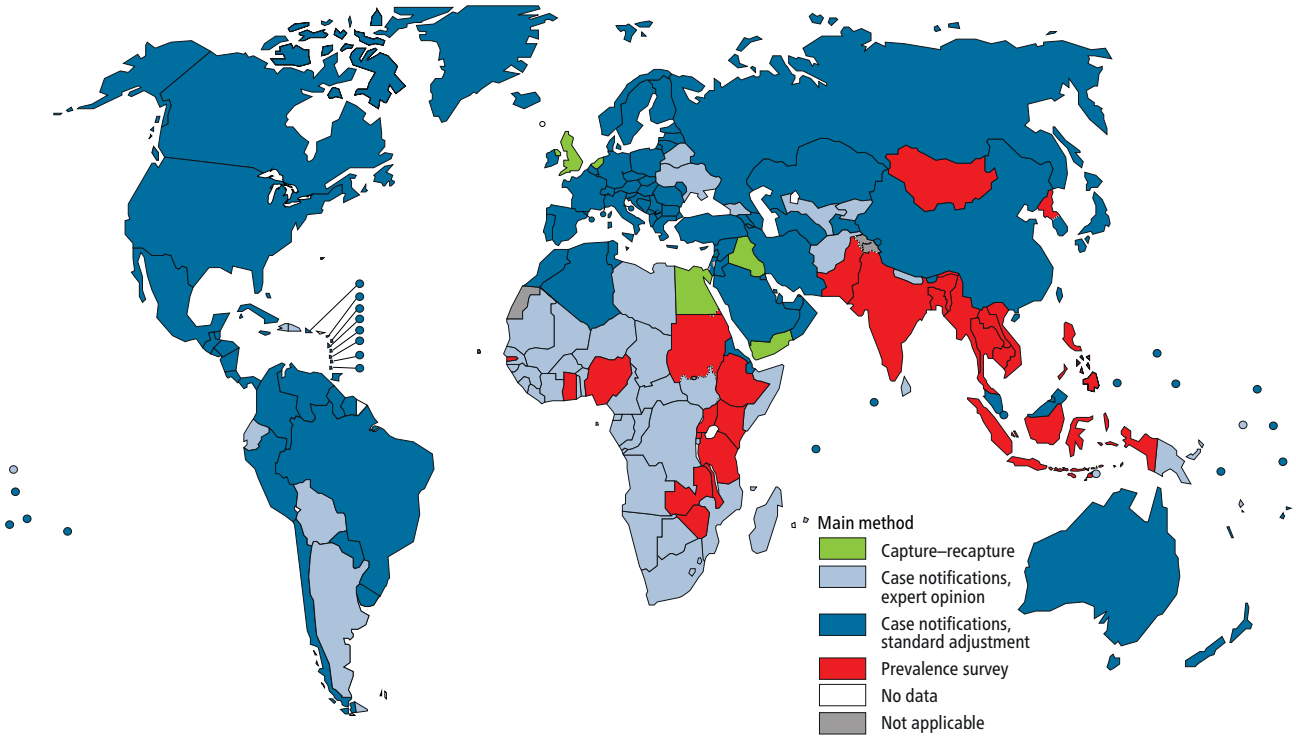


FIG. 3.2

Main methods used to estimate TB incidence



- **Results from inventory studies and capture–recapture analysis.** This method is used for five countries: Egypt, Iraq, the Netherlands, the United Kingdom and Yemen. These countries accounted for 0.5% of the estimated global number of incident cases in 2016.
- **Case notification data combined with expert opinion about case-detection gaps.** Expert opinion, elicited through regional workshops or country missions, is used to estimate levels of underreporting and underdiagnosis. Trends are estimated through mortality data, surveys of the annual risk of infection or exponential interpolation using estimates of case-detection gaps for 3 years. In this report, this method is used for 54 countries that accounted for 17% of the estimated global number of incident cases in 2016.

Of the four methods, the last one is the least preferred and it is relied upon only if one of the other three methods cannot be used. As explained in **Box 3.1**, the underlying principle for the WHO Global Task Force on TB Impact Measurement since its establishment in 2006 has been that estimates of the level of and trends in TB disease burden should be based on direct measurements from routine surveillance and surveys as much as possible, as opposed to indirect estimates that rely on modelling and expert opinion.

Further details about these methods are provided in the **online technical appendix**.[1]

[1] The **online technical appendix** is available at http://www.who.int/tb/publications/global_report/en/.

3.1.2 Estimates of TB incidence in 2016

Globally in 2016 there were an estimated 10.4 million incident cases of TB (range, 8.8 million to 12.2 million),[2] equivalent to 140 cases per 100 000 population (estimates of absolute numbers are shown in **Table 3.2** and estimates of rates per capita are shown in **Table 3.3**).

Most of the estimated number of cases in 2016 occurred in the WHO South-East Asia Region (45%), the WHO African Region (25%) and the WHO Western Pacific Region (17%); smaller proportions of cases occurred in the WHO Eastern Mediterranean Region (7%), the WHO European Region (3%) and the WHO Region of the Americas (3%). The 30 high TB burden countries[3] accounted for 87% of all estimated incident cases worldwide. The five countries that stood out as having the largest number of incident cases in 2016 were (in descending order) India, Indonesia, China, the Philippines and Pakistan (**Fig. 3.3**), which together accounted for 56% of the global total. Of these, China, India and Indonesia alone accounted for 45% of global cases in 2016. Nigeria and South Africa each accounted for 4% of the global total.

The annual number of incident TB cases relative to population size (the incidence rate) varied widely among countries in 2016, from under 10 per 100 000 population in most high-income countries to 150–300 in most of the 30 high TB burden countries (**Fig. 3.4**), and above 500 in a

[2] Here and elsewhere in the report, "range" refers to the 95% uncertainty interval.

[3] These countries are listed in **Table 3.2** and **Table 3.3**. For an explanation of how the list of 30 high TB burden countries was defined, see **Chapter 2**.

TABLE 3.2

Estimated epidemiological burden of TB in 2016 for 30 high TB burden countries, WHO regions and globally. Numbers in thousands.[a]

	POPULATION	HIV-NEGATIVE TB MORTALITY		HIV-POSITIVE TB MORTALITY[b]		INCIDENCE		HIV-POSITIVE TB INCIDENCE	
		BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Angola	29 000	18	10–29	6.9	3.4–12	107	66–156	18	8.5–30
Bangladesh	163 000	66	43–94	0.18	0.09–0.30	360	262–474	0.50	0.25–0.84
Brazil	208 000	5.4	4.9–5.9	1.9	1.4–2.4	87	74–100	11	9.1–13
Cambodia	16 000	3.2	2.1–4.4	0.45	0.29–0.66	54	35–78	1.3	0.85–1.9
Central African Republic	5 000	2.7	1.5–4.2	2.5	1.3–4.0	19	12–27	6.2	3.3–9.9
China	1 404 000	50	34–70	1.8	0.7–3.4	895	766–1 030	11	6.9–15
Congo	5 000	3.1	1.7–4.8	2.1	1.1–3.4	19	12–28	5.1	2.6–8.4
DPR Korea	25 000	11	6.8–16	0.05	0.02–0.09	130	113–148	0.28	0.14–0.46
DR Congo	79 000	53	31–80	8.5	4.0–15	254	165–363	20	13–29
Ethiopia	102 000	26	16–37	4.0	2.7–5.4	182	128–245	14	9.6–19
India[c]	1 324 000	423	324–534	12	6.6–19	2 790	1 440–4 570	87	56–125
Indonesia	261 000	110	75–152	13	6.2–23	1 020	660–1 460	45	21–78
Kenya	48 000	29	16–45	24	14–36	169	103–250	53	32–79
Lesotho	2 000	1.1	0.56–1.8	5.2	3.3–7.7	16	10–23	12	7.3–17
Liberia	5 000	2.8	1.6–4.2	0.96	0.60–1.4	14	9.2–20	2.2	1.4–3.2
Mozambique	29 000	22	13–33	33	20–48	159	103–227	72	46–104
Myanmar	53 000	25	16–35	4.9	3.5–6.6	191	141–249	18	13–24
Namibia	2 000	0.75	0.48–1.1	0.87	0.61–1.2	11	8.5–14	4.2	2.7–6.0
Nigeria	186 000	115	67–176	39	23–58	407	266–579	63	40–93
Pakistan	193 000	44	34–55	2.1	0.98–3.6	518	335–741	6.9	3.2–12
Papua New Guinea	8 000	3.6	2.4–50	0.82	0.45–1.3	35	28–42	3.6	2.0–5.5
Philippines	103 000	22	22–22	0.30	<0.01–2.6	573	321–895	6.0	2.5–11
Russian Federation	144 000	12	11–12	1.7	0.85–2.7	94	61–135	18	12–26
Sierra Leone	7 000	3.4	2.0–5.2	1.0	0.66–1.5	22	14–32	3.1	2.0–4.5
South Africa	56 000	23	17–29	101	67–142	438	304–595	258	176–355
Thailand	69 000	8.6	7.2–10	3.9	2.3–5.9	119	70–180	10	6.1–16
UR Tanzania	56 000	28	13–50	27	12–46	160	75–275	54	35–78
Viet Nam	95 000	13	8.4–18	0.85	0.63–1.1	126	103–151	4.2	3.4–5.1
Zambia	17 000	4.8	2.8–7.3	12	7.9–18	62	40–89	36	23–52
Zimbabwe	16 000	1.2	0.71–1.7	4.4	3.0–6.1	34	24–44	23	15–32
High TB burden countries	4 710 000	1 130	998–1 270	317	268–369	9 060	7 450–10 800	866	755–986
Africa	1 020 000	417	351–488	320	272–372	2 590	2 310–2 900	764	660–876
The Americas	996 000	17	16–18	6.2	5.6–6.9	274	255–294	30	28–33
Eastern Mediterranean	669 000	82	69–95	3.0	1.8–4.5	766	573–985	9.9	5.9–15
Europe	916 000	26	25–27	5.1	3.9–6.4	290	251–333	34	26–42
South-East Asia	1 950 000	652	542–772	35	25–46	4 670	3 190–6 440	163	120–211
Western Pacific	1 890 000	103	85–123	5.0	3.0–7.3	1 800	1 500–2 130	29	23–36
GLOBAL	7 440 000	1 300	1 160–1 440	374	325–427	10 400	8 770–12 200	1 030	915–1 150

[a] Numbers shown to two significant figures if under 100 and to three significant figures otherwise.
[b] Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD-10.
[c] Estimates of TB incidence and mortality for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.

TABLE 3.3

Estimated epidemiological burden of TB in 2016 for 30 high TB burden countries, WHO regions and globally. Rates per 100 000 population except where indicated.

	HIV-NEGATIVE TB MORTALITY		HIV-POSITIVE TB MORTALITY[a]		TOTAL TB INCIDENCE		HIV PREVALENCE IN INCIDENT TB (%)	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Angola	64	36–99	24	12–41	370	230–543	16	10–24
Bangladesh	40	26–58	0.11	0.05–0.18	221	161–291	0.14	0.08–0.22
Brazil	2.6	2.3–2.9	0.90	0.66–1.2	42	36–48	13	12–14
Cambodia	20	14–28	2.9	1.8–4.2	345	223–493	2.5	2.2–2.7
Central African Republic	59	33–92	54	29–87	407	263–581	33	22–45
China	3.6	2.4–5.0	0.13	0.05–0.24	64	55–74	1.2	0.50–2.1
Congo	60	34–93	41	21–66	378	240–547	26	17–37
DPR Korea	43	27–63	0.20	0.09–0.35	513	446–584	0.21	0.11–0.35
DR Congo	67	39–101	11	5.1–19	323	209–461	8.0	4.6–12
Ethiopia	25	16–36	3.9	2.6–5.3	177	125–239	7.6	7.0–8.3
India[b]	32	24–40	0.92	0.50–1.5	211	109–345	3.1	2.8–3.5
Indonesia	42	29–58	5.1	2.4–8.7	391	253–558	4.4	2.5–6.8
Kenya	60	33–93	50	30–75	348	213–516	31	29–33
Lesotho	49	26–80	238	148–350	724	468–1 030	72	64–80
Liberia	60	35–91	21	13–30	308	199–440	16	14–18
Mozambique	75	44–115	114	70–167	551	356–787	45	40–50
Myanmar	47	30–66	9.3	6.7–12	361	266–471	9.5	8.7–10
Namibia	30	20–44	35	25–48	446	342–565	38	37–40
Nigeria	62	36–95	21	12–31	219	143–311	16	13–18
Pakistan	23	18–29	1.1	0.51–1.9	268	174–383	1.3	0.74–2.1
Papua New Guinea	44	29–62	10	5.5–16	432	352–521	10	6.0–15
Philippines	21	21–22	0.29	<0.01–2.5	554	311–866	1.1	0.60–1.6
Russian Federation	8.2	7.8–8.6	1.2	0.59–1.9	66	42–94	19	18–21
Sierra Leone	47	28–70	14	9.0–20	304	195–435	14	13–15
South Africa	41	31–52	181	120–254	781	543–1 060	59	53–65
Thailand	13	10–15	5.7	3.4–8.6	172	102–261	8.8	7.9–9.6
UR Tanzania	51	23–90	48	22–83	287	136–495	34	30–38
Viet Nam	14	8.9–19	0.90	0.66–1.2	133	109–159	3.3	3.1–3.6
Zambia	29	17–44	74	48–107	376	244–535	58	53–63
Zimbabwe	7.2	4.4–11	27	19–38	208	152–273	67	65–69
High TB burden countries	24	21–27	6.7	5.7–7.8	192	158–230	9.7	7.5–12
Africa	41	34–48	31	27–36	254	227–284	30	24–35
The Americas	1.7	1.6–1.8	0.63	0.56–0.70	27	26–29	11	9.8–12
Eastern Mediterranean	12	10–14	0.45	0.27–0.68	114	86–147	1.3	0.71–2.1
Europe	2.8	2.8–2.9	0.55	0.43–0.69	32	27–36	12	8.6–15
South-East Asia	33	28–40	1.8	1.3–2.4	240	164–331	3.6	2.1–5.4
Western Pacific	5.4	4.5–6.5	0.26	0.16–0.39	95	79–113	1.6	1.2–2.1
GLOBAL	17	16–19	5.0	4.4–5.7	140	118–164	10	8.1–12

[a] Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD–10.
[b] Estimates of TB incidence and mortality for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.

FIG. 3.3

Estimated TB incidence in 2016, for countries with at least 100 000 incident cases

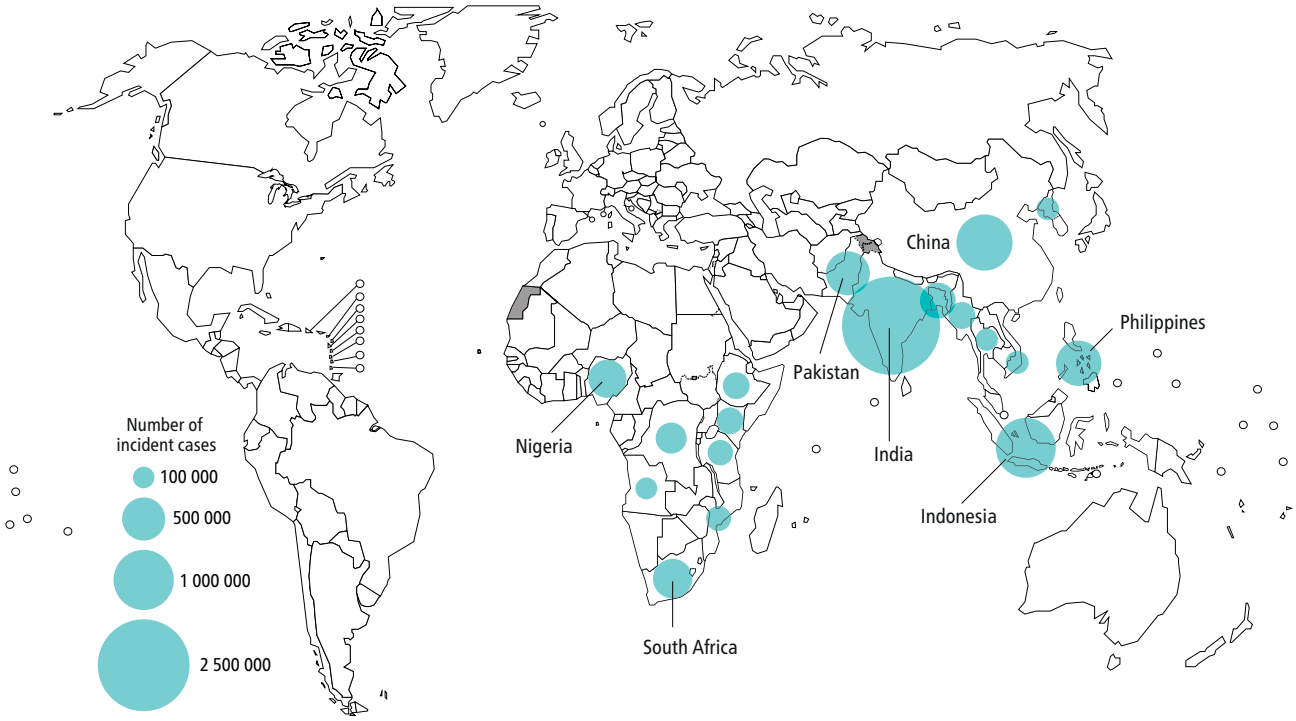


FIG. 3.4

Estimated TB incidence rates, 2016

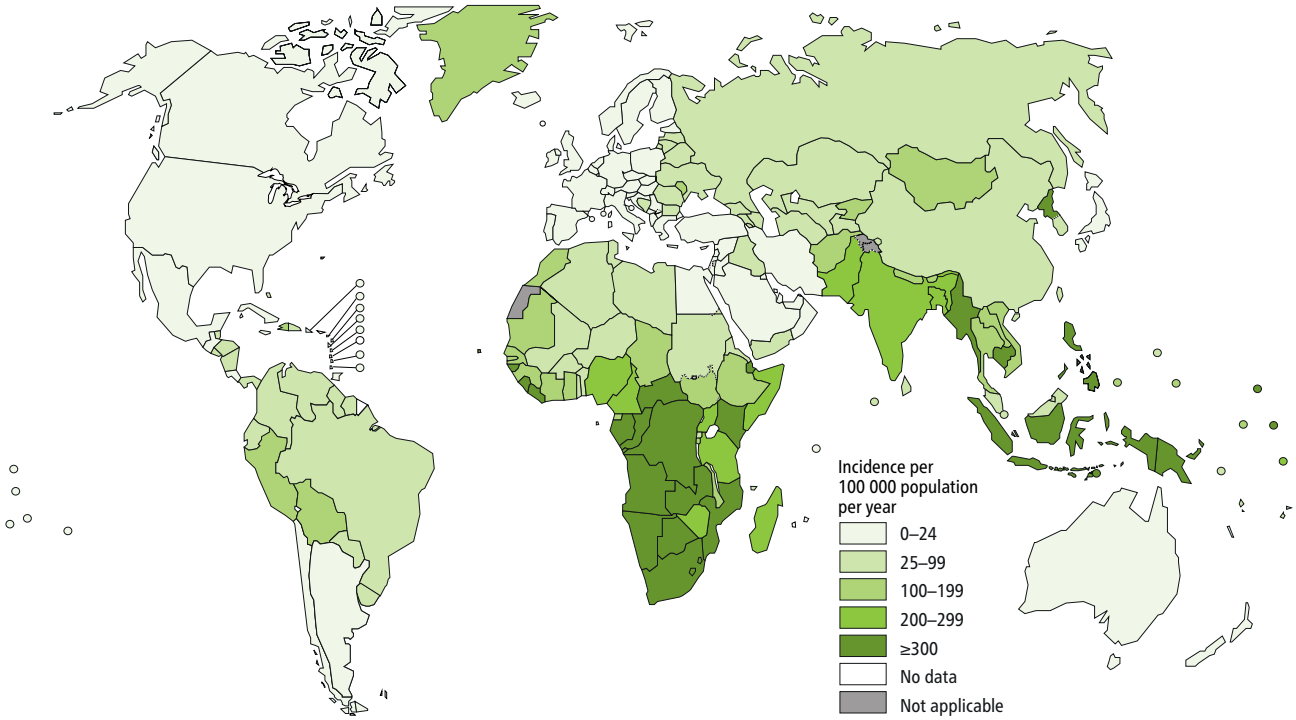
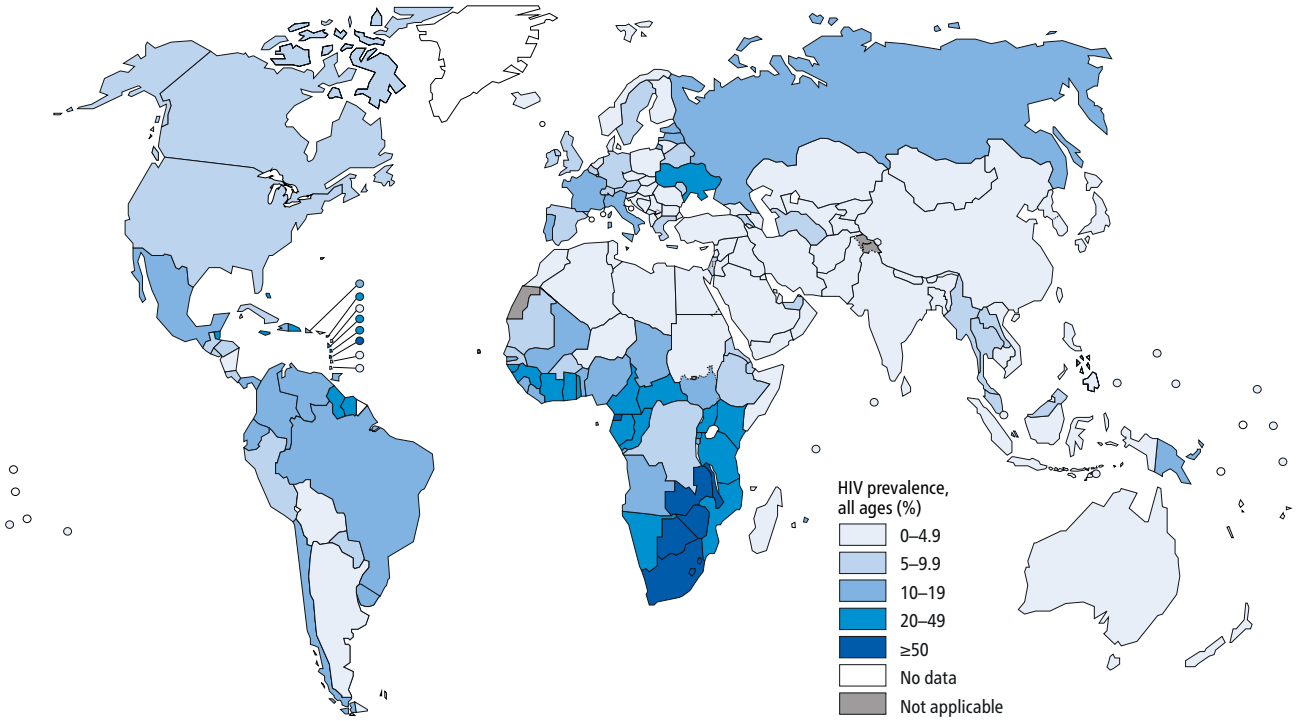


FIG. 3.5

Estimated HIV prevalence in new and relapse TB cases, 2016



few countries including the Democratic People's Republic of Korea, Lesotho, Mozambique, the Philippines and South Africa (Table 3.3).

An estimated 10% (range, 8–12%) of the incident TB cases in 2016 were among people living with HIV (Table 3.2, Table 3.3). The proportion of TB cases coinfected with HIV was highest in countries in the WHO African Region, exceeding 50% in parts of southern Africa (Fig. 3.5). The risk of developing TB in the 37 million people living with HIV was 21 times higher than the risk in the rest of the world population (range, 16–27). The relative risk increases as the prevalence of HIV in the general population decreases.

Estimates of the incidence of zoonotic TB are shown in Box 3.4.

3.1.3 Estimated trends in TB incidence, 2000–2016

Consistent with previous global TB reports, the number of incident cases is falling slowly, in both absolute terms and per capita (Fig. 3.6, Fig. 3.7). Globally, the average rate of decline in the TB incidence rate was 1.4% per year in 2000–2016, and 1.9% between 2015 and 2016. This needs to accelerate to 4–5% per year by 2020 to achieve the milestones for reductions in cases and deaths set in the End TB Strategy (Chapter 2).

Trends are shown for the six WHO regions in Fig. 3.8 and for the 30 high TB burden countries in Fig. 3.9. The fastest declines are in the WHO European Region (4.6% from 2015 to 2016). The estimated decline in the incidence rate since 2010 has exceeded 4% per year in several high TB burden countries, including Zimbabwe (11%), Lesotho (7%), Kenya (6.9%), Ethiopia (6.9%), the United Republic of Tanzania (6.7%), Namibia (6.0%), Zambia (4.8%) and the Russian Federation (4.5%).

3.2 TB mortality

Deaths from TB among HIV-negative people are classified as TB deaths in the most recent version of the *International classification of diseases* (ICD-10).[1] When an HIV-positive person dies from TB, the underlying cause is classified as HIV. For consistency with these international classifications, this section makes a clear distinction between TB deaths in HIV-negative people and TB deaths in HIV-positive people.

3.2.1 Methods to estimate TB mortality

TB mortality among HIV-negative people can be measured directly using data from national vital registration (VR) systems, provided that these systems have high coverage and that causes of death are accurately determined and coded according to ICD-10. Sample VR systems covering representative areas of the country (the approach used, for example, in China) provide an interim solution. Mortality surveys can also be used to estimate deaths caused by TB. In 2016, most countries with a high burden of TB lacked national

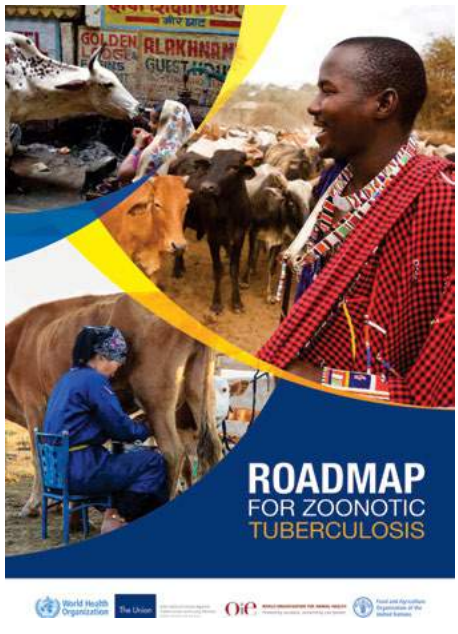
[1] World Health Organization. International statistical classification of diseases and health related problems (The) ICD-10. Geneva: WHO; 2016.(http://apps.who.int/classifications/icd10/browse/2016/en).

BOX 3.4

Zoonotic TB

Zoonotic TB is predominantly caused by *M. bovis*, which belongs to the *M. tuberculosis* complex. In humans, there were an estimated 147 000 new cases of zoonotic TB and 12 500 deaths due to the disease in 2016 (Table B3.4.1). This burden of disease cannot be reduced without improving standards of food safety and controlling bovine TB in the animal reservoir.

The organism is host-adapted to cattle, where it is referred to as bovine TB; it also causes TB in other animal species, including wildlife. Bovine TB has an important economic impact and threatens livelihoods.



In 2016–2017, a roadmap for zoonotic TB was developed by the tripartite of WHO, the World Organisation for Animal Health (OIE) and the Food and Agricultural Organization of the United Nations (FAO), together with the International Union Against Tuberculosis and Lung Disease. The roadmap calls for a multidisciplinary "One Health" approach that includes a more comprehensive analysis of risks, better coverage of interventions, more efficient use of resources, reduced costs and, ultimately, improved health of human and animal populations.

The roadmap is centred on 10 priorities grouped under three core themes:

Improve the scientific evidence base

- Collect and report more complete and accurate data
- Improve diagnosis in people
- Address research gaps

Reduce transmission at the animal–human interface

- Ensure safer food
- Improve animal health
- Reduce the risk to people

Strengthen intersectoral and collaborative approaches

- Increase awareness, engagement and collaboration
- Develop policies and guidelines
- Implement joint interventions
- Advocate for investment

TABLE B3.4.1

Estimated incidence and mortality due to *M. bovis* TB. Best estimates (absolute numbers) are followed by the lower and upper bounds of the 95% uncertainty interval.

	INCIDENT CASES		DEATHS	
REGION	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	72 700	19 500–160 000	9 300	2 460–20 600
The Americas	822	223–1 810	41	11–90
Eastern Mediterranean	7 660	1 930–17 300	654	173–1 450
Europe	1 160	309–2 570	84	23–183
South-East Asia	46 700	11 100–107 000	2 080	548–4 620
Western Pacific	18 000	4 740–40 000	350	92–777
GLOBAL	147 000	71 800–249 000	12 500	4 870–23 700

FIG. 3.6

Global trends in the estimated number of incident TB cases and the number of TB deaths (in millions), 2000–2016. Shaded areas represent uncertainty intervals.

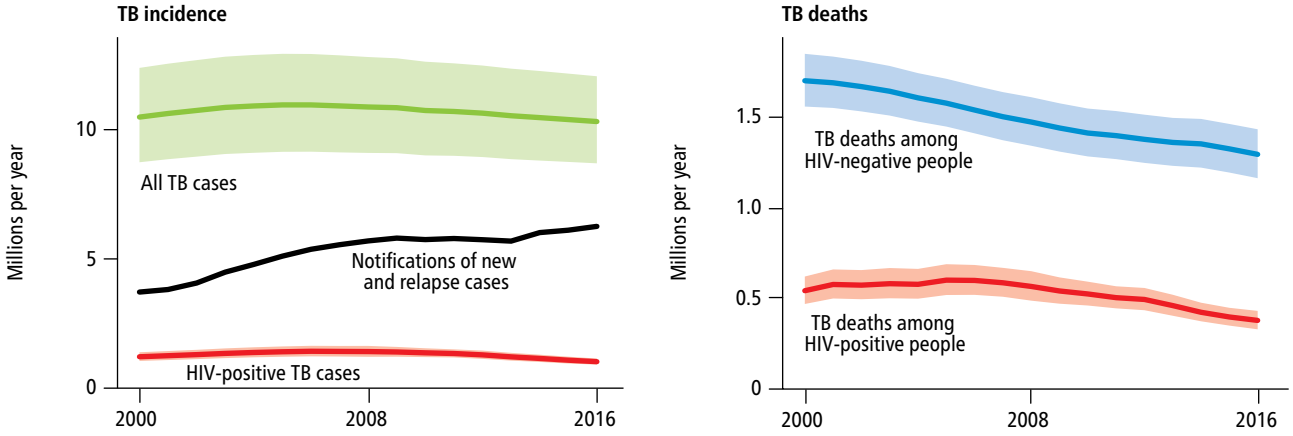
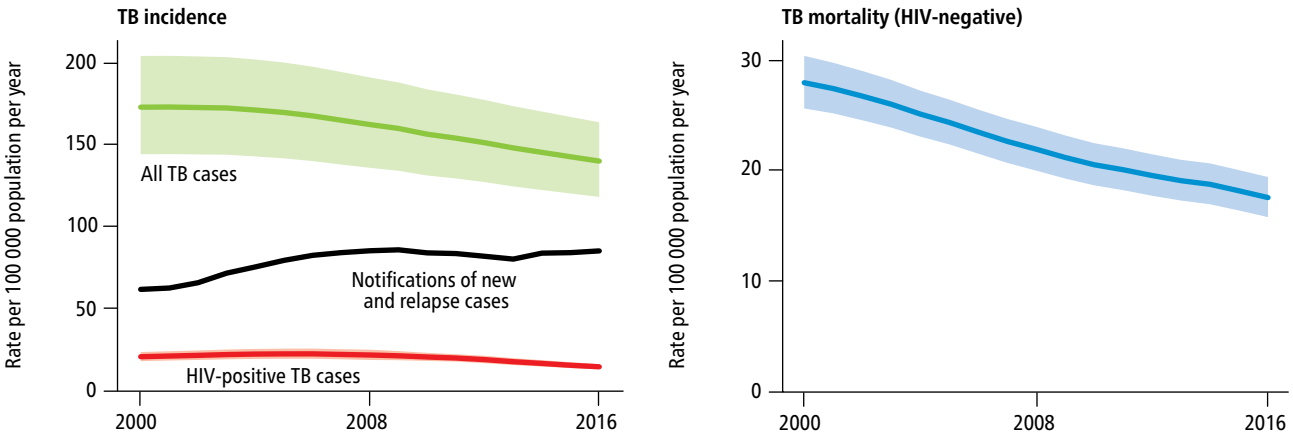


FIG. 3.7

Global trends in estimated TB incidence and mortality rates, 2000–2016. Shaded areas represent uncertainty intervals.



or sample VR systems, and few had conducted mortality surveys. In the absence of VR systems or mortality surveys, TB mortality can be estimated as the product of TB incidence and the case fatality ratio (CFR), or through ecological modelling using mortality data from countries with VR systems.

TB mortality among HIV-positive people is hard to measure even when VR systems are in place, because deaths among HIV-positive people are coded as HIV deaths, and contributory causes (e.g. TB) are often not reliably assessed and recorded. TB deaths among HIV-positive people were estimated as the product of TB incidence and the CFR, with the latter accounting for the protective effect of antiretroviral therapy (ART).

Until 2008, WHO estimates of TB mortality used VR data for only three countries. This was substantially improved to 89 countries in 2009, although most of the data were from countries in the WHO European Region and the WHO Region of the Americas, which accounted for less than 10% of the world's TB cases. For the current report, VR data were used for 129 countries (Fig. 3.10), which collectively accounted for 57% of the estimated number of TB deaths (among HIV-negative people) globally in 2016. For 18 countries, analyses of VR data and resulting estimates of TB deaths published by the Institute of Health Metrics and Evaluation (IHME) at the University of Washington, United States of America (USA) were used.[1] The WHO African Region is the part of the world that has the greatest need to introduce or strengthen VR systems in which causes of death are classified according to ICD-10.

Details about the methods used to produce estimates of TB mortality are provided in the **online technical appendix**.[2]

3.2.2 Estimates of TB mortality in 2016

Estimates of the number of deaths caused by TB are shown globally, for the six WHO regions and for the 30 high TB

[1] Downloaded from http://ghdx.healthdata.org/gbd-results-tool, July 2017.

[2] The **online technical appendix** is available at http://www.who.int/tb/publications/global_report/en/.