



# GLOBAL TUBERCULOSIS REPORT 2017

# Abbreviations

aDSM	active TB drug-safety monitoring and management	NCD	noncommunicable disease
AIDS	acquired immunodeficiency syndrome	NFC	near-field communication
ART	antiretroviral therapy	NHI	national health insurance
BCG	bacille Calmette-Guérin	NTP	national TB programme
BRICS	Brazil, Russian Federation, India, China and South Africa	OECD	Organisation for Economic Co-operation and Development
CFR	case fatality ratio	OIE	World Organisation for Animal Health
CHOICE	CHOosing Interventions that are Cost-Effective (WHO)	OOP	out-of-pocket
CI	confidence interval	PEPFAR	President's Emergency Plan For AIDS Relief
CRS	creditor reporting system	PMDT	programmatic management of drug-resistant TB
DST	drug susceptibility testing	P:N	prevalence to notification (ratio)
EBA	early bactericidal activity	PPM	public-public and public-private mix
EECA	Eastern Europe and Central Asia	RR-TB	rifampicin-resistant TB
FIND	Foundation for Innovative New Diagnostics	SDG	Sustainable Development Goal
GAF	Global Action Framework for TB Research	SHA	System of Health Accounts
GDP	gross domestic product	SMS	short message service
Global Fund	The Global Fund to Fight AIDS, Tuberculosis and Malaria	SPARKS	Social Protection Action Research & Knowledge Sharing
HBC	high-burden country	SRL	supranational reference laboratory
HIV	human immunodeficiency virus	TB	tuberculosis
IGRA	interferon gamma release assay	TBTC	TB Trial Consortium
IHME	Institute of Health Metrics and Evaluation	TDR	Special Programme for Research and Training in Tropical Diseases
ILO	International Labour Organization	TNF	tumour necrosis factor
LED	light-emitting diode	TPP	target product profile
LMIC	low- and middle-income country	TST	tuberculin skin test
LPA	line probe assay	UHC	universal health coverage
LTBI	latent TB infection	UN	United Nations
MAMS-TB	multi-arm, multi-stage TB	UNAIDS	Joint United Nations Programme on HIV/AIDS
MDG	Millennium Development Goal	UNICEF	United Nations Children's Fund
MDR/RR-TB	multidrug-resistant TB or rifampicin-resistant (but isoniazid-susceptible) TB	US	United States
MDR-TB	multidrug-resistant TB, defined as resistance to rifampicin and isoniazid	USAID	US Agency for International Development
M:F	male to female (ratio)	VICTORY	Viet Nam Integrated Center for TB and Respiratory Research
MoH	ministry of health	VR	vital registration
MOLISA	Ministry of Labour – Invalids and Social Affairs (Viet Nam)	WHO	World Health Organization
		WRD	WHO-recommended rapid diagnostic
		XDR-TB	extensively drug-resistant TB



**LEAVE  
NO ONE  
BEHIND**



**UNITE TO END TB**

## CHAPTER 1.

# Introduction

Tuberculosis (TB) has existed for millennia and remains a major global health problem. It causes ill-health for approximately 10 million people each year and is one of the top ten causes of death worldwide. For the past 5 years, it has been the leading cause of death from a single infectious agent, ranking above HIV/AIDS.<sup>1</sup> This is despite the fact that, with a timely diagnosis and correct treatment, most people who develop TB disease can be cured. Basic facts about TB are summarized in **Box 1.1**.

WHO has published a global TB report every year since 1997. The main aim of the report is to provide a comprehensive and up-to-date assessment of the TB epidemic, and of progress in prevention, diagnosis and treatment, at global, regional and country levels. This is done in the context of recommended global TB strategies and associated targets, as well as broader development goals set by the United Nations (UN). For the period 2016–2035, these are the End TB Strategy and Sustainable Development Goals (SDGs).

The End TB Strategy was endorsed by WHO's 194 Member States during the 2014 World Health Assembly, and is for the period 2016–2035. The SDGs were adopted by UN Member States in September 2015, and are for the period 2016–2030. The SDGs and the End TB Strategy share a common aim: to end the global TB epidemic. Targets set in the End TB Strategy include a 90% reduction in TB deaths and an 80% reduction in TB incidence by 2030, compared with 2015.

As usual, the 2017 global TB report is based primarily on data gathered from countries and territories. WHO has implemented annual rounds of global TB data collection since 1996, with an online system<sup>2</sup> used since 2009. In 2017, this system was opened for reporting in April. Following the May deadline for reporting, and subsequent review and follow-up of submitted data between June and August, data were available for 201 countries and territories that collectively account for more than 99% of the world's population and estimated TB cases. Data reported in 2017 were analysed alongside data collected in previous rounds of global TB data collection. Other data sources used in the report include the HIV department in WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS), which collect information about the provision of TB preventive treatment to people living with HIV, and about antiretroviral therapy for HIV-positive TB patients; the creditor reporting system of the Organisation for Economic Co-operation and Development

(OECD); the World Bank, for development indicators; and the WHO national health accounts database. All data are stored in WHO's global TB database.<sup>3</sup>

The years 2017 and 2018 are landmark ones for global and national efforts to end TB. In November 2017, WHO will host the first global Ministerial Conference on TB in Moscow, Russian Federation, with the theme of ending TB in the era of the SDGs. In the second half of 2018, this will be followed by the first UN General Assembly high-level meeting on TB, at which a multisectoral approach to ending TB and an associated multisectoral accountability framework will be discussed by Heads of State. This global TB report, published shortly in advance of the WHO Ministerial Conference, provides the latest data and analysis to inform discussions and deliberations at both events.

Chapter 2 provides an overview of the SDGs, the End TB Strategy, and a new TB-SDG monitoring framework developed by WHO in 2017. This framework goes beyond the TB-specific indicators of the End TB Strategy and the SDG target that is specific to TB, focusing attention on 14 other indicators under seven SDGs that will influence the future course of the TB epidemic. Chapter 3 provides estimates of TB disease burden, and Chapter 4 provides data on diagnosis and treatment of TB, HIV-associated TB and drug-resistant TB, for the period 2000–2016. The topics of Chapter 5 and Chapter 6 are TB prevention services and TB financing, respectively. Chapter 7 assesses progress towards universal health coverage and analyses the latest status of, and trends in, other indicators in the TB-SDG monitoring framework. Chapter 8 discusses TB research and development, which is critical to achieving the technological breakthroughs required to end TB.

The report also has four annexes. Annex 1 describes the online WHO global TB database and provides further details about the 2017 round of global TB data collection. Annex 2 contains country profiles for the 30 high TB burden countries (profiles for other countries are available online<sup>4</sup>) and Annex 3 contains global and regional profiles. Annex 4 provides data tables that give details of key indicators for the most recent year for which data or estimates are available, for all countries.

<sup>1</sup> Further details are provided in **Chapter 3**.

<sup>2</sup> <https://extranet.who.int/tme>

<sup>3</sup> Further details are provided in **Annex 1**.

<sup>4</sup> [www.who.int/tb/data](http://www.who.int/tb/data)

## BOX 1.1

### Basic facts about TB

TB is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. It typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB). The disease is spread when people who are sick with pulmonary TB expel bacteria into the air, for example by coughing. Overall, a relatively small proportion (5–15%) of the estimated 1.7 billion people infected with *M. tuberculosis* will develop TB disease during their lifetime. However, the probability of developing TB disease is much higher among people infected with HIV, and also higher among people affected by risk factors such as under-nutrition, diabetes, smoking and alcohol consumption.

Diagnostic tests for TB disease include the following:

- **Rapid molecular tests** – The only rapid test for diagnosis of TB currently recommended by WHO is the Xpert® MTB/RIF assay (Cepheid, USA). It can provide results within 2 hours, and was initially recommended (in 2010) for diagnosis of pulmonary TB in adults. Since 2013, it has also been recommended for use in children and to diagnose specific forms of extrapulmonary TB. The test has much better accuracy than sputum smear microscopy;
- **Sputum smear microscopy** – Developed more than 100 years ago, this technique requires the examination of sputum samples using a microscope to determine the presence of bacteria. In the current case definitions recommended by WHO, one positive result is required for a diagnosis of smear-positive pulmonary TB;
- **Culture-based methods** – The current reference standard, they require more developed laboratory capacity and can take up to 12 weeks to provide results.

Globally, use of rapid molecular tests is increasing, and many countries are phasing out the use of smear microscopy for diagnostic purposes (although microscopy and culture remain necessary for treatment monitoring). Despite advances in diagnostics, a considerable proportion of the TB cases reported to WHO are still clinically diagnosed rather than bacteriologically confirmed. In 2016, for example, only 57% of the pulmonary cases reported to WHO were bacteriologically confirmed.

There are also tests for TB that is resistant to first-line and second-line anti-TB drugs. They include Xpert MTB/RIF, which simultaneously tests for TB and resistance to rifampicin (the most effective first-line anti-TB drug); rapid line probe assays (LPAs) that test for resistance to rifampicin and isoniazid (referred to as first-line LPAs); a rapid LPA that tests for resistance to fluoroquinolones and injectable anti-TB drugs (referred to as a second-line LPA); and sequencing technologies. First-line LPAs were

first recommended by WHO in 2008; the second-line LPA was first recommended in May 2016. Culture-based methods currently remain the reference standard for drug susceptibility testing.

Without treatment, the mortality rate from TB is high. Studies of the natural history of TB disease in the absence of treatment with anti-TB drugs (conducted before drug treatments became available) found that about 70% of individuals with sputum smear-positive pulmonary TB died within 10 years of being diagnosed, as did about 20% of people with culture-positive (but smear-negative) pulmonary TB.<sup>a</sup>

Effective drug treatments were first developed in the 1940s. The currently recommended treatment for cases of drug-susceptible TB is a 6-month regimen of four first-line drugs: isoniazid, rifampicin, ethambutol and pyrazinamide. The Global TB Drug Facility supplies a complete 6-month course for about US\$ 40 per person. Treatment success rates of at least 85% for cases of drug-susceptible TB are regularly reported to WHO by its 194 Member States. Treatment for rifampicin-resistant TB (RR-TB) and multidrug-resistant TB (MDR-TB)<sup>b</sup> is longer, and requires more expensive and more toxic drugs. Until early 2016, the treatment regimens recommended by WHO typically lasted for 20 months, and cost about US\$ 2000–5000 per person. As a result of new evidence from several countries, WHO issued updated guidance in May 2016. Shortened regimens of 9–12 months are now recommended for patients (other than pregnant women) with pulmonary RR-TB or MDR-TB that is not resistant to second-line drugs. The cost of a shortened drug regimen is about US\$ 1000 per person. The latest data reported to WHO show a treatment success rate for MDR-TB of 54%, globally, reflecting high rates of loss to follow-up, unevaluated treatment outcomes and treatment failure.

There are 17 TB drugs in clinical trials and combination regimens that include new compounds as well as other drugs are also being tested in clinical trials. The bacille Calmette-Guérin (BCG) vaccine, which was developed almost 100 years ago and has been shown to prevent severe forms of TB in children, is still widely used. However, there is currently no vaccine that is effective in preventing TB disease in adults, either before or after exposure to TB infection. There are 12 TB vaccines in Phase I, Phase II or Phase III trials.

<sup>a</sup> Tiemersma EW, van der Werf MJ, Borgdorff MW, Williams BG, Nagelkerke NJ. Natural history of tuberculosis: duration and fatality of untreated pulmonary tuberculosis in HIV negative patients: a systematic review. *PLoS One*. 2011;6(4):e17601 (<http://www.ncbi.nlm.nih.gov/pubmed/21483732>, accessed 27 July 2016).

<sup>b</sup> Defined as resistance to isoniazid and rifampicin, the two most powerful anti-TB drugs.



**Children in Batad, Philippines**

IAN TROWER / ALAMY STOCK PHOTO

## CHAPTER 2.

# The Sustainable Development Goals and the End TB Strategy

From 2000 to 2015, global and national efforts to reduce the burden of tuberculosis (TB) disease were focused on achieving targets set within the context of the Millennium Development Goals (MDGs). The MDGs were established by the United Nations (UN) in 2000 and targets were set for 2015. Target 6c of MDG 6 was to “halt and reverse” TB incidence. The Stop TB Partnership, established in 2001, adopted this target and set two additional targets. These were to halve TB prevalence and TB mortality rates by 2015 compared with their levels in 1990. The global TB strategy developed by WHO for the decade 2006–2015, the Stop TB Strategy, had the overall goal of reaching all three targets. In October 2015, WHO published its assessment of whether the 2015 global TB targets for reductions in TB incidence, prevalence and mortality were achieved.<sup>1</sup>

In 2016, the MDGs were succeeded by a new set of goals, known as the Sustainable Development Goals (SDGs). Adopted by the UN in September 2015 following 3 years of consultations, the SDG framework of goals, targets and indicators is for the period 2016–2030.<sup>2</sup> Similarly, WHO initiated work on a new global TB strategy in 2012, which was completed in 2014. The End TB Strategy was unanimously endorsed by all WHO Member States at the 2014 World Health Assembly, and is for the period 2016–2035.<sup>3</sup>

This chapter provides an overview of both the SDGs (Section 2.1) and the End TB Strategy (Section 2.2). It then defines and explains a new TB-SDG monitoring framework that has been developed by WHO in 2017 (Section 2.3). This framework is designed to focus attention on, and encourage analysis of, SDG targets and indicators that will influence the course of the TB epidemic. This is important, because achieving the ambitious targets set in the SDGs and End TB Strategy requires that these broader influences on the risks of developing TB and the consequences of TB disease are addressed.<sup>4</sup>

For the first 5 years of the SDGs and End TB Strategy (2016–2020), WHO has defined three lists of high burden countries (HBCs): for TB, TB/HIV and multidrug-resistant TB (MDR-TB). Particular attention is given to the countries in each of these lists throughout this report, and for this reason they are presented and explained in Section 2.4.

## 2.1 The Sustainable Development Goals

The 17 SDGs are shown in Box 2.1. Departures from the MDGs include a broader agenda (17 goals compared with the previous eight), one consolidated goal on health compared with three health-related MDGs, and a desire for universal relevance rather than a focus on issues mostly of concern to developing countries.

The consolidated goal on health is SDG 3. It is defined as “Ensure healthy lives and promote well-being for all at all ages”, and 13 targets have been set for this goal (Box 2.2). One of these targets, Target 3.3, explicitly mentions TB: “By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases”. The language of “ending epidemics” is also now a prominent element of global health strategies developed by WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS) for the post-2015 era,<sup>5</sup> including the End TB Strategy (Section 2.2). Such language is much more ambitious than the MDG language of “halting and reversing” epidemics (or “stopping” them, as in the Stop TB Strategy). The TB indicator for Target 3.3 is TB incidence per 100 000 population per year.

SDG 3 also includes a target (Target 3.8) related to universal health coverage (UHC) in which TB is explicitly mentioned. The WHO/World Bank definition of UHC is that all people receive the health services they need, while at the same time ensuring that the use of these services does not expose the user to financial hardship.<sup>6</sup> Target 3.8 includes an indicator on the coverage of essential prevention, treatment and care interventions. This is a composite indicator based

<sup>1</sup> World Health Organization. Global tuberculosis report 2015. Geneva: WHO; 2015 ([http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf), accessed 2 August 2017).

<sup>2</sup> United Nations. Sustainable Development Goals (<https://sustainabledevelopment.un.org/topics/sustainabledevelopmentgoals>, accessed 2 August 2017).

<sup>3</sup> Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's new End TB Strategy. *Lancet*. 2015;385(9979):1799–1801 (<http://www.sciencedirect.com/science/article/pii/S0140673615605700?via%3Dihub>, accessed 2 August 2017).

<sup>4</sup> Analysis of these indicators is featured in Chapter 7. In Annex 2, the latest data and recent trends for each indicator are shown for high TB burden countries. In Annex 4, the latest data for each indicator are shown for all countries.

<sup>5</sup> World Health Organization. Accelerating progress on HIV, tuberculosis, malaria, hepatitis and neglected tropical diseases: A new agenda for 2016–2030. Geneva: WHO; 2015 (<http://www.who.int/about/structure/organigram/htm/progress-hiv-tb-malaria-ntd/en/>, accessed 2 August 2017).

<sup>6</sup> World Health Organization/World Bank Group. Tracking universal health coverage: first global monitoring report. Geneva: WHO; 2015 ([http://apps.who.int/iris/bitstream/10665/174536/1/9789241564977\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/174536/1/9789241564977_eng.pdf?ua=1), accessed 2 August 2017).

**BOX 2.1**

## The Sustainable Development Goals

- Goal 1. End poverty in all its forms everywhere
- Goal 2. End hunger, achieve food security and improved nutrition and promote sustainable agriculture
- Goal 3. Ensure healthy lives and promote well-being for all at all ages
- Goal 4. Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all
- Goal 5. Achieve gender equality and empower all women and girls
- Goal 6. Ensure availability and sustainable management of water and sanitation for all
- Goal 7. Ensure access to affordable, reliable, sustainable and modern energy for all
- Goal 8. Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all
- Goal 9. Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation
- Goal 10. Reduce inequality within and among countries
- Goal 11. Make cities and human settlements inclusive, safe, resilient and sustainable
- Goal 12. Ensure sustainable consumption and production patterns
- Goal 13. Take urgent action to combat climate change and its impacts<sup>a</sup>
- Goal 14. Conserve and sustainably use the oceans, seas and marine resources for sustainable development
- Goal 15. Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss
- Goal 16. Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels
- Goal 17. Strengthen the means of implementation and revitalize the Global Partnership for Sustainable Development



<sup>a</sup> Acknowledging that the United Nations Framework Convention on Climate Change is the primary international, intergovernmental forum for negotiating the global response to climate change.



**BOX 2.2**

## Sustainable Development Goal 3 and its 13 targets

### SDG3: Ensure healthy lives and promote well-being for all at all ages

#### Targets

- 3.1 By 2030, reduce the global maternal mortality ratio to less than 70 per 100 000 live births
- 3.2 By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1000 live births and under-5 mortality to at least as low as 25 per 1000 live births
- 3.3 By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases
- 3.4 By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being
- 3.5 Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol
- 3.6 By 2020, halve the number of global deaths and injuries from road traffic accidents
- 3.7 By 2030, ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes
- 3.8 Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all
- 3.9 By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination
- 3.a Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries, as appropriate
- 3.b Support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade-Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all
- 3.c Substantially increase health financing and the recruitment, development, training and retention of the health workforce in developing countries, especially in least developed countries and small island developing States
- 3.d Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks

TRIPS, Trade-Related Aspects of Intellectual Property Rights

on the coverage of 16 so-called “tracer interventions”,<sup>1</sup> one of which is TB treatment.

In contrast with the MDGs, the SDGs include considerable emphasis on disaggregated analysis and reporting of data (as well as reporting for an entire country). Depending on the indicator, examples include disaggregation by age, sex, location and economic status (e.g. bottom 40%, or bottom versus top income quintiles). Some indicators also give particular attention to specific subpopulations, such as

pregnant women, people with disabilities, victims of work injuries and migrants. In addition to the specification of such disaggregation for many SDG indicators under SDGs 1–16, SDG 17 includes two targets and associated indicators under the subheading of “Data, monitoring and accountability”, which specifically refer to disaggregated data and mechanisms needed to generate such data (Table 2.1). Emphasis is also given to the importance of death registration within national vital registration systems for accurate tracking of causes of death (this is Part b of Indicator 17.19). Strengthening national vital registration systems as the basis for direct measurement of the number of TB deaths is one of the five strategic

<sup>1</sup> There are many different prevention and treatment interventions. In this context, 16 interventions have been selected as “tracers” for progress towards UHC for all interventions.

**TABLE 2.1**

**SDG 17, and targets and indicators related to data, monitoring and accountability**

SDG 17: Strengthen the means of implementation and revitalize the global partnership for sustainable development	
TARGETS	INDICATORS
<p><b>17.18</b> By 2020, enhance capacity-building support to developing countries, including for least developed countries and small island developing States, to increase significantly the availability of high-quality, timely and reliable data disaggregated by income, gender, age, race, ethnicity, migratory status, disability, geographic location and other characteristics relevant in national contexts</p>	<p><b>17.18.1</b> Proportion of sustainable development indicators produced at the national level <i>with full disaggregation when relevant to the target</i>, in accordance with the Fundamental Principles of Official Statistics</p>
<p><b>17.19</b> By 2030, build on existing initiatives to develop measurements of progress on sustainable development that complement gross domestic product, and support statistical capacity-building in developing countries</p>	<p><b>17.19.2</b> Proportion of countries that (a) have conducted at least one population and housing census in the last 10 years; and (b) have achieved 100 per cent birth registration and 80 per cent death registration</p>

areas of work of the WHO Global Task Force on TB Impact Measurement, as discussed further in [Chapter 3](#).

Disaggregation is intended to inform analysis of within-country inequalities and associated assessments of equity, with findings used to identify particular areas or subpopulations where progress is lagging and greater attention is needed. Such disaggregation is also an important consideration for the TB community, given the influence of sex, age, socioeconomic status and differential access to health care on the risks for and consequences of TB infection and disease. [Chapter 3](#) and [Chapter 4](#) of this report include analyses of TB data disaggregated by age, sex and location.

**2.2 The End TB Strategy**

The End TB Strategy “at a glance” is shown in [Box 2.3](#).

The overall goal is to “End the global TB epidemic”, and there are three high-level, overarching indicators and related targets (for 2030, linked to the SDGs, and for 2035) and milestones (for 2020 and 2025). The three indicators are:

- the number of TB deaths per year;
- the TB incidence rate per year; and
- the percentage of TB-affected households that experience catastrophic costs as a result of TB disease.

The 2035 targets are a 95% reduction in TB deaths and a 90% reduction in the TB incidence rate, compared with levels in 2015. The 2030 targets are a 90% reduction in TB deaths and an 80% reduction in the TB incidence rate, compared with levels in 2015. The most immediate milestones, set for 2020, are a 35% reduction in TB deaths and a 20% reduction in the TB incidence rate, compared with levels in 2015. The trajectories of TB incidence and TB deaths that are required to reach these milestones and targets are shown in [Fig. 2.1](#). For the third indicator (the percentage of TB-affected households that experience catastrophic costs as a result of TB disease), the milestone for 2020 is zero, to be sustained thereafter.

The Stop TB Partnership has developed a *Global Plan to End TB, 2016–2020*,<sup>1</sup> which focuses on the actions and funding

needed to reach the 2020 milestones of the End TB Strategy. More details about this plan are provided in [Chapter 6](#).

Progress towards UHC and actions to address health-related risk factors for TB as well as broader social and economic determinants of TB will be fundamental to achieving the targets and milestones for reductions in TB cases and deaths. There are two reasons for this. First, reaching the milestones for reductions in TB cases and deaths set for 2020 and 2025 requires the annual decline in the global TB incidence rate to accelerate from 1.5% per year in 2015 to 4–5% per year by 2020, and then to 10% per year by 2025. A decline of 10% per year is equivalent to the best-ever performance to date at national level – for example, in countries in western Europe during the 1950s and 1960s. Declines of 10% per year have only been documented in the context of UHC combined with broader social and economic development. Second, the global proportion of people with TB who die from the disease (the case fatality ratio, or CFR) needs to be reduced to 10% by 2020 and then to 6.5% by 2025. A CFR of 6.5% is similar to the current level in many high-income countries, but is only possible if all those with TB disease can access high-quality treatment. Analysis of CFRs at global and national levels is included in [Chapter 3](#).

The percentage of TB patients and their households facing catastrophic costs is a good tracer for progress towards UHC as well as social protection. If UHC and social protection are in place, then people with TB should be able to access high-quality diagnosis and treatment without incurring catastrophic costs.

After 2025, an unprecedented acceleration in the rate at which TB incidence falls globally is required if the 2030 and 2035 targets are to be reached. Such an acceleration will depend on a technological breakthrough that can substantially reduce the risk of developing TB disease among the approximately 1.7 billion people<sup>2</sup> who are already infected with *Mycobacterium tuberculosis*. Examples include an effective post-exposure vaccine or a short, efficacious and

<sup>1</sup> The Global Plan to End TB, 2016–2020. Geneva: Stop TB Partnership; 2015 (<http://www.stoptb.org/global/plan/>, accessed 2 August 2017).

<sup>2</sup> Houben RM, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. *PLoS Med*. 2016;13(10):e1002152 (<https://www.ncbi.nlm.nih.gov/pubmed/27780211>, accessed 2 August 2017).

## BOX 2.3 The End TB Strategy at a glance

VISION	A WORLD FREE OF TB — zero deaths, disease and suffering due to TB			
GOAL	END THE GLOBAL TB EPIDEMIC			
INDICATORS	MILESTONES		TARGETS	
	2020	2025	SDG 2030 <sup>a</sup>	END TB 2035
Percentage reduction in the absolute number of TB deaths (compared with 2015 baseline)	35%	75%	90%	95%
Percentage reduction in the TB incidence rate (compared with 2015 baseline)	20%	50%	80%	90%
Percentage of TB-affected households experiencing catastrophic costs due to TB (level in 2015 unknown)	0%	0%	0%	0%

### PRINCIPLES

1. Government stewardship and accountability, with monitoring and evaluation
2. Strong coalition with civil society organizations and communities
3. Protection and promotion of human rights, ethics and equity
4. Adaptation of the strategy and targets at country level, with global collaboration

### PILLARS AND COMPONENTS

#### 1. INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION

- A. Early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
- B. Treatment of all people with TB including drug-resistant TB, and patient support
- C. Collaborative TB/HIV activities, and management of comorbidities
- D. Preventive treatment of persons at high risk, and vaccination against TB

#### 2. BOLD POLICIES AND SUPPORTIVE SYSTEMS

- A. Political commitment with adequate resources for TB care and prevention
- B. Engagement of communities, civil society organizations, and public and private care providers
- C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
- D. Social protection, poverty alleviation and actions on other determinants of TB

#### 3. INTENSIFIED RESEARCH AND INNOVATION

- A. Discovery, development and rapid uptake of new tools, interventions and strategies
- B. Research to optimize implementation and impact, and promote innovations

<sup>a</sup> Targets linked to the Sustainable Development Goals (SDGs).

safe treatment for latent TB infection (LTBI). The latest status of the development pipelines for new TB diagnostics, drugs and vaccines is presented in [Chapter 8](#).

To achieve the targets and milestones, the End TB Strategy has four underlying principles and three pillars. The principles are government stewardship and accountability, with monitoring and evaluation; a strong coalition with civil society organizations and communities; protection and promotion of human rights, ethics and equity; and adaptation of the strategy and targets at country level, with global collaboration. The three pillars are integrated, patient-centred TB care and prevention; bold policies and supportive systems (including UHC, social protection and action on TB determinants); and intensified research and innovation.

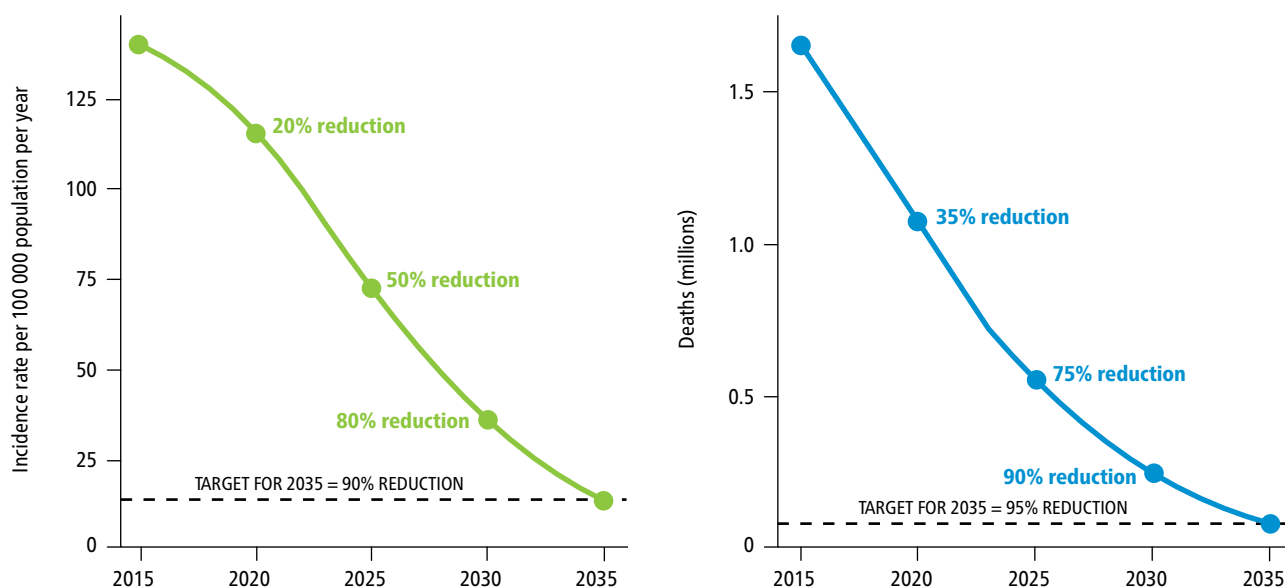
The 10 components of the three pillars are shown in [Box 2.3](#), and the 10 priority indicators (defined in March 2015 in association with the publication of a journal article about

the End TB Strategy)<sup>1</sup> to monitor their implementation are shown in [Table 2.2](#). The table also indicates the particular chapter of this report in which available data for each indicator can be found.

Data for five of the 10 indicators cannot be captured routinely using the standard recording and reporting forms for paper-based systems that are included in the latest revision of WHO's framework for TB case definitions and reporting.<sup>2</sup> Collection of data on the costs faced by TB patients

<sup>1</sup> Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's new End TB Strategy. *Lancet*. 2015;385(9979):1799–1801 (<http://www.sciencedirect.com/science/article/pii/S0140673615605700?via%3Dihub>, accessed 2 August 2017). The 10 indicators are defined and explained in an appendix.

<sup>2</sup> World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision (updated December 2014) (WHO/HTM/TB/2013.2). Geneva: WHO; 2013 ([www.who.int/iris/bitstream/10665/79199/1/9789241505345\\_eng.pdf](http://www.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf), accessed 2 August 2017).

**FIG. 2.1****Projected incidence and mortality curves that are required to reach End TB Strategy targets and milestones, 2015–2035**

and their households, and assessment of whether these are catastrophic (Indicator 3 in [Table 2.2](#)) requires periodic surveys of a representative sample of TB patients; further details are provided in [Chapter 7](#). For the other four indicators (Indicators 4, 5, 6 and 8 in [Table 2.2](#)), data may already be captured routinely in countries with electronic case-based systems for recording and reporting of data, or these systems can be adapted to do so. Alternatively, periodic surveys of the medical records or patient cards of a random sample of TB patients can be done. Further guidance is provided in WHO operational guidance on the End TB Strategy.<sup>1</sup>

### 2.3 A TB-SDG monitoring framework

Monitoring of TB-specific indicators is well established at global and national levels. For example, standardized monitoring of notifications of TB cases and their treatment outcomes at global and national levels has been in place since 1995, and estimates of TB incidence and mortality have been published annually by WHO for more than a decade. In the era of the End TB Strategy and SDGs, such monitoring will continue, alongside continued efforts to strengthen notification and vital registration systems so that they can be reliably used for direct measurement of TB incidence and TB deaths (see also [Chapter 3](#)), and expanded monitoring to include new priority indicators (five of those listed in [Table 2.2](#) have been introduced in the context of the End TB Strategy).

As explained in [Section 2.2](#), achieving the End TB Strategy targets and milestones requires progress in reducing health-related risk factors for TB infection and disease, as well as

broader social and economic determinants of TB infection and disease. As explained in [Section 2.1](#), the SDG framework includes targets and indicators related to these risk factors and determinants. In this context, TB monitoring needs to be further expanded to include analysis of selected SDG indicators that will influence the course of the TB epidemic, to inform broader actions in the health sector and beyond that will be necessary to end the TB epidemic.

Previously published work has identified clear linkages between various SDG indicators and TB incidence.<sup>2,3,4,5</sup> In 2017, building on this previous work as well as further analysis of the relationship between SDG indicators and TB incidence,<sup>6</sup> WHO has developed a TB-SDG monitoring framework that comprises 14 indicators under seven SDGs ([Table 2.3](#)).

<sup>1</sup> World Health Organization. Implementing the End TB Strategy: the essentials. Geneva: WHO, 2016 ([http://www.who.int/tb/publications/2015/The\\_Essentials\\_to\\_End\\_TB/en/](http://www.who.int/tb/publications/2015/The_Essentials_to_End_TB/en/), accessed 2 August 2017). See in particular Part II, Section 2.4.

<sup>2</sup> Lönnroth K, Jaramillo E, Williams B, Dye C, Raviglione M. Tuberculosis: the role of risk factors and social determinants. In: Blas E & Kurup A (eds.), Equity, social determinants and public health programmes, WHO. 2010 ([http://apps.who.int/iris/bitstream/10665/44289/1/9789241563970\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44289/1/9789241563970_eng.pdf), accessed 2 August 2017).

<sup>3</sup> Lönnroth K, Castro KG, Chakaya JM, Chauhan LS, Floyd K, Glaziou P et al. Tuberculosis control and elimination 2010–50: cure, care, and social development. *Lancet*. 2010;375(9728):1814–1829 (<http://www.sciencedirect.com/science/article/pii/S0140673610604837?via%3Dihub>, accessed 2 August 2017).

<sup>4</sup> Lienhardt C, Glaziou P, Uplekar M, Lönnroth K, Getahun H, Raviglione M. Global tuberculosis control: lessons learnt and future prospects. *Nat Rev Microbiol*. 2012;10(6):407–416 (<https://www.nature.com/nrmicro/journal/v10/n6/full/nrmicro2797.html>, accessed 2 August 2017).

<sup>5</sup> Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Soc Sci Med*. 2009;68(12):2240–2246 (<http://www.sciencedirect.com/science/article/pii/S0277953609002111?via%3Dihub>, accessed 2 August 2017).

<sup>6</sup> Monitoring and evaluation of TB in the context of the Sustainable Development Goals: Background Paper for WHO Ministerial Conference on “TB in the context of the Sustainable Development Goals”. Available on request.

**TABLE 2.2**

**Top 10 indicators (not ranked) for monitoring implementation of the End TB Strategy at global and national levels, with recommended target levels that apply to all countries.** The target level is for 2025 at the latest.

	INDICATOR	RECOMMENDED TARGET LEVEL	MAIN RATIONALE FOR INCLUSION IN TOP 10	MAIN METHOD OF MEASUREMENT, AND RELEVANT CHAPTER OF THIS REPORT
1	<b>TB treatment coverage</b> <i>Number of new and relapse cases that were notified and treated, divided by the estimated number of incident TB cases in the same year, expressed as a percentage.</i>	≥90%	High-quality TB care is essential to prevent suffering and death from TB and to cut transmission. High coverage of appropriate treatment is a fundamental requirement for achieving the milestones and targets of the End TB Strategy. In combination, it is likely that these two indicators will be used as tracer indicators for monitoring progress towards UHC within the SDGs.	Routinely collected notification data used in combination with estimate of TB incidence. <a href="#">Chapter 4</a>
2	<b>TB treatment success rate</b> <i>Percentage of notified TB patients who were successfully treated. The target is for drug-susceptible and drug-resistant TB combined, although outcomes should also be reported separately.</i>	≥90%		Routinely collected data. <a href="#">Chapter 4</a>
3	<b>Percentage of TB-affected households that experience catastrophic costs due to TB<sup>a</sup></b> <i>Number of people treated for TB (and their households) who incur catastrophic costs (direct and indirect combined), divided by the total number of people treated for TB.</i>	0%	One of the End TB Strategy's three high-level indicators; a key marker of financial risk protection (one of the two key elements of UHC) and social protection for TB-affected households.	National survey of notified TB patients. <a href="#">Chapter 7</a>
4	<b>Percentage of new and relapse TB patients tested using a WHO-recommended rapid diagnostic (WRD) at the time of diagnosis</b> <i>Number of new and relapse TB patients tested using a WRD at the time of diagnosis, divided by the total number of new and relapse TB patients, expressed as a percentage.</i>	≥90%	Accurate diagnosis is a fundamental component of TB care. Rapid molecular diagnostic tests help to ensure early detection and prompt treatment.	Routinely collected data (as part of case-based surveillance), or national survey of medical records or patient cards of TB patients. <a href="#">Chapter 4</a>
5	<b>Latent TB infection (LTBI) treatment coverage</b> <i>Number of people living with HIV newly enrolled in HIV care and the number of children aged &lt;5 years who are household contacts of cases started on LTBI treatment, divided by the number eligible for treatment, expressed as a percentage (separately for each of the two groups).</i>	≥90%	Treatment of LTBI is the main treatment intervention available to prevent development of active TB disease in those already infected with <i>Mycobacterium tuberculosis</i> .	Routinely collected data (as part of case-based surveillance), or national survey of medical records or patient cards of people living with HIV and TB patients. <a href="#">Chapter 5</a>
6	<b>Contact investigation coverage</b> <i>Number of contacts of people with bacteriologically confirmed TB who were evaluated for TB, divided by the number eligible, expressed as a percentage.</i>	≥90%	Contact tracing is a key component of TB prevention, especially in children.	As above for LTBI.
7	<b>Drug-susceptibility testing (DST) coverage for TB patients</b> <i>Number of patients with bacteriologically confirmed pulmonary TB with a DST result for at least rifampicin, divided by the total number of notified cases of bacteriologically confirmed pulmonary TB in the same year, expressed as a percentage. DST coverage includes results from molecular (e.g. Xpert MTB/RIF) as well as conventional phenotypic DST results.</i>	100%	Testing for drug susceptibility for WHO-recommended drugs is essential to provide the right treatment for every person diagnosed with TB.	Routinely collected data (as part of case-based surveillance), or national survey of medical records or patient cards of TB patients. <a href="#">Chapter 4</a>
8	<b>Treatment coverage, new TB drugs</b> <i>Number of TB patients treated with regimens that include new (endorsed after 2010) TB drugs, divided by the number of notified patients eligible for treatment with new TB drugs, expressed as a percentage.</i>	≥90%	An indicator that is relevant to monitoring the adoption of innovations in all countries. <i>The definition of which patients are eligible patients for treatment with new drugs may differ among countries.</i>	As above for DST.
9	<b>Documentation of HIV status among TB patients</b> <i>Number of new and relapse TB patients with documented HIV status, divided by the number of new and relapse TB patients notified in the same year, expressed as a percentage.</i>	100%	One of the core global indicators used to monitor collaborative TB/HIV activities. Documentation of HIV status is essential to provide the best care for HIV-positive TB patients, including antiretroviral therapy.	Routinely collected data for all TB patients. <a href="#">Chapter 4</a>
10	<b>Case fatality ratio (CFR)</b> <i>Number of TB deaths divided by estimated number of incident cases in the same years, expressed as a percentage.</i>	≤5%	This is a key indicator for monitoring progress towards the 2020 and 2025 milestones. A CFR of 6% is required to achieve the 2025 global milestone for reductions in TB deaths and cases.	Mortality divided by incidence. In countries with a high-performance surveillance system, notifications approximate incidence. <a href="#">Chapter 3</a>

CFR, case fatality ratio; DST, drug-susceptibility testing; HIV, human immunodeficiency virus; LTBI, latent TB infection; SDG, Sustainable Development Goal; TB, tuberculosis; UHC, universal health coverage; WHO, World Health Organization; WRD, WHO-recommended rapid diagnostic.

<sup>a</sup> Catastrophic costs are provisionally defined as total costs that exceed 20% of annual household income.

**TABLE 2.3A**

**TB-SDG monitoring framework: indicators to monitor within SDG 3**

SDG 3: Ensure healthy lives and promote well-being for all at all ages					
SDG TARGETS FOR 2030	SDG INDICATORS	ALTERNATIVE INDICATORS TO MONITOR	RATIONALE	DATA SOURCE	COLLECT DATA FOR TB PATIENTS SPECIFICALLY?
3.3 End the epidemics of AIDS, TB, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases	3.3.1 Number of new HIV infections per 1000 uninfected population 3.3.2 TB incidence per 100 000 population	HIV prevalence	HIV is a strong risk factor for development of TB disease and is associated with poorer treatment outcomes. HIV prevalence (rather than incidence) will be monitored because it is directly measured and those newly infected with HIV are at lower risk of developing TB compared with those who have been infected for more than 1 year.	UNAIDS	Yes, already routinely collected.
				WHO	NA
3.4 Reduce premature mortality by one third from non-communicable diseases and promote mental health and well-being	3.4.1 Mortality rate attributed to cardiovascular disease, cancer, diabetes or chronic respiratory disease	Prevalence of diabetes	Diabetes is a strong risk factor for development of TB disease, although a link with TB incidence at the national (as opposed to individual) level has been difficult to establish due to confounding. Diabetes prevalence is more relevant than mortality for TB since it directly influences the risk of developing TB.	WHO	Could be considered at country level, to inform planning of care for comorbidities.
3.5 Strengthen prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol	3.5.2 Alcohol consumption per capita per year (in litres of pure alcohol) among those aged ≥15 years (harmful level defined nationally)	Prevalence of alcohol use disorder	Alcohol use is a strong risk factor for TB disease and poorer treatment outcomes at the individual level, although a link with TB incidence at the national (as opposed to individual) level has been hard to establish due to confounding. The prevalence of alcohol use disorder is the most relevant indicator in the context of TB.	WHO	Could be considered at country level, to inform planning of care for comorbidities.
3.8 Achieve UHC, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all	3.8.1 Coverage of essential health services (composite indicator, including TB treatment coverage as one of 16 tracer indicators) 3.8.2 Proportion of population with large household expenditures on health as a share of total household expenditure or income	NA	Achieving UHC is required to achieve the three high-level targets of the End TB Strategy for reductions in the TB incidence rate, the number of TB deaths and eliminating catastrophic costs for TB patients and their households. TB treatment coverage and treatment success have been monitored for years and the composite indicator of “effective treatment coverage” (the product of treatment coverage and treatment success) is now one of 16 tracer indicators for UHC in the SDG framework. Health expenditure per capita is correlated with TB incidence.	WHO	To assess progress in elimination of catastrophic costs for TB patients and their households, periodic surveys of TB patients are recommended.
		Percentage of total health expenditures that are out-of-pocket Health expenditure per capita			
3.a Strengthen implementation of the WHO Framework Convention on Tobacco Control	3.a.1 Age-standardized prevalence of current tobacco use among those aged ≥15 years	Prevalence of smoking among those aged ≥15 years (%)	Smoking is a strong risk factor for TB disease at the individual level, although a link with TB incidence at the national (as opposed to individual) level has been difficult to establish due to confounding.	WHO	Could be considered (e.g. to inform access to smoking cessation interventions).

AIDS, acquired immune deficiency syndrome; HIV, human immunodeficiency virus; NA, not applicable; SDG, Sustainable Development Goal; TB, tuberculosis; UHC, universal health coverage; UNAIDS, Joint United Nations Programme on HIV/AIDS; WHO, World Health Organization.

**TABLE 2.3B**
**TB-SDG monitoring framework: indicators to monitor beyond SDG 3**

SDG 1: End poverty in all its forms everywhere					
SDG TARGETS FOR 2030	SDG INDICATORS	ALTERNATIVE INDICATORS TO MONITOR	RATIONALE	DATA SOURCE	COLLECT DATA FOR TB PATIENTS SPECIFICALLY?
1.1 Eradicate extreme poverty for all people everywhere  1.3 Nationally appropriate social protection systems and measures for all, including floors	1.1.1 Proportion of population living below the international poverty line  1.3.1 Proportion of population covered by social protection floors/ systems	NA  NA	Poverty is a strong risk factor for TB, operating through several pathways. Reducing poverty should also facilitate prompt health-care seeking. Countries with higher levels of social protection have lower TB burden. Progress on both indicators will help to achieve the End TB Strategy target to eliminate catastrophic costs for TB patients and their households.	UN SDG database, World Bank	No  Could be considered (e.g. to facilitate access to social protection).
SDG 2: End hunger, achieve food security and improved nutrition and promote sustainable agriculture					
2.1 End hunger and ensure access by all people to safe, nutritious and sufficient food year-round	2.1.1 Prevalence of undernourishment	NA	Under-nutrition weakens the body's defence against infections and is a strong risk factor for TB at the national and individual level.	UN SDG database	Could be considered (e.g. to plan food support).
SDG 7: Ensure access to affordable, reliable, sustainable, and modern energy for all					
7.1 Ensure universal access to affordable, reliable and modern energy services	7.1.2 Proportion of population with primary reliance on clean fuels and technology	NA	Indoor air pollution is a risk factor for TB disease at the individual level. There has been limited study of ambient air pollution but it is plausible that it is linked to TB incidence.	WHO	No
SDG 8: Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all					
8.1 Sustain per capita growth with at least 7% growth in GDP per year in the least developed countries	8.1.1 Annual growth rate of real GDP per capita	GDP per capita	Historic trends in TB incidence are closely correlated with changes in the absolute level of GDP per capita (but not with the growth rate).	World Bank	No
SDG 10: Reduce inequality within and among countries					
10.1 Achieve and sustain income growth of the bottom 40% of the population at a rate higher than the national average	10.1.1 Growth rates of household expenditure or income per capita, overall and for the bottom 40% of the population	Gini index for income inequality	TB is a disease of poverty, and decreasing income inequalities combined with economic growth should have an effect on the TB epidemic.	World Bank  OECD	No
SDG 11: Make cities and human settlements inclusive, safe, resilient and sustainable					
11.1 Ensure access for all to adequate, safe and affordable housing and basic services and upgrade slums	11.1.1 Proportion of urban population living in slums, informal settlements or inadequate housing	NA	Living in a slum is a risk factor for TB transmission due to its link with overcrowding. It is also a risk factor for developing TB disease, due to links with air pollution and under-nutrition.	UN SDG database	No

GDP, gross domestic product; NA, not applicable; OECD, Organisation for Economic Co-operation and Development; SDG, Sustainable Development Goal; TB, tuberculosis; UN, United Nations; WHO, World Health Organization.

For SDG 3, the seven indicators selected for monitoring are:

- coverage of essential health services;
- percentage of total health expenditures that are out-of-pocket;
- health expenditure per capita;
- HIV prevalence;
- prevalence of smoking;
- prevalence of diabetes; and
- prevalence of alcohol use disorder.

For SDGs 1, 2, 7, 8, 10 and 11, the seven indicators selected for monitoring are:

- proportion of the population living below the international poverty line;
- proportion of the population covered by social protection floors/systems;
- prevalence of undernourishment;
- proportion of the population with primary reliance on clean fuels and technology;
- gross domestic product (GDP) per capita;
- Gini index for income inequality;<sup>1</sup> and
- proportion of the urban population living in slums.

The rationale for the selection of these 14 indicators, data sources and comments on whether it is relevant to collect data for TB patients specifically are provided in [Table 2.3](#).

The framework includes only indicators for which a relationship with TB incidence could be established. It excludes:

- indicators that are additional sub-indicators under indicators that have already been included (e.g. sub-indicators related to UHC, under SDG 3); and
- indicators that are much more remotely associated with TB risks, and that operate mainly through other SDGs (e.g. education under SDG 4, gender equality under SDG 5 and resilient infrastructure under SDG 9).

Collection and reporting of data for the 14 indicators shown in [Table 2.3](#) does not require any additional data collection and reporting efforts by national TB programmes. Nor does it require data collection and reporting efforts that go beyond those to which countries have already committed in the context of the SDGs. At the global level, the UN has established a monitoring system for SDG indicators, and countries are expected to report data on an annual basis via the appropriate UN agencies (including WHO). Therefore, analysis of the status of, and trends in, the 14 indicators related to TB will be based primarily on accessing the data held in the UN's SDG database, as shown in [Table 2.3](#). In those cases where the SDG indicator is not considered the best metric, and a better (but closely related) alternative has been identified and justified (five indicators under SDG 3, one under SDG 8 and one under SDG 10), data sources are

<sup>1</sup> The index can take values between 0 and 1, with 0 representing perfect equality and 1 representing perfect inequality.

either WHO, the Organisation for Economic Co-operation and Development (OECD), UNAIDS or the World Bank (also shown in [Table 2.3](#)).

The data for the indicators shown in [Table 2.3](#) that will be available in the WHO, OECD, UN and World Bank databases will be for national populations. They will not be available for TB patients specifically, with the exception of HIV prevalence (HIV status among TB patients has been routinely monitored as part of national TB surveillance for more than a decade). This is not a problem for monitoring of TB risk factors and determinants, since it is the population-level prevalence that influences population-level TB risks.

Collection of data for a few of the indicators included in [Table 2.3](#) could be considered for TB patients specifically. However, there is a clear risk of making routine TB surveillance far too complex, and this risk needs to be avoided. If the indicator is considered important enough to monitor among TB patients at country level, periodic surveys should be considered as an alternative to routine surveillance (in which data would be collected for all TB patients).

Analysis of the indicators in the TB-SDG monitoring framework for high TB burden countries is included in [Chapter 7](#). The latest status and recent trends in each indicator are also shown for these countries on the second page of the country profiles in [Annex 2](#) (this information is shown for other countries in profiles that are available online<sup>2</sup>).

## 2.4 Lists of high-burden countries being used by WHO during the period 2016–2020

During the period 1998 to 2015, the concept of an HBC became familiar and widely used in the context of TB. In 2015, three HBC lists – for TB, TB/HIV and MDR-TB – were in use. The HBC list for TB (22 countries) had remained unchanged since 2002, and the HBC lists for TB/HIV (41 countries) and MDR-TB (27 countries) had not been updated since 2009 and 2008, respectively. With 2015 marking the end of the MDGs and a new era of SDGs, and the last year of the Stop TB Strategy before its replacement with the End TB Strategy, it was an ideal time to revisit these three HBC lists.

Following a wide consultation process,<sup>3</sup> WHO defined three new HBC lists for the period 2016–2020: one for TB, one for MDR-TB and one for TB/HIV ([Fig. 2.2](#), [Table 2.4](#)).<sup>4</sup> Each list contains 30 countries ([Table 2.4](#)). These are defined as the top 20 in terms of the absolute number of estimated incident cases, plus the additional 10 countries with the most severe burden in terms of incidence rates per capita that do

<sup>2</sup> [http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/) (Accessed 2 August 2017)

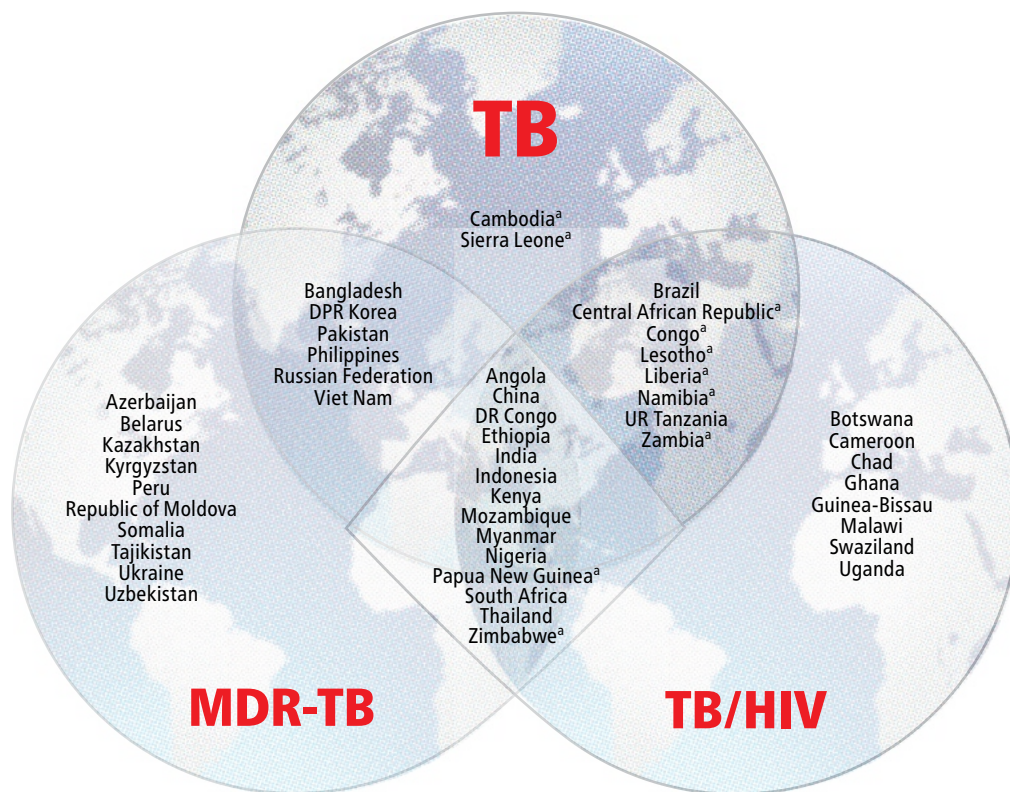
<sup>3</sup> World Health Organization Strategic and Technical Advisory Group for TB. Use of high burden country lists for TB by WHO in the post-2015 era (discussion paper). Geneva: WHO; 2015 ([http://www.who.int/tb/publications/global\\_report/high\\_tb\\_burdencountrylists2016-2020.pdf?ua=1](http://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020.pdf?ua=1), accessed 28 July 2017).

<sup>4</sup> As explained in the last row of [Table 2.4](#), the three lists have a lifetime of 5 years, and the countries included in each list and the criteria used to define each list will be reviewed in June 2020.



**FIG. 2.2**

**Countries in the three high-burden country lists for TB, TB/HIV and MDR-TB being used by WHO during the period 2016–2020, and their areas of overlap**



DPR Korea, Democratic People's Republic of Korea; DR Congo, Democratic Republic of the Congo; HIV, human immunodeficiency virus; MDR, multidrug-resistant; TB, tuberculosis; UR Tanzania, United Republic of Tanzania; WHO, World Health Organization.

<sup>a</sup> Indicates countries that are included in the list of 30 high TB burden countries on the basis of the severity of their TB burden (i.e. TB incidence per 100 000 population), as opposed to the top 20, which are included on the basis of their absolute number of incident cases per year.

not already appear in the top 20 and that meet a minimum threshold in terms of their absolute numbers of incident cases (10 000 per year for TB, and 1000 per year for TB/HIV and MDR-TB). The lists were defined using the latest estimates of TB disease burden available in October 2015. Each list accounts for about 90% of the global burden, with most of this accounted for by the top 20 countries in each list.

There is overlap among the three lists, but 48 countries appear in at least one list. The 14 countries that are in all three lists (shown in the central diamond in [Fig. 2.2](#)) are Angola, China, the Democratic Republic of the Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Papua New Guinea, South Africa, Thailand and Zimbabwe.

The 30 high TB burden countries are given particular attention in the main body of this report. Where estimates of disease burden and assessment of progress in the response are for TB/HIV and MDR-TB specifically, the countries in the TB/HIV and MDR-TB lists, respectively, are given particular attention. [Annex 2](#) contains a two-page profile for each of the 30 high TB burden countries, with a clear demarcation between the 20 countries included on the basis of absolute numbers of incident cases and the 10 additional countries included on the basis of the incidence rate per capita.

Data for all countries are included in [Annex 4](#) and in WHO's online global TB database. Country profiles for all countries (with the same content as those presented in [Annex 2](#)) are also available online.<sup>1</sup>

<sup>1</sup> [www.who.int/tb/data](http://www.who.int/tb/data)

**TABLE 2.4**
**The three high-burden country lists for TB, TB/HIV and MDR-TB being used by WHO during the period 2016–2020**

LIST	THE 30 HIGH TB BURDEN COUNTRIES		THE 30 HIGH TB/HIV BURDEN COUNTRIES		THE 30 HIGH MDR-TB BURDEN COUNTRIES	
<b>Purpose and target audience</b>	To provide a focus for global action on TB in the countries where progress is most needed to achieve End TB Strategy and SDG targets and milestones, to help build and sustain national political commitment and funding in the countries with the highest burden in terms of absolute numbers or severity, and to promote global monitoring of progress in a well-defined set of countries.		To provide a focus for global action on HIV-associated TB in the countries where progress is most needed to achieve End TB Strategy, UNAIDS and SDG targets and milestones, to help build and sustain national political commitment and funding in the countries with the highest burden in terms of absolute numbers or severity, and to promote global monitoring of progress in a well-defined set of countries.		To provide a focus for global action on the MDR-TB crisis in the countries where progress is most needed to achieve End TB Strategy targets and milestones, to help build and sustain national political commitment and funding in the countries with the highest burden in terms of absolute numbers or severity, and to promote global monitoring of progress in a well-defined set of countries.	
<b>Definition</b>	The 20 countries with the highest estimated numbers of incident TB cases, plus the top 10 countries with the highest estimated TB incidence rate that are not in the top 20 by absolute number (threshold, >10 000 estimated incident TB cases per year).		The 20 countries with the highest estimated numbers of incident TB cases among people living with HIV, plus the top 10 countries with the highest estimated TB/HIV incidence rate that are not in the top 20 by absolute number (threshold, >1000 estimated incident TB/HIV cases per year).		The 20 countries with the highest estimated numbers of incident MDR-TB cases, plus the top 10 countries with the highest estimated MDR-TB incidence rate that are not in the top 20 by absolute number (threshold, >1000 estimated incident MDR-TB cases per year).	
<b>Countries in the list</b>	<i>The top 20 by estimated absolute number (in alphabetical order):</i> Angola Bangladesh Brazil China DPR Korea DR Congo Ethiopia India Indonesia Kenya Mozambique Myanmar Nigeria Pakistan Philippines Russian Federation South Africa Thailand UR Tanzania Viet Nam	<i>The additional 10 by estimated incidence rate per 100 000 population and with a minimum number of 10 000 cases per year (in alphabetical order):</i> Cambodia Central African Republic Congo Lesotho Liberia Namibia Papua New Guinea Sierra Leone Zambia Zimbabwe	<i>The top 20 by estimated absolute number (in alphabetical order):</i> Angola Brazil Cameroon China DR Congo Ethiopia India Indonesia Kenya Lesotho Malawi Mozambique Myanmar Nigeria South Africa Thailand Uganda UR Tanzania Zambia Zimbabwe	<i>The additional 10 by estimated incidence rate per 100 000 population and with a minimum number of 1000 cases per year (in alphabetical order):</i> Botswana Central African Republic Chad Congo Ghana Guinea-Bissau Liberia Namibia Papua New Guinea Swaziland	<i>The top 20 by estimated absolute number (in alphabetical order):</i> Bangladesh China DPR Korea DR Congo Ethiopia India Indonesia Kazakhstan Kenya Mozambique Myanmar Nigeria Pakistan Philippines Russian Federation South Africa Thailand Ukraine Uzbekistan Viet Nam	<i>The additional 10 by estimated rate per 100 000 population and with a minimum number of 1000 cases per year (in alphabetical order):</i> Angola Azerbaijan Belarus Kyrgyzstan Papua New Guinea Peru Republic of Moldova Somalia Tajikistan Zimbabwe
<b>Share of global incidence in 2016 (%)</b>	84%	2.8%	85%	4.4%	84%	5.7%
<b>Lifetime of list</b>	5 years (review criteria and included countries in June 2020).		5 years (review criteria and included countries in June 2020).		5 years (review criteria and included countries in June 2020).	

DPR Korea, Democratic People's Republic of Korea; DR Congo, Democratic Republic of the Congo; HIV, human immunodeficiency virus; MDR, multidrug resistant; SDG, Sustainable Development Goal; TB, tuberculosis; UNAIDS, Joint United Nations Programme on HIV/AIDS; UR Tanzania, United Republic of Tanzania; WHO, World Health Organization.





**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.<sup>a</sup>

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.

<sup>a</sup> 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).<sup>1</sup> 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**

INDICATORS	MILESTONES		TARGETS	
	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.<sup>2</sup> 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

<sup>1</sup> 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/](http://www.who.int/tb/post2015_strategy/en/), accessed 8 August 2016).

<sup>2</sup> 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.

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.<sup>3,4</sup> 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.<sup>5</sup> 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.<sup>6</sup> By August 2017, a total of

<sup>3</sup> The [online technical appendix](http://www.who.int/tb/publications/global_report/en/) is available at [http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/)

<sup>4</sup> 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.

<sup>5</sup> 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/](http://www.who.int/tb/publications/inventory_studies/en/), accessed 15 August 2016).

<sup>6</sup> 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).<sup>a</sup> 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,<sup>b</sup> and efforts to introduce such systems were supported.
- Development of a guide on inventory studies to measure underreporting of detected TB cases,<sup>c</sup> 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.<sup>d</sup>

## 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.<sup>e</sup>

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;<sup>f</sup> an up-to-date summary is provided in the latest brochure about its work.<sup>g</sup>

- <sup>a</sup> 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).
- <sup>b</sup> 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/](http://www.who.int/tb/publications/electronic_recording_reporting/en/), accessed 11 September 2017).

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

<sup>d</sup> 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/](http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/consultation_april_2015_tb_estimates_subgroup/en/), accessed 11 September 2017).

<sup>e</sup> 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](http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf6_report.pdf?ua=1), accessed 11 September 2017).

<sup>f</sup> Available at: [http://www.who.int/tb/areas-of-work/monitoring-evaluation/impact\\_measurement\\_taskforce/en/](http://www.who.int/tb/areas-of-work/monitoring-evaluation/impact_measurement_taskforce/en/)

<sup>g</sup> Available at: [http://www.who.int/tb/publications/factsheet\\_tb\\_impactmeasurement.pdf?ua=1](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](#).

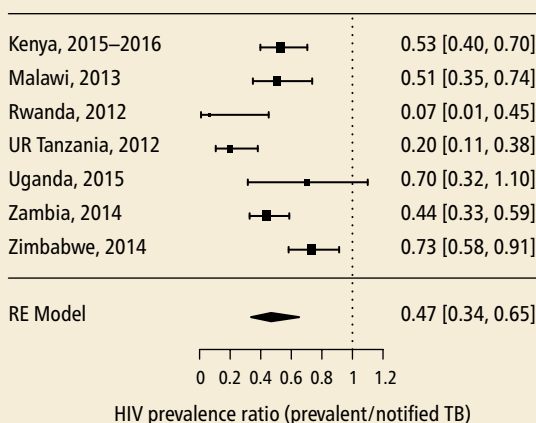
The best estimate of TB incidence in Kenya based on the prevalence survey was higher than the pre-survey estimate, but with overlapping uncertainty intervals. The post-survey estimate of TB incidence for Bangladesh was slightly lower, and for the Democratic Republic of Korea it was similar to the pre-survey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

<sup>a</sup> Downloaded from <http://ghdx.healthdata.org/gbd-results-tool>, July 2017

<sup>b</sup> 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).

<sup>c</sup> 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.<sup>a</sup>

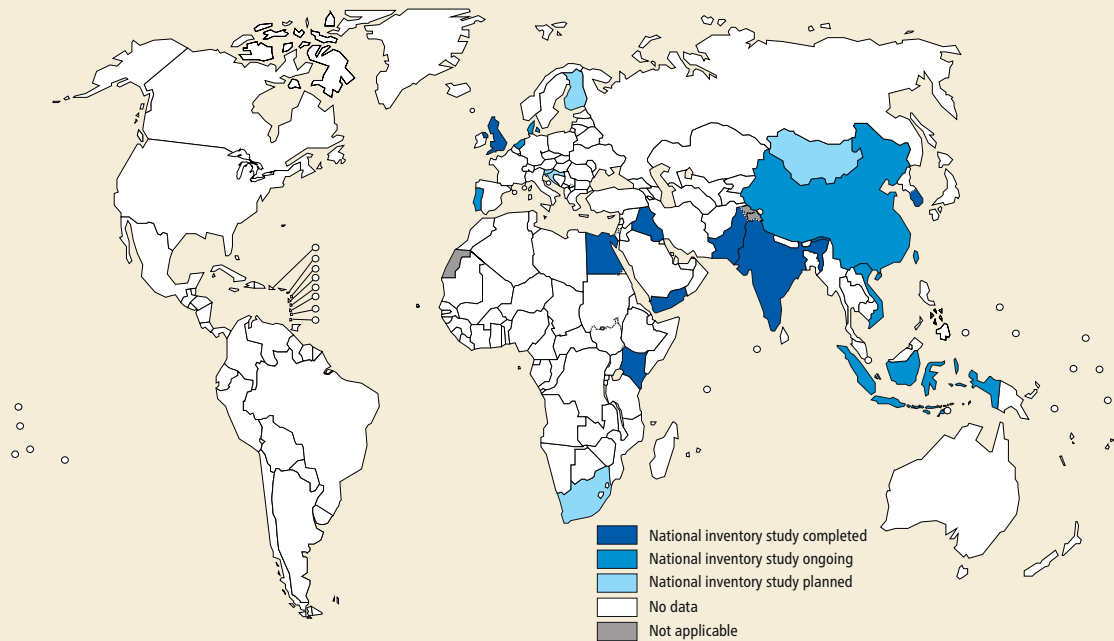
Countries in which a national inventory study has been implemented since 2000 are shown in **Fig. B3.3.1**. Progress in 2016–2017 includes the completion of a study focused on the underreporting of TB cases

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.

<sup>a</sup> World Health Organization. Assessing tuberculosis underreporting through inventory studies. Geneva: WHO; 2012 ([http://www.who.int/tb/publications/inventory\\_studies/en/](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)<sup>a</sup>**

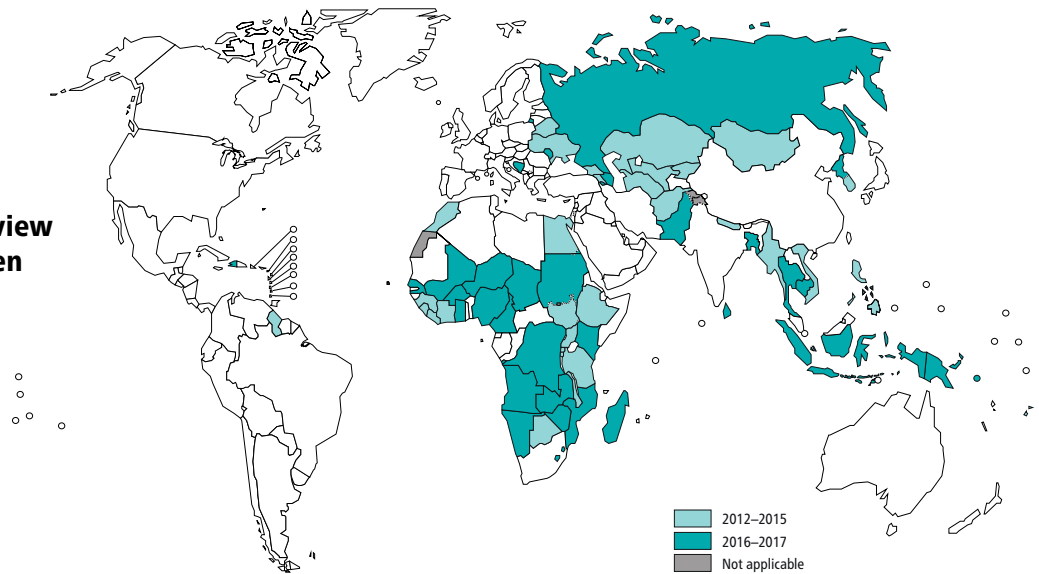


<sup>a</sup> Pakistan has completed a second inventory study focusing on children with TB. Nigeria is planning to undertake a subnational level study (in metropolitan Lagos). The Netherlands is carrying out a repeat of the inventory study conducted in 2006.

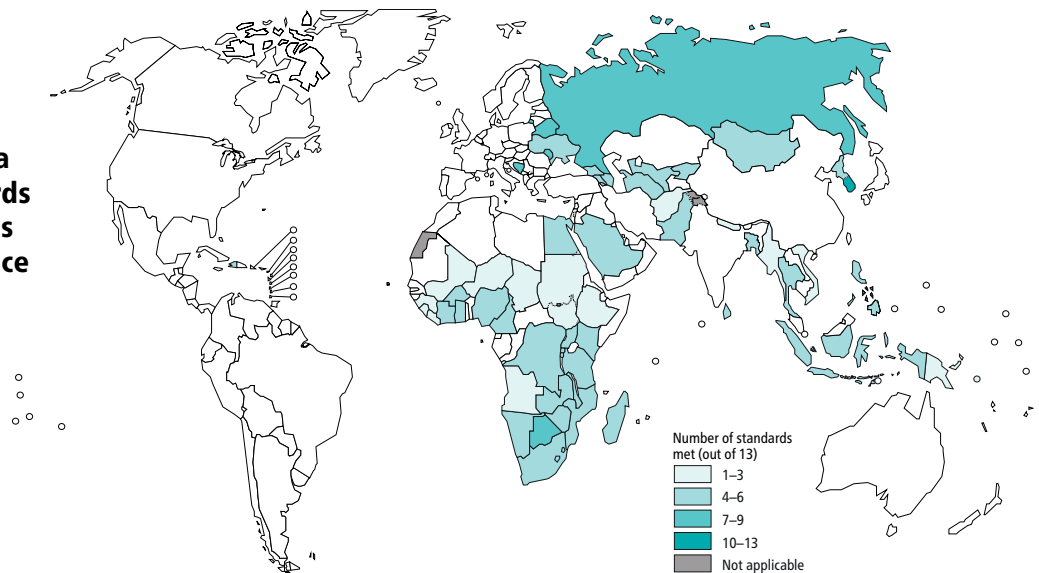
**FIG. 3.1**

**Strengthening national TB surveillance (status in August 2017)**

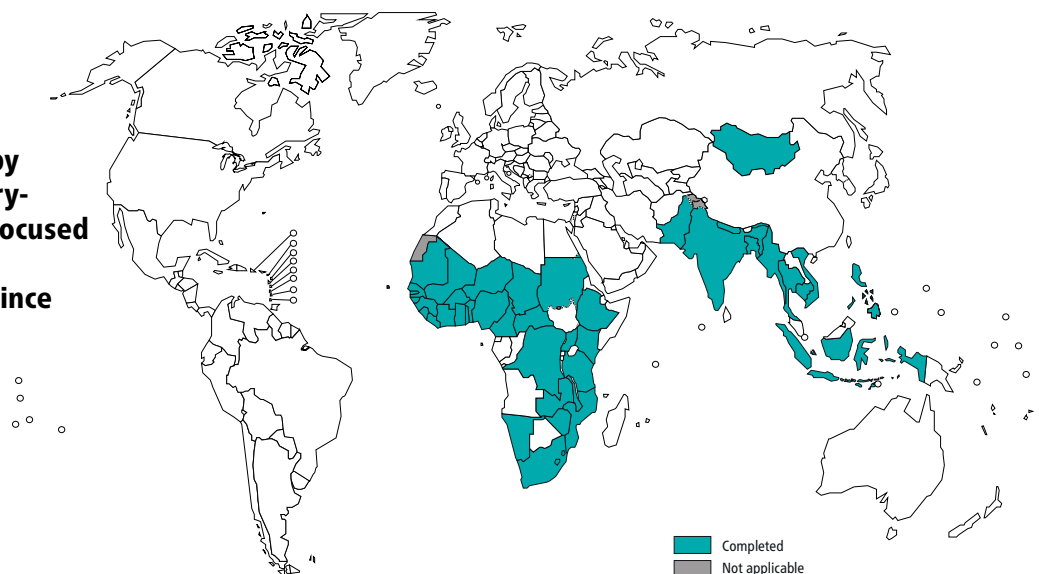
**Countries in which a national TB epidemiological review has been undertaken since July 2012**

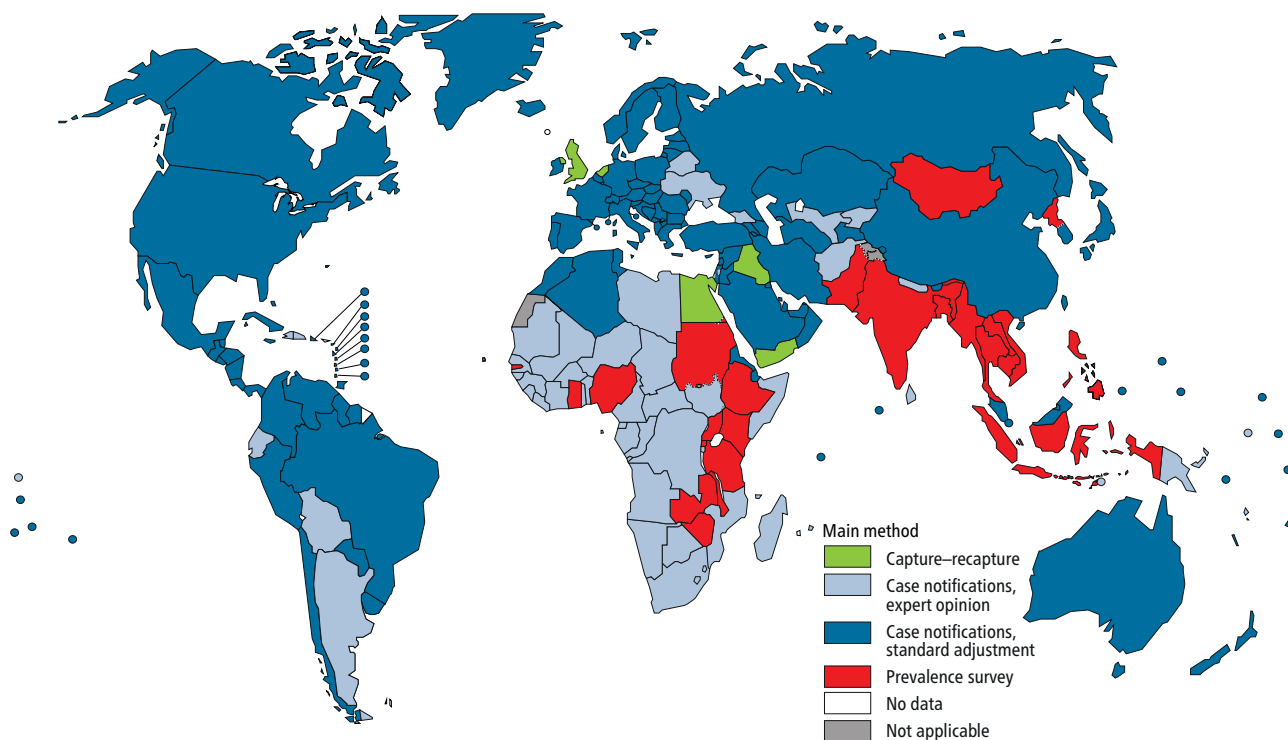


**Countries in which a checklist of standards and benchmarks has been completed since January 2013**



**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](#).<sup>1</sup>

<sup>1</sup> The [online technical appendix](#) is available at [http://www.who.int/tb/publications/global\\_report/en/](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),<sup>2</sup> 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<sup>3</sup> 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

<sup>2</sup> Here and elsewhere in the report, “range” refers to the 95% uncertainty interval.

<sup>3</sup> 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.<sup>a</sup>**

	POPULATION	HIV-NEGATIVE TB MORTALITY		HIV-POSITIVE TB MORTALITY <sup>b</sup>		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 <sup>c</sup>	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
<b>High TB burden countries</b>	<b>4 710 000</b>	<b>1 130</b>	<b>998–1 270</b>	<b>317</b>	<b>268–369</b>	<b>9 060</b>	<b>7 450–10 800</b>	<b>866</b>	<b>755–986</b>
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
<b>GLOBAL</b>	<b>7 440 000</b>	<b>1 300</b>	<b>1 160–1 440</b>	<b>374</b>	<b>325–427</b>	<b>10 400</b>	<b>8 770–12 200</b>	<b>1 030</b>	<b>915–1 150</b>

<sup>a</sup> Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

<sup>b</sup> Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD-10.

<sup>c</sup> 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.

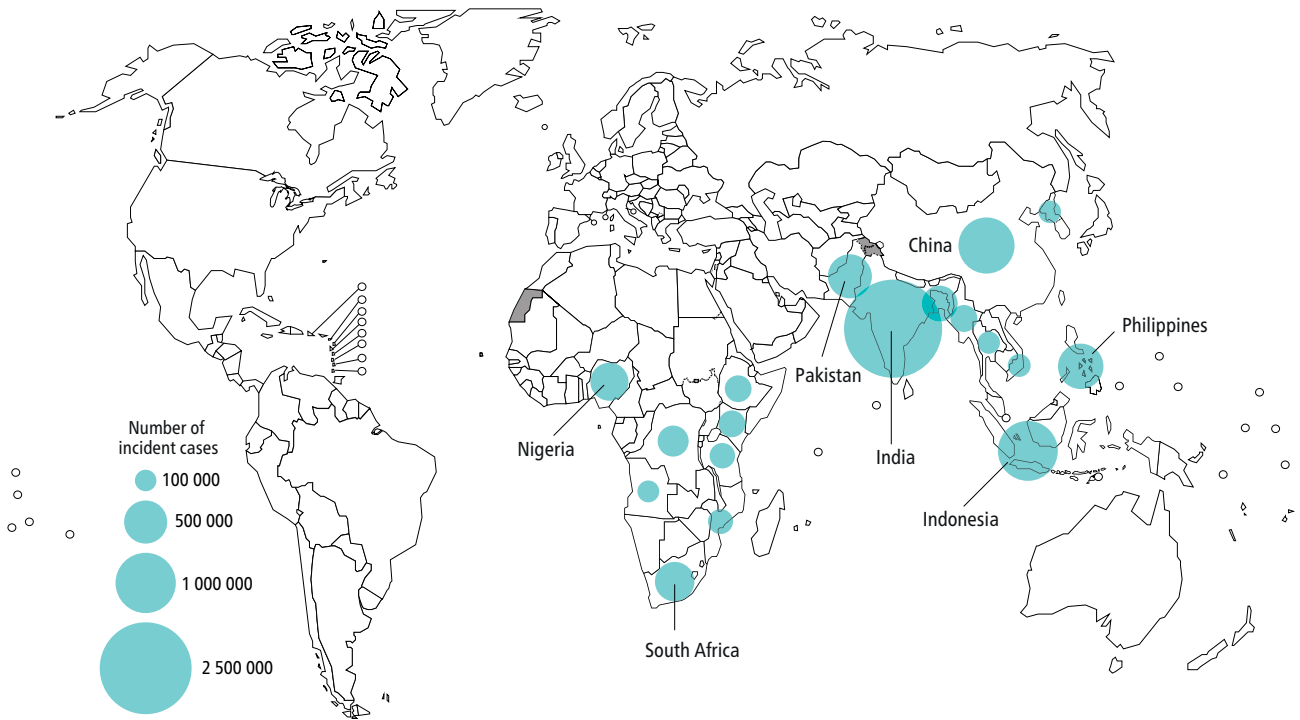
	HIV-NEGATIVE TB MORTALITY		HIV-POSITIVE TB MORTALITY <sup>a</sup>		TOTAL TB INCIDENCE		HIV PREVALENCE IN INCIDENT TB (%)	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Angola	64	36–99	24	12–41	370	230–543	16	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 <sup>b</sup>	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
<b>High TB burden countries</b>	<b>24</b>	<b>21–27</b>	<b>6.7</b>	<b>5.7–7.8</b>	<b>192</b>	<b>158–230</b>	<b>9.7</b>	<b>7.5–12</b>
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

<sup>a</sup> Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD–10.

<sup>b</sup> Estimates of TB incidence and mortality for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.

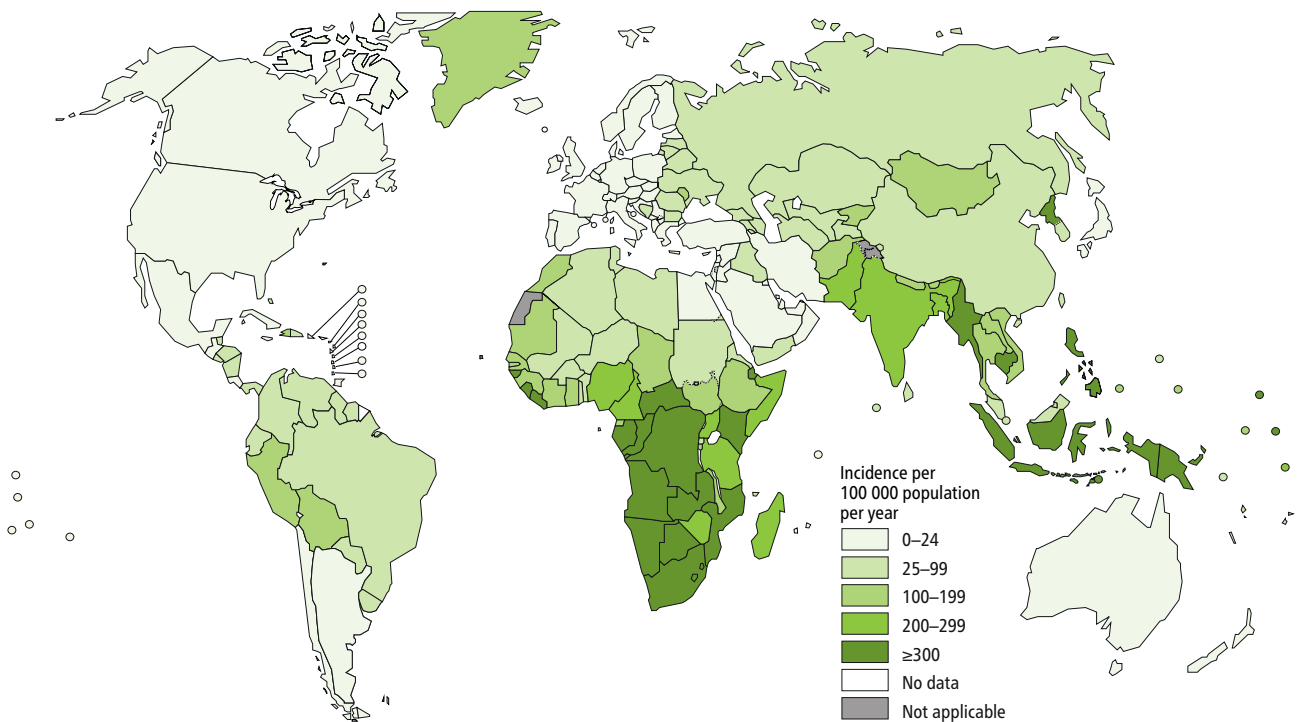
**FIG. 3.3**

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

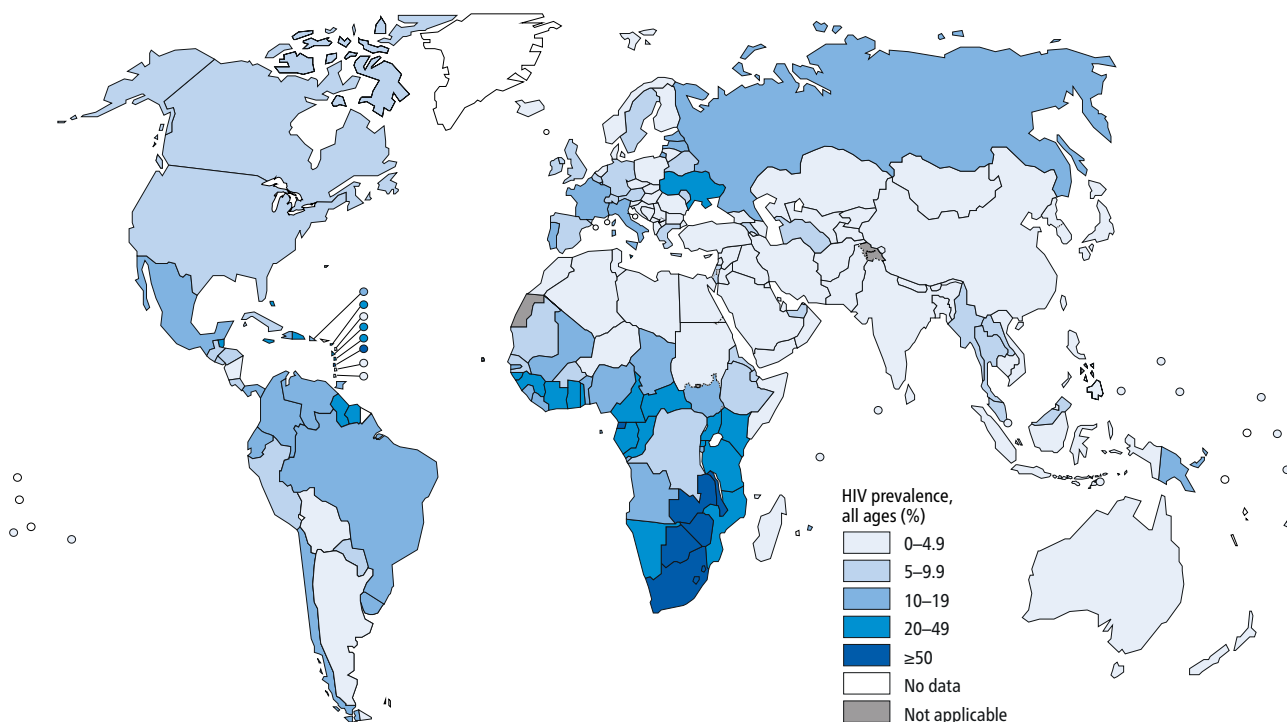


**FIG. 3.4**

**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 coinfecting 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).<sup>1</sup> 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

<sup>1</sup> 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*

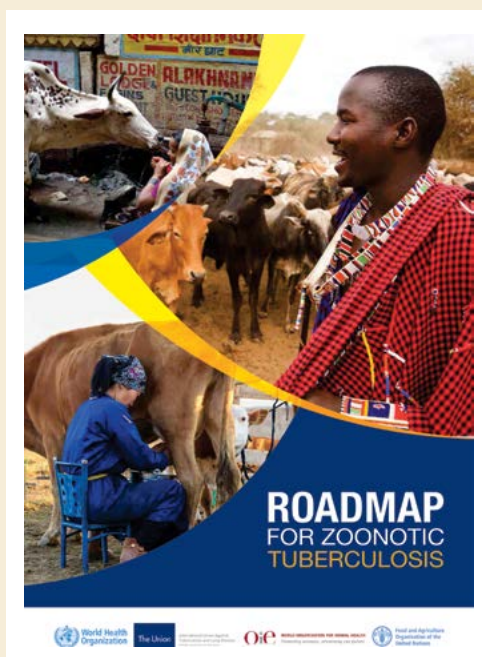
- Collect and report more complete and accurate data
- Improve diagnosis in people
- Address research gaps

*Reduce transmission at the animal–human interface*

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

*Strengthen intersectoral and collaborative approaches*

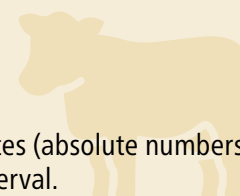
- Increase awareness, engagement and collaboration
- Develop policies and guidelines
- Implement joint interventions
- Advocate for investment



**TABLE B3.4.1**

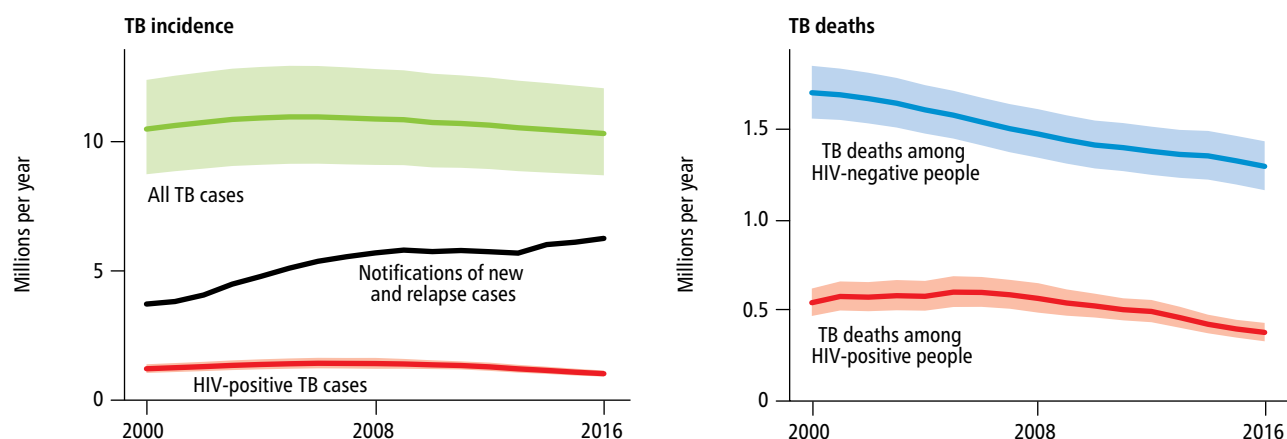
**Estimated incidence and mortality due to *M. bovis* TB.** Best estimates (absolute numbers) are followed by the lower and upper bounds of the 95% uncertainty interval.

REGION	INCIDENT CASES		DEATHS	
	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

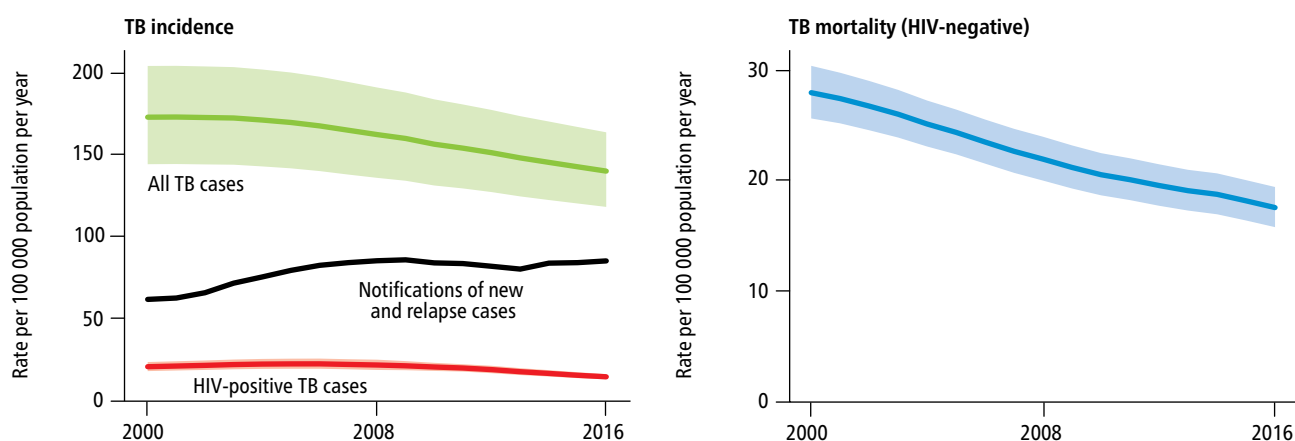


**FIG. 3.6**

**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.<sup>1</sup> 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](#).<sup>2</sup>

### 3.2.2 Estimates of TB mortality in 2016

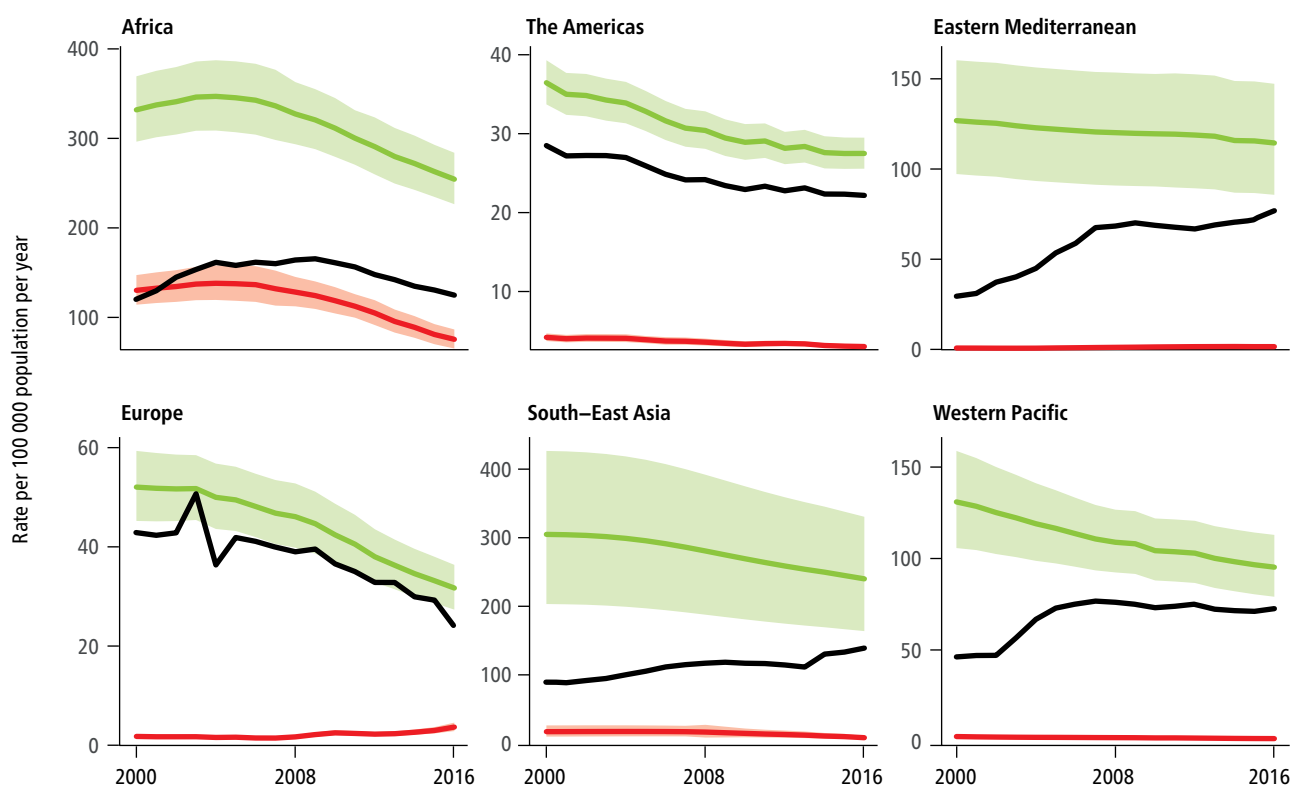
Estimates of the number of deaths caused by TB are shown globally, for the six WHO regions and for the 30 high TB

<sup>1</sup> Downloaded from <http://ghdx.healthdata.org/gbd-results-tool>, July 2017.

<sup>2</sup> The [online technical appendix](#) is available at [http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/).

**FIG. 3.8**

**Regional trends in estimated TB incidence rates by WHO region, 2000–2016.** Total TB incidence rates are shown in **green** and incidence rates of HIV-positive TB are shown in **red**. Shaded areas represent uncertainty intervals. The **black** lines show notifications of new and relapse cases for comparison with estimates of the total incidence rate.



burden countries, in [Table 3.2](#). There were an estimated 1.3 million (range, 1.2 million to 1.4 million) deaths from TB among HIV-negative people in 2016 and an additional 374 000 (range, 325 000–427 000) deaths from TB among HIV-positive people. TB is the ninth leading cause of death worldwide, and for the past five years (2012–2016) has been the leading cause of death from a single infectious agent, ranking above HIV/AIDS ([Fig. 3.11](#), [Fig. 3.12](#), [Fig. 3.13](#)).<sup>1</sup> Most of these deaths could be prevented with early diagnosis and appropriate treatment ([Chapter 1](#)). For example, among people whose TB was detected, reported and treated in 2015, the treatment success rate was 83% globally ([Chapter 4](#)); and in high-income countries with universal health coverage the proportion of people who die from TB can be under 5% ([section 3.2.4](#)).

About 82% of TB deaths among HIV-negative people occurred in the WHO African Region and the WHO South-East Asia Region in 2016; these regions accounted for 85% of the combined total of TB deaths in HIV-negative and HIV-positive people. India accounted for 33% of global TB deaths among HIV-negative people, and for 26% of the combined total TB deaths in HIV-negative and HIV-positive people.

Estimates of TB mortality rates (per 100 000 population)

<sup>1</sup> WHO Global Health Observatory data repository, available at <http://apps.who.int/gho/data/node.main.GHECOD?lang=en> (accessed 23 August 2017).

are shown globally, for the six WHO regions and for the 30 high TB burden countries, in [Table 3.3](#). Globally, the number of TB deaths among HIV-negative people per 100 000 population was 17 in 2016, and 22 when TB deaths among HIV-positive people were included. There was considerable variation among countries ([Fig. 3.14](#)), ranging from less than one TB death per 100 000 population in many high-income countries to 40 or more deaths per 100 000 population in much of the WHO African Region and in five high TB burden countries in Asia (Bangladesh, the Democratic People's Republic of Korea, Indonesia, Myanmar and Papua New Guinea).

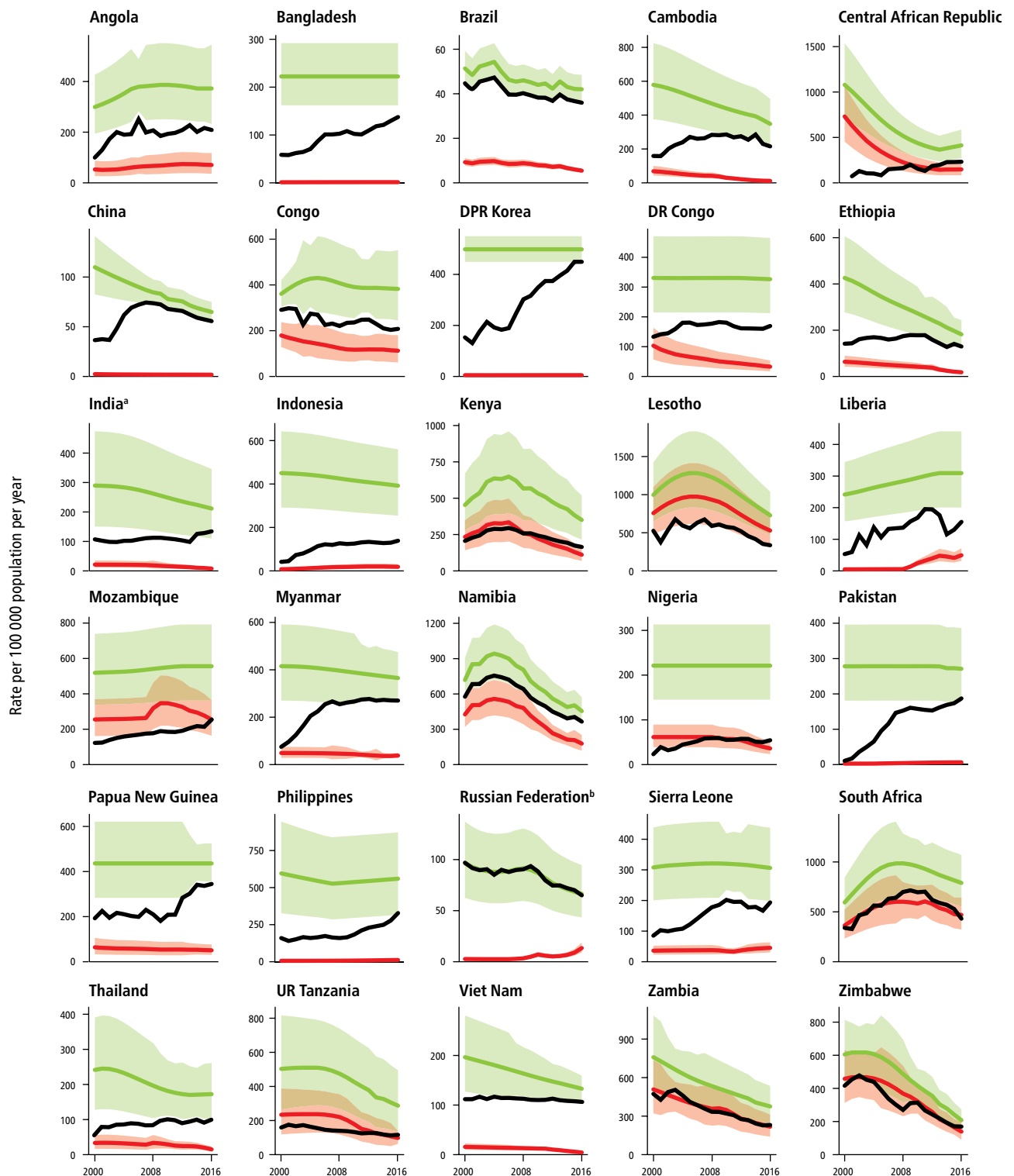
Estimates of the number of deaths caused by zoonotic TB are shown in [Box 3.4](#).

### 3.2.3 Estimated trends in TB mortality, 2000–2016

Globally, the absolute number of TB deaths among HIV-negative people has been falling since 2000, from 1.7 million in 2000 to 1.3 million in 2016 ([Fig. 3.6](#)). The TB mortality rate (per 100 000 population) fell by 37% between 2000 and 2016 ([Fig. 3.7](#)), and by 3.4% between 2015 and 2016. Rates have also been falling in all six of the WHO regions ([Fig. 3.15](#)). Since 2010, the fastest average rates of decline in the mortality rate have been in the WHO European Region and the WHO Western Pacific Region (6.0% and 4.6% per year, respectively), and slowest in the WHO Eastern Mediterranean

**FIG. 3.9**

**Trends in estimated TB incidence in the 30 high TB burden countries, 2000–2016.** TB incidence rates are shown in **green** and incidence rates of HIV-positive TB are shown in **red**. Shaded areas represent uncertainty intervals. The **black** lines show notifications of new and relapse cases for comparison with estimates of the total incidence rate.

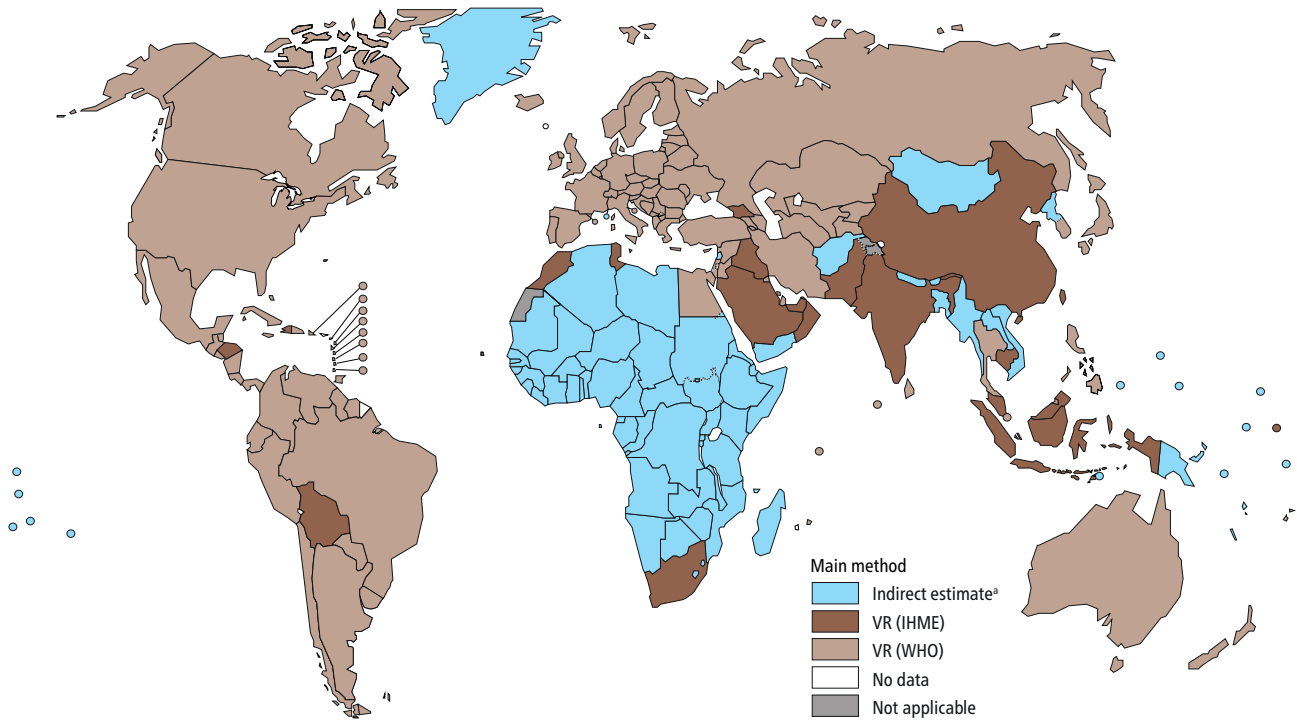


<sup>a</sup> Estimates of TB incidence for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.

<sup>b</sup> For an explanation of why notifications are assumed to be equivalent to TB incidence in the Russian Federation, see [Box 3.5](#).

**FIG. 3.10**

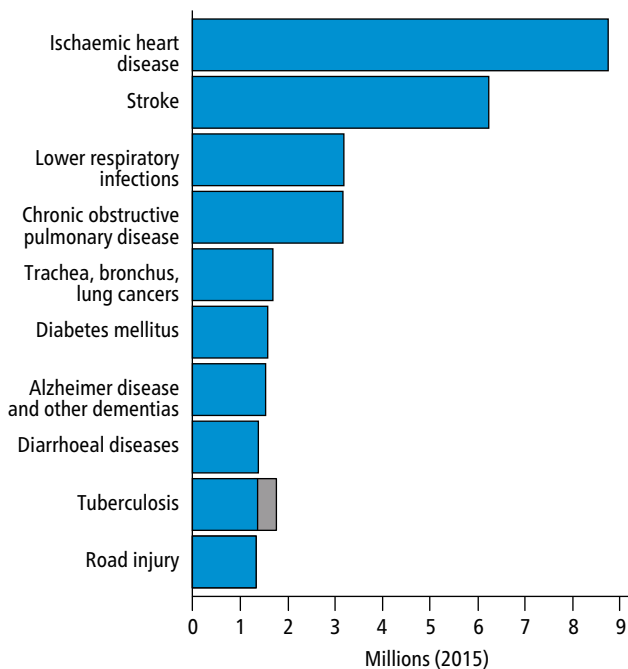
**Main methods used to estimate TB mortality in HIV-negative people**



<sup>a</sup> Mortality is estimated as the product of TB incidence and the TB case fatality ratio. Further details are provided in the [online technical appendix](#).

**FIG. 3.11**

**Top causes of death worldwide in 2015.** <sup>a,b,c</sup> Deaths from TB among HIV-positive people are shown in grey.



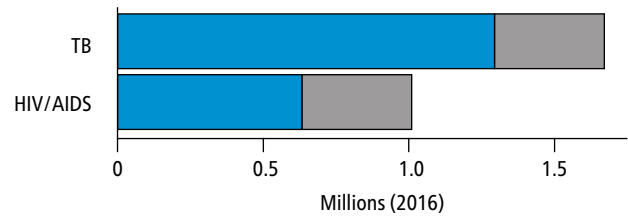
<sup>a</sup> This is the latest year for which estimates for all causes are currently available. See WHO Global Health Observatory data repository, available at <http://apps.who.int/gho/data/node.main.GHECOD> (accessed 28 August 2017).

<sup>b</sup> For HIV/AIDS, the latest estimates of the number of deaths in 2016 that have been published by UNAIDS are available at [www.unaids.org/en/resources/documents/2017/HIV\\_estimates\\_with\\_uncertainty\\_bounds\\_1990-2016](http://www.unaids.org/en/resources/documents/2017/HIV_estimates_with_uncertainty_bounds_1990-2016). For TB, the estimates for 2016 are those published in this report.

<sup>c</sup> Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International classification of diseases.

**FIG. 3.12**

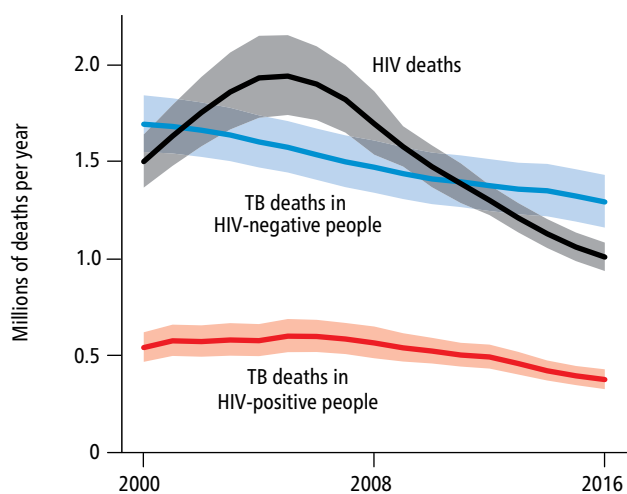
**Estimated number of deaths from HIV/AIDS and TB in 2016.** Deaths from TB among HIV-positive people are shown in grey. <sup>a,b</sup>



<sup>a</sup> For HIV/AIDS, the latest estimates of the number of deaths in 2016 that have been published by UNAIDS are available at [www.unaids.org/en/resources/documents/2017/HIV\\_estimates\\_with\\_uncertainty\\_bounds\\_1990-2016](http://www.unaids.org/en/resources/documents/2017/HIV_estimates_with_uncertainty_bounds_1990-2016). For TB, the estimates for 2016 are those published in this report.

<sup>b</sup> Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International classification of diseases.

**FIG. 3.13**  
**Global trends in the estimated number of deaths caused by TB and HIV (in millions), 2000–2016.<sup>a,b</sup>**  
 Shaded areas represent uncertainty intervals.



<sup>a</sup> For HIV/AIDS, the latest estimates of the number of deaths in 2016 that have been published by UNAIDS are available at [www.unaids.org/en/resources/documents/2017/HIV\\_estimates\\_with\\_uncertainty\\_bounds\\_1990-2016](http://www.unaids.org/en/resources/documents/2017/HIV_estimates_with_uncertainty_bounds_1990-2016). For TB, the estimates for 2016 are those published in this report.  
<sup>b</sup> Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International classification of diseases. Deaths from TB among HIV-positive people accounted for 37% of deaths classified as caused by HIV/AIDS in 2016.

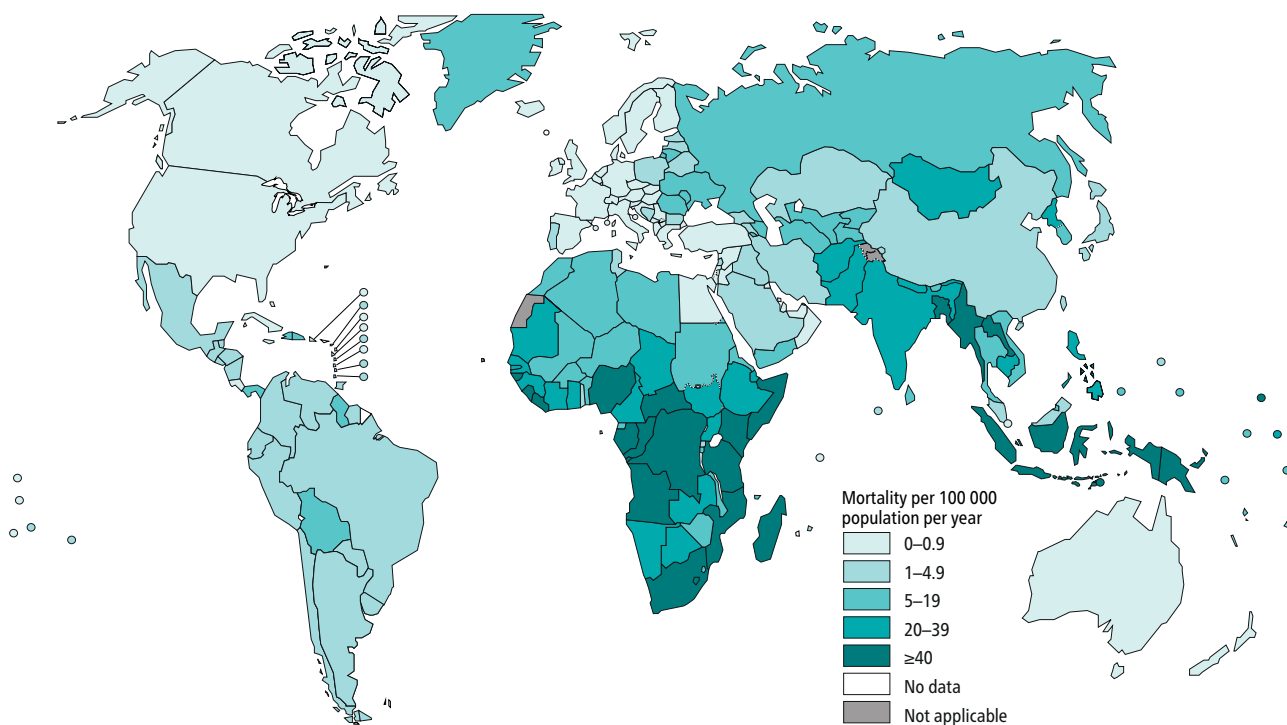
Region (2.2% per year). Trends in mortality rates in the 30 high TB burden countries vary markedly (Fig. 3.16), ranging from substantial reductions since 2000 (e.g. in Cambodia, China, Ethiopia, Myanmar, the Russian Federation and Viet Nam) to limited changes (e.g. in Angola, Congo and South Africa). High TB burden countries with rates of decline exceeding 6% per year since 2010 included Ethiopia, the Russian Federation, the United Republic of Tanzania, Viet Nam and Zimbabwe. Further details about trends in TB disease burden in the Russian Federation, based on an epidemiological review conducted in February 2017, are provided in Box 3.5.

### 3.2.4 The CFR and across-country equity

The CFR is the proportion of people with TB who die from the disease; it can be approximated as the number of TB deaths divided by TB incidence in the same year. The CFR allows assessment of variation in equity in terms of access to TB diagnosis and treatment among countries (because if everyone with TB had access to timely diagnosis and high-quality treatment, the CFR would be low in all countries). To achieve the milestones for reductions in TB deaths set for 2020 and 2025 in the End TB Strategy, the global CFR needs to fall to 10% by 2020 and to 6% by 2025 (Chapter 2).

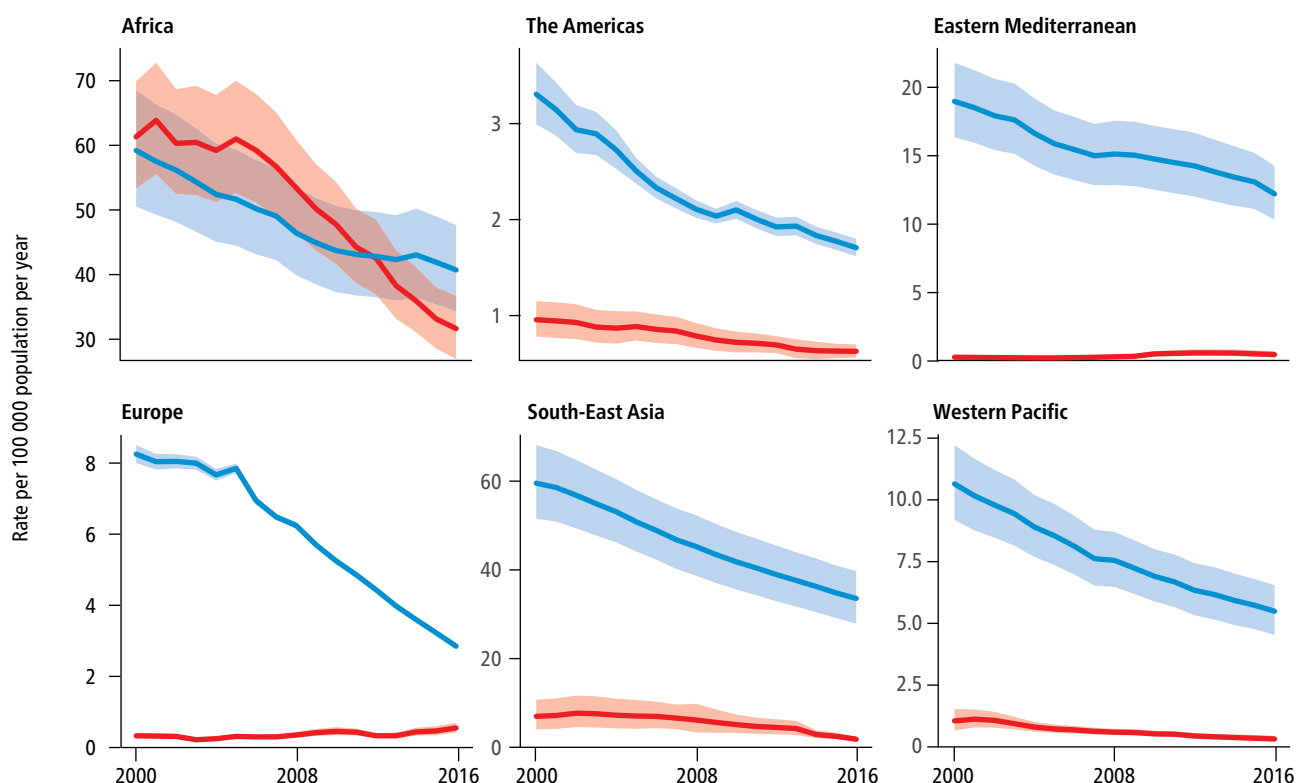
In 2016, the global CFR (calculated as the combined number of TB deaths in HIV-negative people and HIV-positive people, divided by the total number of incident cases in both

**FIG. 3.14**  
**Estimated TB mortality rates excluding TB deaths among HIV-positive people, 2016**



**FIG. 3.15**

**Regional trends in estimated TB mortality rates by WHO region, 2000–2016.** Estimated TB mortality rates in HIV-negative people are shown in **blue**, and estimated mortality rates of HIV-positive TB are shown in **red**. Shaded areas represent uncertainty intervals.



HIV-negative and HIV-positive people)<sup>1</sup> was 16%. It varied widely among countries (Fig. 3.17), from under 5% in a few countries to more than 20% in most countries in the WHO African Region. Intensified efforts are required to reduce the CFR to 10% globally by 2020.

### 3.2.5 Estimated number of deaths averted by TB treatment, 2000–2016

The actual numbers of TB deaths (presented above) can be compared with the number of TB deaths that would have occurred in the absence of TB treatment, to estimate the number of deaths averted by TB interventions. The number of deaths that would have occurred each year in the absence of TB treatment (and without ART provided alongside TB treatment for HIV-positive cases) can be conservatively estimated as the number of estimated incident cases (Section 3.1) multiplied by the relevant estimated CFR for untreated TB.<sup>2</sup> Estimates are

<sup>1</sup> The CFR was calculated based on the combined total of deaths in HIV-negative and HIV-positive people for the purpose of cross-country comparisons, in particular to illustrate the high CFRs in African countries, which could be reduced by effective detection and care programmes. CFRs restricted to HIV-negative TB deaths and cases can also be calculated but are not shown here. At the subnational level, CFRs can also be restricted to HIV-negative TB deaths, depending on the country and its HIV burden.

<sup>2</sup> Further details about methods used to estimate lives saved, including CFRs for different categories of TB case, are provided in the [online technical appendix](http://www.who.int/tb/publications/global_report/en/), available at [http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/).

conservative because they do not account for the impact of TB services or the availability of ART on the level of TB incidence, or for the indirect, downstream impact of these interventions on future levels of infections, cases and deaths.

Between 2000 and 2016, TB treatment alone averted an estimated 44 million deaths among HIV-negative people (Table 3.4). Among HIV-positive people, TB treatment supported by ART averted an additional 8.5 million deaths.

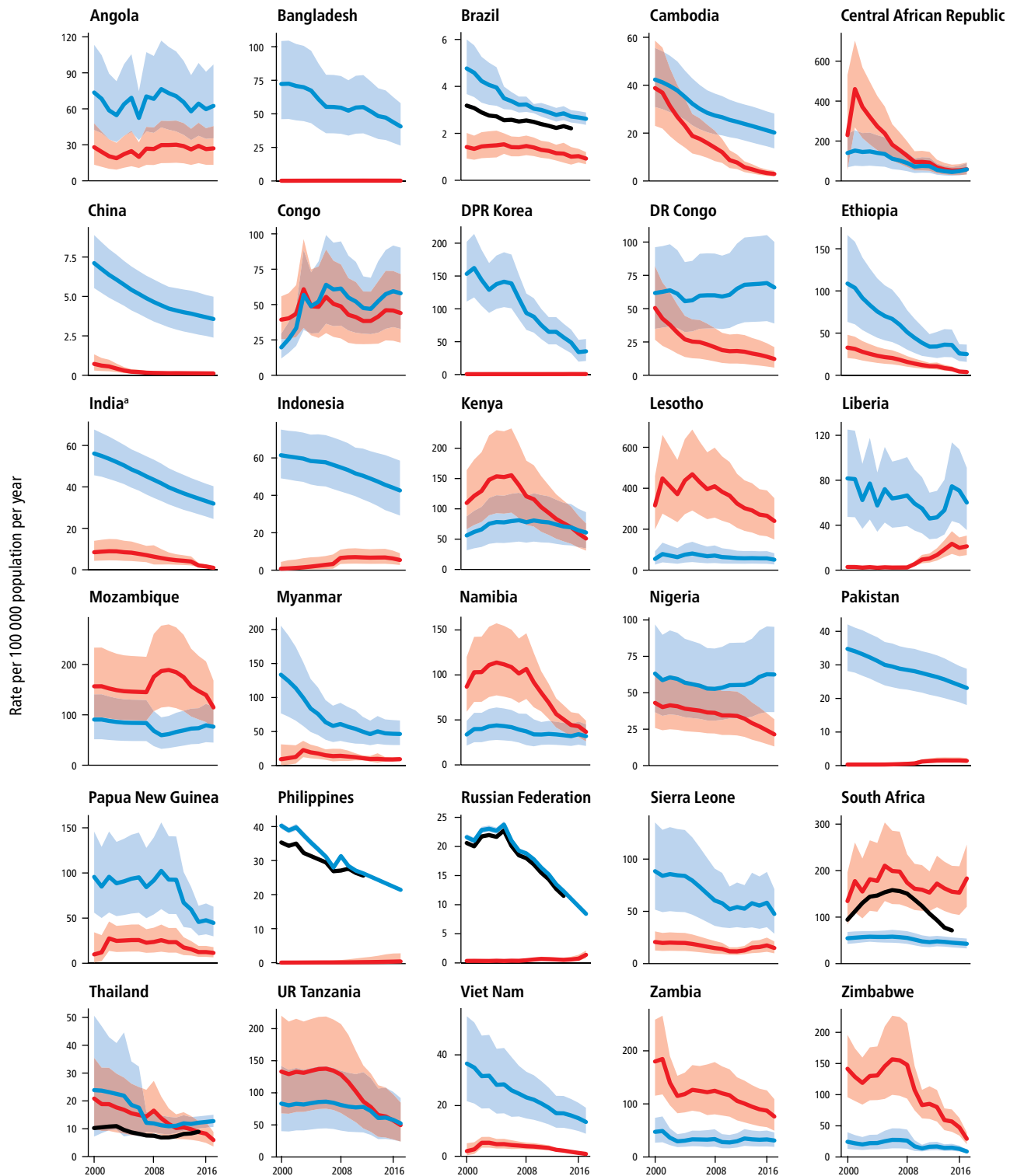
### 3.3 Drug-resistant TB

Drug-resistant TB threatens global TB care and prevention, and remains a major public health concern in many countries. Three major categories are used for global surveillance and treatment. MDR-TB is TB that is resistant to both rifampicin and isoniazid, the two most powerful anti-TB drugs; it requires treatment with a second-line regimen. RR-TB also requires treatment with second-line drugs.<sup>3</sup> With increasing use of Xpert® MTB/RIF for simultaneous detection of TB and resistance to rifampicin, a growing number of RR-TB cases (without further testing for isoniazid resistance) are being detected and notified (Chapter 4). Extensively drug-resistant TB (XDR-TB) is defined as MDR-TB plus resistance to

<sup>3</sup> World Health Organization. WHO treatment guidelines for drug-resistant tuberculosis (2016 update) (WHO/HTM/TB/2016.04). Geneva: WHO; 2016 (<http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/>, accessed 16 August 2017).

**FIG. 3.16**

**Trends in estimated TB mortality rates in the 30 high TB burden countries, 2000–2016.** TB mortality rates in HIV-negative people are shown in **blue** and mortality rates of HIV-positive TB are shown in **red**. The **black** lines show observations from vital registration systems. Shaded areas represent uncertainty intervals.



<sup>a</sup> Estimates of TB mortality for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.



**BOX 3.5**

**The burden of TB disease is falling in the Russian Federation, but the incidence of MDR-TB is increasing**

A national TB epidemiological review was undertaken in the Russian Federation in February 2017. It included a thorough review of the latest epidemiological data, including TB case notifications, death registration data from the national VR system and results from DST for anti-TB drug resistance. The main conclusions from this review were that the burden of TB disease (incidence and mortality) is falling but the incidence of MDR-TB is increasing.

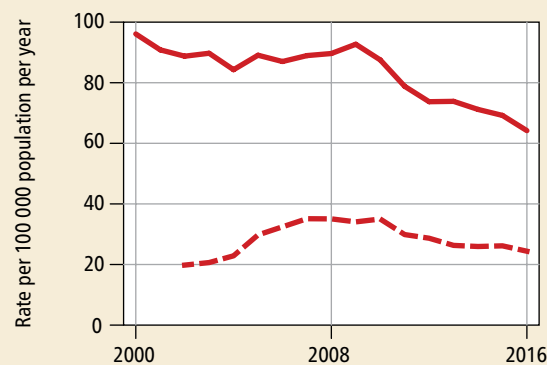
Data from the VR system show that the TB mortality rate (excluding TB deaths in HIV-positive people) has been falling rapidly since 2009, at an average rate of 11% per year. This trend is consistent in all of the eight federal regions (okrugs), although the decline has been especially impressive (at 17% per year) in the North Caucasus region (Fig. B3.5.1).

The case notification rate of new and relapse TB cases has fallen at an average rate of 4.8% per year since 2009 (Fig. B3.5.2). This is considered to be a good proxy for the trend in TB incidence, for four main reasons:

- There is extensive and regular screening for TB. It is mandatory for every citizen aged 17 and above to be screened every 1–2 years (with the frequency depending on residence); this screening is typically done using fluorography, and otherwise using sputum microscopy. Children and adolescents are screened annually using tuberculin skin tests. Contacts of TB cases are also screened (in 2015, 470 000 contacts were screened). The high coverage of active case finding means that there is a low probability of missed diagnoses. Instead, it is more likely that there is some overreporting of cases due to the lower predictive value of laboratory tests among the general population.

**FIG B3.5.2**

**Notifications of new and relapse cases in the Russian Federation, 2000–2016.** The dashed line shows the notification rate of new cases that were bacteriologically confirmed.

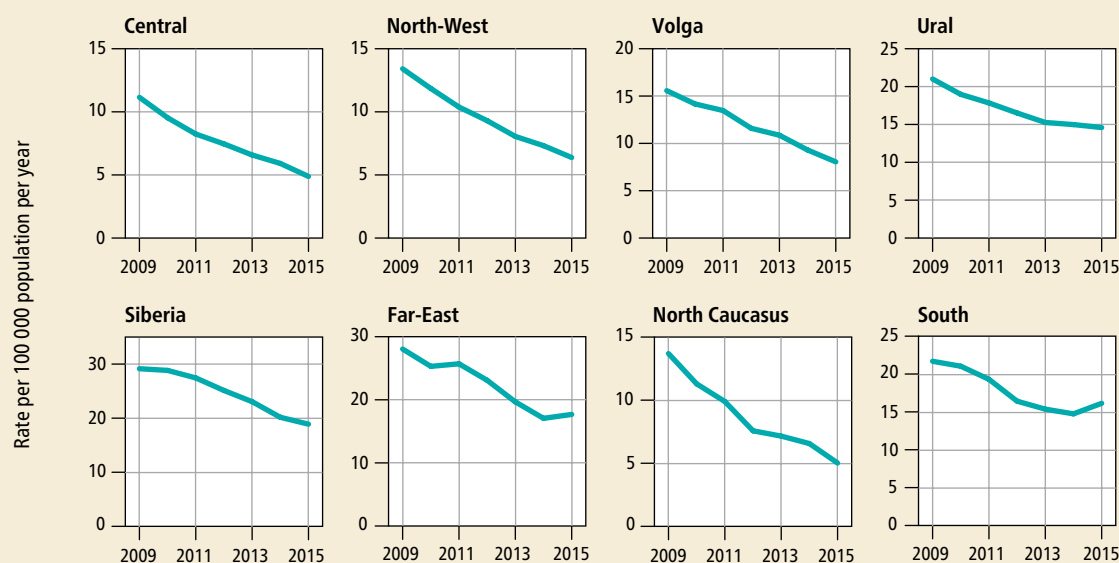


Furthermore, there seems to be an over-reliance on clinical diagnostic criteria, since a large proportion of the notified cases found through screening do not have bacteriological confirmation of pulmonary TB, despite the systematic use of sensitive and modern diagnostic tests.

- Notification of detected TB cases is mandatory, and the TB notification system has complete coverage. Underreporting of detected cases is unlikely.
- Culture or molecular tests are routinely used for diagnosis.
- There have been no major changes to TB screening, diagnostic and reporting practices since 2009. →

**FIG. B3.5.1**

**Annual TB mortality rates per 100 000 population for eight federal regions (okrugs), 2009–2015.** Rates were adjusted for ill-defined causes of death.



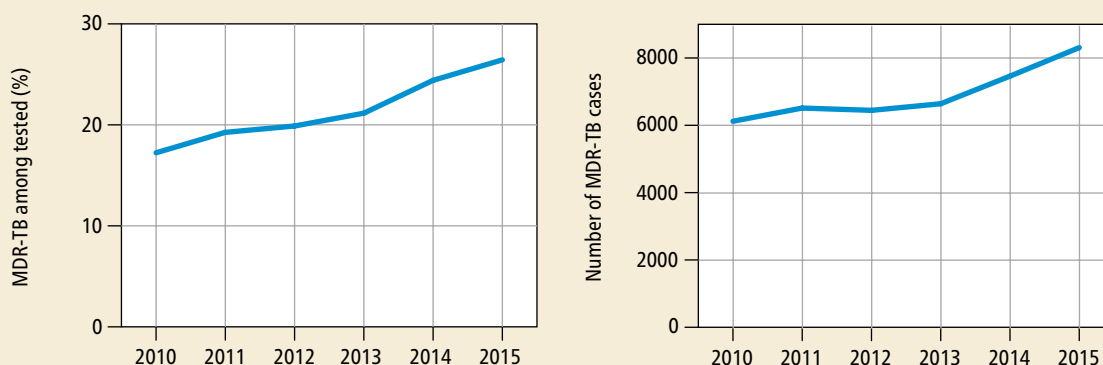
→ Trends in all of the eight federal regions (okrugs) are broadly consistent with the national trend. The far-Eastern region reports the highest notification rates (123/100 000 in 2015); the lowest rates are found in the central region (43/100 000 in 2015) and the North Caucasus region (41/100 000 in 2015).

Despite the steady decline in the overall TB notification rate, a concerning national trend is that the case notification rate for MDR-TB has been increasing, from 8 per 100 000 population in 2010

(6000 cases) to 11 per 100 000 population in 2015 (8000 cases). The proportion of TB cases with a DST result who had MDR-TB has risen from 17% in 2010 to 27% in 2015 (Fig. B3.5.3). Reasons for this increase, which is in contrast to the overall decline in TB burden, are not clear. Coverage of DST among laboratory-confirmed cases has been consistently high over the period (Fig. B3.5.4). It will be important to closely monitor trends and to continuously assess the performance of the national response to MDR-TB.

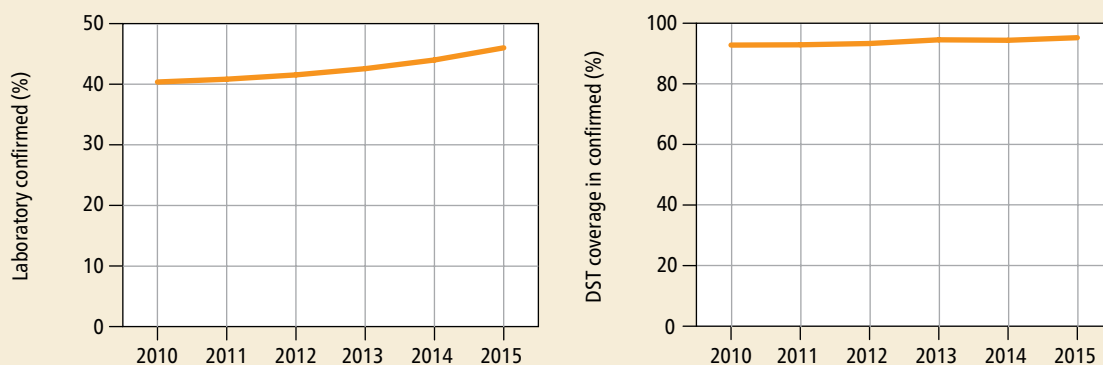
**FIG. B3.5.3**

**MDR-TB detection among new cases of pulmonary TB, 2010–2015**



**FIG. B3.5.4**

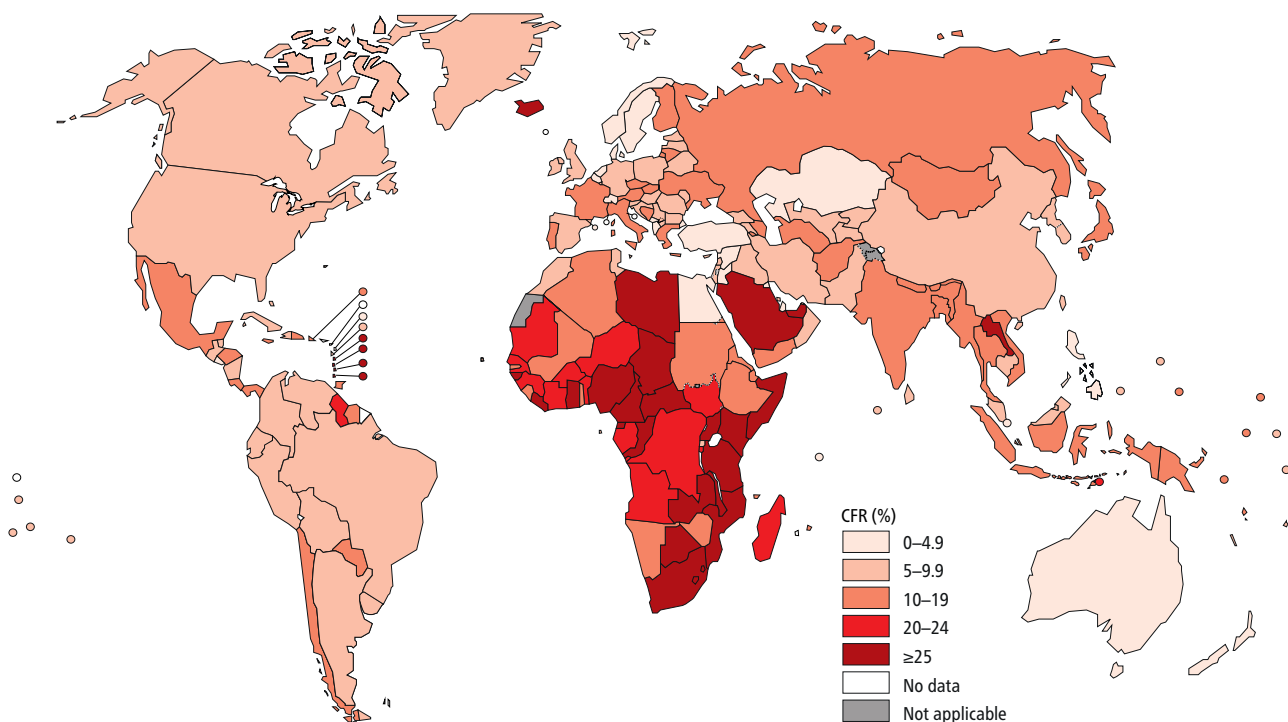
**Culture confirmation and DST coverage among new cases of pulmonary TB, 2010–2015**



**TABLE 3.4**

**Cumulative number of deaths averted by TB and TB/HIV interventions 2000–2016 (in millions), globally and by WHO region**

WHO REGION	HIV-NEGATIVE PEOPLE		HIV-POSITIVE PEOPLE		TOTAL	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	5.1	4.2–6.0	5.7	5.0–6.5	11	10–12
The Americas	1.5	1.3–1.6	0.32	0.29–0.34	1.8	1.7–1.9
Eastern Mediterranean	3.5	3.0–4.0	0.05	0.04–0.06	3.6	3.1–4.0
Europe	1.8	1.6–2.0	0.20	0.18–0.21	2.0	1.8–2.2
South-East Asia	20	16–24	1.9	1.5–2.4	22	18–26
Western Pacific	12	11–13	0.32	0.28–0.36	12	11–13
GLOBAL	44	38–50	8.5	7.5–9.5	53	47–58

**FIG. 3.17****Estimates of the case fatality ratio (CFR), (including HIV-negative and HIV-positive people), 2016**

at least one drug in both of the two most important classes of medicines in an MDR-TB regimen: fluoroquinolones and second-line injectable agents (amikacin, capreomycin or kanamycin).

Estimates of the disease burden caused by drug-resistant TB presented in this chapter focus on MDR/RR-TB.

### 3.3.1 Global surveillance of anti-TB drug resistance

Since the launch of the Global Project on Anti-tuberculosis Drug Resistance Surveillance in 1994, data on drug resistance have been systematically collected and analysed from 160 countries worldwide (82% of the 194 WHO Member States), which collectively have more than 97% of the world's population and TB cases. This includes 90 countries that have continuous surveillance systems based on routine diagnostic drug susceptibility testing (DST) of all TB patients, and 70 countries that rely on epidemiological surveys of representative samples of patients (Fig. 3.18). Surveys conducted about every 5 years represent the most common approach to investigating the burden of drug resistance in resource-limited settings where routine DST is not accessible to all TB patients, owing to lack of laboratory capacity or resources.

Progress towards achieving global coverage of drug resistance surveillance data is shown in Fig. 3.19. Among the 30 high TB burden countries and the 30 high MDR-TB burden countries (which comprise a total of 40 countries,

because of overlap between the two groups<sup>1</sup>), 37 have data on levels of drug resistance. The three countries that have never conducted a drug resistance survey are Angola, Congo and Liberia. Among the other 37 high TB burden or high MDR-TB burden countries, the data for Sierra Leone are from before the year 2000, and four countries (Brazil, Central African Republic, Democratic People's Republic of Korea and Papua New Guinea) rely on drug resistance surveillance data gathered from subnational areas only.

In 2015–2016, the first-ever national drug resistance surveys were completed in Burkina Faso, Democratic Republic of the Congo, Ghana, India and Sudan, and repeat surveys were completed in Côte d'Ivoire, Mongolia and Zimbabwe. In 2016–2017, drug resistance surveys were ongoing in 11 countries, with the first nationwide surveys in four countries (Burundi, Eritrea, Indonesia, Lao People's Democratic Republic, Mali and Togo) and repeat surveys in seven countries (Bangladesh, Cambodia, Ethiopia, Malawi, Sri Lanka, Swaziland, Thailand and the United Republic of Tanzania).

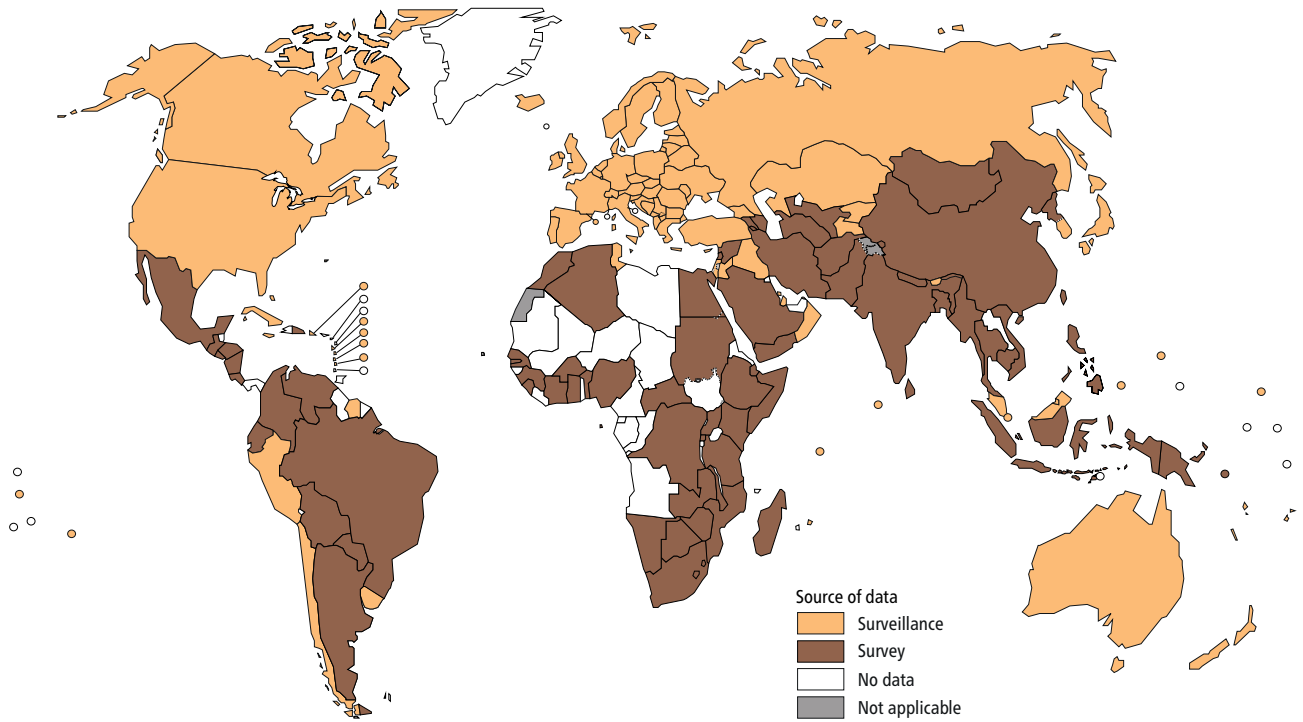
### 3.3.2 Estimates of the disease burden caused by MDR/RR-TB

Globally in 2016, an estimated 4.1% (95% confidence interval [CI]: 2.8–5.3%) of new cases and 19% (95% CI: 9.8–27%) of previously treated cases had MDR/RR-TB (Table 3.5). The proportions of new and previously treated TB cases with

<sup>1</sup> For a full list of the high TB burden and high MDR-TB burden countries, see Chapter 2.

**FIG. 3.18**

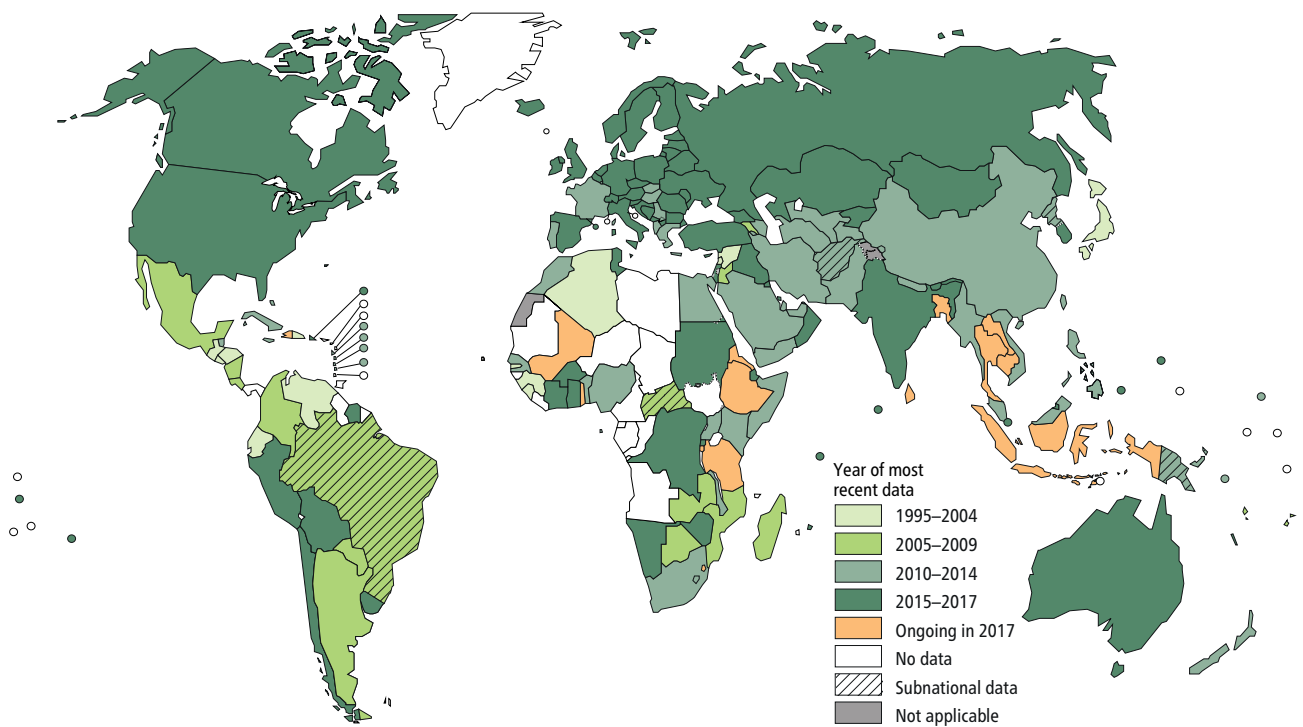
**Data sources available to estimate levels of TB drug resistance<sup>a</sup>**



<sup>a</sup> Data shown refer to new TB cases only.

**FIG. 3.19**

**Global coverage of surveillance data on drug resistance, 1995–2017**



**TABLE 3.5****Estimated incidence of MDR/RR-TB in 2016 for 30 high MDR-TB burden countries, WHO regions and globally**

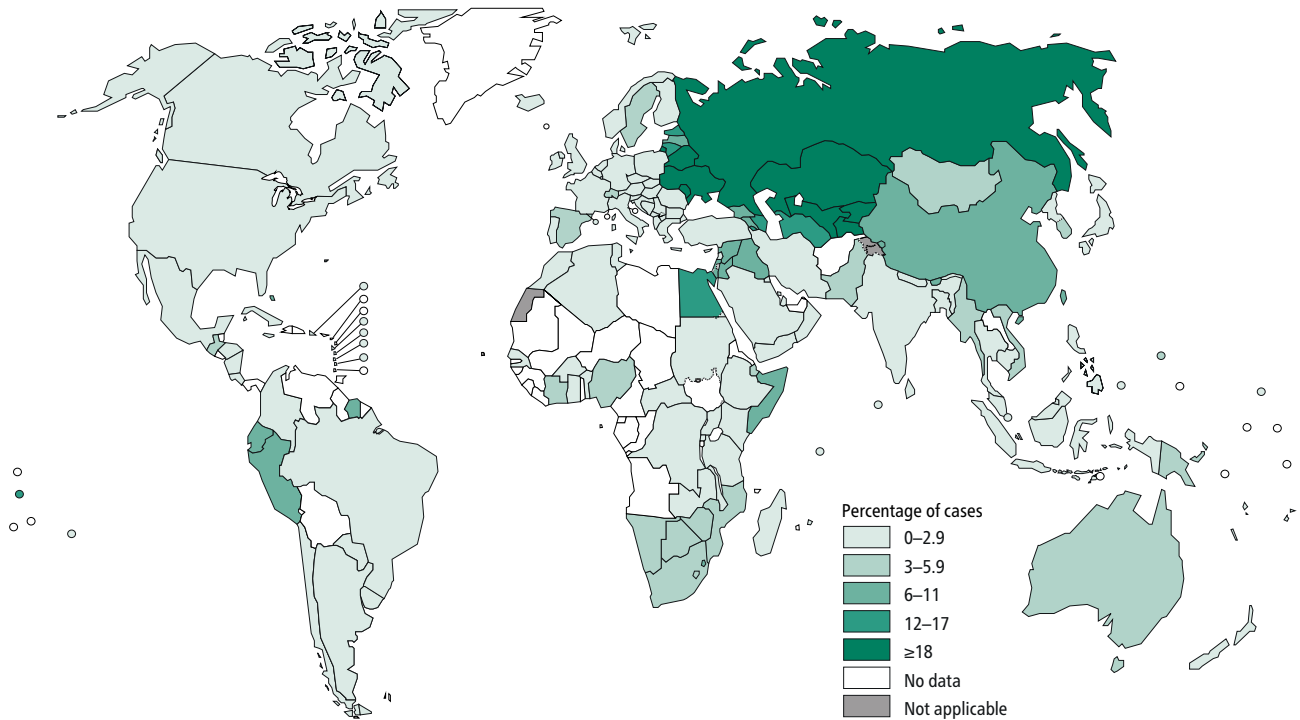
	ESTIMATED % OF NEW CASES WITH MDR/RR-TB		ESTIMATED % OF PREVIOUSLY TREATED CASES WITH MDR/RR-TB		INCIDENCE OF MDR/RR-TB				
	BEST ESTIMATE <sup>a</sup>	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	NUMBER (IN 1000S)	UNCERTAINTY INTERVAL	RATE <sup>b</sup>	UNCERTAINTY INTERVAL	% OF MDR AMONG MDR/RR-TB
Angola	2.6	0.10–5.1	18	0.10–36	4.3	1.4–7.3	15	4.8–25	68
Azerbaijan	13	10–16	39	37–42	2.4	2.0–2.9	25	20–30	77
Bangladesh	1.6	0.59–2.6	29	22–36	8.8	4.8–13	5.4	2.9–7.8	91
Belarus	38	36–40	72	68–75	3.4	2.6–4.1	35	28–43	99
China	7.1	5.6–8.7	24	20–28	73	56–89	5.2	4.0–6.4	75
DPR Korea	2.2	0.51–3.9	16	5.8–27	5.7	3.2–8.1	22	13–32	90
DR Congo	2.2	1.0–3.5	17	9.6–24	7.6	3.9–11	9.7	4.9–15	68
Ethiopia	2.7	1.5–4.0	14	3.6–25	5.8	3.1–8.5	5.7	3.0–8.3	62
India	2.8	2.0–3.5	12	10–13	147	95–199	11	7.2–15	86
Indonesia	2.8	2.2–3.5	16	10–20	32	19–45	12	7.3–17	68
Kazakhstan	26	25–28	44	42–46	7.0	5.4–8.6	39	30–48	91
Kenya	1.3	0.68–1.9	9.4	8.7–10	3.0	1.6–4.4	6.2	3.2–9.1	59
Kyrgyzstan	27	25–29	60	57–63	4.8	4.0–5.5	80	68–92	94
Mozambique	3.7	2.4–5.0	20	2.1–37	7.6	4.5–11	26	16–37	85
Myanmar	5.1	3.2–7.0	27	10–44	13	8.8–18	25	17–34	99
Nigeria	4.3	3.2–5.4	25	19–31	20	12–29	11	6.4–15	66
Pakistan	4.2	3.2–5.3	16	15–17	27	17–37	14	8.8–19	90
Papua New Guinea	3.4	1.7–5.0	26	15–36	1.9	1.2–2.6	23	15–32	78
Peru	6.3	5.9–6.7	24	23–26	3.5	2.9–4.2	11	9.1–13	89
Philippines	2.6	1.8–3.3	29	20–38	30	21–40	30	20–39	75
Republic of Moldova	26	24–28	56	51–60	2.3	1.9–2.6	56	47–65	97
Russian Federation	27	27–28	65	65–66	63	52–74	44	36–51	100
Somalia	8.7	5.9–11	47	23–71	3.9	2.2–5.6	27	16–39	64
South Africa	3.4	2.5–4.3	7.1	4.8–9.5	19	12–25	34	22–45	62
Tajikistan	22	21–24	45	40–50	2.6	2.1–3.1	30	24–36	96
Thailand	2.2	1.5–2.9	24	16–32	4.7	3.0–6.3	6.8	4.4–9.2	86
Ukraine	27	26–27	47	46–48	21	16–26	47	37–58	85
Uzbekistan	24	18–30	63	50–75	10	7.6–13	32	24–40	97
Viet Nam	4.1	2.6–5.5	26	25–27	8.2	6.1–10	8.7	6.5–11	94
Zimbabwe	4.6	3.0–6.2	14	8.9–20	1.9	1.3–2.6	12	8.0–16	41
<b>MDR/RR HBCs</b>	<b>4.4</b>	<b>2.8–6.0</b>	<b>19</b>	<b>8.7–30</b>	<b>546</b>	<b>487–609</b>	<b>12</b>	<b>11–13</b>	<b>83</b>
Africa	2.7	2–3.5	14	8.4–20	93	81–106	9.1	7.9–10	68
The Americas	2.9	1.4–4.3	13	6.9–20	12	11–13	1.2	1.1–1.3	88
Eastern Mediterranean	4.2	1.7–6.7	17	14–19	41	31–52	6.2	4.7–7.8	83
Europe	19	12–26	55	43–67	122	110–134	13	12–15	96
South-East Asia	2.8	2.4–3.1	13	10–15	214	163–272	11	8.4–14	86
Western Pacific	5.3	2.9–7.8	25	20–29	119	101–139	6.3	5.3–7.4	77
<b>GLOBAL</b>	<b>4.1</b>	<b>2.8–5.3</b>	<b>19</b>	<b>9.8–27</b>	<b>601</b>	<b>541–664</b>	<b>8.1</b>	<b>7.3–8.9</b>	<b>82</b>

<sup>a</sup> Best estimates are for the latest available year.

<sup>b</sup> Rates are per 100 000 population.

**FIG. 3.20**

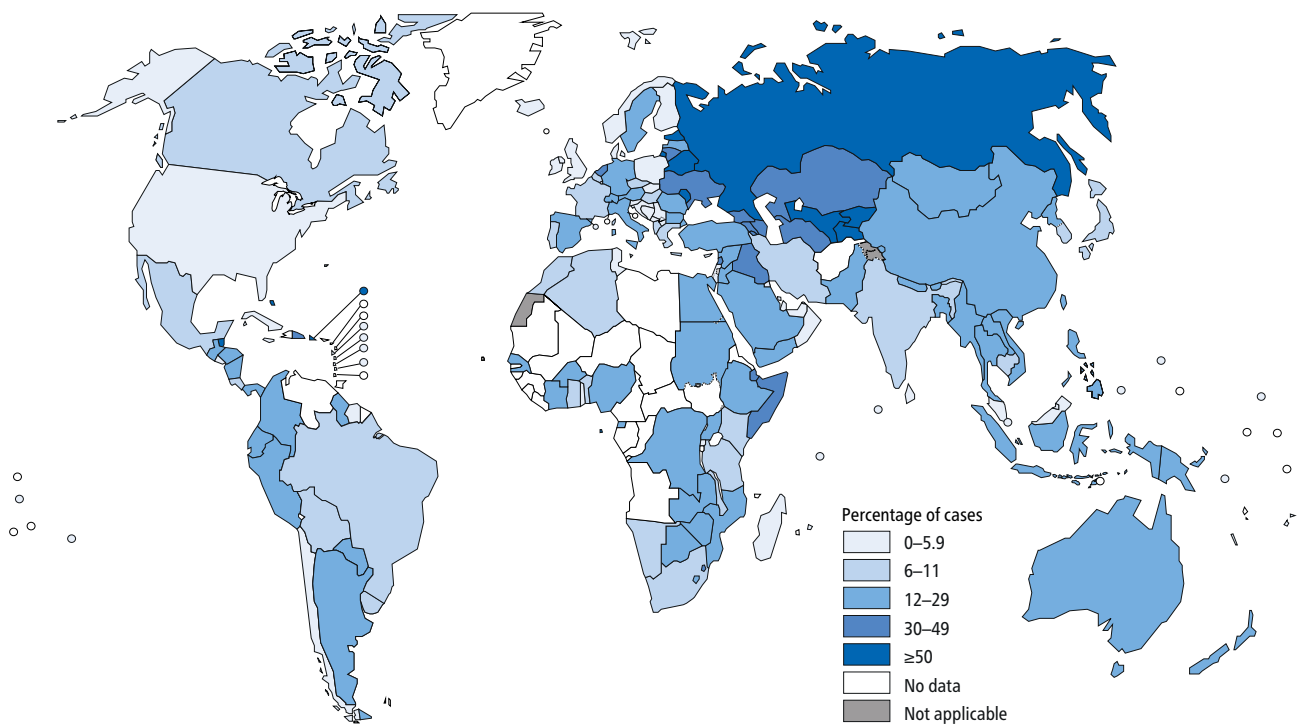
**Percentage of new TB cases with MDR/RR-TB<sup>a</sup>**



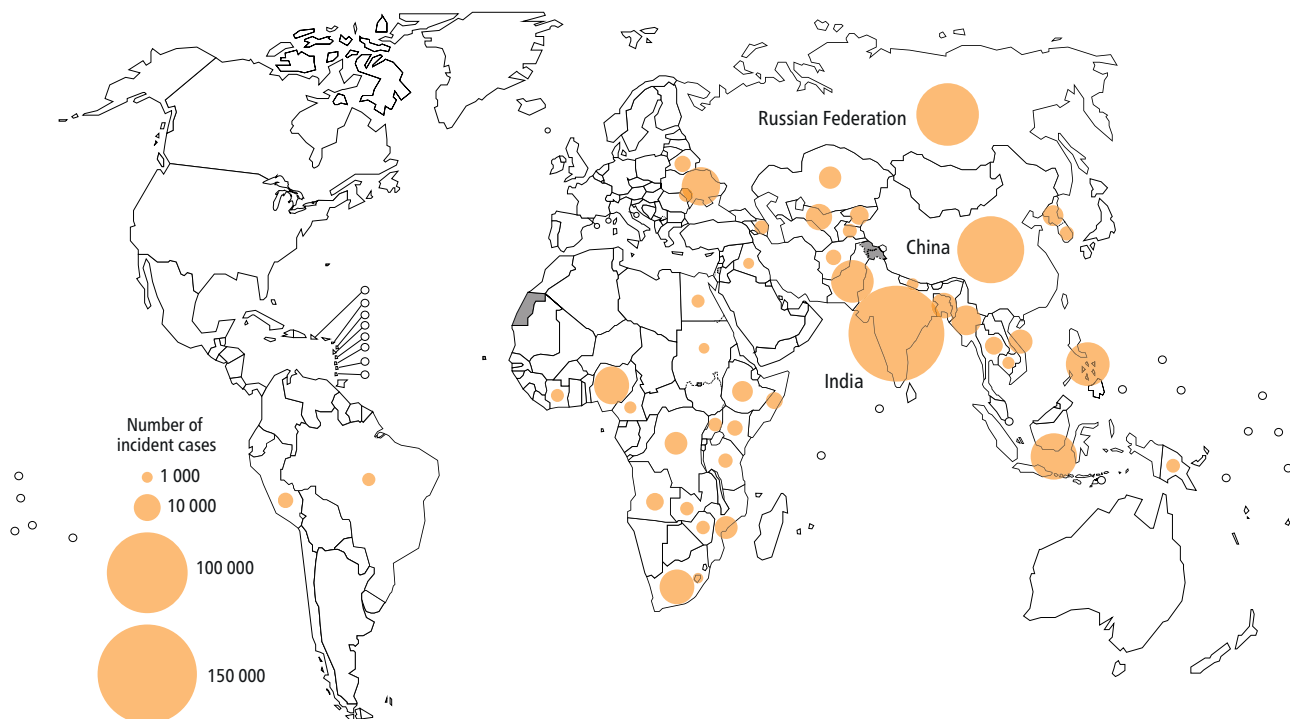
<sup>a</sup> Figures are based on the most recent year for which data have been reported, which varies among countries. Data reported before 2002 are not shown.

**FIG. 3.21**

**Percentage of previously treated TB cases with MDR/RR-TB<sup>a</sup>**



<sup>a</sup> Figures are based on the most recent year for which data have been reported, which varies among countries. Data reported before 2002 are not shown. The high percentages of previously treated TB cases with MDR-TB in Bahamas, Belize, French Polynesia, Puerto Rico and Sao Tomé and Príncipe refer to only a small number of notified cases (range: 1-8 notified previously treated TB cases).

**FIG. 3.22****Estimated incidence of MDR/RR-TB in 2016, for countries with at least 1000 incident cases**

MDR/RR-TB at the country level are shown in [Fig. 3.20](#) and [Fig. 3.21](#).

There were an estimated 600 000 (range, 540 000–660 000) incident cases of MDR/RR-TB in 2016, with cases of MDR-TB accounting for 82% (490 000) of the total ([Table 3.5](#)). The countries with the largest numbers of MDR/RR-TB cases (47% of the global total) were China, India and the Russian Federation ([Fig. 3.22](#)). There were about 240 000 (range, 140 000–340 000) deaths from MDR/RR-TB in 2016, similar to the best estimate for 2015 that was published in the 2016 edition of the WHO global TB report.

Data compiled from surveys and continuous surveillance of drug resistance among TB patients also allow estimation of the number of MDR/RR-TB cases among notified TB patients with pulmonary TB. These are the MDR/RR-TB cases that could be detected if all notified patients were tested for drug resistance to rifampicin and isoniazid using WHO-recommended diagnostic tests. Globally in 2016, there were an estimated 350 000 (range, 330 000–370 000) MDR/RR-TB cases among notified TB patients.

### 3.3.3 Trends in drug resistance

Of the 40 countries with a high TB or MDR-TB burden (or both), only 22 have repeated a survey at least once to evaluate trends in drug resistance. Among these countries, nine have at least 3 years of data: Belarus, Kazakhstan, Myanmar, Peru, Republic of Moldova, Russian Federation, Thailand, Ukraine and Viet Nam. For these settings, [Fig. 3.23](#) shows trends in

the number of new TB cases notified, the proportion of new TB cases with MDR, and per capita TB and MDR-TB rates. Based on these data, there is a slight trend for cases of MDR-TB to increase as a proportion of all TB cases in these countries, with the burden of MDR-TB either increasing faster or decreasing more slowly than the overall TB burden in each country.

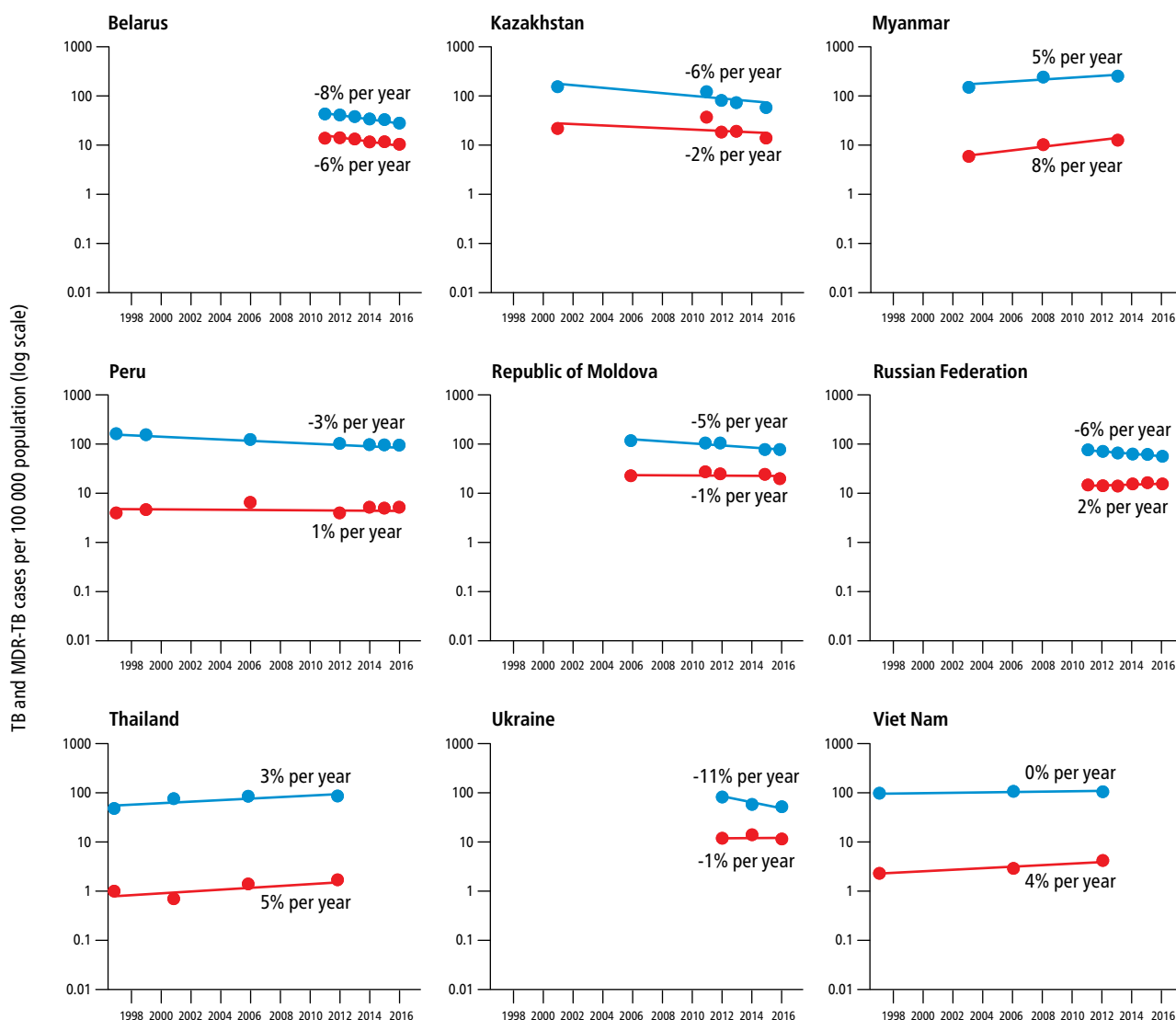
### 3.3.4 Resistance to isoniazid and to second-line anti-TB drugs

Levels of resistance to isoniazid without concurrent rifampicin resistance are available for 158 countries over the period 2002–2016. The proportions of TB patients resistant to isoniazid but susceptible to rifampicin in each country were weighted according to the number of new TB cases that were notified in the country to generate a global average. Among all TB cases, the global average of isoniazid resistance without concurrent rifampicin resistance was 8.5% (95% CI: 7.4–9.7). In new and previously treated TB cases, the global averages were 7.3% (95% CI: 6.1–8.6) and 14% (95% CI: 12–17), respectively.

By the end of 2016, XDR-TB had been reported by 123 WHO Member States. Of these, 91 countries and five territories reported representative data from continuous surveillance or surveys regarding the proportion of MDR-TB cases that had XDR-TB. Combining their data, the average proportion of MDR-TB cases with XDR-TB was 6.2% (95% CI: 3.6–9.5%), with the best estimate lower than those based on data available in previous years (9.5% in 2015, 9.7% in 2014

**FIG. 3.23**

**Trends in levels of drug resistance in selected high MDR-TB burden countries with at least three years of data.** The **blue** line shows the number of new notified MDR-TB cases per 100 000 population. The **red** line shows the number of MDR-TB cases among new TB patients per 100 000 population.



and 9.0% in 2013). This decrease is explained by the use of a larger quantity of routine surveillance data and more precise country-specific measures of the prevalence of second-line drug resistance among MDR/RR-TB cases.

Among the 40 countries with a high TB or MDR-TB burden, 22 have surveillance data on resistance to second-line anti-TB drugs. The proportion of MDR-TB/RR-TB cases with resistance to any fluoroquinolone for which testing was done – including ofloxacin, levofloxacin and moxifloxacin – was 20% (95% CI: 14–26%).

### 3.4 National TB prevalence surveys

The prevalence of TB disease is not an indicator in the SDGs or a high-level indicator of the End TB Strategy, and no global target has been set for the period 2016–2035.<sup>1</sup> Furthermore, indirect estimates of prevalence suffer from considerable uncertainty, because they are derived from incidence and assumptions about disease duration. For these two reasons, indirect estimates of TB prevalence (i.e. estimates that are not from a national TB prevalence survey) are not presented in this chapter.<sup>2</sup>

In an important subset of countries with a large proportion of the world's TB burden, however, national TB prevalence

<sup>1</sup> This is in contrast to the era of the Millennium Development Goals (MDGs) and Stop TB Strategy, when one of the global targets for reductions in TB disease burden was to halve prevalence between 1990 and 2015.

<sup>2</sup> WHO will continue to produce indirect estimates of TB prevalence. These can be provided upon request to [tbddata@who.int](mailto:tbddata@who.int).



surveys continue to provide the best method for measuring the burden of TB disease (both in absolute terms and to assess trends when repeat surveys are done, and by age and sex). Findings can inform assessment of actions needed to reduce this burden as well as estimates of TB incidence (Fig. 3.2), thus contributing to monitoring of progress towards SDG and End TB Strategy targets. The WHO Global Task Force on TB Impact Measurement has retained national TB prevalence surveys within its strategic areas of work 2016–2020 (Box 3.1), and defined the group of countries where they continue to be relevant as those with a relatively high burden of TB (about 150 incident cases per 100 000 population) that do not yet have health, national notification and VR systems of the quality and coverage required to provide reliable and routine direct measurements of the number of TB cases and deaths.<sup>1</sup> An excellent recent example of a prevalence survey that has informed understanding of trends in TB disease burden, estimates of TB incidence and identification of actions required to reduce the burden of TB disease is the 2016 survey in the Philippines (Box 3.6).

Countries in which national prevalence surveys were implemented in 2000–2016 or are planned for 2017–2018 are shown in Fig. 3.24 and Fig. 3.25. An unprecedented number of surveys were implemented in 2007–2015, a period in which the WHO Global Task Force on TB Impact Measurement defined national TB prevalence surveys in 22 global focus countries as one of its three strategic areas of work (Box 3.1). Between 2007 and the end of 2016, a total of 25 surveys that used the screening and diagnostic methods recommended in the second edition of the WHO handbook on prevalence surveys<sup>2</sup> were completed. This included 13 surveys in Asian countries (of which two were in the Philippines) and 12 in African countries. In 2016, surveys were completed in Bangladesh, the Democratic People’s Republic of Korea, Kenya and the Philippines. A further 10 surveys will be implemented in 2017 or 2018, including in India, Mozambique, Myanmar, South Africa and Viet Nam. The surveys in Myanmar and Viet Nam are repeat surveys.

A comparison of estimates of TB prevalence before and after the implementation of a national survey is shown for the 25 surveys in Fig. 3.26. Post-survey prevalence estimates were almost always more precise (i.e. had narrower uncertainty intervals). For 18 countries, estimates were within the

<sup>1</sup> In the Task Force’s April 2016 meeting, epidemiological criteria for conducting a survey were defined for two groups of countries: those that implemented a survey in 2009–2015 and in which a repeat survey could be considered; and those that have never conducted a survey. There were 24 countries in the first group and 33 in the second group. For any of these 57 countries, it was emphasized that feasibility criteria must also be considered. In particular, the prerequisites for conducting a survey defined in the WHO handbook on national TB prevalence surveys (see next footnote) should be met. For further details, see 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](http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf6_report.pdf?ua=1), accessed 11 September 2017).

<sup>2</sup> World Health Organization. Tuberculosis prevalence surveys: a handbook (WHO/HTM/TB/2010.17). Geneva: WHO; 2011 ([www.who.int/tb/advisory\\_bodies/impact\\_measurement\\_taskforce/resources\\_documents/thelimebook/](http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/resources_documents/thelimebook/), accessed 24 August 2017).

**FIG. 3.24**

**Global progress in implementing national surveys of the prevalence of TB disease, actual (2000–2017) and expected (2018)**

2000	China				
2001					
2002	Cambodia				
2003	Malaysia				
2004	Indonesia				
2005	Eritrea <sup>a</sup>				
2006	Thailand				
2007	Philippines	Viet Nam			
2008	Bangladesh <sup>a</sup>				
2009	Myanmar				
2010	China				
2011	Cambodia	Ethiopia	Lao PDR	Pakistan	
2012	Gambia	Nigeria	Rwanda	UR Tanzania	Thailand
2013	Malawi	Ghana	Sudan		
2014	Indonesia	Zambia	Zimbabwe		
2015	Bangladesh	Kenya	Mongolia	Uganda	
2016	DPR Korea	Philippines			
2017	Mozambique <sup>b</sup>	South Africa <sup>b</sup>	Myanmar <sup>b</sup>	Namibia <sup>b</sup>	Viet Nam <sup>b</sup>
2018	Botswana	India	Lesotho	Nepal	Swaziland

<sup>a</sup> The surveys in Bangladesh (2008) and Eritrea (2005) collected sputum samples from all individuals (aged ≥15 years), and did not use chest X-ray and/or a symptom questionnaire to screen individuals for sputum submission.

<sup>b</sup> These surveys have started or field operations are scheduled to start in 2017.

pre-survey uncertainty interval, whereas for the other seven countries the survey found a burden that was either significantly above (six countries) or below (one country) the burden that had been estimated in the absence of survey data.

The distribution of TB disease by age (in adults) and sex based on prevalence survey data is shown in Fig. 3.27 and Fig. 3.28. In Asia and some African countries (e.g. Ghana, Malawi, Rwanda, the United Republic of Tanzania and Zimbabwe), prevalence increases with age. However, in several African countries (e.g. Ethiopia, Gambia, Nigeria, Sudan, Uganda and Zambia), prevalence per 100 000 population peaks among those aged 35–54 years. The male to female (M:F) ratio of cases for the same set of surveys shows a systematically higher burden of TB disease among men, with ratios ranging from 1.2 (in Ethiopia) to 4.5 (in Viet Nam) for bacteriologically confirmed TB. In most countries, the ratio was in the range 2–4.

The ratio of prevalence to notifications (P:N) can be used to compare detection and reporting gaps (Fig. 3.29a) and variation in these gaps by sex (Fig. 3.29b). The P:N ratios from surveys implemented in 2007–2016 suggest that women are accessing available diagnostic and treatment services more effectively than men. The higher disease burden in men, combined with larger gaps in detection and reporting, also suggests that strategies to improve access to and use of health services among men are required.

## BOX 3.6 ■ The 2016 national TB prevalence survey in the Philippines: results and lessons learned

The fourth national survey of the prevalence of TB disease in the Philippines was conducted from March to December 2016, following surveys in 1981–1983, 1997 and 2007. It was implemented by the Foundation for the Advancement of Clinical Epidemiology, under the National TB Control Programme, Department of Health and the Philippine Council for Health Research and Development. The main survey objective was to estimate the prevalence of pulmonary TB (bacteriologically confirmed; i.e. culture-positive TB or Xpert MTB/RIF, or both) among the general population aged 15 years or more.

### Methods

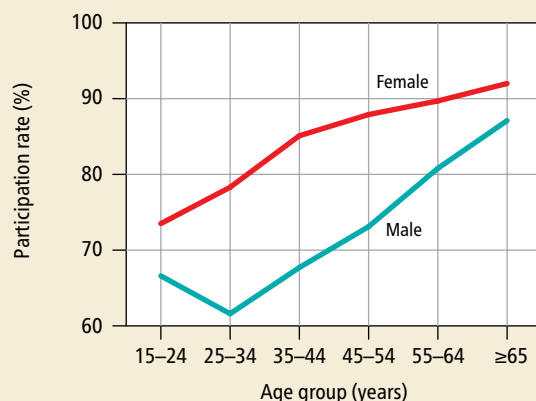
Survey design and overall methods followed the international recommendations of the WHO Global Task Force on TB Impact Measurement (Box 3.1). All survey participants were screened for symptoms by interview and by digital chest X-ray examination. Participants with any of the following – cough of at least 2 weeks and/or haemoptysis (screening symptoms) or radiological lesion(s) in the lung consistent with TB – were asked to submit two sputum specimens (one spot and one early morning). These were examined by direct light-emitting diode (LED-FM) microscopy, culture (Ogawa solid media) and Xpert MTB/RIF in one of six laboratories.<sup>a</sup>

A total of 89 663 people of all ages were enumerated during the survey, which covered 106 randomly selected clusters across four strata.<sup>b</sup> Of these, 61 466 (69%) were eligible and invited to participate in the survey based on age ( $\geq 15$  years) and residency status. Residents were defined as having spent at least the past 2 weeks in the cluster or having slept in the household more than 50% of the time in the past month.

Of those who were eligible, 46 689 people (76%) participated in the survey's cluster operations. Participation was higher for females (82%) than males (70%) (Fig. B3.6.1). The average number of participants per cluster was 440 (range 149–576). Of all participants, 13 517 (29%) screened positive for TB by both screening methods. A further 5080 participants who were asymptomatic but did not have a chest X-ray were also

FIG. B3.6.1

### Survey participation rate by age group and sex



asked to submit sputum samples (Fig. B3.6.2). Among the 18 597 participants eligible for sputum collection, 16 242 (87%) submitted at least one sputum specimen.

Best-practice analytical methods were used to estimate TB prevalence, taking into account clustered sampling, as well as non-participation and other missing data.<sup>c</sup>

### Main results

A total of 466 bacteriologically confirmed pulmonary TB cases were found in the survey, of whom 173 had smear-positive TB and 293 had smear-negative TB. Of the 466 cases, 238 (51%) were diagnosed by Xpert MTB/RIF only, 159 (34%) were diagnosed by Xpert MTB/RIF and culture, and 69 (15%) were diagnosed by culture only.

Of the 466 bacteriologically confirmed cases, 150 (32%) reported screening symptoms, and 430 (92%) screened positive on chest X-ray. Of the 173 smear-positive TB cases, 88 (51%) reported screening symptoms and 159 (92%) screened positive on chest X-ray.

TB prevalence per 100 000 population aged 15 years or more was estimated as 434 (95% CI: 350–518) for smear-positive TB, and 1159 (95% CI: 1016–1301) for bacteriologically confirmed TB. Prevalence was much higher among men than women: 673 (95% CI: 528–819) per 100 000 population compared with 205 (95% CI: 141–270) per 100 000 population for smear-positive TB, and 1713 (95% CI: 1482–1943) compared with 627 (95% CI: 516–739) per 100 000 population for bacteriologically confirmed TB. Prevalence was highest in the 45–54 year age group (Fig. B3.6.3). There was no statistically significant variation between the four geographical strata.

Comparing the prevalence of smear-positive TB among participants aged 15 years or more to the case notification rate for smear-positive TB cases in 2016 (142 per 100 000 population) in the same age group gave a P:N ratio of 3.1 (Fig. B3.6.4). The P:N ratio was higher in men than women, and was particularly high in the 15–24 year age group.

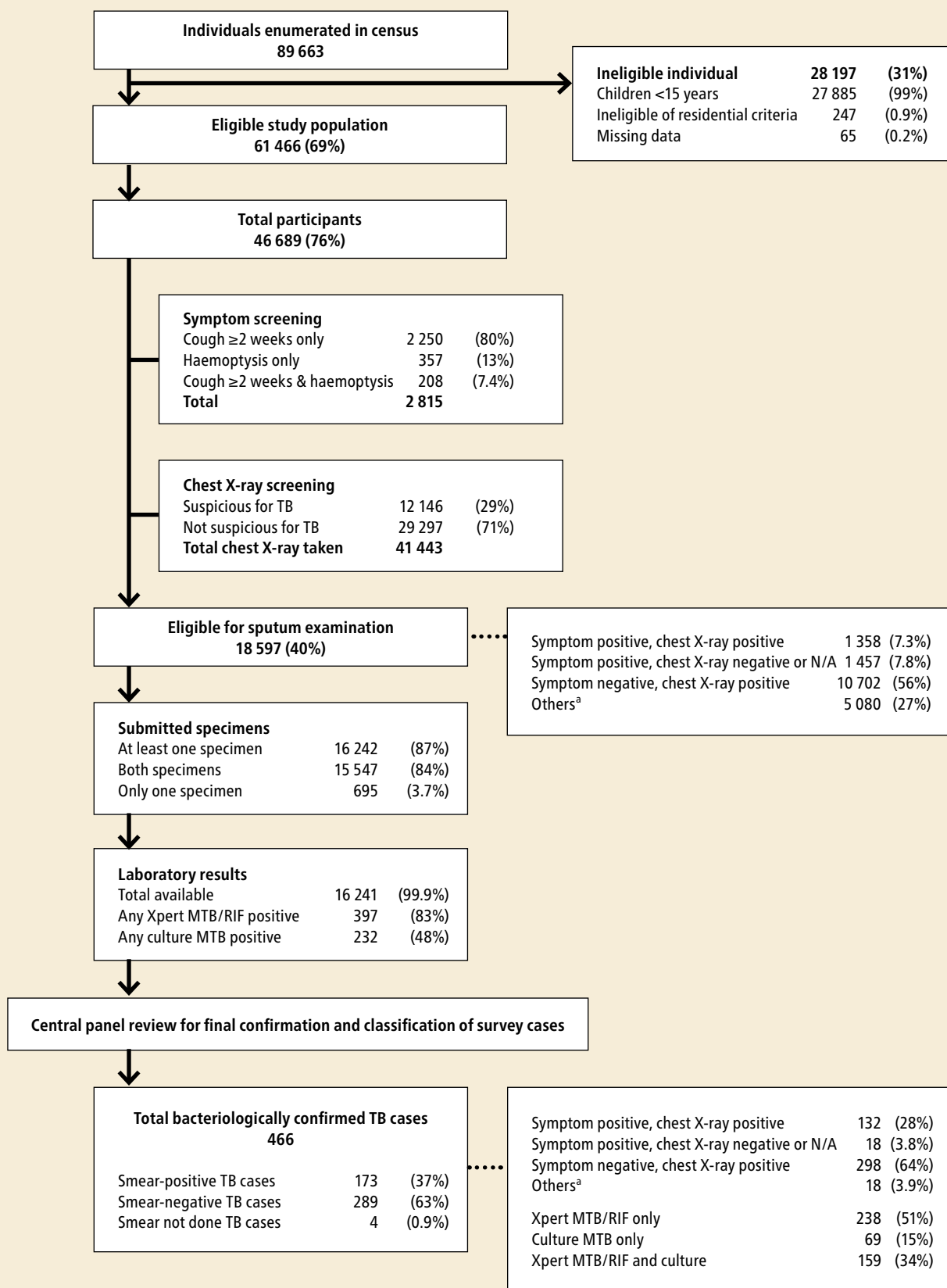
A total of 170 survey participants (0.4%) reported being on TB treatment at the time of the survey (111 men and 59 women). Most of these people reported taking or obtaining treatment in local health centres or in TB clinics (77%), followed by private pharmacies (12%), private clinics or hospitals (7.6%), and provincial hospitals or public medical centres (1.8%). There were 2615 (5.6%) survey participants who reported a past history of TB treatment (1595 men and 1020 women).

A total of 2815 (6%) survey participants reported the presence of screening symptoms at the time of interview. Of the 2815 participants, only 534 (19%) consulted a health-care worker, with more females (23%) seeking a consultation compared with males (16%); 1143 (41%) took no action (younger more so than older participants, and men more than women) and 1130 (40%) self-medicated (predominantly women).

Of the 466 bacteriologically confirmed TB cases identified in the survey, 150 (32.3%) had screening symptoms of at least 2 weeks cough or haemoptysis, or both. However, →

**FIG. B3.6.2**

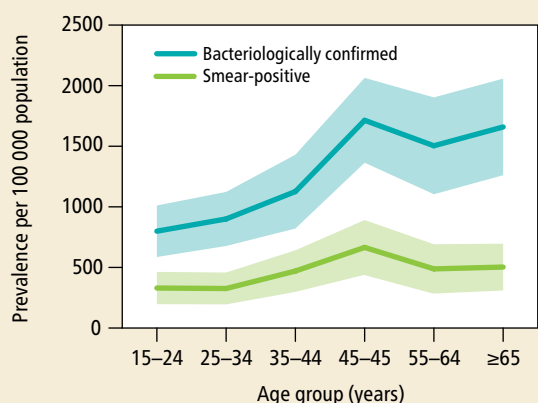
**Consort diagram of the 2016 national TB prevalence survey in the Philippines**



<sup>a</sup> Symptom screening negative but chest X-ray exempted.

**FIG. B3.6.3**

**Prevalence of smear and bacteriologically confirmed pulmonary TB**



→ only 44 (29%) of these people consulted a health-care worker, with 33 (75%) consulting a public provider and 10 (23%) going to a private provider. There were 56 (37%) people who self-medicated and 51 (34%) who did not take any action at the time they experienced the symptoms.

The sample size in 2016 was not designed to detect a specified effect size in comparison with the 2007 survey, but rather to obtain an estimate of prevalence in 2016 with a specified precision. The 2016 survey was therefore not powered to detect small differences with the 2007 survey. Nonetheless, this limitation did not prevent an assessment of the trend in TB disease burden since 2007. Adjustments were made to ensure that the two data sets and methods were as comparable as possible, resulting in an upward adjustment of the 2007 survey results to account for the more sensitive screening and diagnostic methods used in the 2016 survey. Based on these adjustments, the prevalence of culture-positive TB was 463 per 100 000 population (95% CI: 333–592) in 2007 and 512 per 100 000 population (95% CI: 420–603) in 2016. The probability that prevalence did not decline over the period 2007–2016 was estimated at 75%.

**Updated estimates of TB disease burden**

Results from the 2016 prevalence survey were used to update estimates of TB incidence and mortality,<sup>d</sup> with both revised upwards (see also **Box 3.2**). The estimate of TB incidence after the survey was 554 (311–866) per 100 000 population, compared with the pre-survey WHO estimate (which had assumed a decline in incidence since 2007) of 322 per 100 000 (95% CI 277–370). The estimated mortality rate based on the survey was 21 (21–22) per 100 000 population in 2016, compared to a pre-survey estimate of 13 (8.7–19).

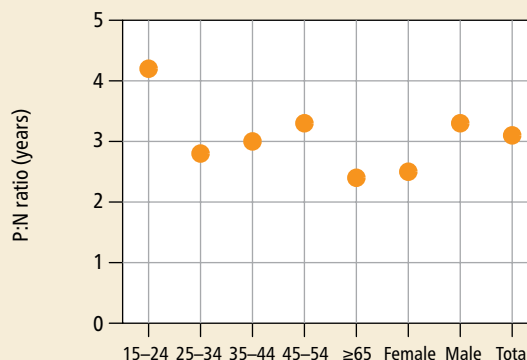
**Programmatic implications**

Notwithstanding the limitation of a 76% participation rate, survey results are of high quality and have provided a robust and up-to-date measurement of the burden of TB disease in the Philippines.

Of the 23 surveys implemented since 2009, when the WHO Global Task Force on TB Impact Measurement agreed on a standard recommendation for diagnostic and screening practices in surveys, the survey in the Philippines found the highest prevalence of bacteriologically-confirmed TB. Although it is not surprising that use of Xpert MTB/RIF increased the diagnostic yield, the prevalence of culture-confirmed TB alone was high (587 per 100 000; 95% CI:

**FIG. B3.6.4**

**Ratio of prevalence to notification<sup>a</sup>**



<sup>a</sup> Prevalence is for bacteriologically confirmed smear-positive TB cases, ≥15 years. Notifications are for all pulmonary smear-positive TB in 2016, ≥15 years.

488–687). The Philippines is thus facing one of the highest burdens of TB in the world. When prevalence is extrapolated to all ages and all forms of TB, it is estimated that there are about 1 million people in the Philippines with TB disease, which is equivalent to 1 in 15 of all prevalent cases globally.

The lack of decline in TB prevalence since 2007 can be explained by a combination of case-detection gaps, possibly significant delays in diagnosis, health system weaknesses, and broader social and economic influences on the TB epidemic. These broader influences include the level of undernourishment, with a prevalence of 14% in 2015 and no improvement since 2008; the level of poverty, with 25% of people living below the national poverty line in 2012; and low coverage of health insurance and social protection, with coverage of only 4% in the poorest quintile in 2013, leading to 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.

In response to the high estimate of TB prevalence, the NTP and partners have defined eight strategic actions at the local level under the general approach of “REACH, CURE and PROTECT.” These are:

1. Replace smear microscopy with a rapid point-of-care diagnostic test, such as Xpert MTB/RIF, in all DOTS facilities and enhance sputum delivery mechanism at all levels.
2. Increase engagement of private providers by expanding the TB service delivery network and human resources and by enforcing the policy of mandatory TB case notification.<sup>e</sup>
3. Improve the availability of patient-centred health facilities providing quality services through a revised certification programme, an improved Phil Health TB package and social protection.
4. Use integrated communication strategies to influence community health-care seeking behaviour.
5. Implement chest X-ray screening among high-risk groups, including 4Ps members (these are beneficiaries of a conditional cash transfer programme for maternal child health, the elderly, contacts, inmates, indigenous populations, people with diabetes and smokers).
6. Undertake intensive supervision and monitoring based on electronic case-based management systems.

7. Network with other government agencies and other key stakeholders to address social determinants.
8. Ensure the governance and sustainable funding of local governance units to support implementation of the End TB Strategy.

The main priorities are protecting those who are financially vulnerable to TB through expanded social insurance and health insurance coverage, preventing TB among those who do not yet have it, and reducing the percentage of TB patients and their households facing catastrophic costs as a result of TB to zero.<sup>f</sup>

It is anticipated that the eight strategic actions can be implemented with the full support of the Department of Health, full mobilization of the health sector with deployment of sufficient human resources at national and subnational levels, increased domestic funding, a presidential executive order for drug regulation, establishment of a high-level steering group, and ensuring financial protection for more than 90% of the poor through increased coverage of Phil Health and expanded social protection programmes.

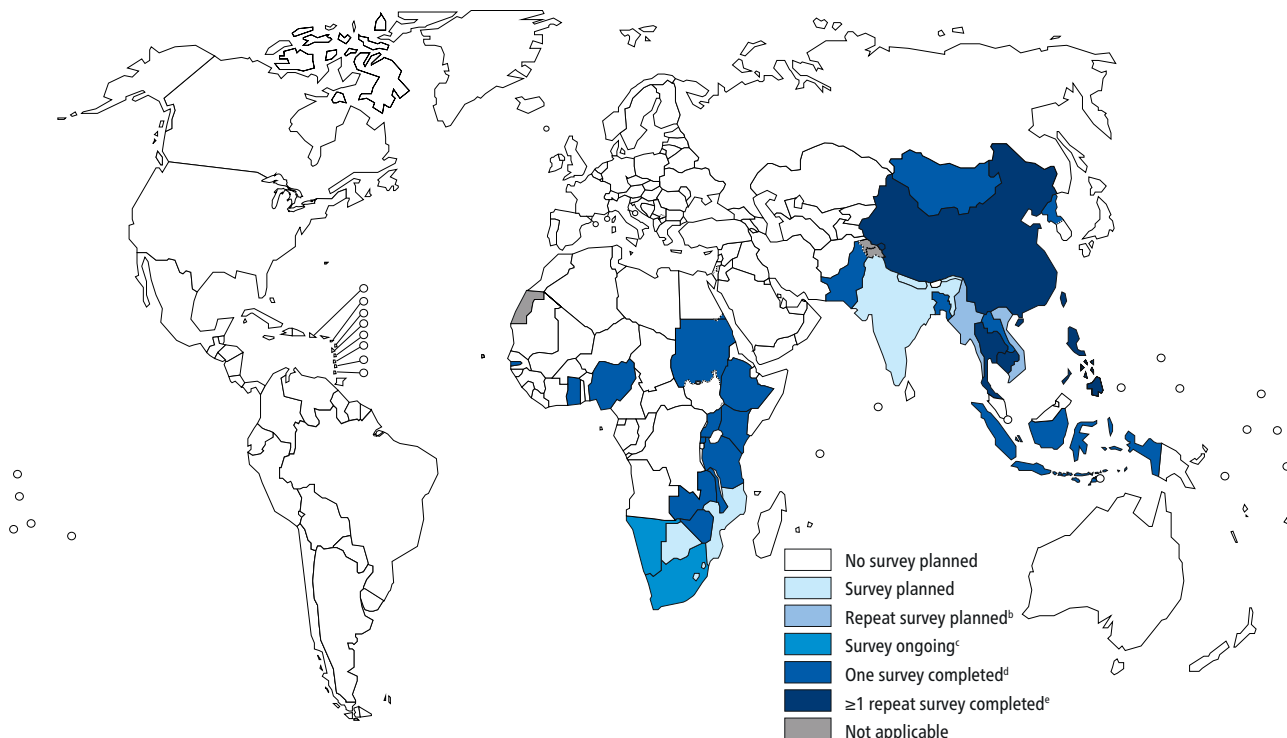
At the most fundamental level, ending TB will require not only greater investment to find and cure TB cases but also

comprehensive and sustained poverty alleviation efforts, linked to the SDGs and multisectoral partnerships at the national and local levels.

- a National TB Reference Laboratory; Medical Research Laboratory, Philippine General Hospital; Cebu TB Reference Laboratory; Region 2 TB Reference Laboratory; Davao TB Reference Laboratory; and Northern Mindanao TB Reference Laboratory.
- b Stratum 1: the National Capital Region, Region 3 and 4A; Stratum 2: the rest of Luzon; Stratum 3: Visayas; and Stratum 4: Mindanao.
- c Floyd S, Sismanidis C, Yamada N, Daniel R, Lagahid J, Mecatti F et al. Analysis of tuberculosis prevalence surveys: new guidance on best-practice methods. *Emerg Themes Epidemiol.* 2013;10(1):10 (<https://www.ncbi.nlm.nih.gov/pubmed/24074436>, accessed 11 September 2017).
- d Incidence is indirectly estimated from prevalence using plausible distributions of disease duration, and mortality is indirectly estimated from prevalence using CFRs estimated from VR data. Other details are provided in the [online technical appendix](#), which is available at [http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/).
- e Mandatory notification of TB cases (Republic Act No. 10767), enacted in April 2016, still needs to be effectively implemented.
- f The NTP implemented a survey of costs faced by TB patients and their households from December 2016 to July 2017. Preliminary results indicate that 35% of TB-affected households spent at least 20% of their household income on costs related to TB, rising to 67% for those with drug-resistant TB.

**FIG. 3.25**

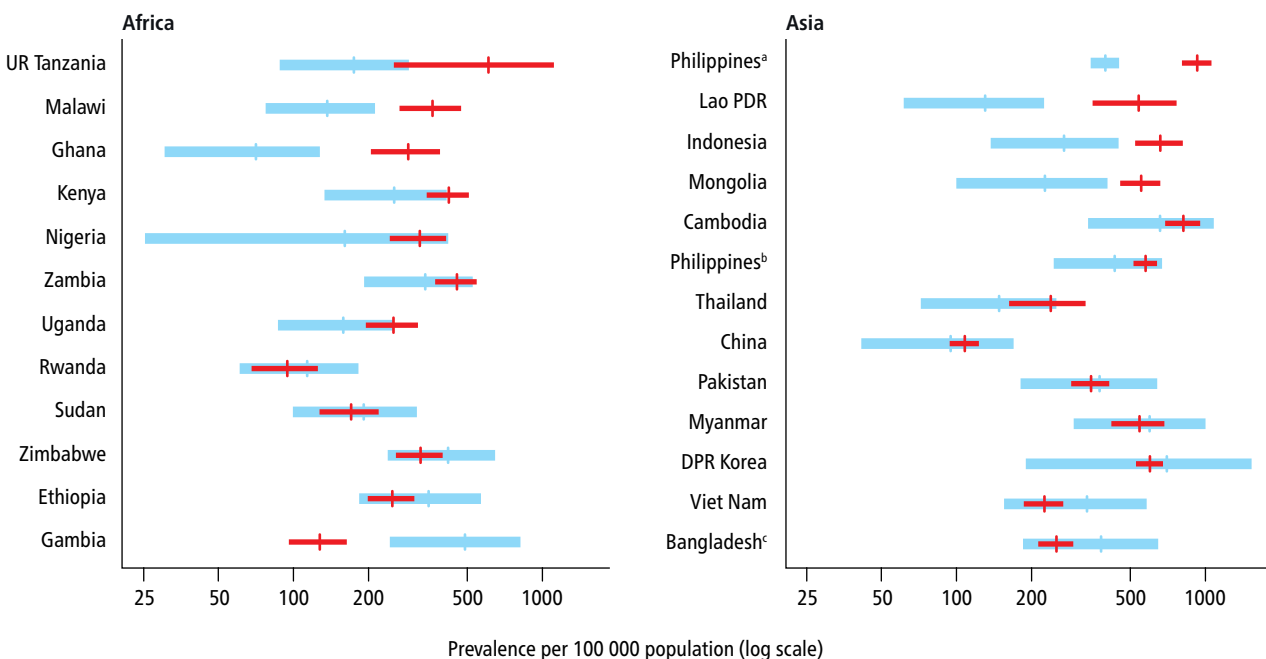
**Countries in which national population-based surveys of the prevalence of TB disease have been implemented using currently recommended screening and diagnostic methods<sup>a</sup> since 2000 or are planned in the future (status in August 2017)**



- a Screening methods include field chest X-ray; at least culture was used to confirm diagnosis. Recent surveys completed in Bangladesh, Kenya and the Philippines used both culture and Xpert MTB/RIF to confirm diagnosis.
- b A country has submitted at least a draft survey protocol and a budget plan to the WHO Global Task Force on TB Impact Measurement.
- c Countries were implementing field operations in August 2017 or were undertaking data cleaning and analysis.
- d A survey was conducted in accordance with WHO recommendations as outlined in *Tuberculosis prevalence surveys: a handbook (2011)* and at least a preliminary report has been published.
- e A repeat national survey is one in which participants were screened with chest X-ray, and (at least) culture was used to diagnose TB cases.

**FIG. 3.26**

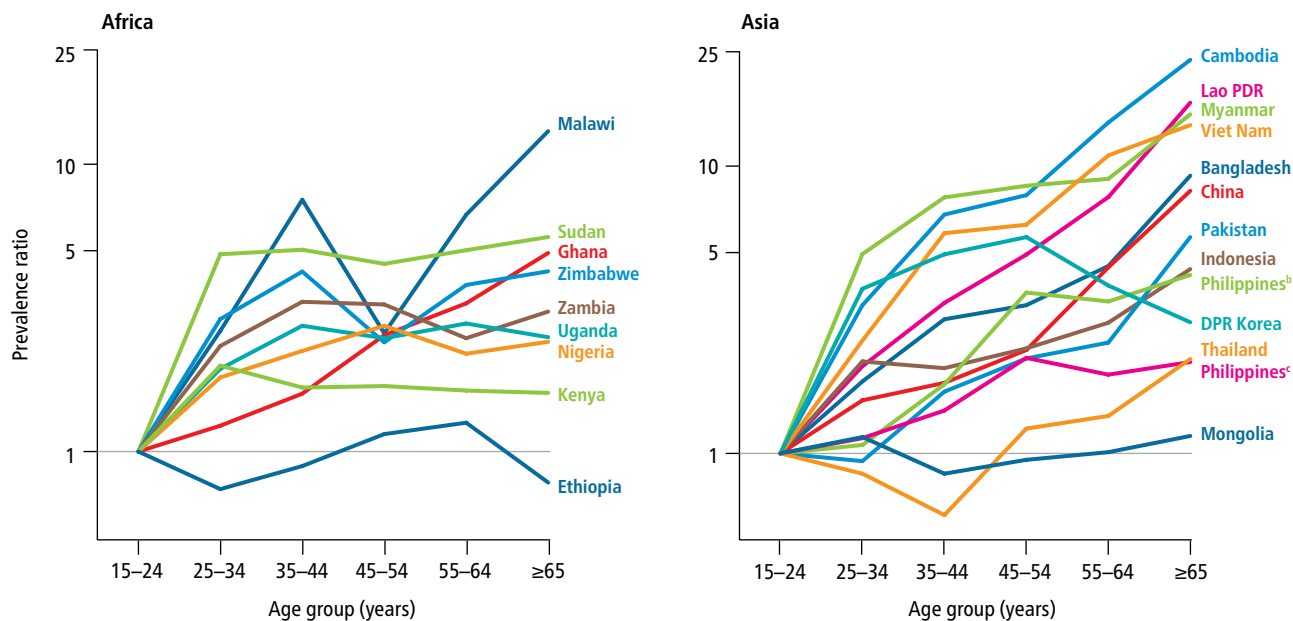
Estimates of TB prevalence (all ages, all forms of TB) for 25 countries, before (in blue) and after (in red) results from national TB prevalence surveys became available since 2007. Panels are ordered according to the before-after difference.



<sup>a</sup> These data relate to the repeat prevalence survey conducted in 2016.  
<sup>b</sup> These data relate to the prevalence survey conducted in 2007.  
<sup>c</sup> These data relate to the prevalence survey conducted in 2015–2016.

**FIG. 3.27**

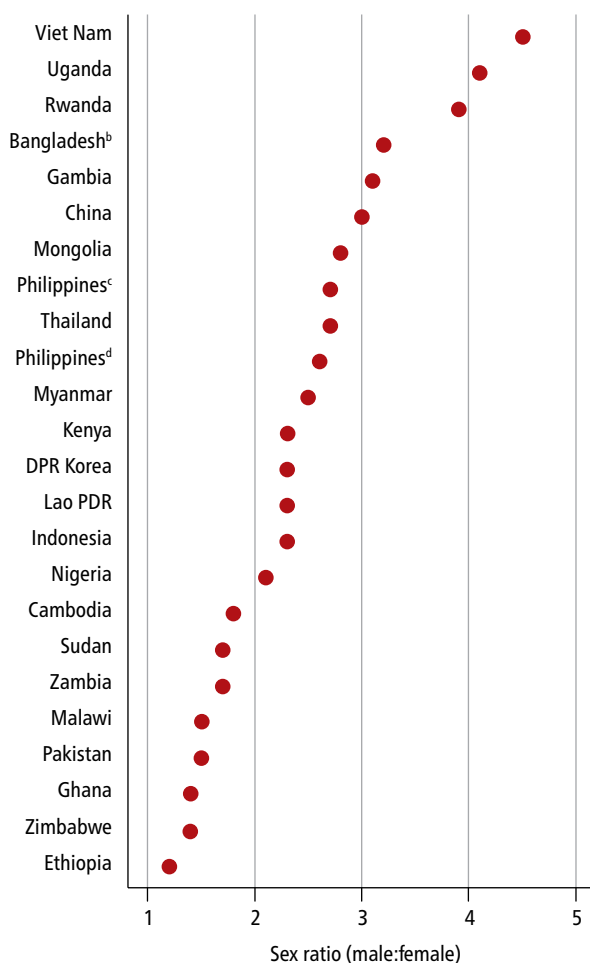
Age-specific prevalence rate ratio of bacteriologically confirmed TB in surveys implemented 2007–2016<sup>a</sup>



<sup>a</sup> Age-specific prevalence ratios were calculated using the prevalence of the 15–24 year age group as the baseline. Data in the presented age groups were not available for Gambia and Rwanda. Data are not shown for UR Tanzania because laboratory challenges during the survey meant that it was only possible to directly estimate the prevalence of smear-positive (as opposed to bacteriologically confirmed) TB.  
<sup>b</sup> These data relate to the prevalence survey conducted in 2007.  
<sup>c</sup> These data relate to the repeat prevalence survey conducted in 2016.

**FIG. 3.28**

The male to female ratio of bacteriologically confirmed adult TB cases detected in prevalence surveys implemented 2007–2016<sup>a</sup>



<sup>a</sup> A value is not shown for UR Tanzania because laboratory challenges during the survey meant that it was only possible to directly estimate the prevalence of smear-positive (as opposed to bacteriologically confirmed) TB.

<sup>b</sup> These data relate to the prevalence survey conducted in 2015–2016.

<sup>c</sup> These data relate to the repeat prevalence survey conducted in 2016.

<sup>d</sup> These data relate to the prevalence survey conducted in 2007.

### 3.5 Estimates of TB incidence and mortality disaggregated by age and sex

This section presents estimates of TB incidence and TB mortality disaggregated by age and sex.

#### 3.5.1 Methods to disaggregate estimates by age and sex

Estimates of TB incidence in children (aged under 15 years) were based on case notifications adjusted for underdiagnosis and underreporting<sup>1</sup> combined with estimates derived from dynamic modelling.<sup>2</sup> Results for the 0–14 age group (0–4 and 5–14 years) in each country were then further disaggregated using outputs from an established deterministic model,<sup>2</sup> followed by disaggregation by sex using results from a meta-analysis of the M:F notification ratio. Estimates of TB incidence in adults were derived by first subtracting incidence in children from incidence in all ages. The estimate for adults was then disaggregated into six age groups (15–24, 25–34, 35–44, 45–54, 55–64 and ≥65 years) using data from national TB prevalence surveys implemented in 2007–2016 (Section 3.4). Country-specific distributions were used for countries that had implemented a survey, whereas for other countries the age distribution was predicted using prevalence survey data. Disaggregation by sex was based on actual M:F ratios for countries that had implemented surveys. For other countries, this disaggregation was based on regional M:F ratios from a systematic review and meta-analysis.<sup>3</sup>

TB mortality in children was estimated for the two age groups using a previously published approach derived from dynamic modelling,<sup>4</sup> and then by sex, on the assumption that the pattern was the same as that for incidence. If available, data on TB deaths among adults were disaggregated for six age groups (15–24, 25–34, 35–44, 45–54, 55–64 and ≥65 years) using VR data. For countries whose mortality estimates were not based on VR data, a CFR was applied to the adult age- and sex-disaggregated incidence. This CFR accounted for differences between HIV-positive and HIV-negative TB cases, and variation in HIV prevalence by age and sex.

Details of the methods used are provided in the [online technical appendix](#).<sup>5</sup>

<sup>1</sup> Jenkins HE, Tolman AW, Yuen CM, Parr JB, Keshavjee S, Pérez-Vélez CM et al. Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. *The Lancet*. 2014;383(9928):1572–1579 (<http://www.sciencedirect.com/science/article/pii/S0140673614601951?via%3Dihub>, accessed 24 August 2017).

<sup>2</sup> Dodd PJ, Gardiner E, Coghlan R, Seddon JA. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Glob Health*. 2014;2(8):e453–459 (<http://www.sciencedirect.com/science/article/pii/S2214109X14702451?via%3Dihub>, accessed 24 August 2017).

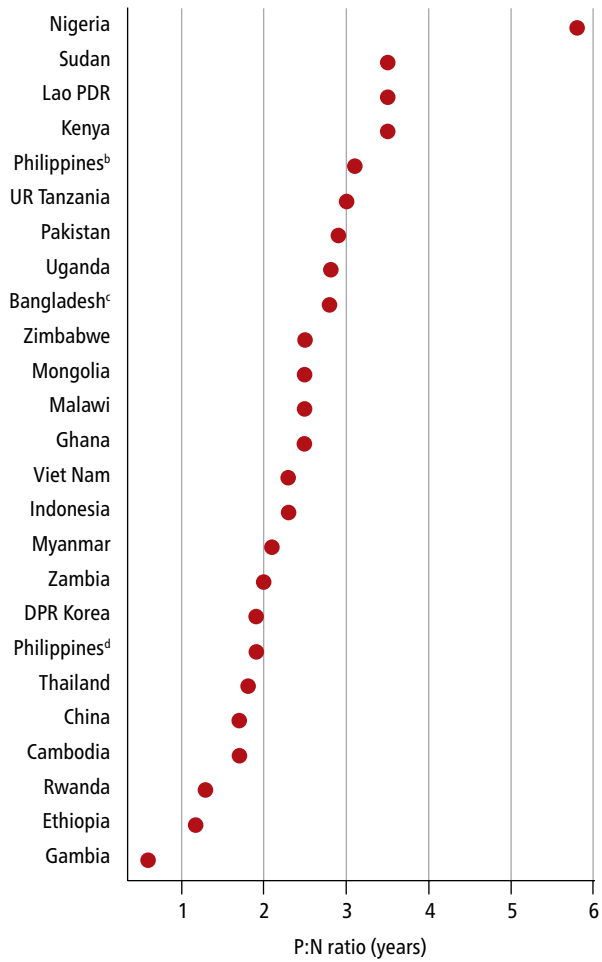
<sup>3</sup> World Health Organization Global Task Force on TB Impact Measurement. Report of the sixth meeting of the full task force; 19–21 April 2016, Gion-sur-Montreux, Switzerland. Geneva: WHO; 2015 ([http://www.who.int/tb/advisory\\_bodies/impact\\_measurement\\_taskforce/meetings/tf6\\_report.pdf?ua=1](http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf6_report.pdf?ua=1), accessed 11 September 2017).

<sup>4</sup> Dodd PJ, Yuen CM, Sismanidis C, Seddon JA, Jenkins HE. The global burden of tuberculosis mortality in children: a mathematical modelling study. *Lancet Glob Health*. 2017;5(9):e898–e906 (<http://www.sciencedirect.com/science/article/pii/S2214109X17302899?via%3Dihub>, accessed 11 September 2017).

<sup>5</sup> The [online technical appendix](#) is available at [http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/).

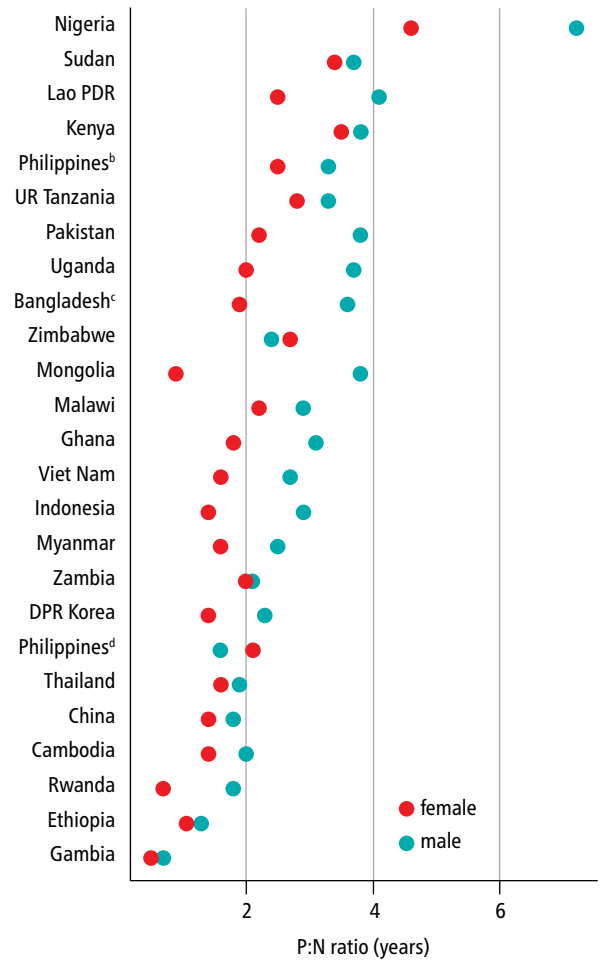
**FIG. 3.29A**

The prevalence to notification (P:N) ratio of adult TB cases in prevalence surveys implemented 2007–2016<sup>a</sup>



**FIG. 3.29B**

The prevalence to notification (P:N) ratio by sex for adult TB cases in prevalence surveys implemented 2007–2016<sup>a</sup>



<sup>a</sup> The P:N ratio is for smear-positive TB, except for Uganda and Zimbabwe where it is based on bacteriologically confirmed TB. Prevalence estimates are from a cross-sectional survey, and therefore only represent one point in time. Notification data are from the main year of the survey (shown in Fig. 3.24).  
<sup>b</sup> These data relate to the repeat prevalence survey conducted in 2016.  
<sup>c</sup> These data relate to the prevalence survey conducted in 2015–2016.  
<sup>d</sup> These data relate to the prevalence survey conducted in 2007.



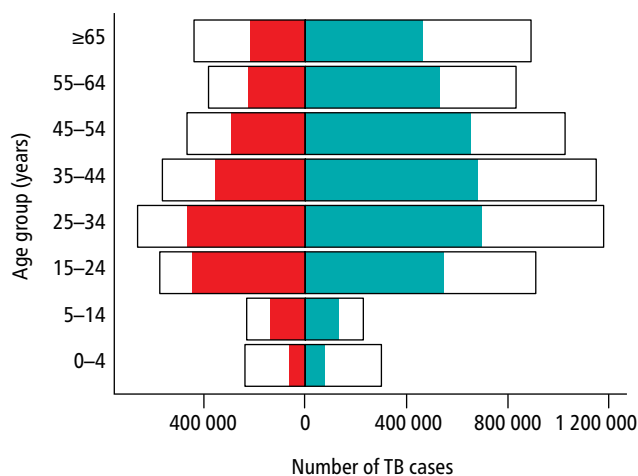
### 3.5.2 TB incidence disaggregated by age and sex

Estimates of TB incidence disaggregated by age and sex are shown in **Fig. 3.30** (global), **Fig. 3.31** (WHO regions) and **Fig. 3.32** (30 high TB burden countries). Globally in 2016, there were an estimated 6.7 million (range, 4.0 million to 9.4 million) incident cases of TB among males, of which 6.2 million (range, 3.7 million to 8.6 million) were adults and 550 000 (range, 340 000–760 000) were children. There were 3.7 million (range, 2.2 million to 5.2 million) incident cases of TB in females, of which 3.2 million (range, 1.9 million to 4.5 million) were adults and 490 000 (range, 300 000–680 000) were children. These numbers correspond to 65% of cases being males and 35% females, and 90% of cases being adults and 10% children.<sup>1</sup>

The M:F ratio of incident TB cases for all ages ranged from 1.3 in the WHO Eastern Mediterranean Region to 2.1 in the WHO Western Pacific Region. Similar M:F ratios were estimated for adults, whereas for children the M:F ratio was close to 1.1 in all WHO regions. Most of the estimated cases among males in 2016 were in Asia (64%) and the WHO African Region (24%), whereas for females the percentages were 59%

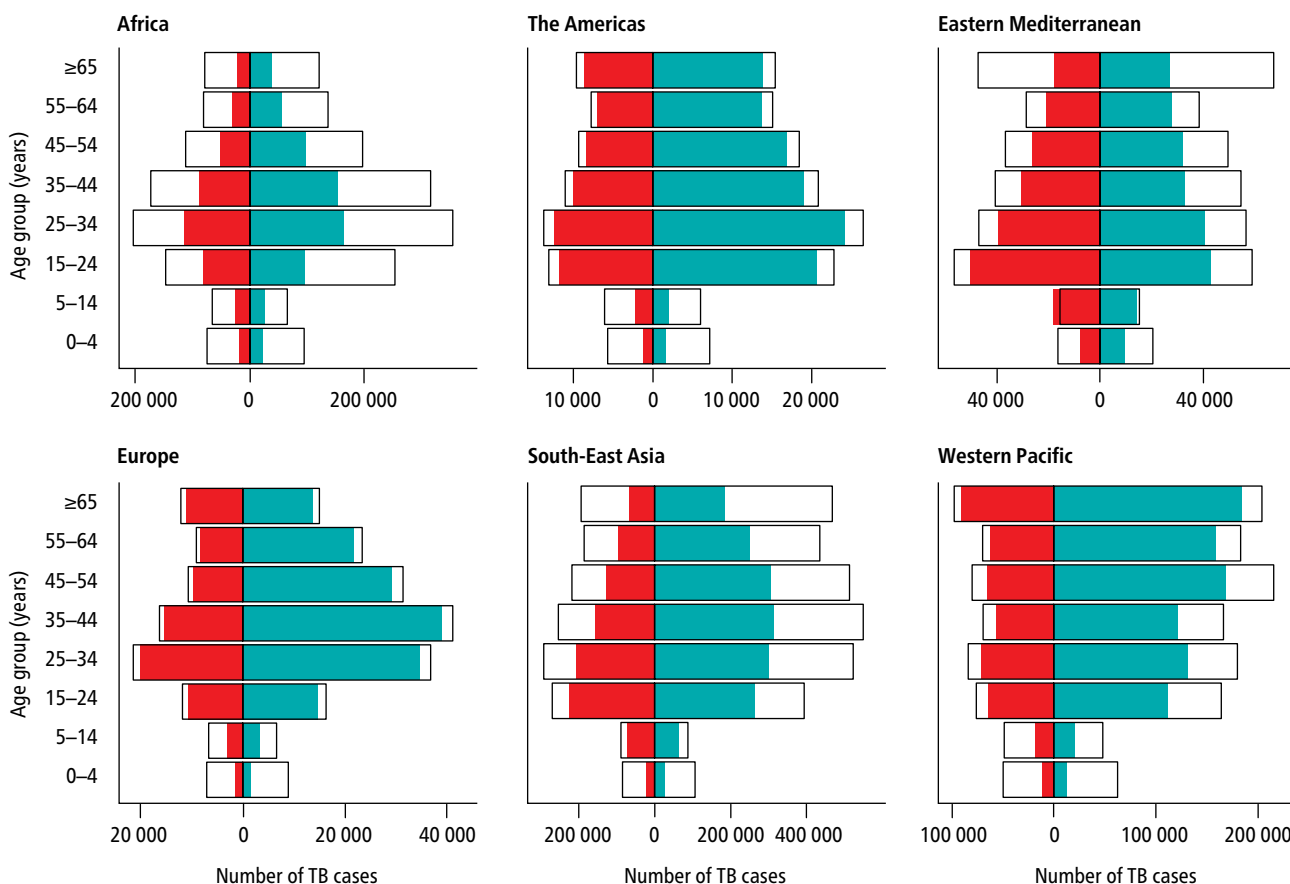
**FIG. 3.30**

**Global estimates of TB incidence (black line) and case notifications disaggregated by age and sex (female in red; male in green), 2016**



**FIG. 3.31**

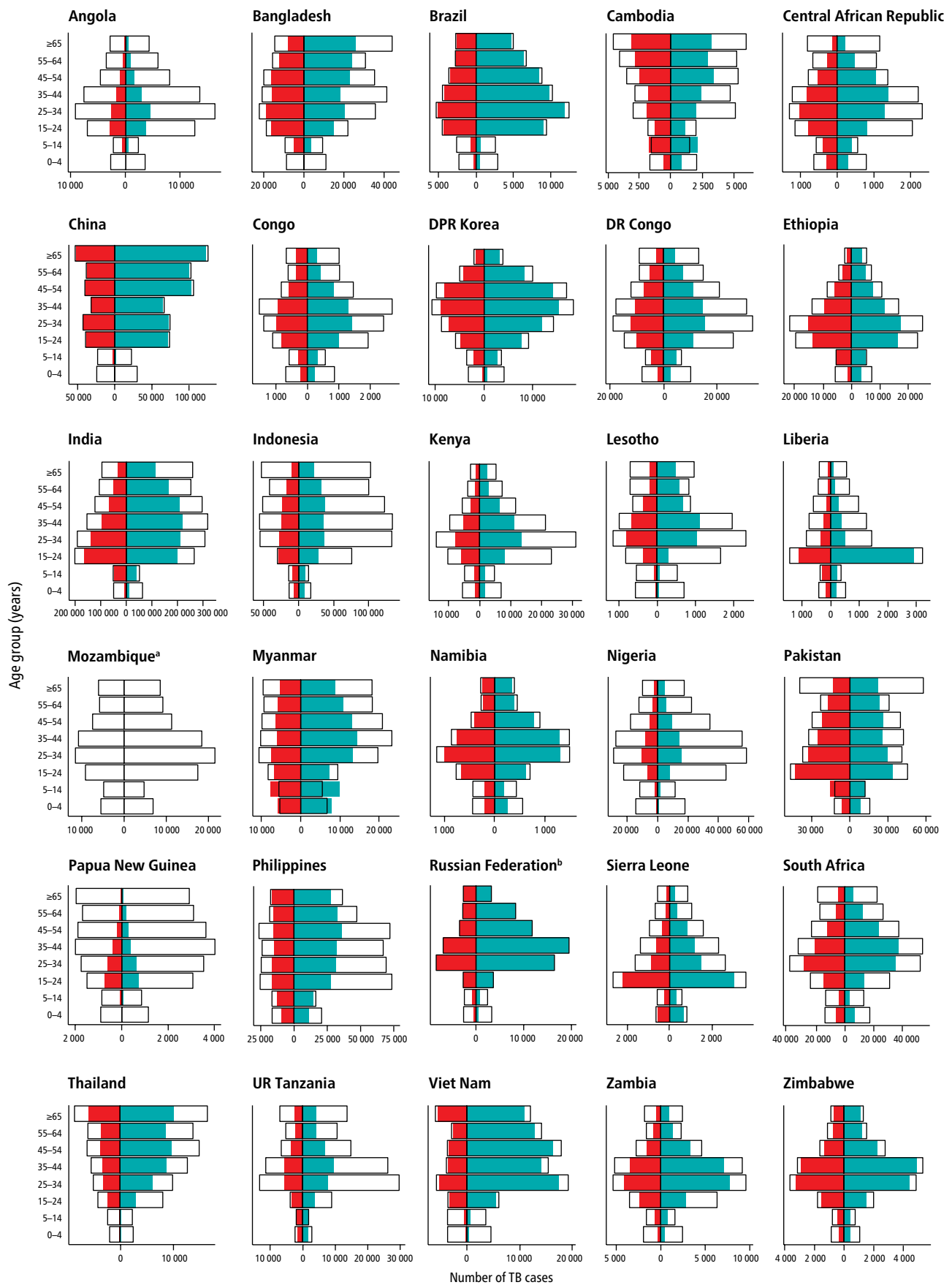
**Regional estimates of TB incidence (black line) and case notifications disaggregated by age and sex (female in red; male in green), 2016**



<sup>1</sup> Further breakdowns by HIV status are not possible, because data on the HIV status of TB cases by age and sex are not available.

**FIG. 3.32**

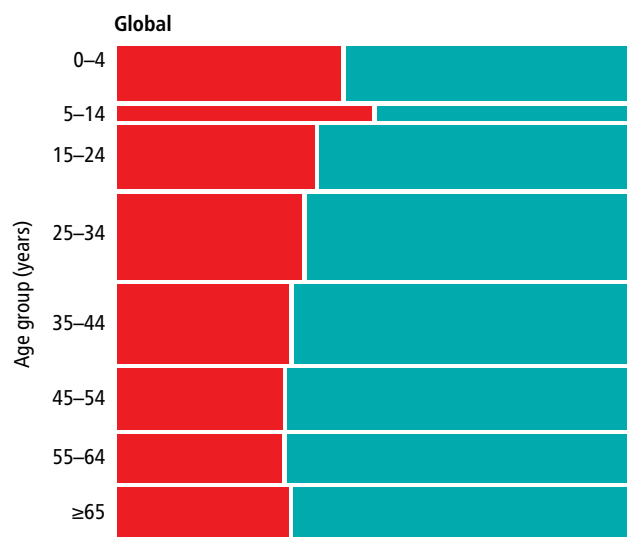
Estimates of TB incidence (black line) and case notifications disaggregated by age and sex (female in red; male in green), 2016, in the 30 high TB burden countries



<sup>a</sup> No age and sex disaggregated case notifications were available for Mozambique.

<sup>b</sup> For an explanation of why notifications are assumed to be equivalent to TB incidence in the Russian Federation, see [Box 3.5](#).

**FIG. 3.33**  
**Global distribution of TB mortality in HIV-negative people by age group and sex (female in red; male in green), 2016<sup>a</sup>**



<sup>a</sup> The total area represents global TB mortality and all rectangles are proportional to their share of total TB mortality.

for Asia and 27% for the WHO African Region. For children, the top three regions were the WHO South-East Asia Region with 35% of incident TB cases in 2015, followed by the WHO African Region with 30% and the WHO Western Pacific Region with 20%.

### 3.5.3 TB mortality disaggregated by age and sex

Estimates of TB mortality disaggregated by age and sex are shown in **Fig. 3.33** (global), **Fig. 3.34** (WHO regions) and **Fig. 3.35** (30 high TB burden countries), and in **Table 3.6**. Estimates are shown for HIV-positive and HIV-negative people separately, given that the cause of TB deaths among HIV-positive people is classified as HIV in ICD-10 (see also **Section 3.2**).

#### TB mortality among HIV-negative people

Globally in 2016, there were an estimated 718 000 (range, 619 000–824 000) deaths from TB among HIV-negative men and 110 000 (range, 75 000–151 000) among boys. There were an additional 378 000 (range, 308 000–454 000) deaths from TB among HIV-negative women and 91 000 (range, 60 000–129 000) among girls. These numbers correspond to 55% of

**FIG. 3.34**  
**Regional distribution of TB mortality in HIV-negative people by age group and sex (female in red; male in green), 2016<sup>a</sup>**



<sup>a</sup> The total area represents TB mortality and all rectangles are proportional to their share of total TB mortality by region.

**FIG. 3.35**

**Distribution of TB mortality in HIV-negative people in the 30 high TB burden countries by age group and sex (female in red; male in green), 2016<sup>a</sup>**



<sup>a</sup> The total area represents TB mortality and all rectangles are proportional to their share of total TB mortality by country.

**TABLE 3.6**

**Estimated number of TB deaths (in thousands) by HIV status in children and adults, globally and for WHO regions, 2016<sup>a</sup>**

HIV-NEGATIVE										
WHO REGION	TOTAL		MALE 0–14 YEARS		FEMALE 0–14 YEARS		MALE ≥15 YEARS		FEMALE ≥15 YEARS	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	417	351–488	32	16–55	27	13–48	231	183–285	126	92–165
The Americas	17	16–18	2.5	2.1–2.9	2.1	1.8–2.4	8.3	7.7–8.9	4.1	3.7–4.6
Eastern Mediterranean	82	69–95	7.1	3.8–11	5.7	2.9–9.5	39	31–49	30	22–38
Europe	26	26–27	2.6	2.4–2.8	2.2	2.0–2.4	16	15–16	5.5	5.2–5.8
South-East Asia	652	542–772	48	22–84	39	16–72	375	293–467	191	133–258
Western Pacific	103	85–123	17	9.4–28	14	7.3–24	49	38–62	22	15–31
GLOBAL	1 300	1 160–1 440	110	75–151	91	60–129	718	619–824	378	308–454

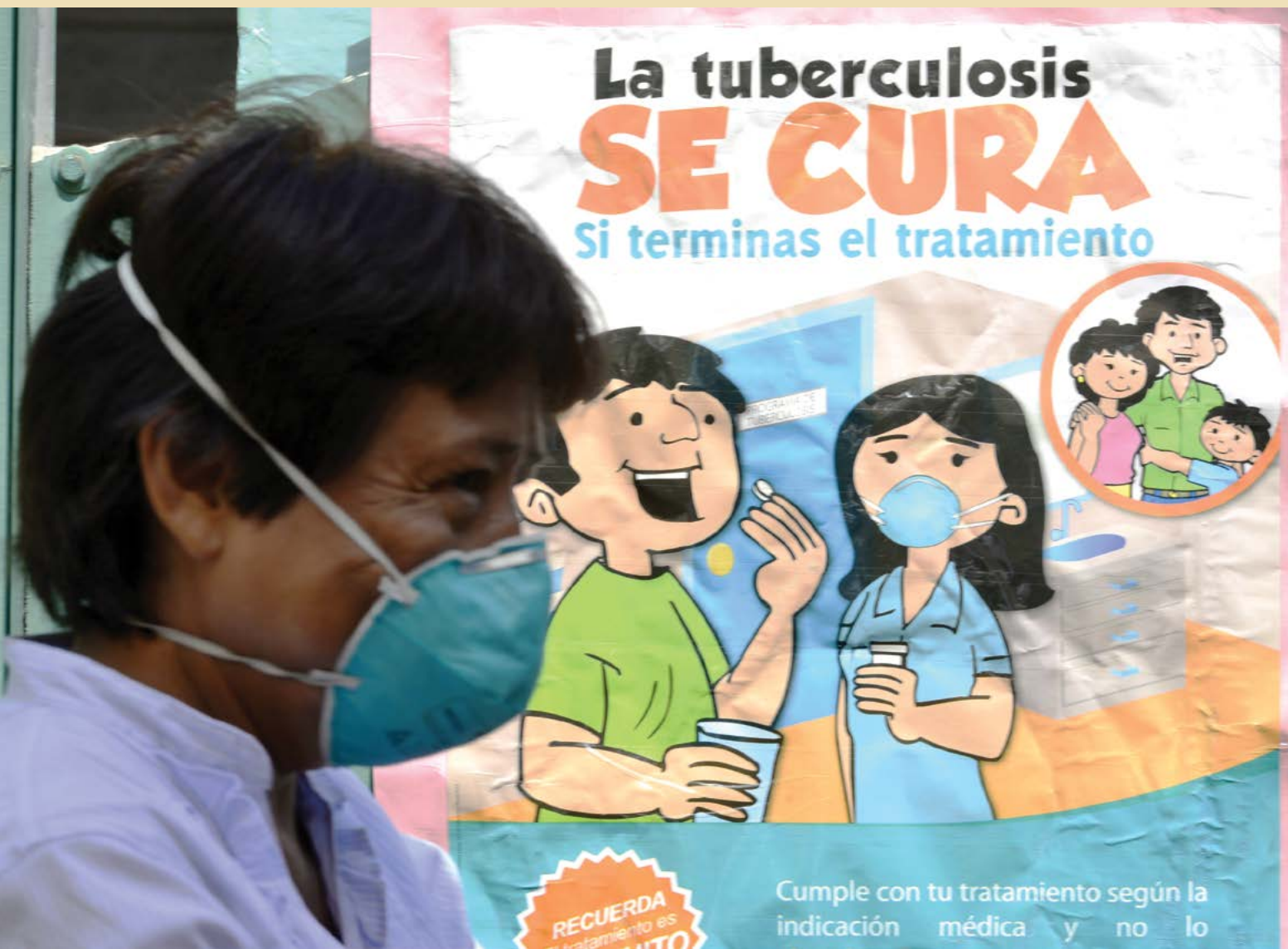
HIV-POSITIVE										
WHO REGION	TOTAL		MALE 0–14 YEARS		FEMALE 0–14 YEARS		MALE ≥15 YEARS		FEMALE ≥15 YEARS	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	320	272–372	23	20–27	20	17–23	177	151–206	100	85–116
The Americas	6.2	5.6–6.9	1.0	0.91–1.1	0.86	0.76–0.95	2.9	2.6–3.2	1.5	1.3–1.6
Eastern Mediterranean	3.0	1.8–4.5	0.26	0.15–0.39	0.21	0.12–0.31	1.4	0.87–2.2	1.1	0.70–1.7
Europe	5.1	3.9–6.4	0.47	0.36–0.59	0.39	0.30–0.49	3.0	2.3–3.7	1.2	0.95–1.6
South-East Asia	35	25–46	2.4	1.7–3.2	0.20	1.4–2.7	20	15–27	9.9	7.1–13.2
Western Pacific	5.0	3.0–7.3	0.93	0.57–1.4	0.78	0.48–1.2	2.2	1.4–3.3	1.0	0.62–1.5
GLOBAL	374	325–427	28	24–32	24	20–27	207	179–236	115	99–131

<sup>a</sup> Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

deaths occurring in men, 29% in women, and 16% in children. Higher numbers of TB deaths among men are consistent with the estimate that 65% of incident cases were among men in 2016. They are also consistent with evidence from prevalence surveys, which show that TB disease affects men more than women (Fig. 3.28), and that gaps in case detection and reporting are higher among men (Fig. 3.29b).

### ***TB mortality among HIV-positive people***

There were an estimated 207 000 (range, 179 000–236 000) TB deaths among HIV-positive men, 115 000 (range, 99 000–131 000) among HIV-positive women and 52 000 (range, 46 000–57 000) among HIV-positive children in 2016 (Table 3.6). The WHO African Region accounted for 86% of these deaths, with the M:F ratio being 1.8. The M:F ratio in other regions varied from 1.3 in the WHO Eastern Mediterranean Region to 2.4 in the WHO European Region.



A TB patient passes a health promotion poster about TB in Lima, Peru

CRIS BOURONCLE / GETTY IMAGES

## CHAPTER 4.

# Diagnosis and treatment: TB, HIV-associated TB and drug-resistant TB

### ■ KEY FACTS AND MESSAGES ■

Globally in 2016, 6.6 million people with tuberculosis (TB) were notified to national TB programmes (NTPs) and reported to WHO. Of these, just over 6.3 million had an incident episode (new or relapse) of TB. The global number of new and relapse TB cases notified and the notification rate per 100 000 population have both been increasing since 2013, mostly explained by a 37% increase in notifications in India.

In 2016, 39% of the 3.6 million new bacteriologically confirmed and previously treated TB cases notified globally were reported to have been tested for resistance to rifampicin, up from 31% in 2015. Coverage was 33% for new TB patients and 60% for previously treated TB patients. Globally, 153 119 cases of multidrug-resistant TB and rifampicin-resistant TB (MDR/RR-TB) were notified in 2016, and 129 689 were enrolled in treatment.

Globally in 2016, 57% of notified TB patients had a documented HIV test result, up from 55% in 2015 and a 19-fold increase since 2004. In the WHO African Region, where the burden of HIV-associated TB is highest, 82% of TB patients had a documented HIV test result. A total of 476 774 TB cases among HIV-positive people were reported and of these, 85% were on antiretroviral therapy (ART).

Despite increases in notifications of TB, MDR/RR-TB and HIV-associated TB, progress in closing detection and treatment gaps is slow and big gaps remain. In 2016, there was a gap of 4.1 million (39%) between notifications of new and relapse cases and the best estimate of the number of incident cases, reflecting a mixture of underreporting of detected TB cases (especially in countries with large private sectors) and underdiagnosis (especially in countries where there are major geographical or financial barriers to accessing care). The number of MDR/RR-TB cases started on treatment in 2016 was only 22% of the estimated incidence of MDR/RR-TB. The number of notified HIV-positive TB cases was only 46% of the estimated incidence of TB among people living with HIV.

From a global perspective, closing detection and treatment gaps requires progress in a particular subset of countries. Ten countries account for 76% of the total estimated gap between TB incidence and notifications, with India, Indonesia and Nigeria accounting for almost half of the total. Ten countries accounted for 75% of the gap between enrolments in MDR-TB treatment in 2016 and the estimated number of incident MDR/RR-TB cases in 2016; China and India accounted for 39% of the total gap. Most of the gaps in detection of HIV-positive TB cases and provision of ART in 2016 were accounted for by the African Region.

The global male:female (M:F) ratio for notifications was 1.7. Results from national TB prevalence surveys of adults show higher M:F ratios, indicating that notification data understate the share of the TB burden accounted for by men in some countries. Globally, children (aged <15 years) accounted for 6.9% of the new and relapse cases that were notified in 2016.

The WHO-recommended rapid diagnostic test for detection of TB and rifampicin resistance currently available is the Xpert MTB/RIF<sup>®</sup> assay. The number of cartridges procured by countries eligible for concessional prices was 6.9 million in 2016. Of the 48 countries in at least one of the lists of high burden countries, 28 had adopted national algorithms positioning Xpert MTB/RIF as the initial diagnostic test for all people suspected of having pulmonary TB by the end of 2016.

The latest treatment outcome data show treatment success rates of 83% for TB (2015 cohort), 78% for HIV-associated TB (2015 cohort), 54% for MDR/RR-TB (2014 cohort) and 30% for extensively drug-resistant TB (XDR-TB) (2014 cohort). At least 35 countries in Africa and Asia have introduced shorter regimens for treatment of MDR/RR-TB, with high treatment success rates (87–90%). As part of efforts to improve outcomes for MDR/XDR-TB, 89 countries and territories had started using bedaquiline and 54 had used delamanid by June 2017.

Prompt and accurate diagnosis of tuberculosis (TB), HIV-associated TB and drug-resistant TB, followed by provision of treatment in line with international standards, prevents deaths and limits ill-health among people who develop the disease. It also prevents further transmission of infection to others. The 2020 and 2025 milestones for reductions in TB incidence and TB deaths set in the End TB Strategy ([Chapter 2](#)) require the case fatality ratio (the proportion of people with TB who die from the disease) to fall to 10% by 2020 and to 6.5% by 2025. The latter is only feasible if all people with TB are promptly diagnosed and effectively treated. Patient-centred care and prevention – backed by bold policies and supportive systems such as universal health coverage (UHC) and social protection – are Pillars 1 and 2 of the End TB Strategy ([Box 4.1](#)). They are among the major themes that will be discussed at the WHO Global Ministerial Conference on ending TB in the era of the Sustainable Development Goals (SDGs), which is to be held in November 2017.<sup>1</sup>

This chapter provides the latest national data reported to WHO on the diagnosis and treatment of TB, HIV-associated TB and drug-resistant TB, and highlights progress in the compilation, safeguarding and use of subnational data. [Section 4.1](#) presents and discusses data for 2016 on notifications of TB cases and associated coverage of diagnostic testing, as well as trends since 2000. It includes data on the contribution of community engagement and public–public and public–private mix (PPM) initiatives to case-finding efforts. [Section 4.2](#) focuses on treatment coverage (and detection and treatment gaps) for patients with TB, HIV-associated TB and drug-resistant TB, comparing numbers detected

and treated with underlying estimates of disease burden. [Section 4.3](#) provides the most recent data on treatment outcomes, for new and relapse TB patients, TB patients living with HIV and patients with multidrug-resistant TB and rifampicin-resistant TB (MDR/RR-TB), as well as global trends for these three groups between 2012 and 2015. [Section 4.4](#) describes a global initiative to help countries make better use of subnational data, summarizes the number of countries for which regional- or district-level data have now been stored for a time period of at least 5 years, and illustrates how such data can be used through a country case study.

Throughout the chapter, data are presented at global, regional and country levels, giving particular attention to high burden countries (HBCs).<sup>2</sup> Further country-specific details for all of the indicators covered in this chapter are provided in [Annex 2](#) and [Annex 4](#).

New guidance related to the topics covered in this chapter that was issued by WHO in 2017 is featured in [Box 4.2](#).

## 4.1 Case notifications and testing coverage

### 4.1.1 TB case notifications and bacteriological confirmation

In 2016, 6.6 million people with TB were notified to national TB programmes (NTPs) and reported to WHO ([Table 4.1](#)). Of these, close to 6.3 million had a new or relapse (incident) episode of TB (shown as the total of new and relapse cases), and an additional 300 000 had been previously diagnosed with TB but their treatment was changed to a retreatment regimen.

## BOX 4.1 Pillars 1 and 2 of the End TB Strategy

Pillar 1 of the End TB Strategy is “Integrated, patient-centred care and prevention”. It has four components:

- early diagnosis of TB including universal drug-susceptibility testing (DST), and systematic screening of contacts and high-risk groups;
- treatment of all people with TB, including drug-resistant TB, and patient support;
- collaborative TB/HIV activities, and management of comorbidities; and
- preventive treatment of persons at high risk, and vaccination against TB.

The fourth component of Pillar 1 is the topic of [Chapter 5](#).

Pillar 2 of the End TB Strategy is “Bold policies and supportive systems”. This pillar also has four components:

- political commitment with adequate resources for TB care and prevention;
- engagement of communities, civil society organizations, and providers of public and private care;
- UHC policy and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control; and
- social protection, poverty alleviation and actions on other determinants of TB.

The components of Pillar 2 are primarily discussed in [Chapter 7](#).

For an overview of all aspects of the End TB Strategy, see [Chapter 2](#).

<sup>1</sup> WHO Global Ministerial Conference. Ending tuberculosis in the SDG era: a multisectoral response – November 2017. World Health Organization ([www.who.int/conferences/tb-global-ministerial-conference/en/](http://www.who.int/conferences/tb-global-ministerial-conference/en/), accessed 21 August 2017).

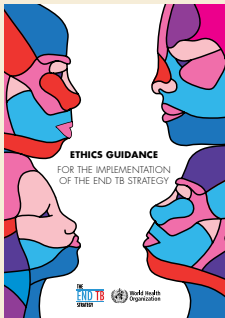
<sup>2</sup> The three lists of HBCs (for TB, HIV-associated TB and MDR-TB) are explained in [Chapter 2](#).



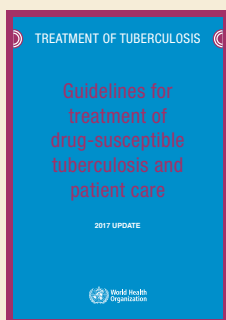
**BOX 4.2**

## New guidelines on ethics in TB and treatment of drug-susceptible TB issued by WHO in 2017

**Guidelines on ethics in TB:** Protecting human rights, ethics and equity is one of the four key principles of the End TB Strategy. In all countries, TB remains closely associated with the most vulnerable and marginalized populations, and there are barriers to the equitable and ethical delivery of care. New guidance on ethics for TB care and prevention that addresses these challenges was released on World TB Day 2017.<sup>a</sup> The guidance was produced by affected individuals and a broad constituency of other experts from NTPs, civil society and the fields of public health, ethics, health law and human rights.



**Guidelines on the treatment of drug-susceptible TB:** An updated edition of guidelines on the treatment of drug-susceptible TB was published in April 2017.<sup>b</sup> The revised guidelines include a strong recommendation to treat new pulmonary TB patients with drug-susceptible TB with a 6-month regimen of 2HRZE/4HR (i.e. 2 months of isoniazid, rifampicin, pyrazinamide and ethambutol, followed by 4 months of isoniazid and rifampicin). If the 8-month regimen of 2HRZE/6HE (i.e. 2 months of isoniazid, rifampicin, pyrazinamide and ethambutol, followed by 6 months of isoniazid and ethambutol) for



such patients is still in use, it is recommended that it be phased out. The recommendations also state that daily therapy is preferred to thrice weekly dosing, and that fixed-dose combination tablets are preferred to single drug formulations. Wider use of DST is supported so that people with drug-resistant TB are treated with regimens appropriate for their pattern of drug resistance.

WHO is updating the 2016 treatment guidelines for drug-resistant TB to include evidence-based recommendations for the treatment of rifampicin-susceptible but isoniazid-resistant TB. This update follows a Guideline Development Group meeting held in April 2017.

A compendium that summarizes all WHO policies on TB diagnosis and treatment in one document is scheduled for publication in late 2017.

- <sup>a</sup> World Health Organization. Ethics guidance for the implementation of the End TB Strategy. Geneva: WHO; 2017 (<http://apps.who.int/iris/bitstream/10665/254820/1/9789241512114-eng.pdf>, accessed 11 July 2017).
- <sup>b</sup> World Health Organization. Treatment of tuberculosis: guidelines for treatment of drug-susceptible tuberculosis and patient care (2017 update) (WHO/HTM/TB/2017.05). Geneva: WHO; 2017 (<http://apps.who.int/iris/bitstream/10665/255052/1/9789241550000-eng.pdf>, accessed 11 July 2017).

The number of new and relapse TB cases notified and the notification rate per 100 000 population increased between 2000 and 2009, then fell slowly until 2013, and has subsequently increased (Fig. 4.1). The increase since 2013 is mostly explained by a continuous increase in notifications in India (+37% between 2013 and 2016), following the introduction of a national policy of mandatory notification in 2012 and the rollout (also since 2012) of a nationwide web-based and case-based reporting system (called “Nikshay”) that facilitates reporting of detected cases by care providers in the public and private sectors.

The distribution of notified cases in 2016 by age and sex is shown globally and for WHO regions in Fig. 4.2. The global male:female (M:F) ratio for notifications was 1.7. In contrast, the M:F ratio of cases identified in 25 national TB disease prevalence surveys of adults in African and Asian countries implemented in 2007–2016 approximated 2.4 overall, and reached 4.5 in Viet Nam. This indicates that notification data understate the share of the TB burden accounted for by men in some countries (see Chapter 3 for further details). Children (aged <15 years) accounted for 6.9% of the new and relapse cases that were notified globally. In the WHO Eastern Mediterranean, South-East Asia and Western Pacific regions, the TB epidemic is a markedly ageing one, with a

progressive increase in the notification rate with age, and a peak among those aged 65 years or over. Elsewhere, and most noticeably in the WHO African Region, notification rates were highest among younger adults. In several central and eastern European countries, as well as three high TB burden countries in Asia – China, Thailand and Viet Nam – less than 2% of notified cases were children (Fig. 4.3). Variation among countries in the child:adult and M:F ratios of cases may reflect real differences in epidemiology, differential access to or use of health-care services, or differential reporting practices.

Of the nearly 5.4 million new and relapse pulmonary TB patients notified globally in 2016, 57% were bacteriologically confirmed.<sup>1</sup> The remaining patients were diagnosed clinically; that is, based on symptoms, abnormalities on chest radiography or suggestive histology. The percentage of cases with bacteriological confirmation worldwide has declined slightly since 2013 (Fig. 4.4), mainly reflecting trends in the WHO South-East Asia (67% to 61%) and Western Pacific regions (43% to 38%). There was an improvement in the WHO African (57% to 67%) and European regions (59% to 66%).

<sup>1</sup> A bacteriologically confirmed case is one from whom a biological specimen is positive by smear microscopy, culture or WHO-recommended rapid diagnostic, such as Xpert MTB/RIF.

**TABLE 4.1**

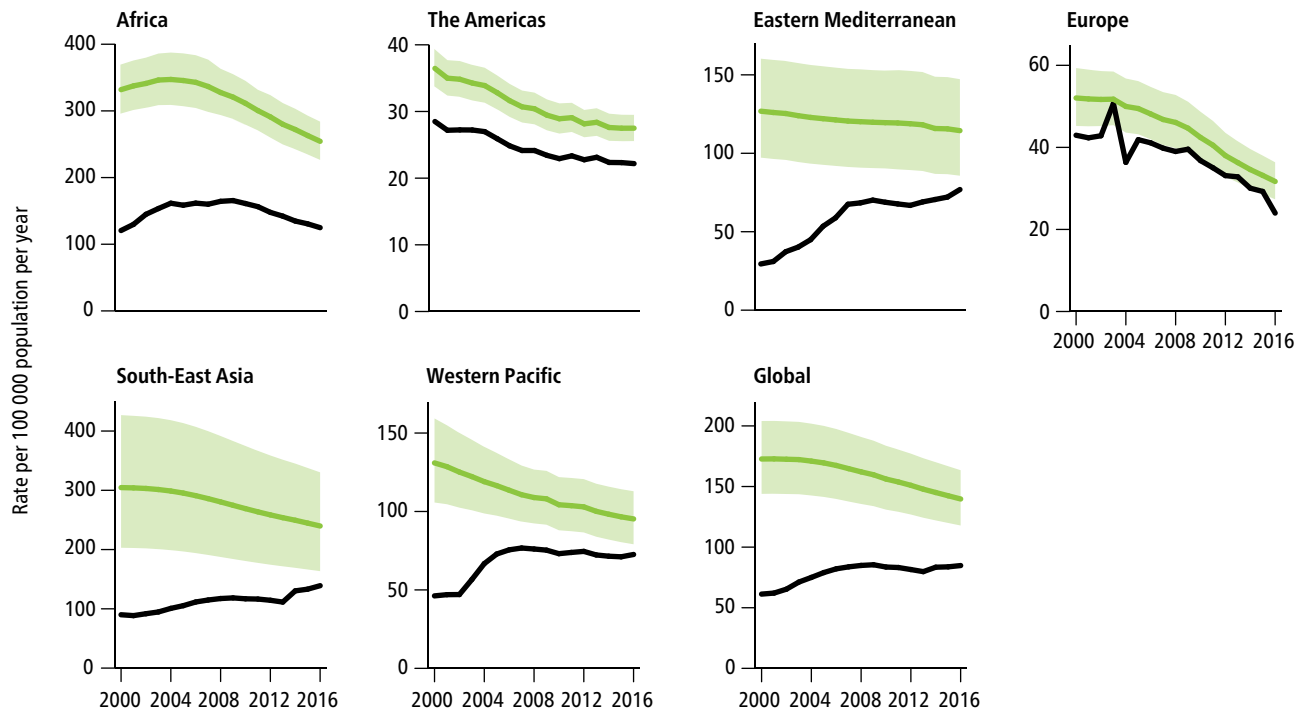
**Notifications of TB, HIV-positive TB and MDR/RR-TB cases, globally and for WHO regions, 2016**

	TOTAL NOTIFIED	NEW AND RELAPSE <sup>a</sup>	PULMONARY NEW AND RELAPSE		EXTRAPULMONARY NEW AND RELAPSE (%)	HIV-POSITIVE NEW AND RELAPSE	MDR/RR-TB	XDR-TB
			NUMBER	OF WHICH BACTERIOLOGICALLY CONFIRMED (%)				
Africa	1 303 483	1 273 560	1 065 327	66%	16%	358 237	27 828	1 092
The Americas	233 793	221 008	186 940	77%	15%	20 528	3 715	112
Eastern Mediterranean	527 693	514 449	390 367	53%	24%	1 367	4 713	152
Europe	260 434	219 867	187 898	64%	15%	24 871	49 442	3 114
South-East Asia	2 898 482	2 707 879	2 291 793	61%	15%	60 245	46 269	2 926
Western Pacific	1 400 638	1 372 371	1 268 798	38%	8%	11 526	21 152	618
GLOBAL	6 624 523	6 309 134	5 391 123	57%	15%	476 774	153 119	8 014

<sup>a</sup> New and relapse includes cases for which the treatment history is unknown. It excludes cases that have been re-registered as treatment after failure, as treatment after lost to follow up or as other previously treated (whose outcome after the most recent course of treatment is unknown or undocumented).

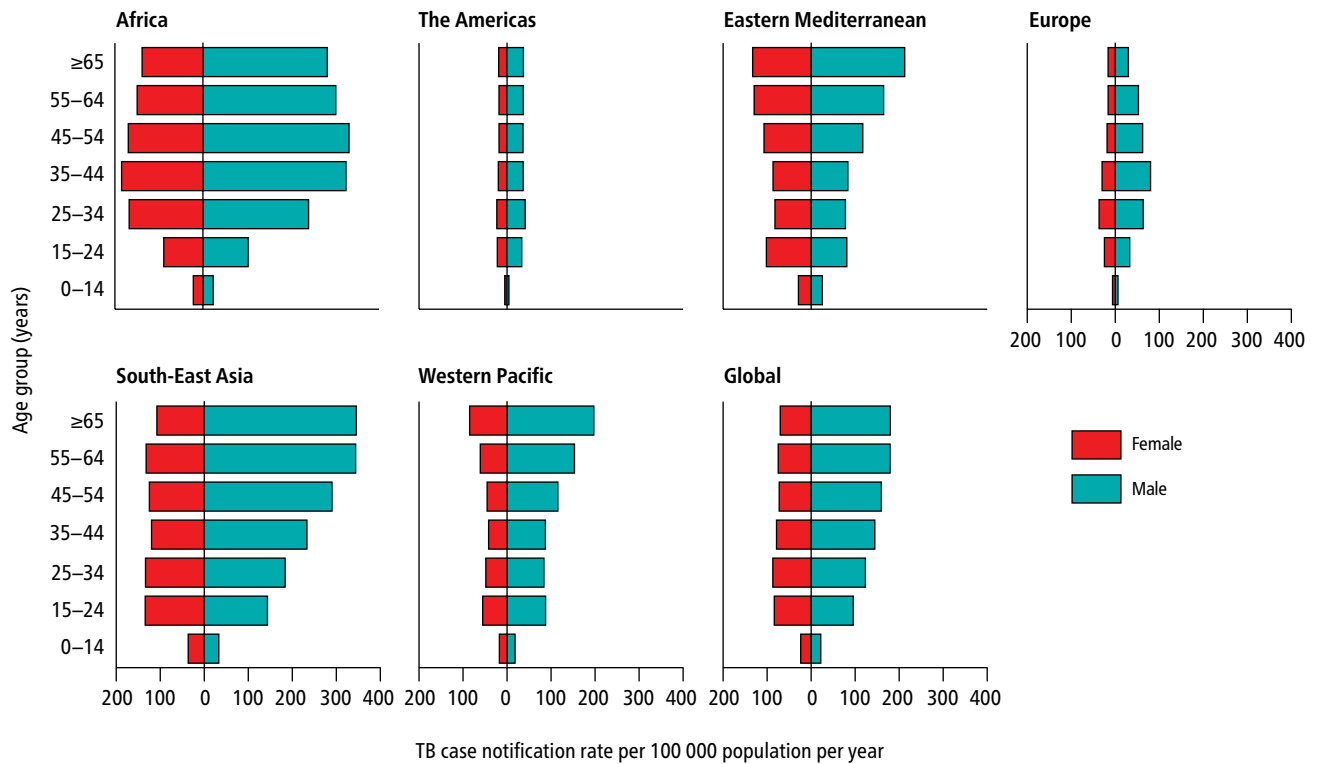
**FIG. 4.1**

**Case notification rates (new and relapse cases, all forms) (black) compared with estimated TB incidence rates (green), globally and for WHO regions, 2000–2016. Shaded areas represent uncertainty bands.**



**FIG. 4.2**

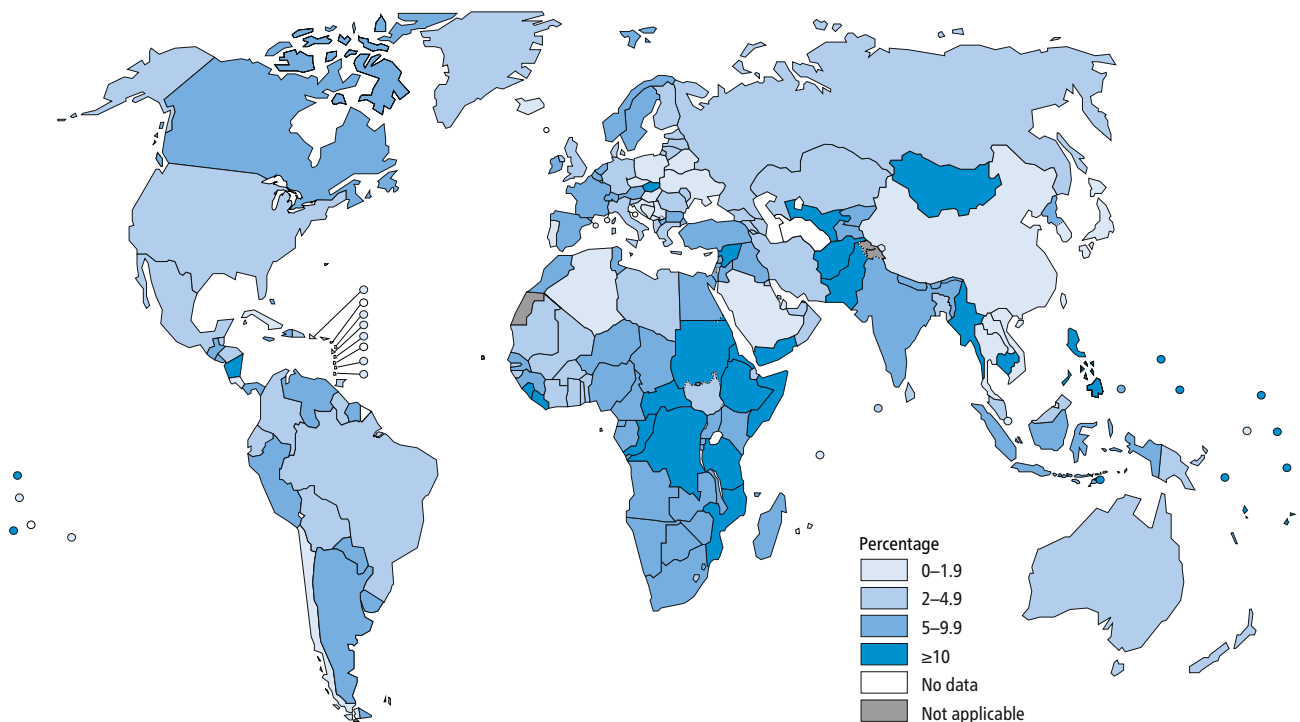
**New and relapse TB case notification rates by age and sex<sup>a</sup> in 2016, globally and for WHO regions**



<sup>a</sup> Countries not reporting cases in these categories are excluded. Cases included account for 89% of reported cases.

**FIG. 4.3**

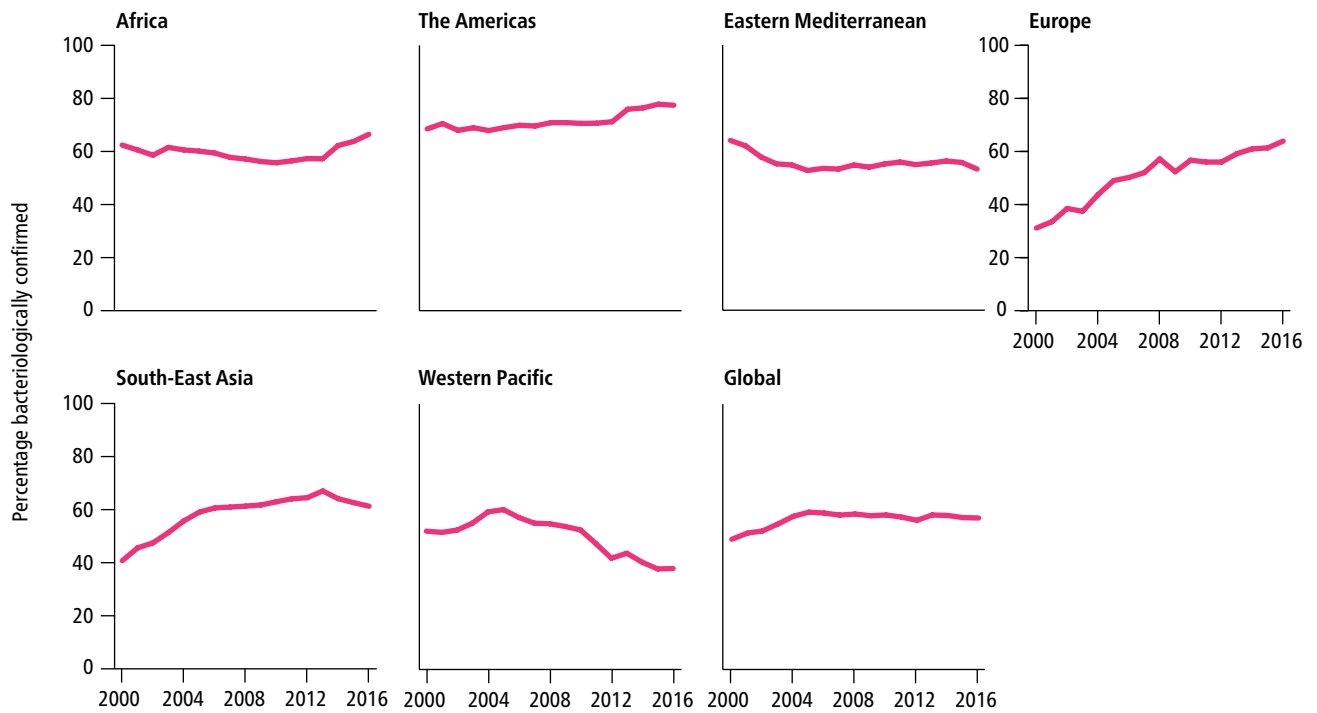
**Percentage of new and relapse TB cases that were children (aged <15), 2016<sup>a</sup>**



<sup>a</sup> 2015 data were used for 15 countries.

**FIG. 4.4**

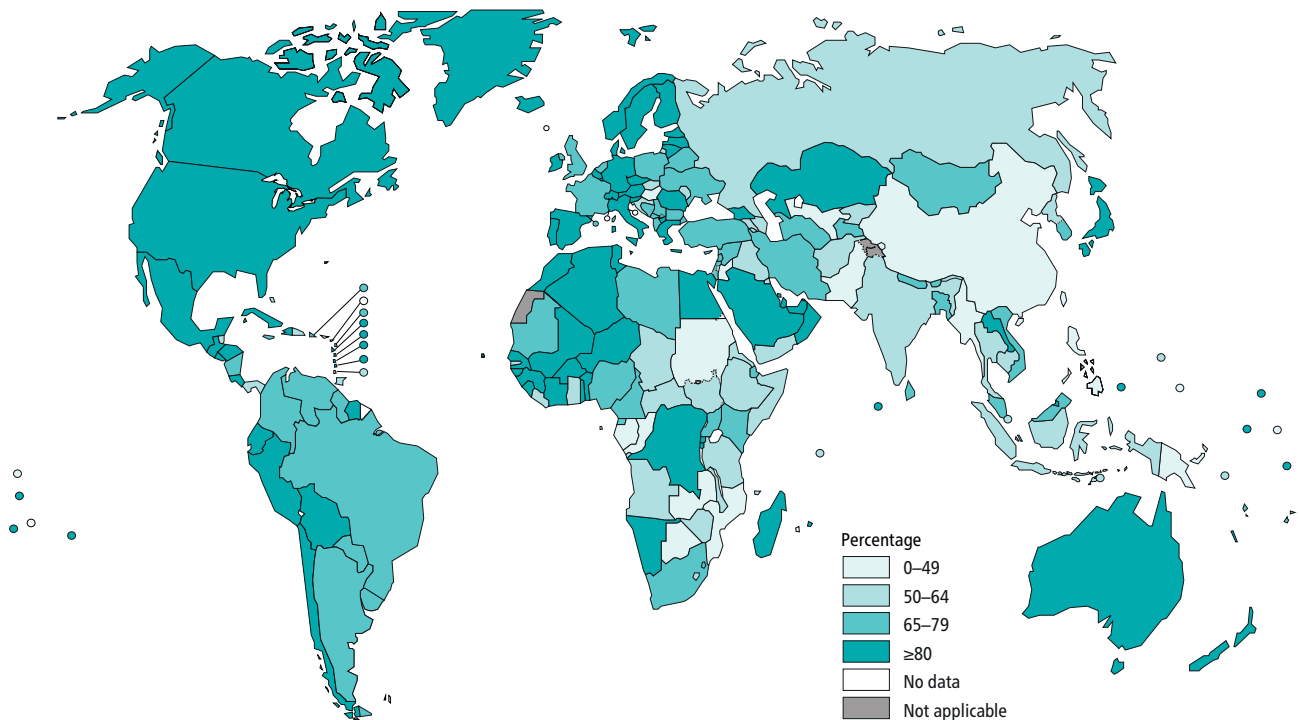
**Percentage of new and relapse<sup>a</sup> pulmonary TB cases with bacteriological confirmation, globally and for WHO regions, 2000–2016**



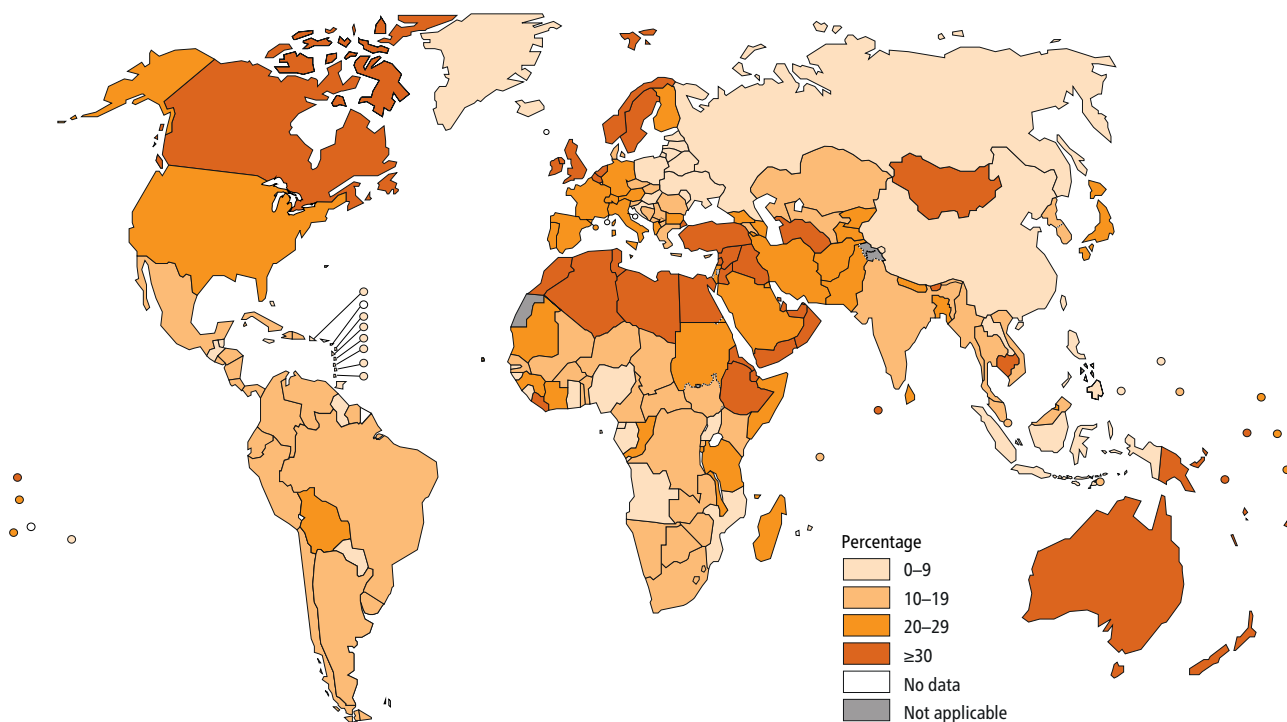
<sup>a</sup> The calculation is for new pulmonary cases in years prior to 2013 based on smear results, except for the European Region where data on confirmation by culture were also available for the period 2002–2012.

**FIG. 4.5**

**Percentage of new and relapse pulmonary TB cases with bacteriological confirmation, 2016<sup>a</sup>**



<sup>a</sup> 2015 data were used for 17 countries.

**FIG. 4.6****Percentage of extrapulmonary cases among new and relapse TB cases, 2016<sup>a</sup>**

<sup>a</sup> 2015 data were used for 17 countries.

Considerable variation in the percentage of new and relapse pulmonary TB patients that are bacteriologically confirmed is evident even among countries with a similar epidemiological profile (Fig. 4.5).

Reasons for a low proportion of cases being bacteriologically confirmed should be assessed at country level, as should reductions over time. The microbiological detection of TB allows patients to be correctly diagnosed and started on the most effective treatment regimen as early as possible, and is critical for infection control. Most clinical features of TB and abnormalities on chest radiography or histology results generally associated with TB have low specificity, which may lead to false diagnoses of TB, and hence to people being enrolled in TB treatment unnecessarily. Extrapulmonary TB represented 15% of the 6.3 million incident cases that were notified in 2016, ranging from 8% in the WHO Western Pacific Region to 24% in the WHO Eastern Mediterranean Region (Fig. 4.6 and Table 4.1).

Engagement of all care providers in the public and private sectors should be integral components of national TB strategies, and PPM initiatives have particular relevance to HBCs in Asia and Africa. The contribution of PPM to total notifications in countries that have reported PPM data for several years are shown in Box 4.3. In areas where monitoring was in place, the contribution of PPM to total notifications increased by more than 10% between 2012 and 2016 in Bangladesh, India and the Philippines. Elsewhere, trends have remained static or declined.

#### 4.1.2 HIV testing for TB patients, detection of HIV-associated TB and screening for TB among people living with HIV

In 2016, 167 countries reported 3.6 million notified new and relapse TB patients with a documented HIV test result, equivalent to 57% of notified TB cases (up from 55% in 2015). This represented a 19-fold increase in testing coverage since 2004, when WHO first asked countries to report data (Fig. 4.7). In 116 countries and territories, at least 75% of TB cases knew their HIV status (Fig. 4.8). Documentation of HIV status averaged 66% of TB patients in the 30 high TB/HIV burden countries, but varied considerably, from 14% in Indonesia to above 80% in 18 high TB/HIV burden countries in the WHO African Region.<sup>1</sup> In the Russian Federation, reported testing coverage increased from 66% in 2015 to 87% in 2016, following inclusion of data from prisons. In the WHO African Region, which accounted for 74% of the global burden of HIV-associated TB in 2016 (Chapter 3), 82% of TB patients had their HIV status documented.

Globally, 476 774 cases of TB among people living with HIV were notified in 2016 (Table 4.1), equivalent to 13% of TB patients with an HIV test result. The number notified was only 46% of the estimated number of incident cases among people living with HIV (Fig. 4.9),<sup>2</sup> similar to the gap in 2015.

<sup>1</sup> Although the national figure for China was 43%, in the counties defined as having a high burden of HIV-associated TB the figure was 87%.

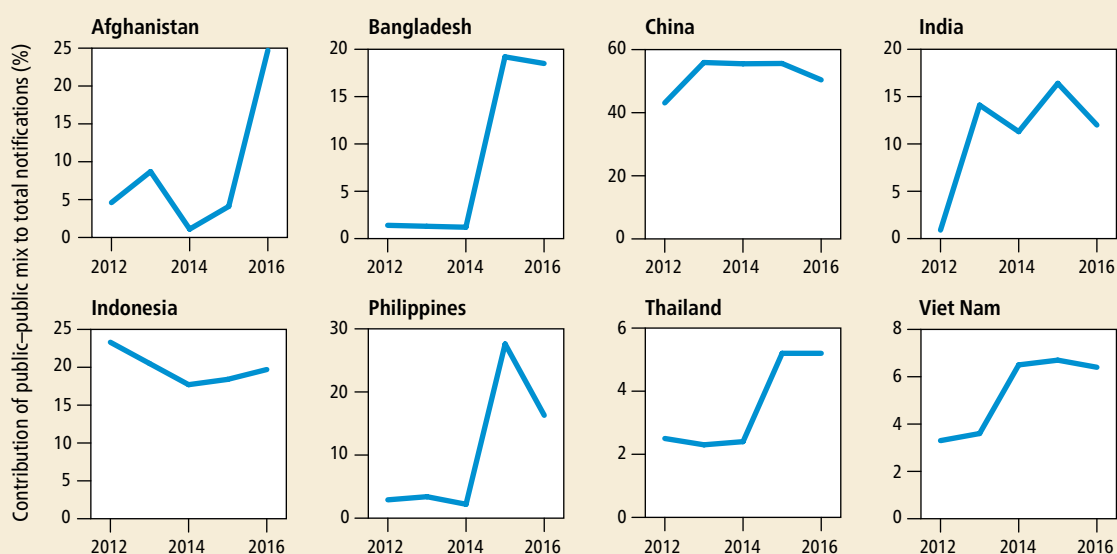
<sup>2</sup> See also Table 3.2 in Chapter 3 for the global estimate of TB incidence among people living with HIV.

**BOX 4.3** ■ **Trends in the contribution of PPM to TB case notifications**

Public–public mix is defined as engagement by the NTP of public sector providers of TB care that are not under the direct purview of the NTP, including public hospitals, public medical colleges, prisons or detention centres, military facilities, railways and public health insurance organizations. Public–private mix is defined as engagement by the NTP of private sector providers of TB care; these include private individual and institutional providers, the corporate or business sector, mission hospitals, nongovernmental organizations and faith-based organizations. In all countries, especially those with many public providers of TB care operating outside the remit of the ministry of health or a large private health sector, PPM is needed to ensure prompt referral by non-treating providers, reporting of all detected cases, and use of international standards of care for diagnosis and treatment.

Examples of approaches used to engage public and private care providers include strengthening coordination within hospitals, establishing linkages between hospitals and peripheral health centres, public sector support to private providers (with or without financial incentives, including linking TB insurance payments to notification), and regulatory approaches such as enforcing mandatory TB case notification and the rational use of TB medicines.

**FIG. B4.3.1**  
**Contribution of public–public mix to TB case notifications in eight countries, 2012–2016**



As in previous years, the region with the highest proportion of HIV-positive cases among those tested for HIV was the WHO African Region (34%). Overall, the percentage of TB patients testing HIV-positive has been falling globally since 2008. This decline is evident in all WHO regions with the exception of the WHO European Region, where the proportion of TB patients testing HIV-positive has increased from 3% in 2008 to 15% in 2016.

Systematic symptom screening for TB among people living with HIV is recommended by WHO as an essential component of the HIV care package. In 2016, 90 countries reported data on the number of TB cases notified among those newly enrolled in HIV care (up from 76 countries in 2015). In total, 88 200 (7%) of the 1.3 million people who were newly enrolled in HIV care in 2016 were diagnosed with TB during the same year; data for the 14 high TB/HIV burden countries that reported data are shown in **Table 4.2**. Improvements in the coverage and quality of data for this indicator are necessary to track the impact of HIV care – in particular, antiretroviral therapy (ART)

and TB preventive treatment – on the burden of TB among people living with HIV.

**4.1.3 Rapid testing for TB**

Increasing patient access to early and accurate diagnosis using a WHO-recommended rapid diagnostic (WRD<sup>1</sup>) is one of the three main objectives of TB laboratory strengthening efforts under the End TB Strategy. As a first step towards reaching this objective and as the first indicator of the *Framework of indicators and targets for laboratory strengthening under the End TB Strategy*,<sup>2</sup> which was launched in 2016, countries should adopt policies that include diagnostic algorithms in

<sup>1</sup> WRDs use molecular techniques to detect TB among people with signs or symptoms of TB. They include the XpertMTB/RIF<sup>®</sup> assay (Cepheid, United States) and the Loopamp<sup>™</sup> MTBC Detection Kit (Eiken Chemical Company Ltd, Japan).

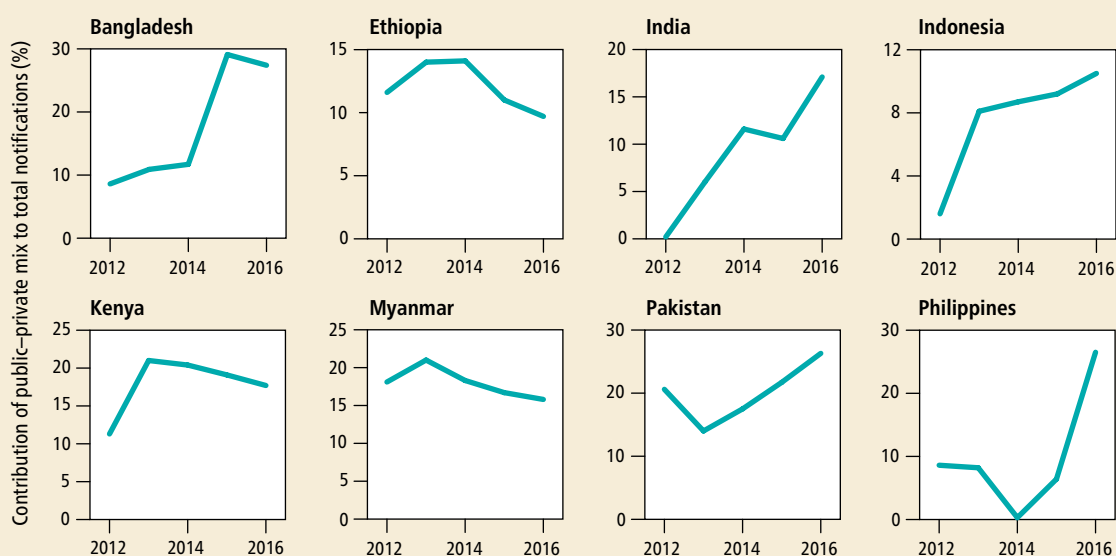
<sup>2</sup> World Health Organization. Framework of indicators and targets for laboratory strengthening under the End TB Strategy (WHO/HTM/TB/2016.18). Geneva: WHO; 2016 (<http://www.who.int/tb/publications/labindicators/en/>, accessed 21 August 2017).

The contribution of PPM to case notifications quantifies the engagement of different providers in the delivery of TB care, and the alignment of their TB management practices with national and international standards. Trends in the contribution of PPM to notifications in selected countries where PPM has been recognized as a priority and from which data have been reported to WHO for each year 2012–2016 are shown in [Fig. B4.3.1](#) and [Fig. B4.3.2](#).

Inventory studies that quantify the underreporting of detected TB cases in both public and private sectors can help to identify where further PPM efforts are needed. They can also indicate the share of notifications that would be accounted for by PPM in the absence of underreporting, and thus inform the setting of targets for the share of notifications that should come from PPM. Of the countries shown in [Fig. B4.3.1](#) and [Fig. B4.3.2](#), inventory studies have been implemented in India and Pakistan, and are underway in China, Indonesia and Viet Nam; further details are provided in [Chapter 3](#). In Pakistan, the level of underreporting of adult cases was 24% in 2014, while PPM accounted for 18% of notifications; to achieve zero underreporting, the targeted level for the contribution of PPM would thus be 43%.<sup>a</sup> By 2016, following further efforts based on the results of the inventory study, the contribution of PPM had risen to 28%.

<sup>a</sup> i.e.  $t = c(1-U) + U$ , where  $t$  is the target level,  $c$  is the overall PPM contribution to total notifications and  $U$  is the level of underreporting measured in an inventory study.

**FIG. B4.3.2**  
**Contribution of public–private mix to TB case notifications in eight countries, 2012–2016**



which a WRD is the initial diagnostic test for all people with signs or symptoms of TB. This is an especially high priority for the 48 countries included in one or more of the lists of high TB, TB/HIV and MDR-TB burden countries, and 28 HBCs reported that such an algorithm was in place by the end of 2016 ([Table 4.3](#)). The second indicator of the framework is the percentage of new and relapse TB cases tested with a WRD as the initial diagnostic test. Of 190 reporting countries and territories, 108 indicated that their routine surveillance system captures the data required to monitor this indicator. Among the 48 HBCs, only Belarus, Kazakhstan, the Republic of Moldova, South Africa and Swaziland reported that more than half of their notified TB cases had received a WRD as the initial diagnostic test.

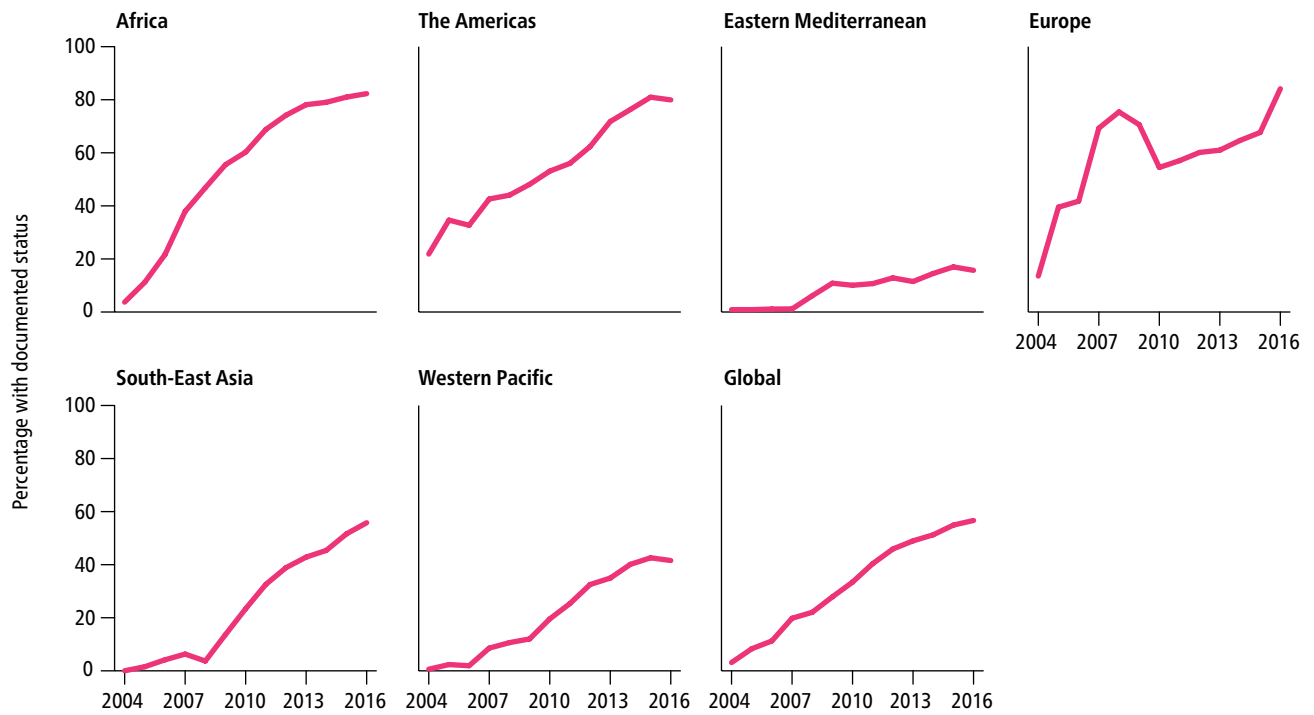
The Xpert MTB/RIF<sup>®</sup> assay (Cepheid, United States) is currently the WRD used most frequently by countries worldwide; it simultaneously detects both TB and resistance to rifampicin. The assay is performed using the GeneXpert<sup>®</sup> platform, a modular testing device that can detect multiple

diseases.<sup>1</sup> Between 2010 and 2016, a cumulative total of 6659 GeneXpert instruments, comprising 29 865 modules, were procured by the public sector in 130 of 145 countries eligible for concessional pricing. In 2016, 6.9 million test cartridges were procured by eligible countries. Of these, 35% (2.4 million) went to South Africa; this percentage has fallen from a high of 63% in 2013, as other parts of the world have adopted the technology. Despite the major scale-up in procurement of cartridges globally, installed instruments are still underused in many countries due to challenges such as network infrastructure, transport of specimens and variation in clinical demand. Outside South Africa (where machine throughput is relatively high), the number of procured cartridges in 2016 compared with the total number of instrument modules as of

<sup>1</sup> World Health Organization (2017). Considerations for adoption and use of multidisease testing devices in integrated laboratory networks (WHO/HTM/TB/2017.05). Geneva: WHO ([http://www.who.int/tb/publications/2017/considerations\\_multidisease\\_testing\\_devices\\_2017/en/](http://www.who.int/tb/publications/2017/considerations_multidisease_testing_devices_2017/en/), accessed 21 August 2017).

**FIG. 4.7**

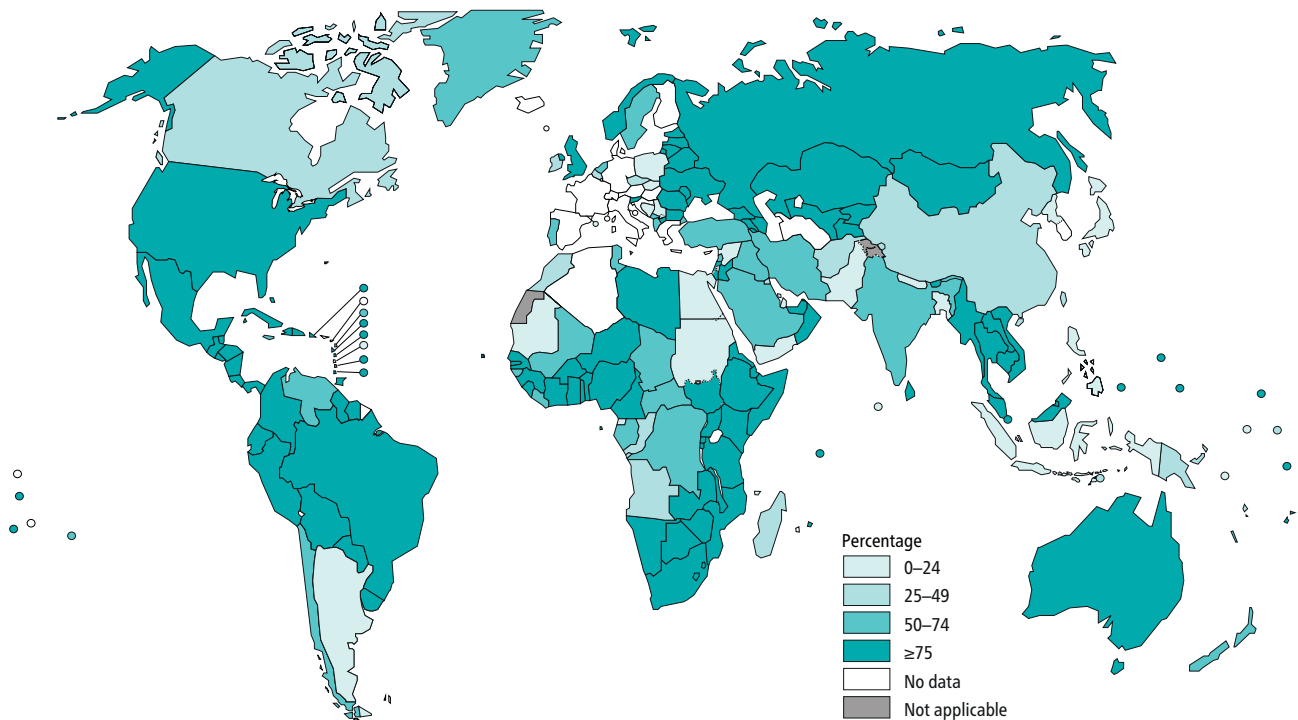
**Percentage of new and relapse<sup>a</sup> TB cases with documented HIV status, 2004–2016, globally and for WHO regions**



<sup>a</sup> The calculation is for all cases in years prior to 2015.

**FIG. 4.8**

**Percentage of new and relapse TB cases with documented HIV status, 2016<sup>a</sup>**

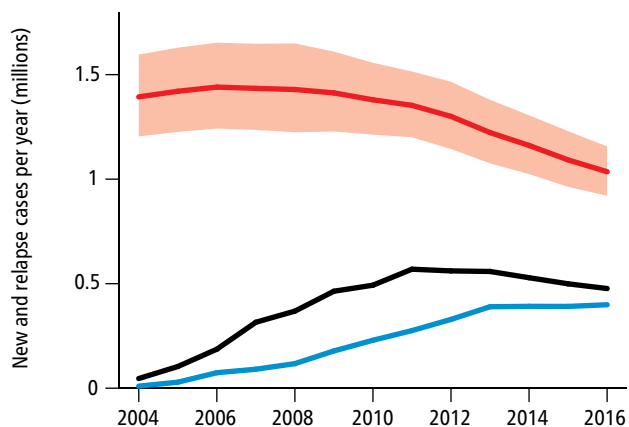


<sup>a</sup> 2015 data were used for 9 countries.



**FIG. 4.9**

**Global numbers of notified new and relapse cases<sup>a</sup> known to be HIV-positive (black), number started on antiretroviral therapy (blue) and estimated number of incident HIV-positive TB cases (red), 2004–2016.** Shaded areas represent uncertainty bands.



<sup>a</sup> The calculation is for all cases in years prior to 2015.

2015 reflects an average rate of only 1.0 test per module per working day globally.

#### 4.1.4 DST and detection of drug-resistant TB

Drug-resistant TB threatens global TB care and prevention, and it remains a major public health concern in many countries. Three categories are used for global surveillance and treatment: RR-TB, MDR-TB and XDR-TB. MDR-TB is TB that is resistant to both rifampicin and isoniazid, the two most powerful anti-TB drugs; it requires treatment with a second-line regimen. RR-TB also requires treatment with second-line drugs.<sup>1</sup> With increasing use of Xpert MTB/RIF for simultaneous detection of TB and resistance to rifampicin, a growing number of RR-TB cases (without further testing for isoniazid resistance) are being detected and notified.<sup>2</sup> Extensively drug-resistant TB (XDR-TB) is defined as MDR-TB plus resistance to at least one fluoroquinolone and a second-line injectable agent (amikacin, capreomycin or kanamycin), the two most important classes of medicines in an MDR-TB regimen.

The End TB Strategy calls for universal access to drug-susceptibility testing (DST); that is, DST for at least rifampicin for all TB cases, plus DST for at least fluoroquinolones and

<sup>1</sup> World Health Organization. WHO treatment guidelines for drug-resistant tuberculosis, 2016 update (October 2016 revision). (WHO/HTM/TB/2016.04). Geneva: WHO; 2016 (<http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/>, accessed 15 August 2017).

<sup>2</sup> Surveillance and survey data show that about 83% of RR-TB cases have MDR-TB. Further details are provided in [Chapter 3](#).

**TABLE 4.2**

**Number of people newly enrolled in HIV care in 2016 who were also notified as a TB case in 2016.**<sup>a</sup> 14 high TB/HIV burden countries that reported data.

	NUMBER OF PEOPLE NEWLY ENROLLED IN HIV CARE	NUMBER NOTIFIED AS A TB CASE	NOTIFIED TB CASES AS A PERCENTAGE OF THOSE NEWLY ENROLLED IN HIV CARE
Angola	16 658	2 884	17
China	110 295	2 931	2.7
Ethiopia	36 761	2 165	5.9
India	174 125	21 032	12
Indonesia	36 294	9 792	27
Liberia	4 528	1 219	27
Malawi	145 117	2 402	1.7
Myanmar	34 765	3 960	11
Nigeria	216 293	14 794	6.8
Papua New Guinea	4 595	425	9.2
Swaziland	138 016	2 342	1.7
Thailand	10 359	1 447	14
Uganda	181 314	13 586	7.5
Zimbabwe	168 968	9 176	5.4
TOTAL	1 278 088	88 155	6.9

second-line injectable agents among all TB cases with rifampicin resistance. DST methods include both phenotypic (conventional) and genotypic (molecular) testing methods. The most widespread technology currently available to test for drug resistance is Xpert MTB/RIF.

#### DST for first-line drugs and detection of MDR/RR-TB

**Fig. 4.10** shows progress in DST coverage since 2009, when WHO intensified efforts to track progress in the programmatic response to drug-resistant TB.<sup>3</sup> In 2016, 1.4 million (39%) of the 3.6 million new bacteriologically confirmed and previously treated TB cases notified globally were tested for rifampicin resistance (up from 31% in 2015), with coverage of 33% for new TB patients and 60% for previously treated TB patients. These figures represent an improvement since 2015, when 25% of new and 53% of previously treated TB cases had a test result for rifampicin resistance; they also represent major progress since 2009, when the figures were 2.9% and 5.9%, respectively. DST coverage increased in five of the six WHO regions between 2015 and 2016, with a high of 84% in the WHO European Region in 2016. There was a reduction in coverage in the WHO African Region, but this reflected a

<sup>3</sup> This happened following a ministerial conference for high MDR-TB burden countries, held in Beijing, China, in April 2009 preceding a World Health Assembly resolution the following month: WHA62.15: Prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. Sixty-second World Health Assembly, Geneva, 18–22 May 2009, Resolutions and decisions; annexes; 2009 ([http://apps.who.int/gb/ebwha/pdf\\_files/WHA62-REC1/WHA62\\_REC1-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA62-REC1/WHA62_REC1-en.pdf), accessed 11 July 2017).

**TABLE 4.3**
**National policies and their implementation to increase access to rapid TB testing and universal DST,<sup>a</sup> 2016**

Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>	HIGH TB BURDEN	HIGH TB/HIV BURDEN	HIGH MDR-TB BURDEN	NATIONAL POLICY AND ALGORITHM INDICATE A WRD AS THE INITIAL DIAGNOSTIC TEST FOR ALL PEOPLE PRESUMED TO HAVE TB	PERCENTAGE OF NOTIFIED NEW AND RELAPSE TB CASES TESTED WITH A WRD AS THE INITIAL DIAGNOSTIC TEST	NATIONAL POLICY AND ALGORITHM INDICATE UNIVERSAL ACCESS TO DST	PERCENTAGE OF NOTIFIED BACTERIOLOGICALLY CONFIRMED TB CASES WITH DST RESULTS FOR RIFAMPICIN	PERCENTAGE OF NOTIFIED RIFAMPICIN-RESISTANT TB CASES WITH DST RESULTS FOR FLUOROQUINOLONES AND SECOND-LINE INJECTABLE AGENTS
Angola	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	0.8	<input checked="" type="checkbox"/>	1.4	0
Azerbaijan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	39	<input checked="" type="checkbox"/>	65	64
Bangladesh	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	30	14
Belarus	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	80	<input checked="" type="checkbox"/>	98	79
Botswana	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	4.7	0
Brazil	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	21	<input checked="" type="checkbox"/>	40	17
Cambodia	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	12	0
Cameroon	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	6.8	100
Central African Republic	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input type="checkbox"/>	3.8	0
Chad	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	3.1	<input type="checkbox"/>	6.8	0
China	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input checked="" type="checkbox"/>	47	–
Congo	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	3.2	<input type="checkbox"/>	8.9	–
DPR Korea	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	2.6	0
DR Congo	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	3.0	31
Ethiopia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	>100 <sup>b</sup>	4.0
Ghana	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	64	0
Guinea-Bissau	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	–	–
India	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	17	<input checked="" type="checkbox"/>	47	60
Indonesia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<0.1	<input type="checkbox"/>	14	39
Kazakhstan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	85	<input checked="" type="checkbox"/>	>100 <sup>b</sup>	–
Kenya	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	26	<input type="checkbox"/>	44	63
Kyrgyzstan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	36	<input checked="" type="checkbox"/>	72	34
Lesotho	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	–	–
Liberia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	60	0
Malawi	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	–	0
Mozambique	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	>100 <sup>b</sup>	95
Myanmar	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	48	–
Namibia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	5.6	15
Nigeria	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	57	–
Pakistan	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input checked="" type="checkbox"/>	15	71
Papua New Guinea	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	–	61
Peru	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	>100 <sup>b</sup>	76
Philippines	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	13	<input type="checkbox"/>	34	8.3
Republic of Moldova	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	51	<input checked="" type="checkbox"/>	86	84
Russian Federation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	70	<input checked="" type="checkbox"/>	74	–
Sierra Leone	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	0	–	0.5	100
Somalia	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input type="checkbox"/>	12	11
South Africa	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	69	<input checked="" type="checkbox"/>	–	62
Swaziland	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	82	<input checked="" type="checkbox"/>	>100 <sup>b</sup>	100
Tajikistan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	73	<input checked="" type="checkbox"/>	89	93
Thailand	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1.4	<input type="checkbox"/>	17	52
Uganda	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	24	<input checked="" type="checkbox"/>	27	21
Ukraine	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	–	<input checked="" type="checkbox"/>	87	100
UR Tanzania	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	8.2	<input type="checkbox"/>	34	49
Uzbekistan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	–	–	–	–	–
Viet Nam	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	6.0	<input type="checkbox"/>	47	18
Zambia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	2.5	0
Zimbabwe	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	–	<input checked="" type="checkbox"/>	–	53

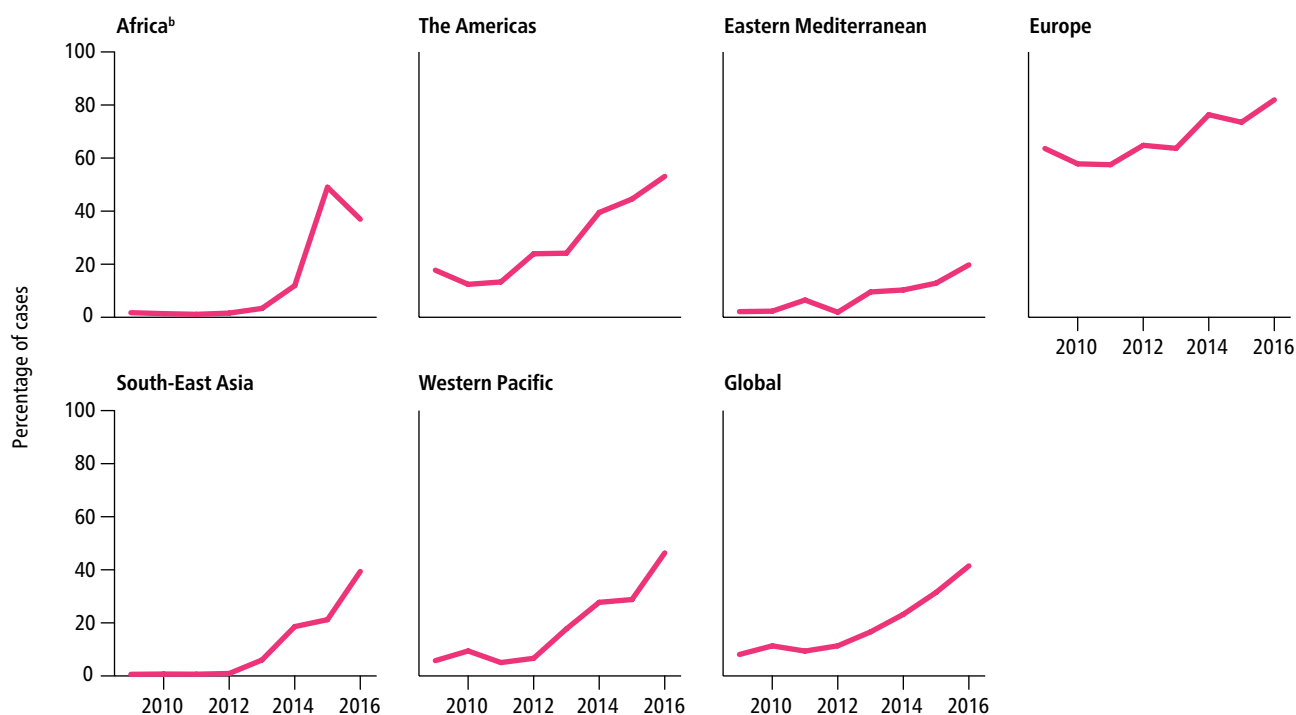
– Data were not available.

<sup>a</sup> The 48 countries shown in the table are the countries that are in one of more of the three lists of high TB, TB/HIV and MDR-TB burden countries (see also [Chapter 2, Figure 2.2](#) and [Table 2.4](#)).

<sup>b</sup> Testing in cases with unknown previous treatment history is not included. The percentage exceeded 100% for several reasons, e.g. samples rather than cases are counted in the numerator; laboratory specimen results are not linked to the denominator data source when enumerated; or there is incomplete reporting of bacteriologically confirmed cases in the denominator. Bacteriologically confirmed extrapulmonary cases are not included in the denominator because they cannot be differentiated from clinically diagnosed ones in the way data are reported to WHO.

**FIG. 4.10**

**Percentage of bacteriologically confirmed TB cases tested for RR-TB, globally and for WHO regions, 2009–2016<sup>a</sup>**



<sup>a</sup> Among new laboratory confirmed and retreatment cases; test results in cases with unknown previous history are not included.

<sup>b</sup> The increase in the African Region from 2014 to 2015 was due to a big increase in reporting of laboratory results for cases in South Africa in 2015.

change in reporting in South Africa.<sup>1</sup> DST coverage varied substantially between countries, even within the same region, and among the 30 high MDR-TB burden countries (Fig. 4.11).

Globally, 153 119 cases of MDR/RR-TB were detected and notified in 2016 (Table 4.1). This was a small increase from 2015 (Fig. 4.12), although aggregate global trends conceal considerable progress in some countries (Fig. 4.13). Between 2015 and 2016, the number of reported MDR/RR-TB cases increased by more than 30% in nine of the 30 high MDR-TB burden countries (Democratic People's Republic of Korea, Democratic Republic of Congo, Mozambique, Nigeria, Papua New Guinea, the Philippines, the Russian Federation, Somalia and Thailand).

The global number of MDR/RR-TB cases notified in 2016 was 26% of the estimated 600 000 incident cases in 2016 (Fig. 4.12; incidence estimates are discussed in more detail in Chapter 3) and 44% of the estimated 350 000 cases of MDR/RR-TB among notified TB cases. Closing these large detection gaps will require improvements in both overall TB detection (Section 4.2) and coverage of diagnostic DST. The latter requires further strengthening of laboratory capacity and wider uptake of new rapid diagnostics.

<sup>1</sup> DST results were reported separately for new and previously treated cases in 2015, but this was not done in 2016.

### **Drug-susceptibility testing for second-line drugs and detection of XDR-TB**

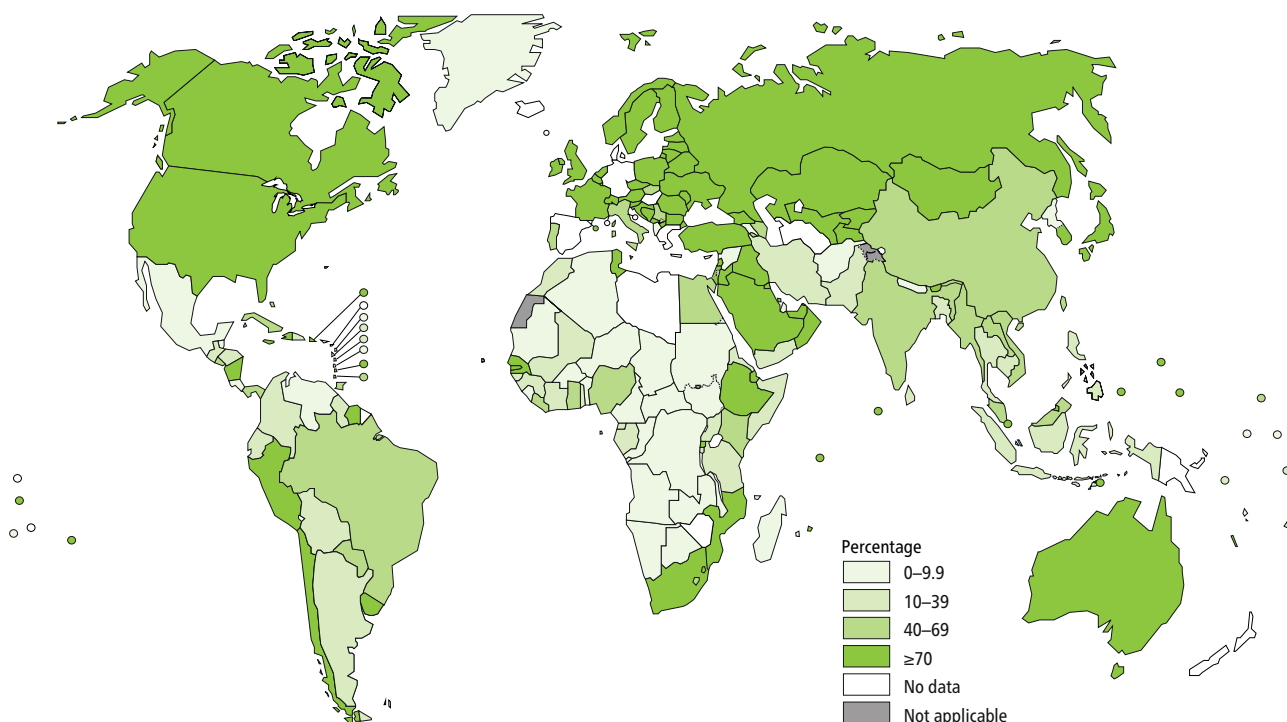
Among MDR/RR-TB patients notified in 2016, 39% were tested for resistance to both fluoroquinolones and second-line injectable agents, a slight increase from 36% in 2015. Coverage varied widely among countries (Fig. 4.14). A total of 8014 cases of XDR-TB were reported by 72 countries, with 75% of cases from the WHO European and South-East Asia regions (Table 4.1). The five countries that reported the largest numbers of cases were China (525), Belarus (572), South Africa (967), Ukraine (1195) and India (2464).

## **4.2 Treatment coverage**

The SDGs include a target to "Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all" (Chapter 2). One of the indicators for Target 3.8 of SDG 3 is the coverage of essential health services; this is a composite indicator based on 16 tracer indicators, one of which is TB treatment coverage. Achieving UHC is a fundamental requirement for achieving the milestones and targets of the End TB Strategy; hence, both TB treatment coverage and the percentage of TB patients and their households that face catastrophic costs as a result of TB disease are priority

**FIG. 4.11**

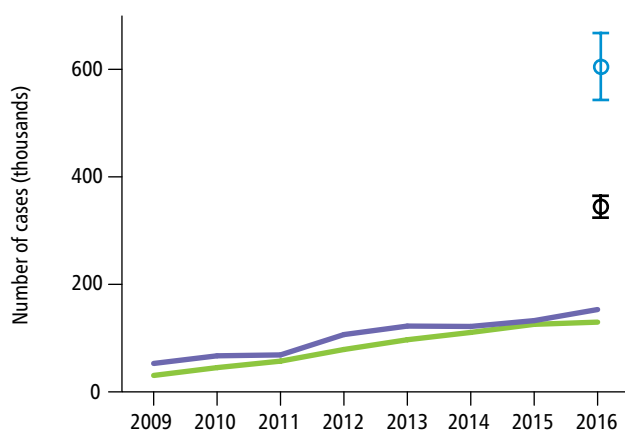
**Percentage of bacteriologically confirmed TB cases tested for RR-TB, 2016<sup>a</sup>**



<sup>a</sup> Among new laboratory confirmed and previously treated cases; cases with unknown previous treatment history are not included. 2015 data were used for 19 countries.

**FIG. 4.12**

**Global number of MDR/RR-TB cases detected (purple) and number enrolled on MDR-TB treatment (green), 2009–2016, compared with estimate for 2016 of the number of incident cases of MDR/RR-TB (uncertainty interval shown in blue) and the number of MDR/RR-TB cases among notified pulmonary cases (uncertainty interval shown in black)**



indicators for monitoring progress in implementing the End TB Strategy (Chapter 2).

TB treatment coverage is defined as the number of new and relapse cases detected and treated in a given year, divided by the estimated number of incident TB cases in the same year, expressed as a percentage. In this section, numbers of notified new and relapse cases in 2016 are used as the numerator for the indicator, because these are the data that are available. However, as discussed further below, there are people with TB who are treated but not notified to national authorities (and in turn are not notified to WHO), and people who are notified but who may not have started treatment.

ART is recommended for all HIV-positive TB patients, and a second-line MDR-TB treatment regimen is recommended for people with MDR/RR-TB. This section includes estimates of treatment coverage for these two interventions as well.

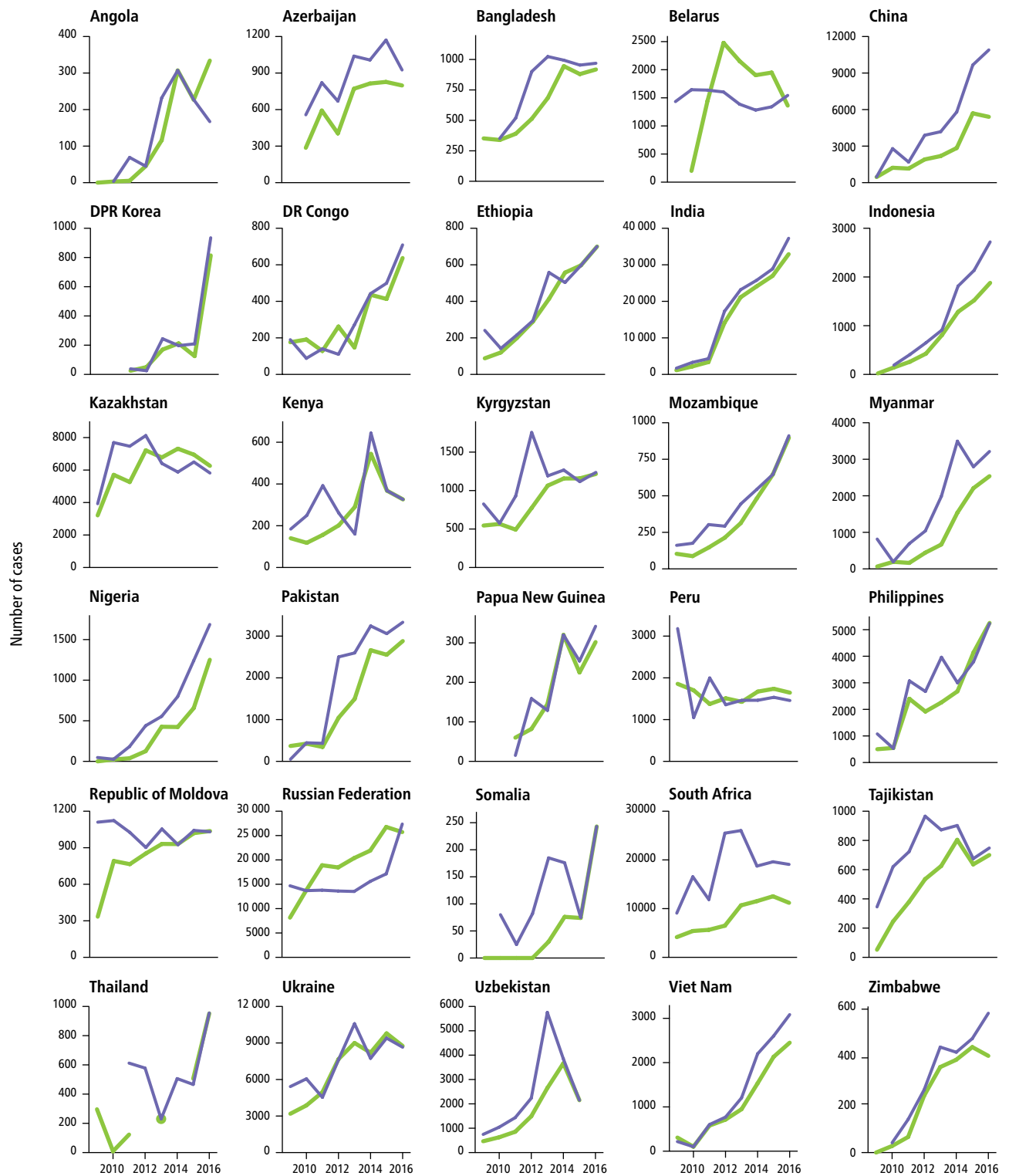
#### 4.2.1 TB treatment coverage

Trends in notifications of new and relapse cases and estimated incidence are shown for the 30 high TB burden countries in Fig. 4.15. Estimates of TB treatment coverage in 2016 (calculated as notifications of new and relapse cases divided by estimated TB incidence) are shown globally, for WHO regions and the 30 high TB burden countries, in Fig. 4.16.

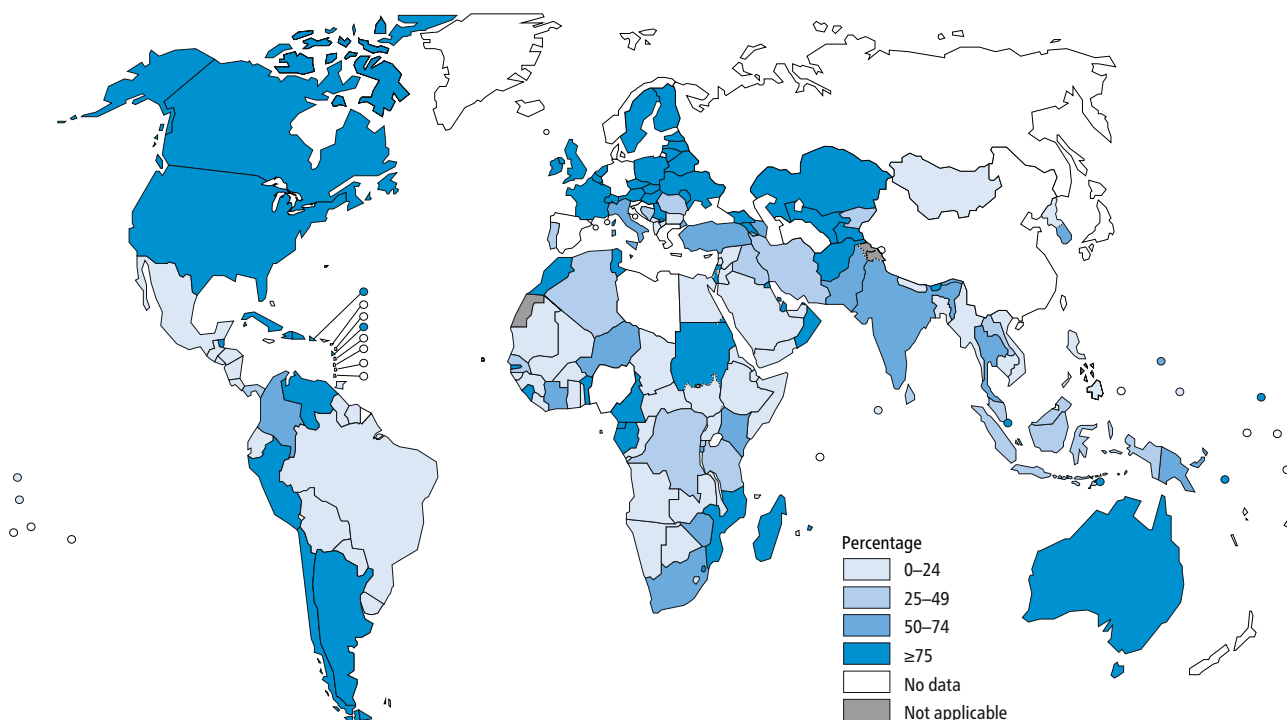
Globally, TB treatment coverage was 61% (range, 52–72%) in 2016, up from 53% (range, 46–64%) in 2010 and 35% (range, 30–43%) in 2000. Three WHO regions achieved levels above 75%: the WHO Region of the Americas, the WHO

**FIG. 4.13**

**Number of MDR/RR-TB cases detected (purple) and enrolled on MDR-TB treatment (green), 2009–2016, 30 high MDR-TB burden countries<sup>a</sup>**



<sup>a</sup> Enrolment may exceed detection of MDR/RR-TB cases for a number of reasons, including the empirical treatment of TB patients considered at risk of having MDR-TB but for whom a laboratory-confirmed diagnosis is missing, incomplete reporting of cases with a laboratory diagnosis of MDR/RR-TB, or enrolment of 'backlogs' of MDR-TB patients who were detected before 2016.

**FIG. 4.14****Percentage of MDR/RR-TB cases tested for susceptibility to second-line drugs, 2016<sup>a</sup>**

<sup>a</sup> 2015 data were used for 20 countries.

European Region and the WHO Western Pacific Region. High TB burden countries with high levels of treatment coverage in 2016 (>80%) included Brazil, China, the Russian Federation, Viet Nam and Zimbabwe. The lowest levels, with best estimates of 50% or less, were in Indonesia, Kenya, Lesotho, Liberia, Mozambique, Nigeria and the United Republic of Tanzania.

Globally in 2016, there was a gap of about 4.1 million (39%) between the 6.3 million new and relapse cases that were notified, and the estimated 10.4 million incident TB cases in the same year (Chapter 3). The global gap has been narrowing, especially in the WHO Eastern Mediterranean and Western Pacific regions, and to a lesser extent in the WHO South-East Asia Region.<sup>1</sup> Ten countries account for 76% of the total estimated gap between incidence and notifications (Fig. 4.17), with India, Indonesia and Nigeria accounting for almost half of the total.

There are three main reasons for a gap between notifications and estimated incidence:

- **Underreporting of detected TB cases.** In many countries, levels of underreporting may be high; this is especially the case for those countries that lack policies on mandatory notification and other measures to ensure reporting of detected cases by all care providers and large private health sectors.

<sup>1</sup> Time trends in countries and regions are shown in Annex 2 and Annex 3, respectively.

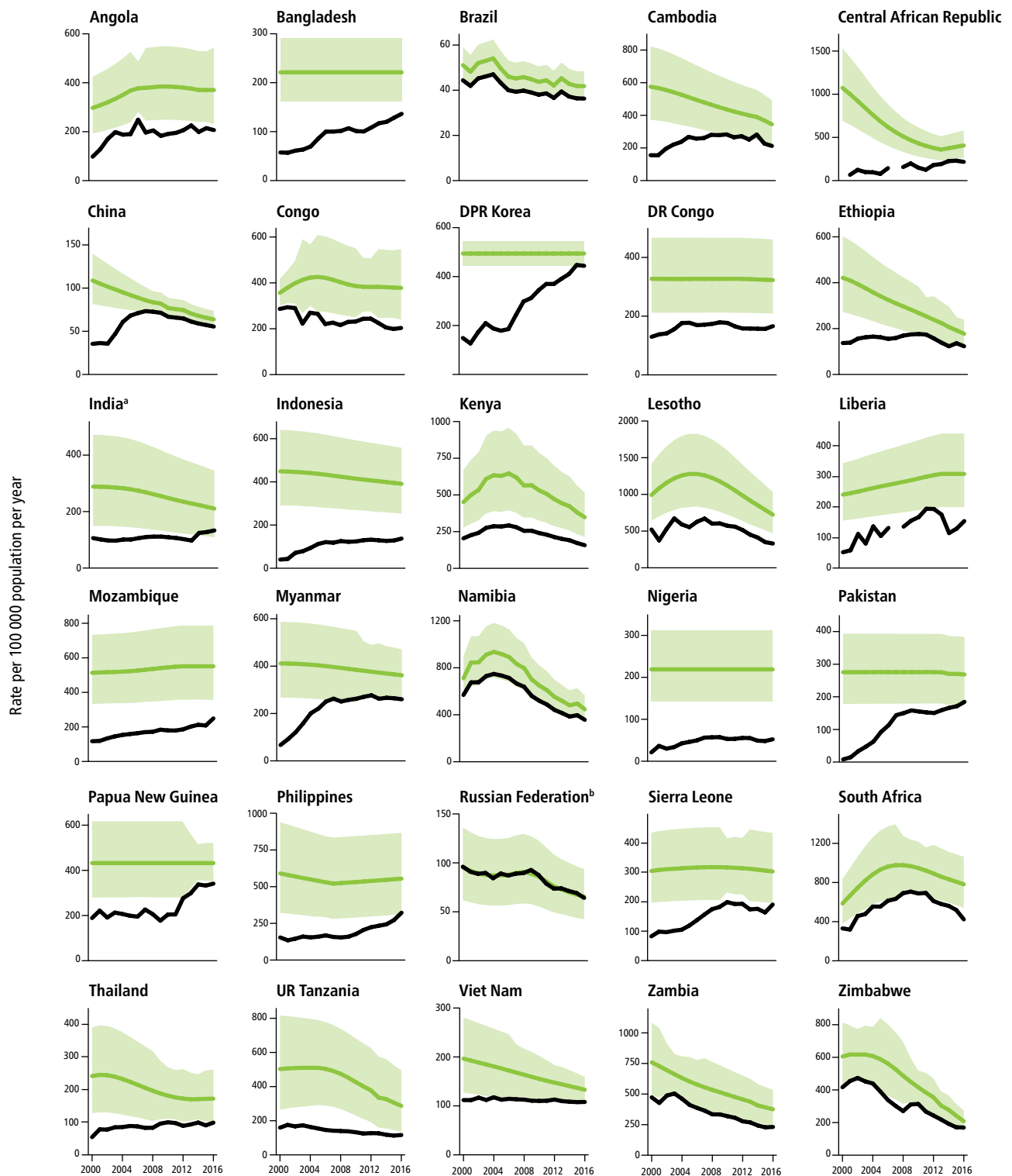
- **Underdiagnosis of people with TB.** Underdiagnosis can occur for reasons such as poor geographical and financial access to health care; lack of or limited symptoms that delay seeking of health care; failure to test for TB when people do present to health facilities; and diagnostic tests that are not sensitive or specific enough to ensure accurate identification of all cases.
- **Uncertainty about the level of TB incidence.** In this report, estimates of TB incidence for 54 countries with 17% of the world's estimated cases are based on expert opinion about levels of underreporting and underdiagnosis, as opposed to direct measurements from surveillance or survey data (Chapter 3). Uncertainty intervals around the best estimates of TB incidence can be wide, and gaps may be lower or higher than the best estimates quoted in this section.

In some of the countries with the largest estimated gaps between notifications and TB incidence, there is already good evidence about the reasons for such gaps, and actions to address them are being taken or are planned. In India, multiple sources of evidence from surveys and surveillance show large underreporting of detected TB cases, especially in the private sector.<sup>2</sup> Three examples of actions that have been taken to close reporting gaps are mandatory notification, a simplified

<sup>2</sup> For further details, see Box 3.3 in World Health Organization. Global tuberculosis report 2016 (WHO/HTM/TB/2016.13). Geneva: WHO; 2016 (<http://apps.who.int/iris/bitstream/10665/250441/1/9789241565394-eng.pdf>, accessed 21 August 2017).

**FIG. 4.15**

Case notification rates (new and relapse cases, all forms) (black) compared with estimated TB incidence rates (green), 2000–2016, 30 high TB burden countries. Shaded areas represent uncertainty bands.

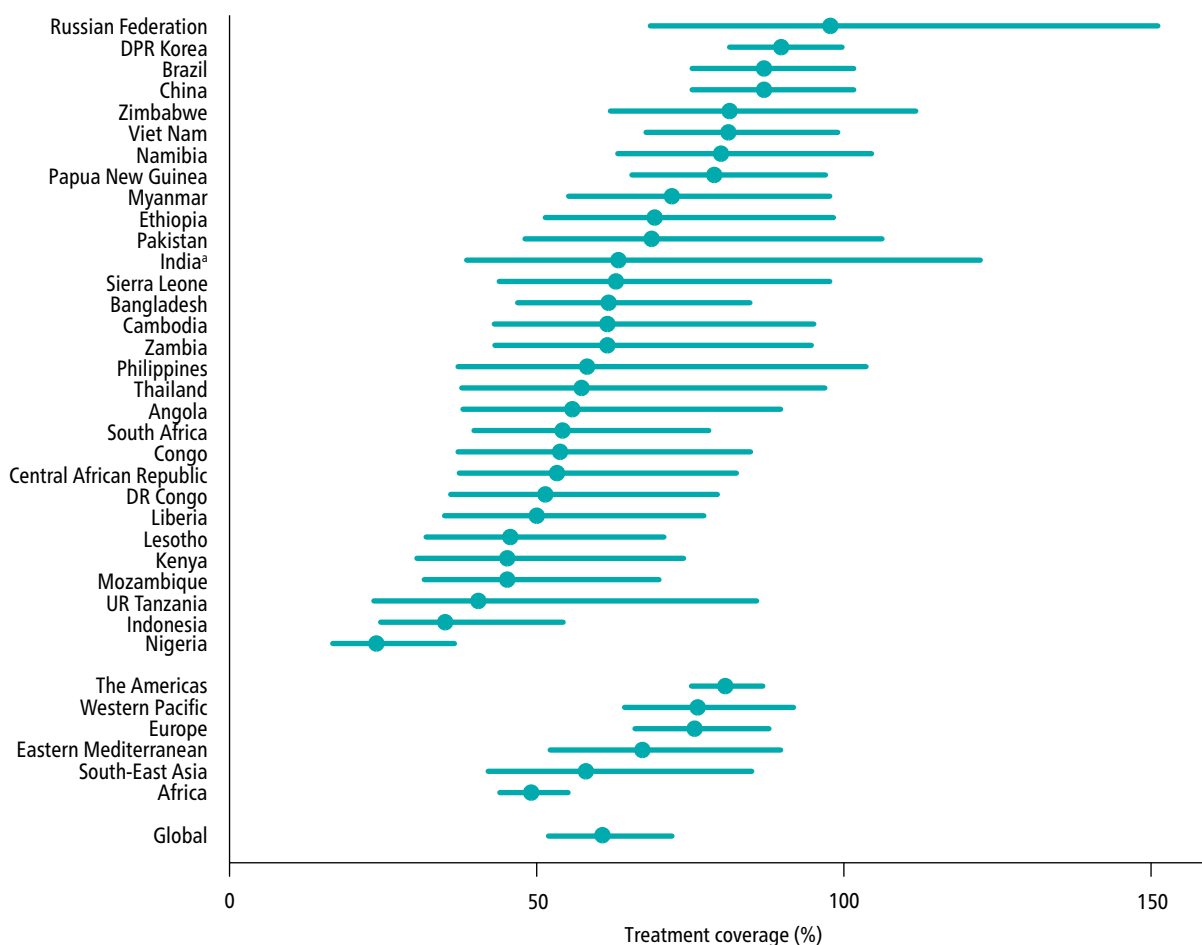


<sup>a</sup> Estimates of TB incidence for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.

<sup>b</sup> For an explanation of why notifications are assumed to be equivalent to TB incidence in the Russian Federation, see [Box 3.5](#) in [Chapter 3](#).

**FIG. 4.16**

**Estimated TB treatment coverage (new and relapse patients as a percentage of estimated TB incidence) in 2016, 30 high TB burden countries, WHO regions and globally**



<sup>a</sup> Estimates of TB incidence for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.

national electronic reporting system that facilitates reporting of cases, and further efforts to engage all care providers through PPM schemes. In Indonesia, the 2013–2014 national TB prevalence survey showed high levels of underreporting of detected TB cases, leading to recommendations such as a mandatory policy on notification (enacted in January 2017), and intensified engagement with public and private hospitals where many people with TB were being treated.<sup>1</sup> Similar findings are emerging from the 2016 national TB prevalence survey in the Philippines (Chapter 3). In Nigeria, the 2012 prevalence survey found that 75% of the smear-positive cases detected had symptoms that met national screening criteria but had not been previously diagnosed, suggesting high levels of underdiagnosis and a need to strengthen access to diagnostic and treatment services.<sup>2</sup>

<sup>1</sup> For further details, see Box 2.4 in World Health Organization. Global tuberculosis report 2015 (WHO/HTM/TB/2015.22). Geneva: WHO; 2015 ([http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf), accessed 27 July 2017).

<sup>2</sup> For further details, see Box 2.2 in World Health Organization. Global tuberculosis report 2014 (WHO/HTM/TB/2014.08). Geneva: WHO; 2014 ([http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf), accessed 15 August 2017).

In countries where underreporting is thought to exist, inventory studies in which electronic lists of notified cases are compared with electronic lists of TB cases detected by all care providers, ideally employing unique identifiers, can be used to quantify levels of underreporting.<sup>3</sup> Such studies have already been used to inform estimates of TB incidence in several countries (Chapter 3), and are planned or underway in six high TB burden countries: China, Indonesia, Nigeria (metropolitan Lagos), the Philippines, South Africa and Viet Nam. When these studies are done prospectively (as opposed to retrospectively, using electronic databases that are already available), the mapping of providers that is required at the beginning can subsequently help with efforts to engage all care providers, including in reporting (Box 4.3).

Examples of mechanisms to ensure reporting of all detected cases include linking reimbursement from health insurance schemes to notification of cases (as in the Republic of Korea)

<sup>3</sup> For a guide to inventory studies, see World Health Organization. Assessing tuberculosis under-reporting through inventory studies. Geneva: WHO; 2012 ([http://www.who.int/tb/publications/inventory\\_studies/en/](http://www.who.int/tb/publications/inventory_studies/en/), accessed 15 August 2017).



**FIG. 4.17**

**The ten countries with the largest gaps between notifications of new and relapse (incident) TB cases and the best estimates of TB incidence, 2016<sup>a</sup>**



<sup>a</sup> The ten countries ranked in order of the size of the gap between notified cases and the best estimates of TB incidence in 2016, are India, Indonesia, Nigeria, the Philippines, South Africa, Pakistan, Bangladesh, DR Congo, China and UR Tanzania. Estimates of TB incidence for India are interim in nature, pending results from the national TB prevalence survey planned for 2018/2019.

and linking the supply of first-line drugs to notification of cases (as in Brazil).

Recent national TB prevalence surveys<sup>1</sup> have also shown that, in both Africa and Asia, detection and reporting gaps are systematically higher for men than for women (Chapter 3). This suggests that specific efforts are needed to improve access to TB diagnosis and treatment for men.

Systematic screening for active TB among specific populations can also help to ensure early diagnosis and reduce levels of underdiagnosis. WHO recommends such screening for contacts of bacteriologically confirmed cases, people living with HIV and people exposed to silica dust.<sup>2,3</sup> Other individuals at risk should be considered for systematic screening based on an assessment of TB epidemiology in each setting. To date, there have been few assessments of the implementation and outcomes of systematic screening in countries that are currently introducing or scaling it up. However, systematic screening is expected to become a

more prominent part of national programme monitoring and evaluation efforts in future. Engaging communities can also add value to efforts to improve case detection and patient support (Box 4.4).

#### 4.2.2 Treatment coverage of ART for HIV-positive TB cases

WHO recommends ART for all HIV-positive TB patients within the first 8 weeks of starting TB treatment. The number of notified HIV-positive TB patients on ART has grown in recent years (Fig. 4.18); it reached 399 146 in 2016, equivalent to 85% of the notified TB patients known to be HIV-positive (Table 4.1).<sup>4</sup> In the 30 high TB/HIV burden countries, overall, 86% of the TB patients known to be HIV-positive were on ART; six of these countries (India, Kenya, Malawi, Mozambique, Namibia and Swaziland) maintained coverage of at least 90% in both 2015 and 2016.<sup>5</sup> In contrast, there were six high TB/HIV burden countries (Brazil, Congo, Ghana, Guinea-Bissau, Indonesia and Liberia) in which less than 50% of HIV-positive TB patients were started on ART in 2016. Angola and Chad did not report data on ART for TB patients.

ART treatment coverage for people with TB can also

<sup>1</sup> See [http://www.who.int/tb/advisory\\_bodies/impact\\_measurement\\_taskforce/meetings/tf6\\_p06\\_prevalence\\_surveys\\_2009\\_2015.pdf](http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf6_p06_prevalence_surveys_2009_2015.pdf)

<sup>2</sup> World Health Organization. Systematic screening for active tuberculosis: principles and recommendations (WHO/HTM/TB.2013.04). Geneva: WHO; 2013 (<http://www.who.int/tb/tbscreening/en/>, accessed 15 August 2017). The data requested in the global monitoring done by WHO focus on screening among people living with HIV and close contacts.

<sup>3</sup> For this reason, the data requested in WHO's annual round of global TB data collection focus on screening among people living with HIV and close contacts. These data are presented in Chapter 5.

<sup>4</sup> There may be discrepancies in data on provision of ART to HIV-positive TB patients that are reported by NTPs and national HIV programmes. These discrepancies have reduced in recent years and are mostly resolved through follow-up and validation efforts.

<sup>5</sup> Further details are provided in Annex 4.

**BOX 4.4**

**Community contributions to TB notifications and treatment support**

Engagement of communities, NGOs and other civil society organizations (CSOs) is one of the four underlying principles as well as one of the core components of the End TB Strategy. Community-based TB activities include a wide range of activities that contribute to the detection, referral and treatment of people with drug-susceptible, drug-resistant and HIV-associated TB that are carried out by community health workers (CHWs) and community volunteers.<sup>a</sup> Such activities can be part of public health services or activities implemented by NGOs or CSOs. In some countries, CHWs are an integral part of the health system, and enjoy the rights and privileges of formal employment. An example is Ethiopia, where the use of CHWs has helped to transform primary health care.

In WHO's 2017 round of global TB data collection, 53 countries reported data about the contribution of communities through CHWs to TB notifications or treatment support. This represents a more than threefold increase in reporting since 2013, when data were first collected on the two core indicators (referrals and treatment support) used to monitor community engagement. In these 53 countries, 57% (30/53) reported nationwide coverage by all basic management units of community engagement in referrals of cases (thus contributing to case notifications) or community-based treatment support in 2016 (Fig B4.4.1). In areas where community-based referral activities were in place, the

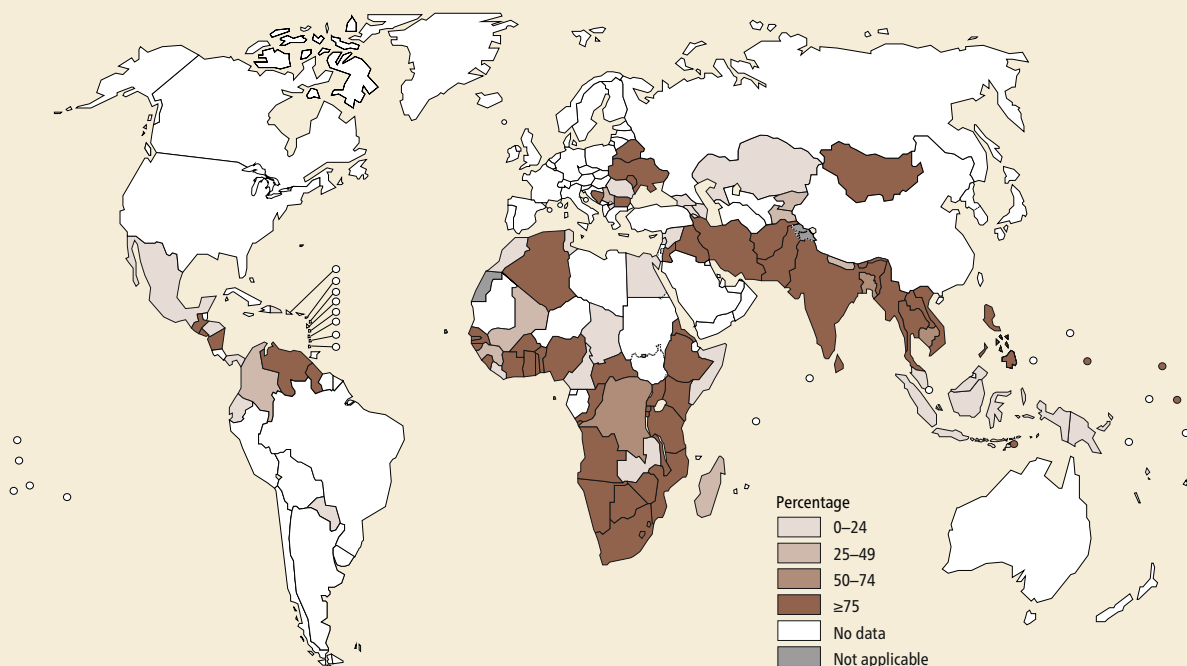
percentage of notified TB patients attributed to community referrals averaged 16%.

Globally, over 1.5 million TB patients received some form of treatment adherence support from CHWs and volunteers in 2016. The proportion of TB patients receiving such community-based treatment support ranged considerably among countries. Almost two thirds of the countries (34/53) reported information about the treatment success rate among TB patients who received treatment support in the community. Treatment success rates ranged from 57% in Colombia to 100% in Afghanistan, Honduras, Jordan and Mozambique.

In 31 other countries, community-based TB activities were carried out and supported TB services, but data collection systems do not allow the contribution of all such activities to be reported at national level. Thirteen of these 31 countries (42%) reported countrywide coverage of community-based activities in all basic management units. Further effort is needed to update the data recording systems in these countries to reflect community contributions.

<sup>a</sup> Community health workers and community volunteers are defined here: World Health Organization. ENGAGE-TB Approach: Operational guidance: integrating community-based tuberculosis activities into the work of nongovernmental and other civil society organizations (WHO/HTM/TB/2012.8). Geneva: WHO; 2012 ([http://www.who.int/tb/publications/2012/engage\\_tb\\_policy/en/](http://www.who.int/tb/publications/2012/engage_tb_policy/en/), accessed 15 August 2017).

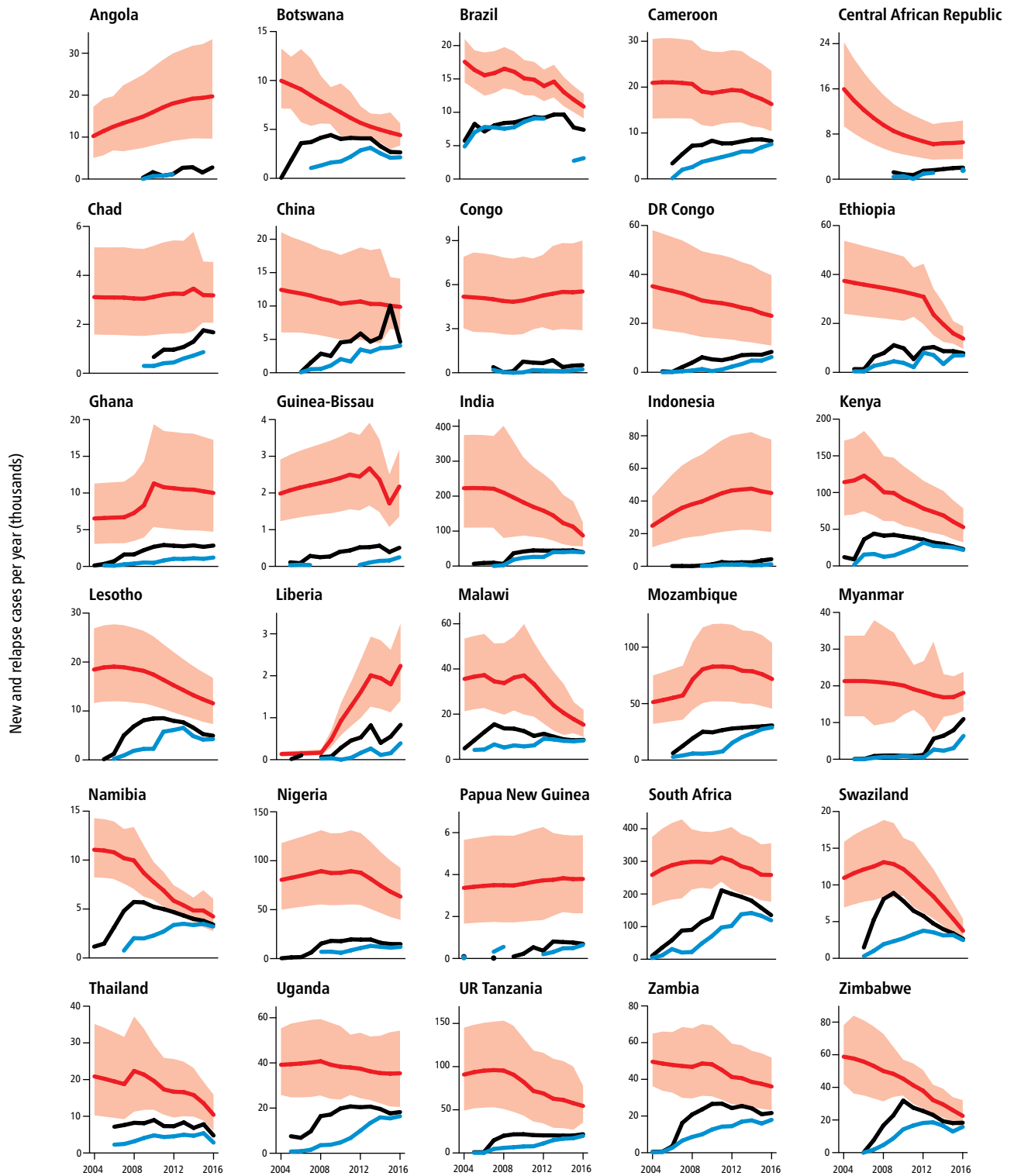
**FIG. B4.4.1**  
**Percentage of basic management units in which there is community contribution to new case finding and/or to treatment adherence support, 2016**



Data only requested from 114 countries.

**FIG. 4.18**

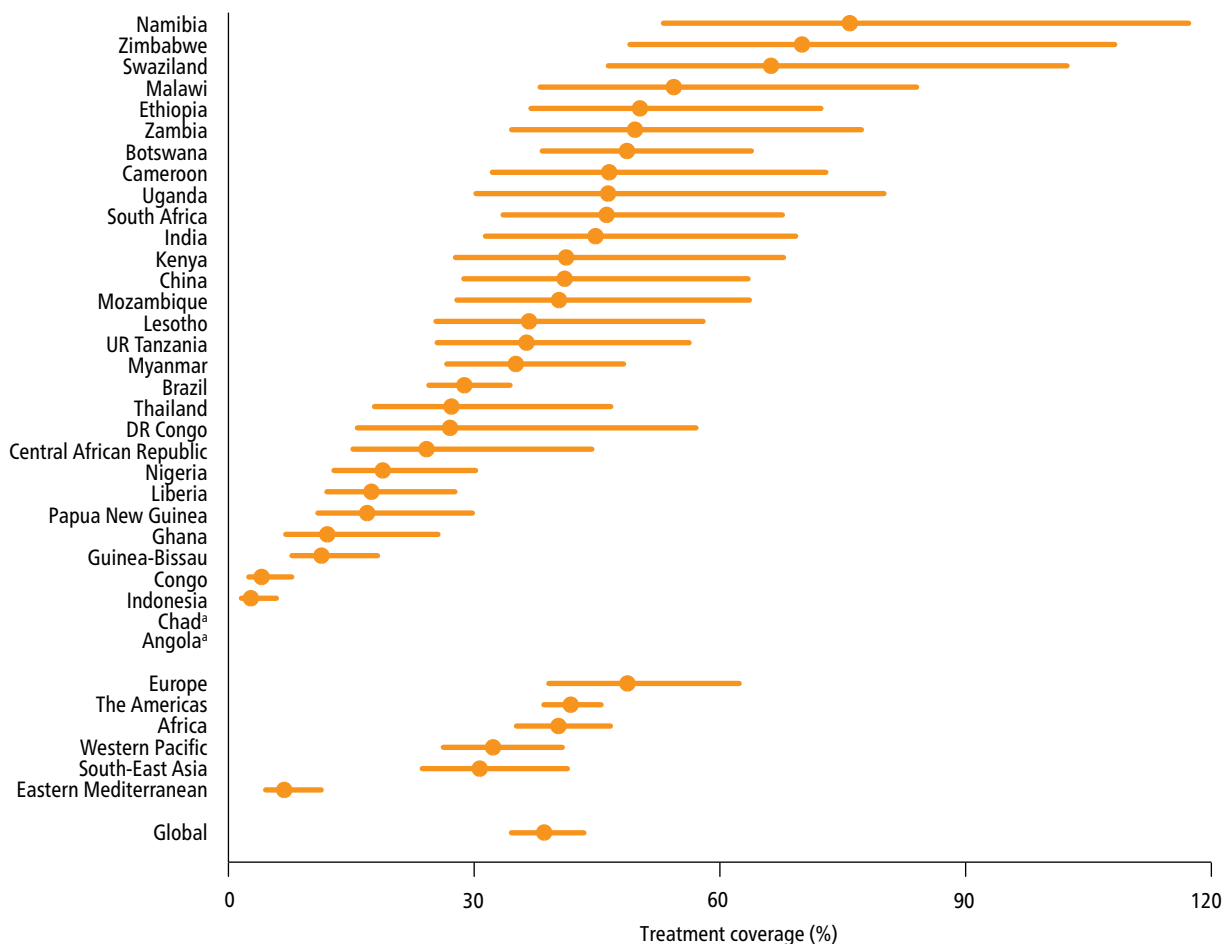
Number of new and relapse cases<sup>a</sup> known to be HIV-positive (black) and number started on ART (blue) compared with estimated number of incident HIV-positive TB cases (red), 2004–2016, 30 high TB/HIV burden countries



<sup>a</sup> The calculation is for all cases in years prior to 2015.

**FIG. 4.19**

**Estimated ART treatment coverage for HIV-positive TB cases (HIV-positive TB patients on ART as a percentage of the estimated incidence of HIV-positive TB) in 2016, 30 high TB/HIV burden countries, WHO regions and globally**



<sup>a</sup> No data.

be assessed by comparing the number of HIV-positive TB patients on ART with the estimated number of HIV-positive incident TB cases (Fig. 4.19). This comparison reveals larger gaps. Globally in 2016, the number of HIV-positive TB patients on ART was 39% of the estimated global number of incident HIV-positive TB cases. There was considerable variation among the high TB/HIV burden countries and, according to best estimates, only five countries achieved ART coverage of more than 50% (Ethiopia, Malawi, Namibia, Swaziland and Zimbabwe).

Improvements are still needed in the detection of active TB disease among HIV-positive people, the coverage of HIV testing among TB patients, and the enrolment of HIV-positive TB patients on ART. An overview of progress and gaps in TB preventive treatment among people living with HIV is provided in Chapter 5.

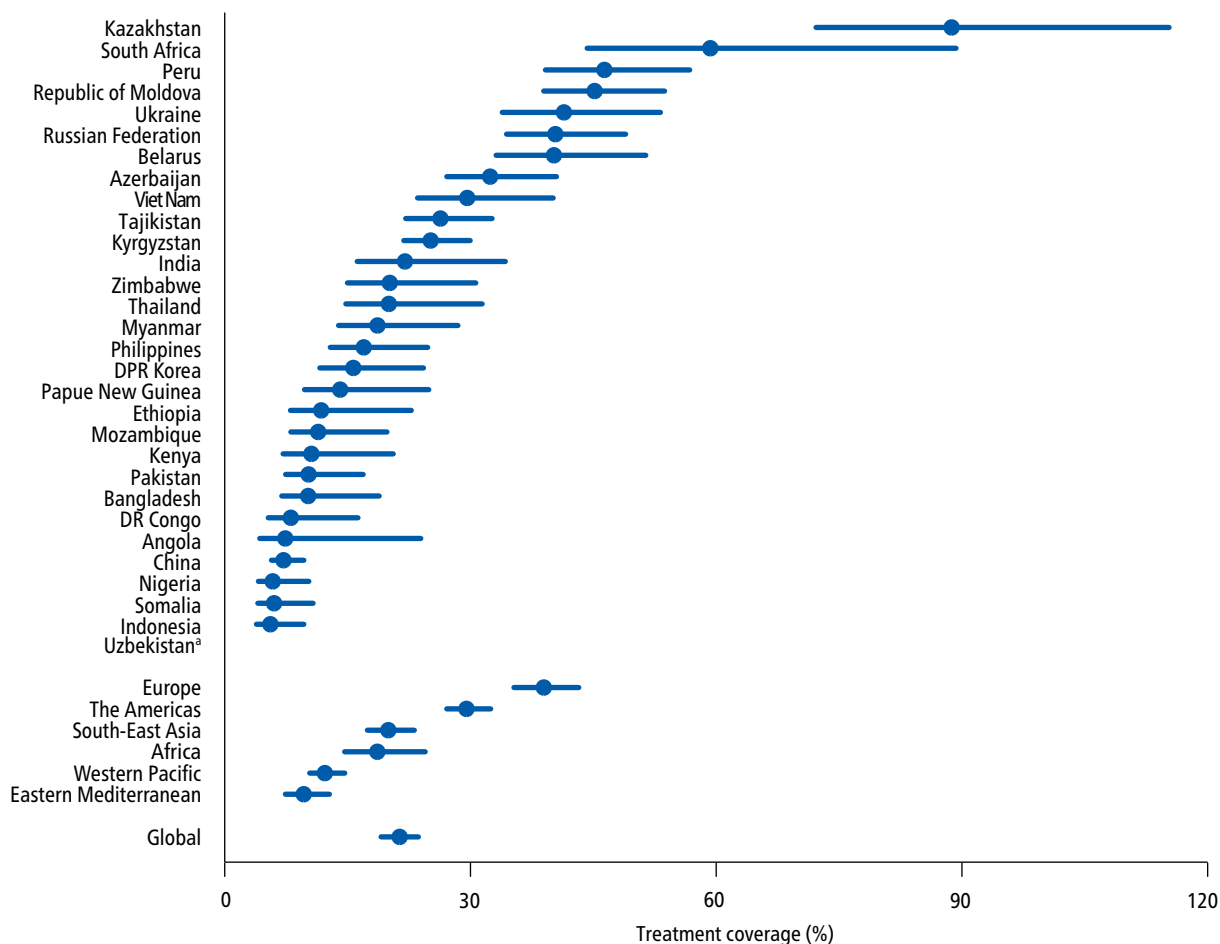
### 4.2.3 Treatment coverage for MDR/RR-TB

Trends in the number of patients enrolled in MDR-TB treatment globally and in the 30 high MDR-TB countries since 2009 are shown in Fig. 4.12 and Fig. 4.13, respectively. The number of people enrolled in treatment globally was 129 689 in 2016, representing a more than fourfold increase since 2009 (when WHO first requested countries to report data), but limited progress since 2015 (when 125 629 people were enrolled in treatment). There was a notable increase in enrolments in India between 2015 and 2016 (from 26 996 to 32 914), and modest increases in several other high MDR-TB burden countries. However, the number of enrolments fell in 10 high MDR-TB burden countries, and fell by more than 1000 patients in the Russian Federation, South Africa and Ukraine.

Globally, the 129 689 patients starting second-line MDR-TB treatment in 2016 represented 22% of the 600 000 estimated MDR/RR-TB incident cases in 2016 (Fig. 4.20). Ten countries accounted for around 75% of the gap between enrolments

**FIG. 4.20**

**Estimated treatment coverage for MDR/RR-TB (patients started on treatment for MDR-TB as a percentage of the estimated incidence of MDR/RR-TB) in 2016, 30 high MDR-TB burden countries, WHO regions and globally**



<sup>a</sup> No data.

in MDR-TB treatment in 2016 and the estimated number of incident MDR/RR-TB cases in 2016; China and India accounted for 39% of the total gap (Fig. 4.21).

The number of cases starting MDR-TB treatment in 2016 was equivalent to 85% of the 153 119 MDR/RR-TB patients notified in 2016 (Fig. 4.12). The figure exceeded 90% in 14 high MDR-TB burden countries (Fig. 4.13) and the WHO European Region and the Region of the Americas; however, it was much lower in the WHO African and Western Pacific regions.<sup>1</sup> Enrolments represented less than 60% of the number of notified MDR/RR-TB cases in two high MDR-TB burden countries in 2016: China (50%) and South Africa (59%). These low percentages show that progress in detection is outstripping capacity to provide treatment; they may also reflect weaknesses in data collection systems. In these settings the risk of transmission of DR-TB is high and efforts are needed to rapidly close enrolment/notification gaps.

<sup>1</sup> For data for WHO regions, see Annex 3.

In many countries, one of the barriers to adequate access to treatment of drug-resistant TB is that the network for the programmatic management of drug-resistant TB (PMDT) is too centralized and reliant on hospital-based models of care. Greater decentralization and more use of outpatient models of care are needed.

Globally, 8511 patients with XDR-TB were enrolled in treatment in 68 countries and territories, a 17% increase compared with 2015. In 29 of these countries, the number of XDR-TB cases enrolled in treatment was less than the number notified. Treatment coverage will not improve globally unless there is an intensification of efforts in the countries with the largest burden, particularly China, India and Indonesia.

**FIG. 4.21**

**The ten countries with the largest gaps between the number of patients started on treatment for MDR-TB and the best estimates of MDR/RR-TB incidence, 2016<sup>a</sup>**



<sup>a</sup> The ten countries ranked in order of the size of the gap between the gap of patients started on MDR-TB treatment and the best estimate of MDR/RR-TB incidence in 2016 are India, China, Indonesia, the Philippines, Pakistan, Russian Federation, Nigeria, Ukraine, Myanmar and Bangladesh.

### 4.3 Treatment outcomes

This section summarizes the latest results of treatment for new and relapse cases of TB who started treatment on a first-line regimen in 2015 (including people with HIV-associated TB), and people detected with RR-TB, MDR-TB or XDR-TB who started a second-line MDR-TB regimen in 2014.<sup>1</sup> The increasing role of digital technologies in treatment support, as a basis for improving treatment outcomes, is discussed in [Box 4.5](#).

Most new and relapse cases do not have MDR/RR-TB, but in some parts of the world, especially countries of the former Soviet Union, more than 20% of new and relapse cases do ([Chapter 3](#)). Universal access to DST is required to ensure that all people with TB receive appropriate treatment, as discussed in [Section 4.1](#).

#### 4.3.1 Treatment outcomes for new and relapse TB patients

Data on treatment outcomes for new and relapse cases of TB in 2015 are shown for the world, the six WHO regions and the 30 high TB burden countries in [Fig. 4.22](#). The global trend

2012–2015 is shown in [Fig. 4.23](#). Globally, the treatment success rate for the 5.9 million new and relapse cases who were treated in the 2015 cohort was 83%, as in 2014. The absolute number of TB patients reported to have been successfully treated has risen substantially over the past 15 years, both globally and in all WHO regions ([Fig. 4.24](#)),

Among the six WHO regions, the highest treatment success rates in 2015 were in the WHO Western Pacific Region (92%) and the WHO Eastern Mediterranean Region (91%). The lowest rates (at 76%) were in the WHO Region of the Americas (due to high levels of loss to follow-up and missing data) and the WHO European Region (due to high rates of treatment failure and death, influenced by the high frequency of MDR/RR-TB).

Only seven of the 30 high TB burden countries reached or exceeded a 90% treatment success rate, although the validity of treatment outcome data was not always ascertained. However, in several high TB burden countries, the completeness of outcome reporting was low. In four countries (Central African Republic, Congo, Liberia and Papua New Guinea), loss to follow-up exceeded 10%, and in four countries (Brazil, Congo, Ethiopia and India), more than 10% of cases were not evaluated. In Brazil (71% success), 21% of cases were either lost to follow-up or their treatment outcome was missing.

<sup>1</sup> For definitions of treatment outcomes, see World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision (updated December 2014) (WHO/HTM/TB/2013.2). Geneva: WHO; 2013 ([www.who.int/iris/bitstream/10665/79199/1/9789241505345\\_eng.pdf](http://www.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf), accessed 1 July 2017).

## BOX 4.5 Digital technologies in support of TB medication adherence and delivery

The updated TB treatment guidelines for drug-susceptible TB published by WHO in April 2017<sup>a</sup> (Box 4.2) include, for the first time, evidence-based recommendations related to the use of digital technologies. These include short message service (SMS, mobile phone texting), video-supported TB treatment and electronic medication monitors. Although data on the impact of these interventions on improving treatment outcomes of TB patients and reducing costs to health services remain limited, several studies that are expected to improve the quality of the evidence and provide more information on their performance in different settings are now underway.

Digital technologies are being used in a variety of ways in TB care (Fig. B4.5.1). Some interventions are pilot projects whereas others are implemented at a much larger scale. Among high TB burden countries, adoption in the public sector has been reported by Cambodia, China, Papua New Guinea, the Russian Federation and Viet Nam; use in the private sector has been reported by the Democratic Republic of the Congo, India, Kenya and Lesotho. Many countries in the WHO African Region report no use whereas several countries – especially high-income ones – are not currently able to report information about the use of digital technologies.

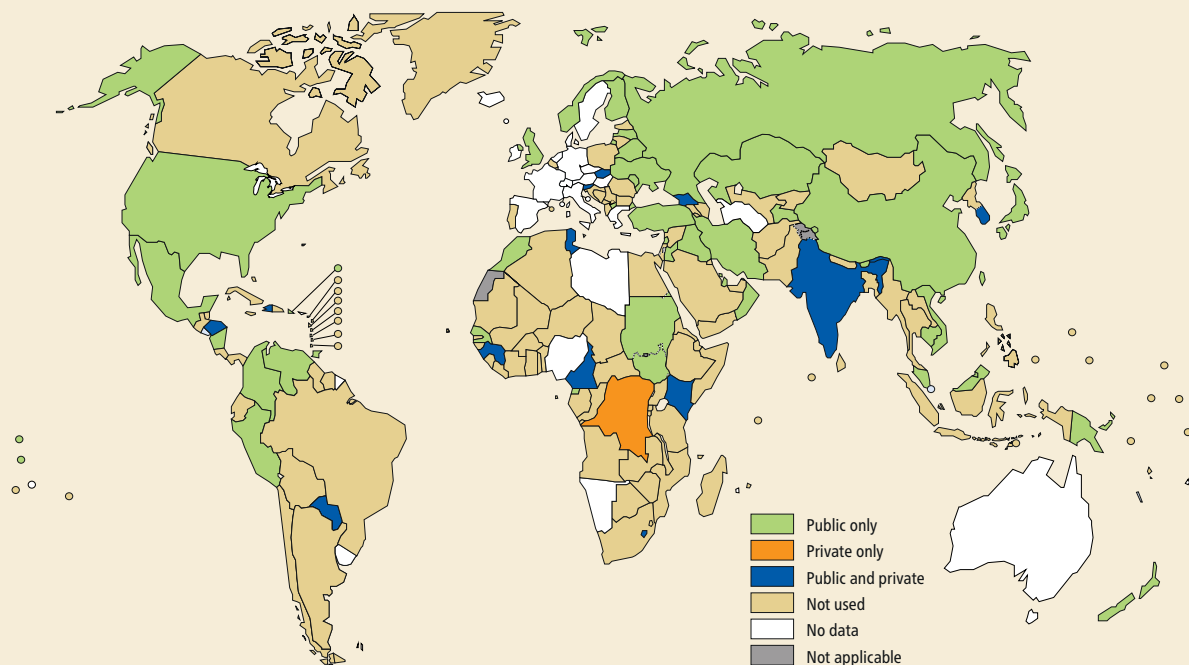
As access to the Internet and to high-performance mobile devices (especially smartphones) grows globally, digital tools are likely to be used (or considered for use) much more widely to help with adherence and other aspects of programmatic work (e.g. surveillance, logistics management and e-learning). Continuous development and diversification of technologies will create new opportunities to make interventions more effective or efficient, while also making it more challenging to generate an evidence base about their effectiveness.

With increasing demand for technical assistance on how to implement digital health interventions at a large scale, the WHO Global Task Force on digital health for TB is developing a practical handbook to address this need.<sup>b</sup>

<sup>a</sup> World Health Organization. Treatment of tuberculosis: guidelines for treatment of drug-susceptible tuberculosis and patient care (2017 update) (WHO/HTM/TB/2017.05). Geneva: WHO; 2017 (<http://apps.who.int/iris/bitstream/10665/255052/1/9789241550000-eng.pdf>, accessed 11 July 2017).

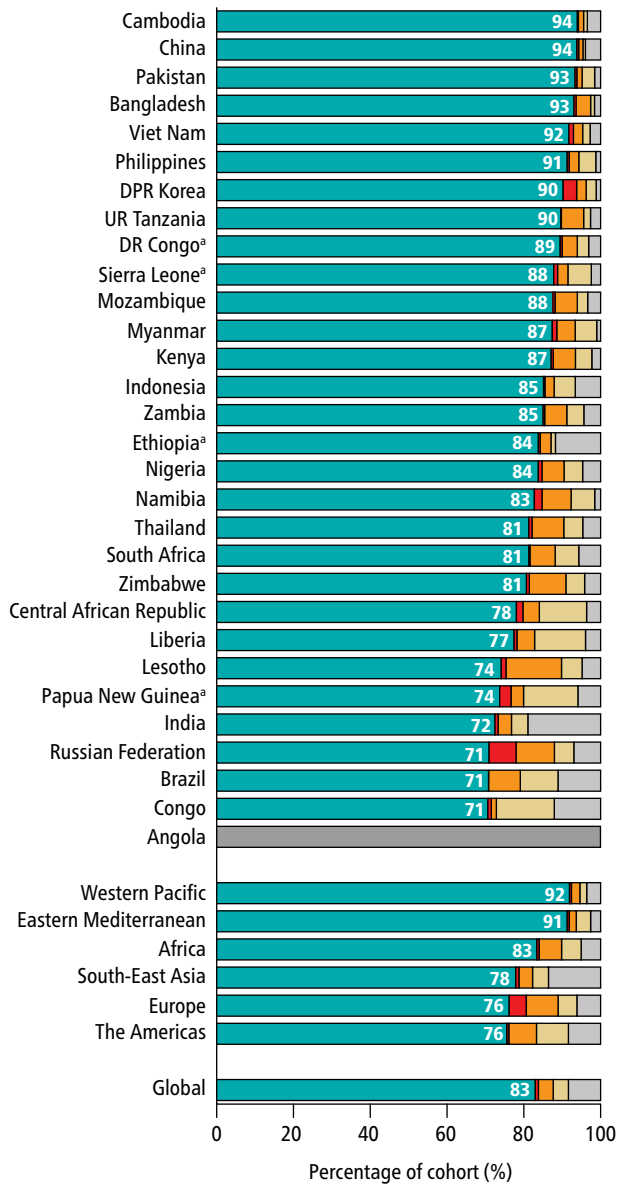
<sup>b</sup> See <http://www.who.int/tb/areas-of-work/digital-health/en/> (accessed 10 August 2017). <http://www.who.int/tb/areas-of-work/digital-health/en/>

**FIG. B4.5.1**  
Use of short message service, video-supported treatment or electronic medication monitors to improve TB treatment adherence and delivery, 2016



**FIG. 4.22**

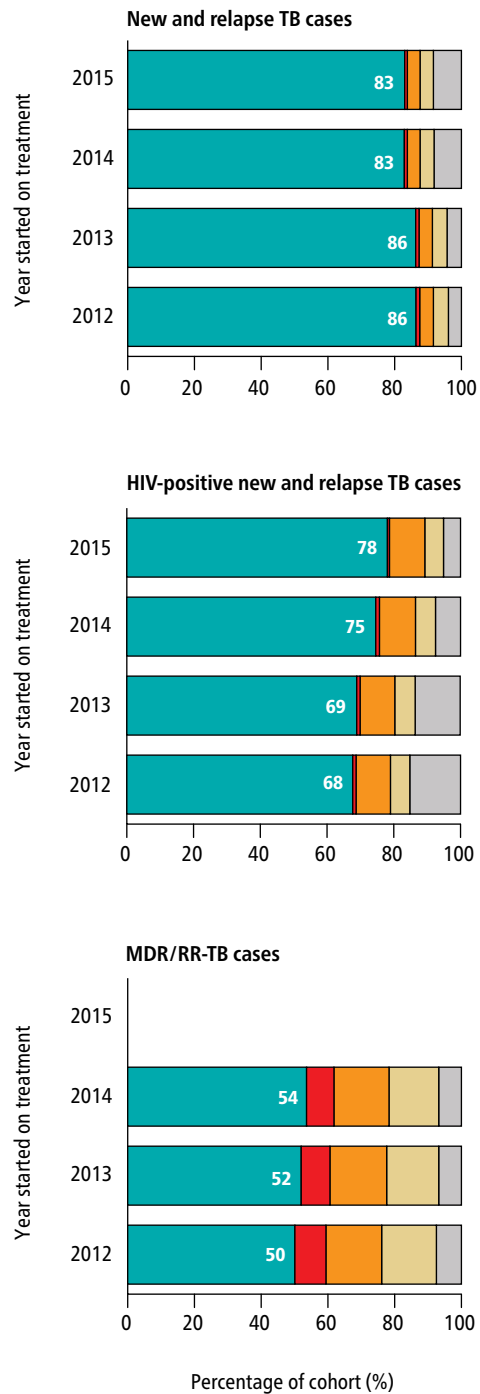
**Treatment outcomes for new and relapse TB cases in 2015, 30 high TB burden countries, WHO regions and globally**



<sup>a</sup> Treatment outcomes are for new cases only.

**FIG. 4.23**

**Treatment outcomes for new and relapse TB cases, new and relapse HIV-positive TB cases, and MDR/RR-TB cases, 2012–2015 globally<sup>a</sup>**

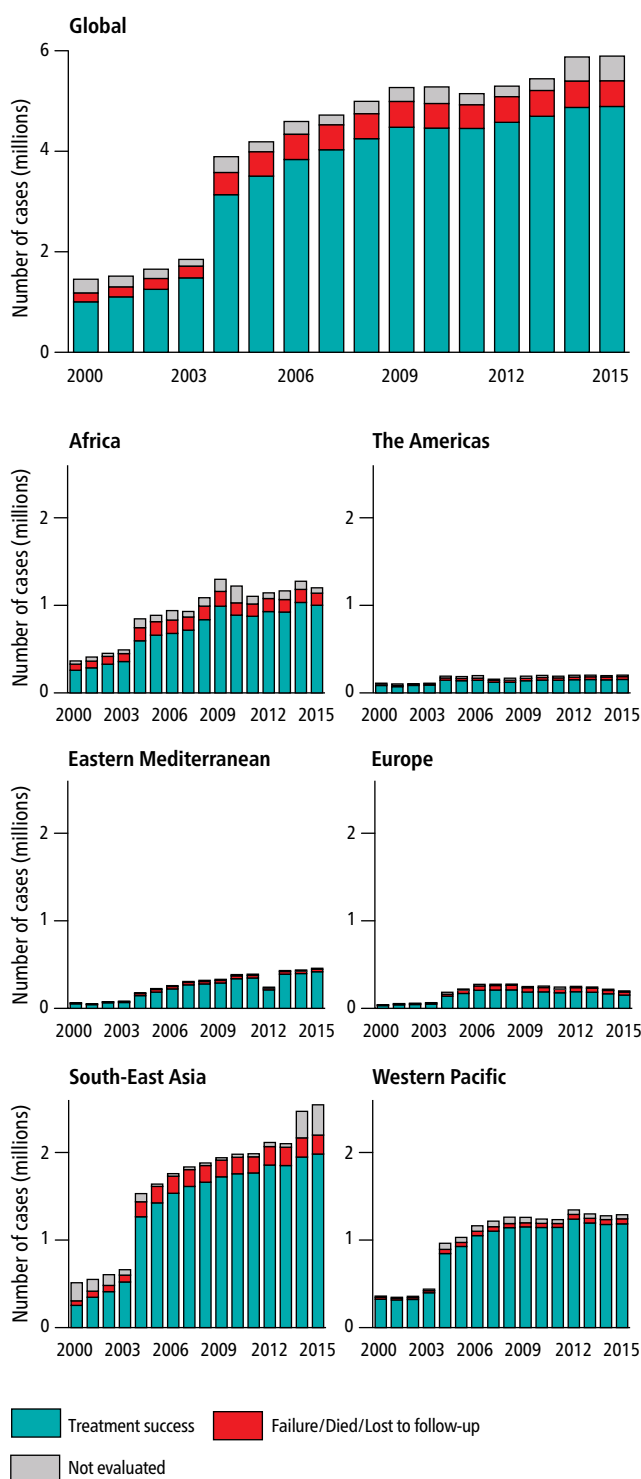


<sup>a</sup> MDR/RR-TB annual treatment cohorts are reported one year later than other TB cohorts.



**FIG. 4.24**

**Treatment outcomes for new and relapse TB cases<sup>a</sup> (absolute numbers), 2000–2015, globally and for WHO regions**



<sup>a</sup> Cohorts before 2012 included new cases only.

**4.3.2 Treatment outcomes for new and relapse TB patients coinfecting with HIV**

A total of 110 countries reported treatment outcomes for the 2015 patient cohort disaggregated by HIV status; collectively, these countries accounted for 93% of the HIV-positive TB patients reported by NTPs in 2015. These 110 countries included 24 of the 30 high TB/HIV burden countries; no data were reported by Angola, Chad, the Democratic Republic of the Congo, Ethiopia, Liberia and Papua New Guinea (Fig. 4.25). Overall, the treatment success rate was 78%, up from 68% in 2012 (Fig. 4.23), although still worse than the level of 83% for all new and relapse TB patients.

Globally, the proportion of HIV-positive TB patients reported having died during treatment was 11%, similar to previous years and about three times the level among all new and relapse cases (4%). The relative difference was smallest in the WHO African Region (9% versus 7%) and highest in the WHO Western Pacific Region (13% versus 2%).

Reasons for comparatively poor outcomes for HIV-positive TB patients include late detection of HIV-associated TB, and delays in starting ART or TB treatment. To reduce excessive TB mortality in HIV-positive people, WHO recommends routine HIV testing among presumptive and diagnosed TB cases; TB screening among people living with HIV; early ART; improved infection control; and provision of TB preventive treatment. Strategic placement of WHO-recommended rapid molecular TB diagnostics such as Xpert MTB/RIF within HIV care settings and uptake of the lateral flow urine lipoarabinamannan assay (LF-LAM) for seriously ill people living with HIV could help to ensure earlier diagnosis.

**4.3.3 Treatment outcomes for TB patients with MDR/RR-TB and XDR-TB**

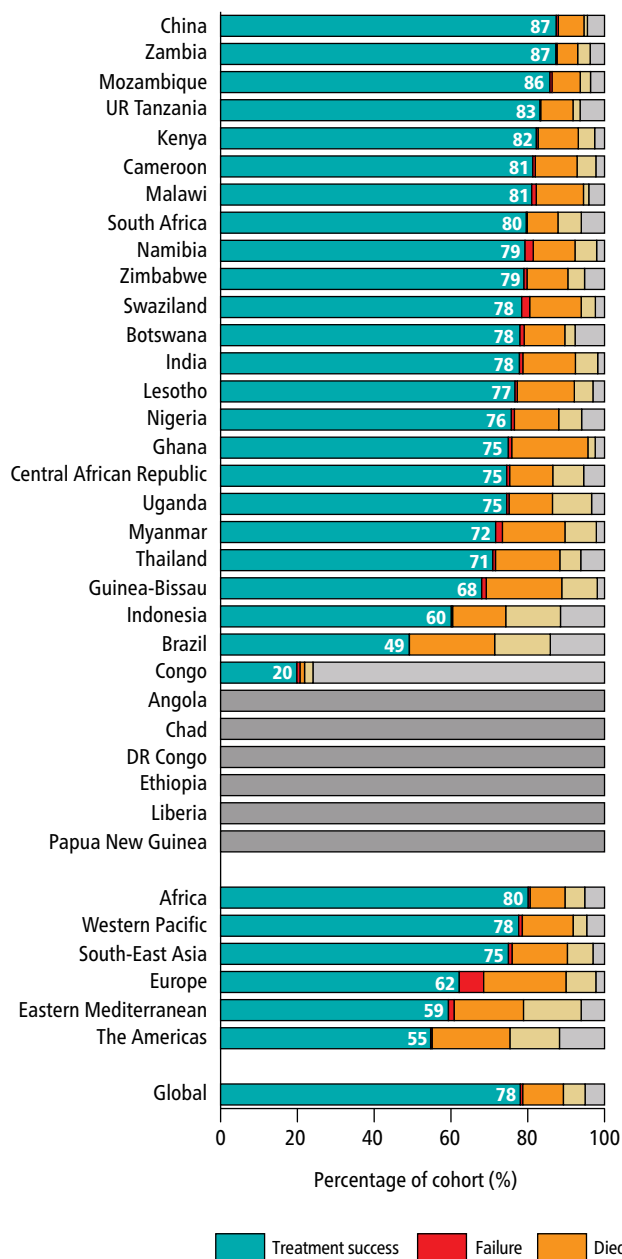
A total of 138 countries and territories reported treatment outcomes for people started on MDR-TB treatment in 2014. The number of cases reported in annual cohorts has steadily increased over time, reaching 99 165 cases globally in the 2014 cohort. Overall, the proportion of MDR/RR-TB patients in the 2014 cohort who successfully completed treatment (i.e. cured or treatment completed) was 54%: in 8% the treatment failed, 16% died, 15% were lost to follow-up and 7% had no outcome information (Fig. 4.26).

Globally, treatment success has increased slightly in recent years, as has the completeness of outcome reporting (Fig. 4.23). In the 2014 cohort, the treatment success rate was highest in the WHO Eastern Mediterranean Region (65%) and lowest in the WHO Region of the Americas (46%). In contrast, treatment failure was highest in the WHO European Region (13%), and the death rate was highest in the WHO African and South-East Asia regions (20%). Loss to follow-up was highest in the WHO Region of the Americas (21%), which also had the highest percentage of cases without outcome data (20%).

Among the 30 high MDR-TB burden countries, 14 had MDR/RR-TB cohorts in 2014 with more than 1000 cases; among these, only Kazakhstan, Myanmar and Viet Nam reported

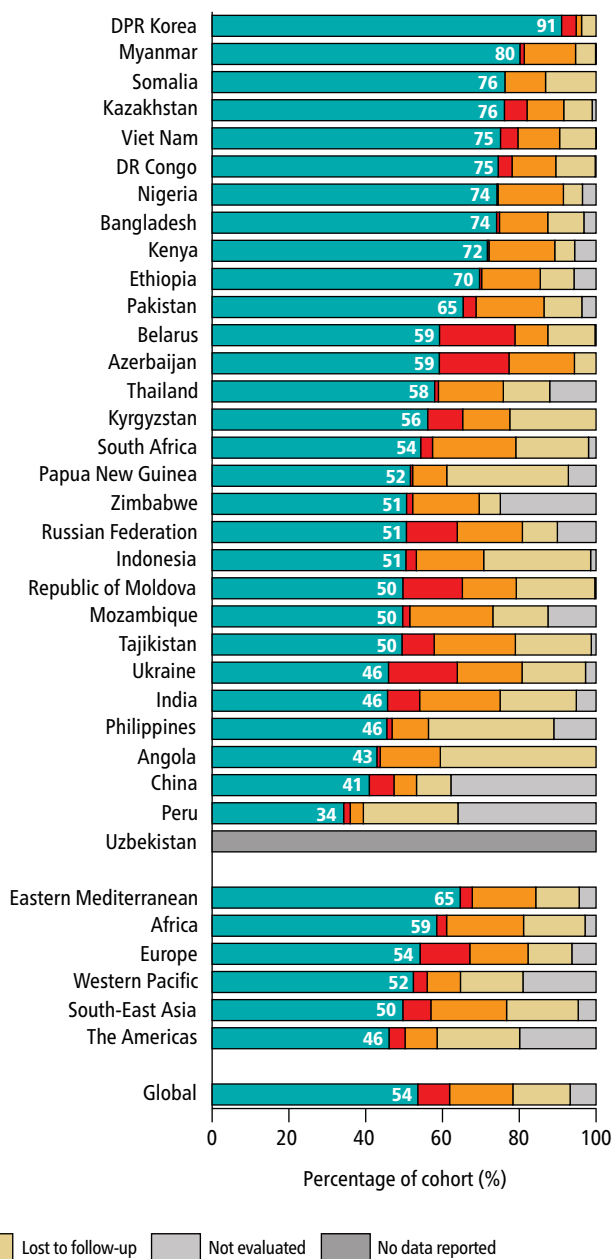
**FIG. 4.25**

**Treatment outcomes for new and relapse HIV-positive TB cases in 2015, 30 high TB/HIV burden countries, WHO regions and globally**



**FIG. 4.26**

**Treatment outcomes for rifampicin-resistant TB cases started on treatment in 2014, 30 high MDR-TB burden countries, WHO regions and globally**



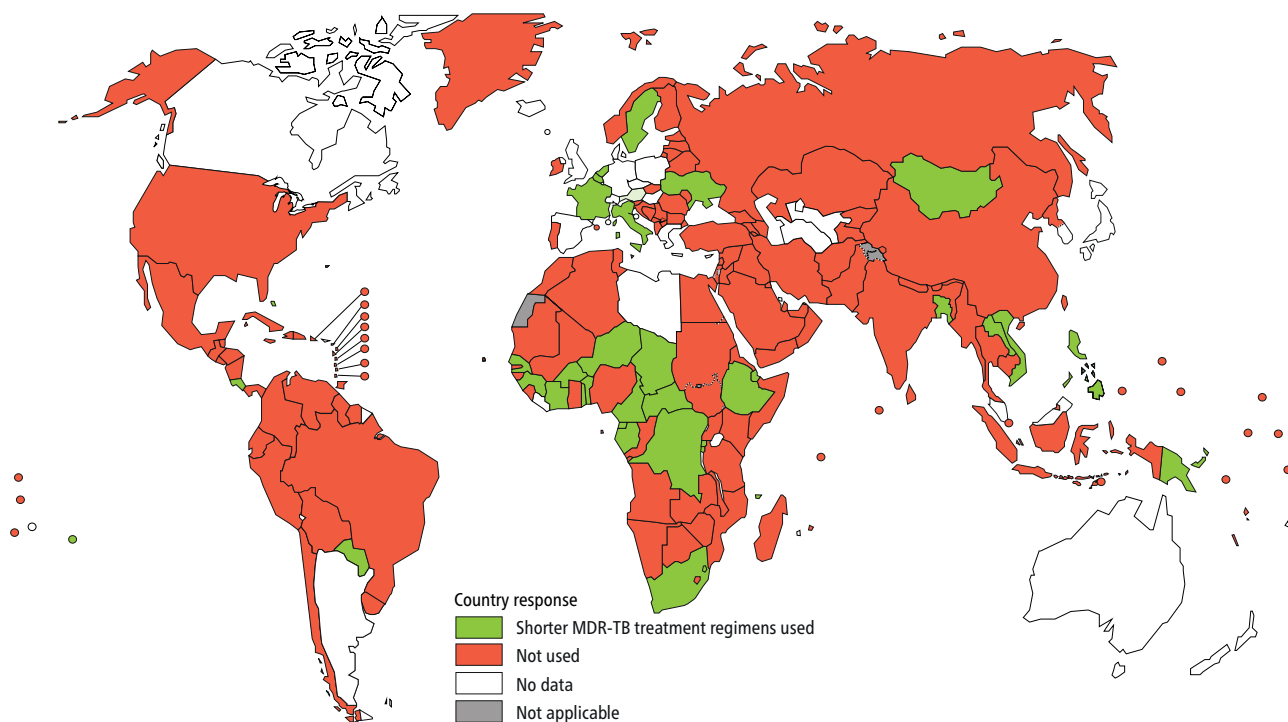
treatment success of more than 75%. Treatment success was less than 50% in China, India, Peru, the Philippines and Ukraine, due to high death rates in India (21%) and Ukraine (17%), high rates of treatment failure in Ukraine (18%) and loss to follow-up or missing data in all five countries (19–60%) (no treatment outcome data were reported by Uzbekistan for the 2014 cohort).

Among 6904 patients started on treatment for XDR-TB in 2014, in 52 countries and territories for which outcomes were reported, 30% completed treatment successfully, 28% died, treatment failed for 21%, and 20% were lost to follow-up or their treatment outcome was not evaluated. India, the

Russian Federation and Ukraine accounted for 68% of the 2014 XDR-TB cohort. Among seven countries with XDR-TB cohorts of more than 100 individuals, mortality was highest (42%) in India and South Africa.

Although improving globally and in some countries, treatment success rates for drug-resistant TB remain unacceptably low. The wider use of shorter MDR-TB treatment regimens of 9–12 months and of new TB drugs for patients with MDR/XDR-TB could help to improve this situation.<sup>1</sup>

<sup>1</sup> World Health Organization. WHO treatment guidelines for drug-resistant tuberculosis (2016 update) (WHO/HTM/TB/2016.04). Geneva: WHO; 2016 (<http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/>, accessed 15 August 2017).

**FIG. 4.27****Countries that had used shorter MDR-TB treatment regimens by the end of 2016**

By 2016, 35 countries, mostly in Africa and Asia, reported having used shorter MDR-TB regimens (Fig. 4.27). These regimens have been reported to achieve high treatment success rates (87–90%) in selected MDR/RR-TB patients and a standardized shorter MDR-TB regimen is recommended by WHO subject to eligibility criteria. By June 2017, 89 countries were known to have imported or started using bedaquiline and 54 countries had used delamanid (Fig. 4.28 and Fig. 4.29). Most (75%) of the patients treated with bedaquiline were reported by two countries: the Russian Federation and South Africa.

With the introduction of new drugs and regimens, there is a need for active TB drug-safety monitoring and management (aDSM), defined as the active and systematic clinical and laboratory assessment of patients on treatment with new TB drugs, novel MDR-TB regimens or XDR-TB regimens to detect, manage and report suspected or confirmed drug toxicities.<sup>1</sup> In 2016, 13 of the 30 high MDR-TB burden countries reported data on adverse events collected from their TB information systems.

#### 4.4 Subnational TB data: availability and use

Notification and treatment outcome data for subnational areas are not routinely requested by WHO in annual rounds of global TB data collection. However, these data are usually available at country level and are a key source of information, including for TB epidemiological reviews and assessment of the performance of TB surveillance.<sup>2</sup> The analysis and use of routinely collected data at both national and subnational levels are essential to understand the TB epidemic, inform national and local response efforts, and track progress.

In countries that still rely on paper-based recording and reporting systems, or have done so until very recently, a major challenge in using and analysing subnational TB data is that the data are not available in electronic format or, if they are in an electronic format, the format is not conducive to analysis (e.g. multiple Microsoft® Excel spreadsheets). In 2016, WHO started an initiative to address this problem, linked to preparations for three regional workshops on the analysis and use of TB data: two in Africa and one in Asia.<sup>3,4,5</sup>

<sup>2</sup> These are discussed in more detail in [Chapter 3](#).

<sup>3</sup> The first workshop included countries in the West African Regional Network for TB (WARN-TB) that has been established by TDR: Benin, Burkina Faso, Cape Verde, Côte d'Ivoire, Gambia, Ghana, Guinea (Conakry), Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo.

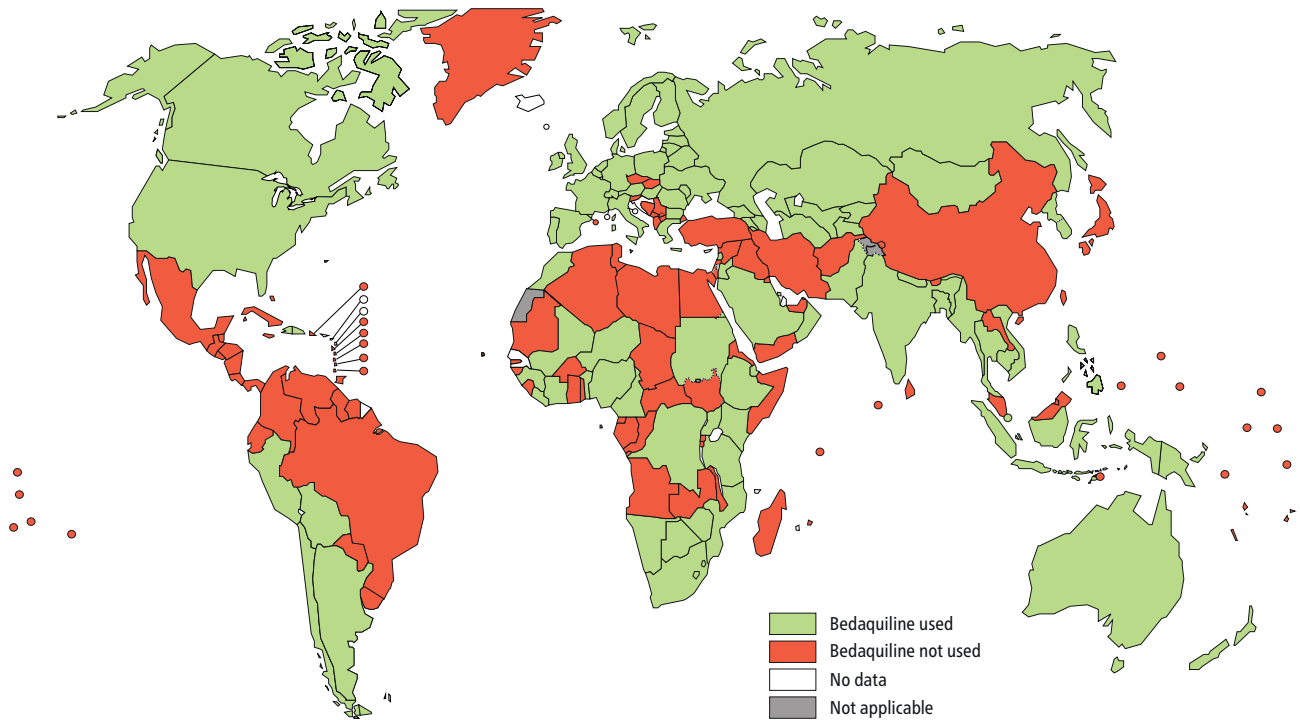
<sup>4</sup> The second workshop included Cameroon, Central African Republic, Chad, the Democratic Republic of the Congo, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Sudan, Swaziland, Uganda, the United Republic of Tanzania, Zambia and Zimbabwe.

<sup>5</sup> The third workshop included Bangladesh, Cambodia, India, Indonesia, Myanmar, Nepal, Pakistan, the Philippines, Thailand and Viet Nam.

<sup>1</sup> World Health Organization. Active tuberculosis drug-safety monitoring and management (aDSM): framework for implementation (WHO/HTM/TB/2015.28). Geneva: WHO; 2015 ([http://apps.who.int/iris/bitstream/10665/204465/1/WHO\\_HTM\\_TB\\_2015.28\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/204465/1/WHO_HTM_TB_2015.28_eng.pdf), accessed 15 August 2017).

**FIG. 4.28**

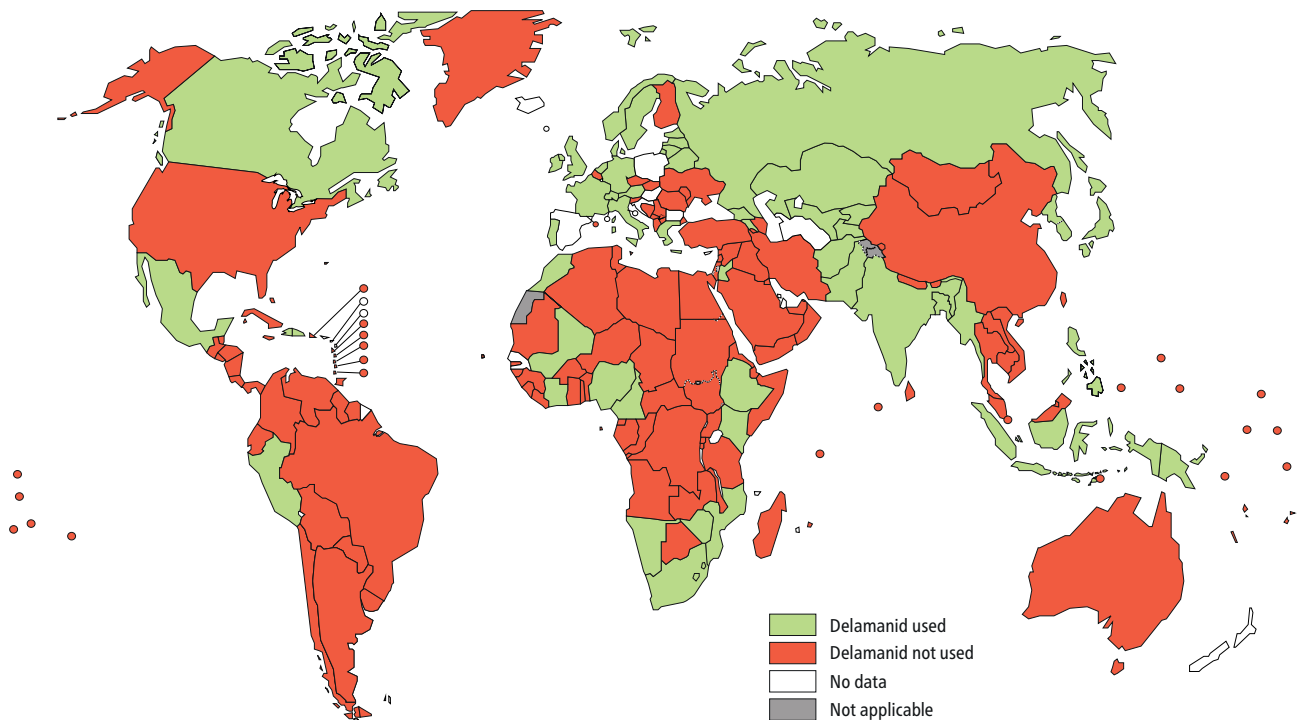
**Countries that had used bedaquiline for the treatment of M/XDR-TB as part of expanded access, compassionate use or under normal programmatic conditions by the end of June 2017<sup>a</sup>**



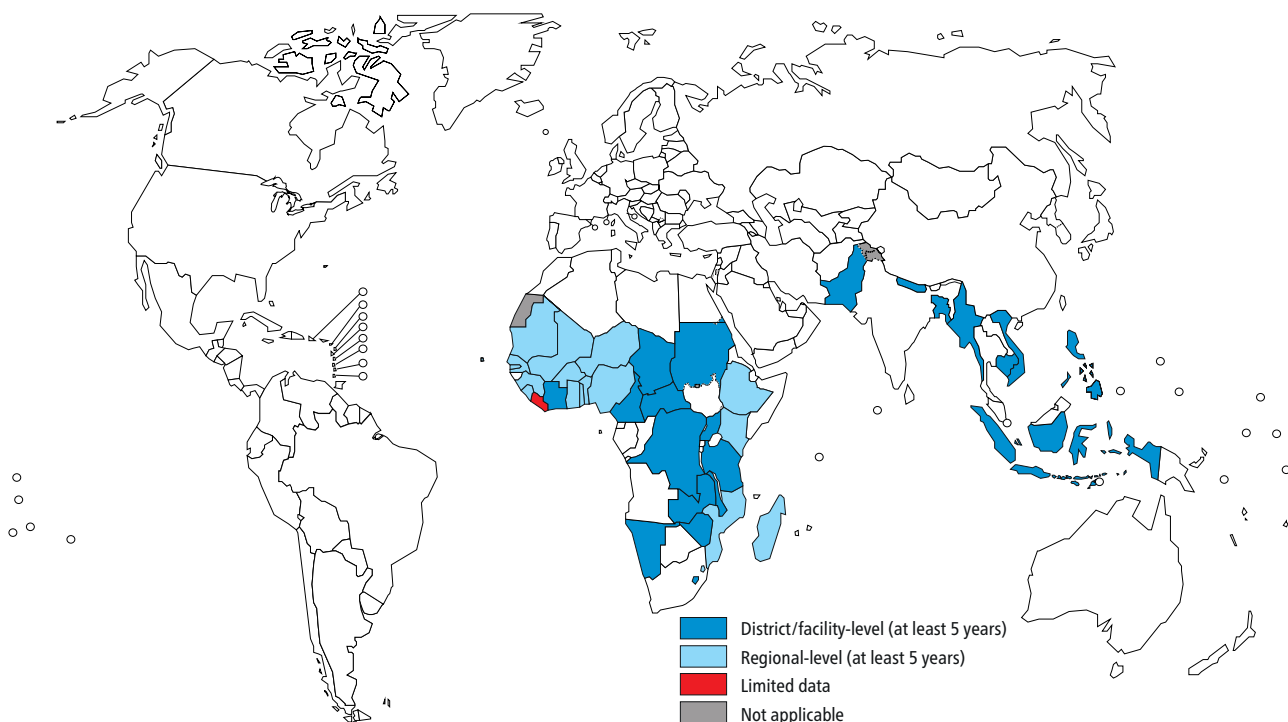
<sup>a</sup> Data shown reflects country reporting supplemented with additional information from pharmaceutical manufacturers.

**FIG. 4.29**

**Countries that had used delamanid for the treatment of M/XDR-TB as part of expanded access, compassionate use or under normal programmatic conditions by the end of June 2017<sup>a</sup>**



<sup>a</sup> Data shown reflects country reporting supplemented with additional information from pharmaceutical manufacturers.

**FIG. 4.30****Subnational data stored in the DHIS2 platform developed by WHO, August 2017<sup>a</sup>**

<sup>a</sup> Information shown only for countries where national TB programme staff participated in DHIS2 workshops in 2016–2017.

The first workshop, for countries in west Africa, was organized in collaboration with the Special Programme for Research and Training in Tropical Diseases (TDR), hosted by WHO and the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund); the second was for countries in east, central and southern Africa with the Global Fund; and the third was for countries in Asia with the Global Fund and the Stop TB Partnership.

Before the workshops, a platform using open-source DHIS2 software<sup>1</sup> was developed to allow the electronic compilation and storage of historical TB surveillance data from quarterly reporting forms (both the 2006 and 2013 versions) in a dedicated module. Subnational population estimates, disaggregated by age and sex wherever possible, were also entered, and geographical information system shape-files were included to allow the generation of maps for each indicator. Standard dashboards for visualizing the results from the analyses recommended in the WHO handbook for understanding and using TB data were also developed.<sup>2</sup>

During the workshops, participants focused on examining data quality and epidemiological indicators displayed as standard graphs and tables, using the data visualization dashboard to help in the discussion and interpretation of

trends, in the context of recent interventions and TB determinants. The workshops also provided an opportunity for discussions between staff responsible for national health information systems and staff from NTPs about the possibility of integrating the TB module into existing DHIS2 systems, for prospective (as opposed to historic) collection of aggregate-level data. Participants used the results to develop monitoring and evaluation investment plans, to identify key activities for strengthening TB surveillance.

The status of the availability of subnational data for the countries that participated in the workshops is shown in Fig. 4.30. Of the 40 countries, 21 now have their district- or facility-level data available in the DHIS2 platform for at least the past 5 years, 18 have regional-level data for at least the past 5 years, and one had uploaded limited data to the platform. A country example of the subnational analyses conducted in the workshops is provided in Box 4.6. Efforts are now underway to obtain the clearances necessary from other countries to feature subnational data in future editions of the global TB report. Other future work includes the development of a module in DHIS2 for entry of patient-level data.

<sup>1</sup> See <https://www.dhis2.org/>

<sup>2</sup> World Health Organization. Understanding and using tuberculosis data. Geneva: WHO Global Task Force on TB Impact Measurement; 2014 ([http://www.who.int/tb/publications/understanding\\_and\\_using\\_tb\\_data/en/](http://www.who.int/tb/publications/understanding_and_using_tb_data/en/), accessed 24 August 2017).

**BOX 4.6**

**Using subnational-level TB surveillance data to guide local action in Cambodia**

Cambodia was one of the 10 Asian countries that participated in a regional workshop on the analysis and use of TB data in April 2017. This workshop included analysis of subnational data for case notification rates, the proportion of new and relapse cases by site of disease and age group, and the coverage of HIV testing. Provincial data for these indicators are shown in [Fig. B4.6.1](#).

In 2016, the national TB case notification rate in Cambodia was 222 per 100 000 population; 34% of all new and relapse TB cases were extrapulmonary; 16% of notified cases were children aged under 15 years; and 86% of all TB cases knew their HIV status. However, these national figures concealed wide geographical variation. The highest TB case notification rates (>300 per 100 000 population) were in the northwest and southeast of the country, and the lowest (75 per 100 000 population) were in the northeast along the border with Lao People’s Democratic Republic and Viet Nam. Extrapulmonary TB accounted for more than 45% of new and relapse TB cases in five provinces, and less than 15% in Preah Vihear province, whereas childhood TB appeared to be either

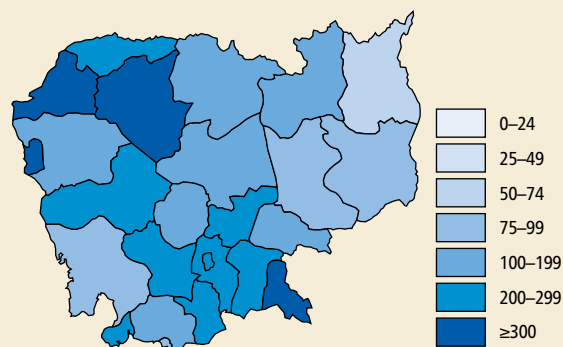
underdiagnosed or underreported (<5% of new and relapse cases) in six provinces, and possibly overdiagnosed in 12 provinces (>15% of new and relapse cases). In four of the 25 provinces, less than 80% of TB patients knew their HIV status, with the lowest coverage being in Mondulkiri province (51%).

This subnational variation may indicate differences in the performance for recording and reporting, possible issues with access to health care, some provinces having large referral centres for diagnosis or treatment, “hot spots” for ongoing transmission, and migration or variation in diagnostic practices for extrapulmonary or childhood TB. Analysis of the data at this level allowed the NTP to generate hypotheses for further investigation, either through operational research or routine monitoring and evaluation mechanisms, and to immediately identify key provinces where local action to improve HIV testing coverage or investigate the possible over or underdiagnosis of childhood TB is required. Future monitoring of indicators at provincial level will allow the impact of corrective actions to be assessed.

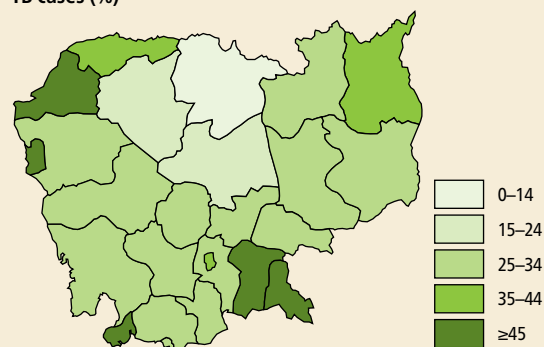
**FIG. B4.6.1**

**Subnational heterogeneity in TB indicators in Cambodia: a difficult interpretation**

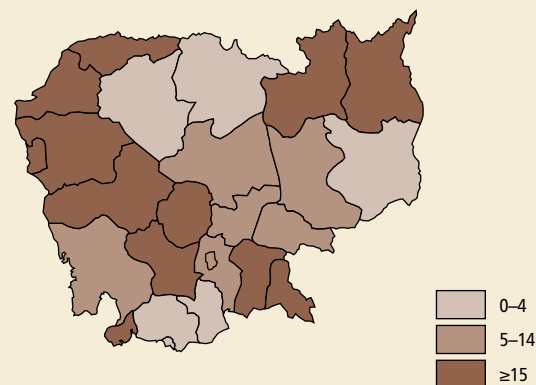
**TB case notification rate per 100 000 population**



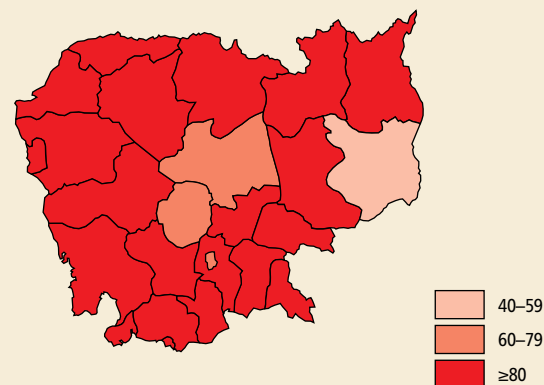
**Proportion of extrapulmonary TB among new and relapse TB cases (%)**



**All new and relapse cases under 15 years old (%)**



**TB patients with known HIV status (%)**



Source: Data provided by the NTP Cambodia for a TB data analysis workshop in Bangkok, Thailand (April 2017).





LOCATION	POPULATION	TB CASES
MIRZAPUR	27874	12
ANANDA	40871	22
ANKUTARA	27657	12
BAKURGA	36623	18
BANAIL	27000	08
BASTAIL	27000	08
BHATGRAM	24771	14
FATERPUR	28874	09
GORAI	38724	16
JAMUKI	31811	05
MAHERA	24372	05
MAHESI	37015	20
TARAF PUR	23854	20
OTHER	---	---

**A patient attending a health facility is given information about TB in Dhaka, Bangladesh**

GARY HAMPTON / WHO



## CHAPTER 5.

# TB prevention services

### KEY FACTS AND MESSAGES

Prevention of new infections of *Mycobacterium tuberculosis* and their progression to tuberculosis (TB) disease is critical to reduce the burden of disease and death caused by TB, and to achieve the End TB Strategy<sup>a</sup> targets set for 2030 and 2035.

Current health interventions for TB prevention are treatment of latent TB infection (LTBI), with particular attention to children aged under 5 years who are household contacts of bacteriologically confirmed pulmonary TB cases, and to people living with HIV; prevention of transmission of *M. tuberculosis* through infection control; and vaccination of children with the bacille Calmette-Guérin (BCG) vaccine.

Globally, in 2016, there were an estimated 1.3 million children aged under 5 years who were household contacts of bacteriologically confirmed pulmonary TB cases and who were eligible for TB preventive treatment according to current policy recommendations. The number of children in this age group reported to have been started on TB preventive treatment increased by 85% between 2015 and 2016 (from 87 242 to 161 740), but was still only 13% of those estimated to be eligible.

Based on data from 60 countries, a total of 940 269 people who were newly enrolled in HIV care were started on TB preventive treatment in 2016. As in previous years, South Africa accounted for the largest share of the total (41%), followed by Mozambique, Zimbabwe and Malawi. In Kenya, data on the number of people newly enrolled in HIV care who were started on TB preventive treatment in 2016 were not available. However, TB preventive treatment was provided to a total of 390 298 people living with HIV in 2016. Combined with data reported by other countries, this means that the global total of people living with HIV who were started on TB preventive treatment in 2016 was at least 1.3 million.

Of the 30 high TB/HIV burden countries, 18 did not report any provision of preventive treatment in 2016. In the 12 high TB/HIV burden countries that did report data, coverage among people newly enrolled in HIV care ranged from 2.4% in Indonesia to 73% in Zimbabwe.

In countries with a low burden of TB, there is a need to improve initiation, completion and reporting of TB preventive treatment for other at-risk populations, including clinical risk groups such as patients with silicosis, patients starting anti-tumour necrosis factor (TNF) therapy and patients preparing for organ transplantation.

The ratio of the TB notification rate among health-care workers to the TB notification rate in the general adult population is a good indicator of the impact of TB infection control in health facilities. In 2016, a total of 8144 health-care workers were reported with TB from 60 countries; China accounted for 39% of these cases. In seven countries (Burkina Faso, Colombia, Dominican Republic, Georgia, Lithuania, Mexico and Venezuela), the number of TB cases per 100 000 health-care workers was more than double the notification rate in the general adult population.

BCG vaccination should be provided as part of national childhood immunization programmes according to a country's TB epidemiology. In 2016, 154 countries reported providing BCG vaccination as a standard part of these programmes, of which 111 reported coverage above 90%.

Monitoring and evaluation of TB prevention services is challenging given the lack of standard systems for recording and reporting data, and the involvement of multiple service providers. WHO has developed a mobile phone application (app) to facilitate monitoring and evaluation of the programmatic management of LTBI.

Development and expanded use of shorter regimens for TB preventive treatment, which require a smaller number of doses and are associated with fewer adverse events, will facilitate large-scale implementation. Additionally, innovative diagnostic tests with improved performance and predictive value are needed to target individuals who will benefit most from TB preventive treatment.

<sup>a</sup> 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/](http://www.who.int/tb/post2015_strategy/en/), accessed 8 August 2016).

Prevention of new infections of *Mycobacterium tuberculosis* and their progression to tuberculosis (TB) disease is critical to reduce the burden of disease and death caused by TB, and to achieve the End TB Strategy targets set for 2030 and 2035.<sup>1</sup> The targets of an 80% reduction in TB incidence from the 2015 level by 2030, and a 90% reduction by 2035, will require a historically unprecedented acceleration in the rate at which TB incidence falls after 2025 (Chapter 2). This accelerated rate is possible only if the probability of progression from latent TB infection (LTBI) to active TB disease among the 1.7 billion people already infected worldwide<sup>2</sup> is drastically reduced below the current lifetime risk of 5–15%.<sup>3</sup> In some low-burden countries, reactivation accounts for about 80% of new cases of disease.<sup>4,5</sup> Interventions that could result in a much greater reduction include more effective treatments for LTBI and development of a vaccine to prevent reactivation of LTBI in adults.

Currently, three major categories of health interventions are available for TB prevention:

- treatment of LTBI through any of the following: isoniazid daily for 6 or 9 months, isoniazid plus rifampicin daily for 3–4 months, rifampicin daily for 3–4 months, or isoniazid plus rifapentine weekly for 3 months;
- prevention of transmission of *M. tuberculosis* through infection control; and
- vaccination of children with the bacille Calmette-Guérin (BCG) vaccine.

The three main sections of this chapter present and discuss progress in provision of these services. Particular attention is given to the 30 high TB burden countries and the 30 high TB/HIV burden countries (Chapter 2).

## 5.1 Treatment of latent TB infection

LTBI is defined as a state of persistent immune response to *M. tuberculosis* without clinically manifested evidence of active TB disease. WHO recommends specific efforts to diagnose and treat LTBI in two particular at-risk groups: children aged under 5 years who are household contacts of bacteriologically-confirmed pulmonary TB cases, and people living with HIV.<sup>6</sup>

<sup>1</sup> 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/](http://www.who.int/tb/post2015_strategy/en/), accessed 8 August 2016).

<sup>2</sup> Houben RM, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. *PLoS Med*. 2016;13(10):e1002152 (<https://www.ncbi.nlm.nih.gov/pubmed/27780211>, accessed 2 August 2017).

<sup>3</sup> Vynnycky E, Fine PE. Lifetime risks, incubation period, and serial interval of tuberculosis. *Am J Epidemiol*. 2000;152(3):247–263.

<sup>4</sup> Heldal E, Docker H, Caugant DA, Tverdal A. Pulmonary tuberculosis in Norwegian patients. The role of reactivation, re-infection and primary infection assessed by previous mass screening data and restriction fragment length polymorphism analysis. *Int J Tuberc Lung Dis*. 2000;4(4):300–307.

<sup>5</sup> Shea KM, Kammerer JS, Winston CA, Navin TR, Horsburgh CR. Estimated rate of reactivation of latent tuberculosis infection in the United States, overall and by population subgroup. *Am J Epidemiol*. 2014;179(2):216–225.

<sup>6</sup> World Health Organization. Guidelines on the management of latent tuberculosis infection. Geneva: WHO; 2015 ([http://www.who.int/tb/publications/lbti\\_document\\_page/en/](http://www.who.int/tb/publications/lbti_document_page/en/), accessed 30 August 2016).

Coverage of contact investigation and treatment of LTBI among child contacts and people living with HIV are among the 10 indicators listed as highest priority for monitoring implementation of the End TB Strategy, with a target of over 90% coverage by 2025 at the latest (Chapter 2, Table 2.2).

Data on provision of TB preventive treatment for people living with HIV have been collected by WHO for more than 10 years. However, until 2016 there was no standardized global guidance on how to monitor the coverage of preventive treatment among child contacts or other high-risk groups. Such guidance was developed by a WHO global LTBI task force in 2016,<sup>7</sup> and the recommended indicators are shown in Table 5.1. The rest of this section presents and discusses data about TB preventive treatment for these three risk groups. The data were gathered from countries and territories in WHO's 2017 round of global TB data collection.

### 5.1.1 Child contacts aged under 5 years who are household contacts of TB cases

There were 191 countries that reported at least one notified bacteriologically confirmed pulmonary TB case in 2016. Of these countries, 118 (63%) reported data about the number of household contacts aged under 5 years who were started on TB preventive treatment (Fig. 5.1), including 16 of the 30 high TB burden countries (compared with nine countries that reported data for 2015). Among the 118 countries, 110 reported at least one child started on preventive treatment (compared with 89 countries in 2015).

A total of 161 740 child household contacts were reported to have been initiated on TB preventive treatment (Table 5.2) in 2016, an 85% increase from 87 242 in 2015. The largest numbers were reported by the WHO African Region (46% of the global total) and the South-East Asia Region (19% of the global total). At country level, Mozambique reported the largest number (19 634), followed by Afghanistan (15 417).

Comparisons of the number of children started on TB preventive treatment in 2016 with national estimates of the number of children aged under 5 years who were contacts of bacteriologically confirmed pulmonary TB cases – and thus eligible for such treatment – are shown in Table 5.2.<sup>8</sup> Globally, the 161 740 children started on TB preventive treatment in 2016 represented 13% of the 1.3 million children estimated to be eligible for treatment. Higher levels of coverage were achieved in the WHO Region of the Americas (best estimate 68%; range, 64–72%), followed by the European Region (best estimate 55%; range, 52–58%).

### 5.1.2 People living with HIV

Provision of TB preventive treatment to those newly enrolled in HIV care has grown substantially since 2009, albeit from low levels, and reached 940 269 people in 2016 (Fig. 5.2). Most of the increase occurred from 2009 to 2014, and has

<sup>7</sup> [http://www.who.int/tb/challenges/task\\_force/en/](http://www.who.int/tb/challenges/task_force/en/)

<sup>8</sup> The online technical appendix is available at [http://www.who.int/tb/publications/global\\_report/en/](http://www.who.int/tb/publications/global_report/en/)

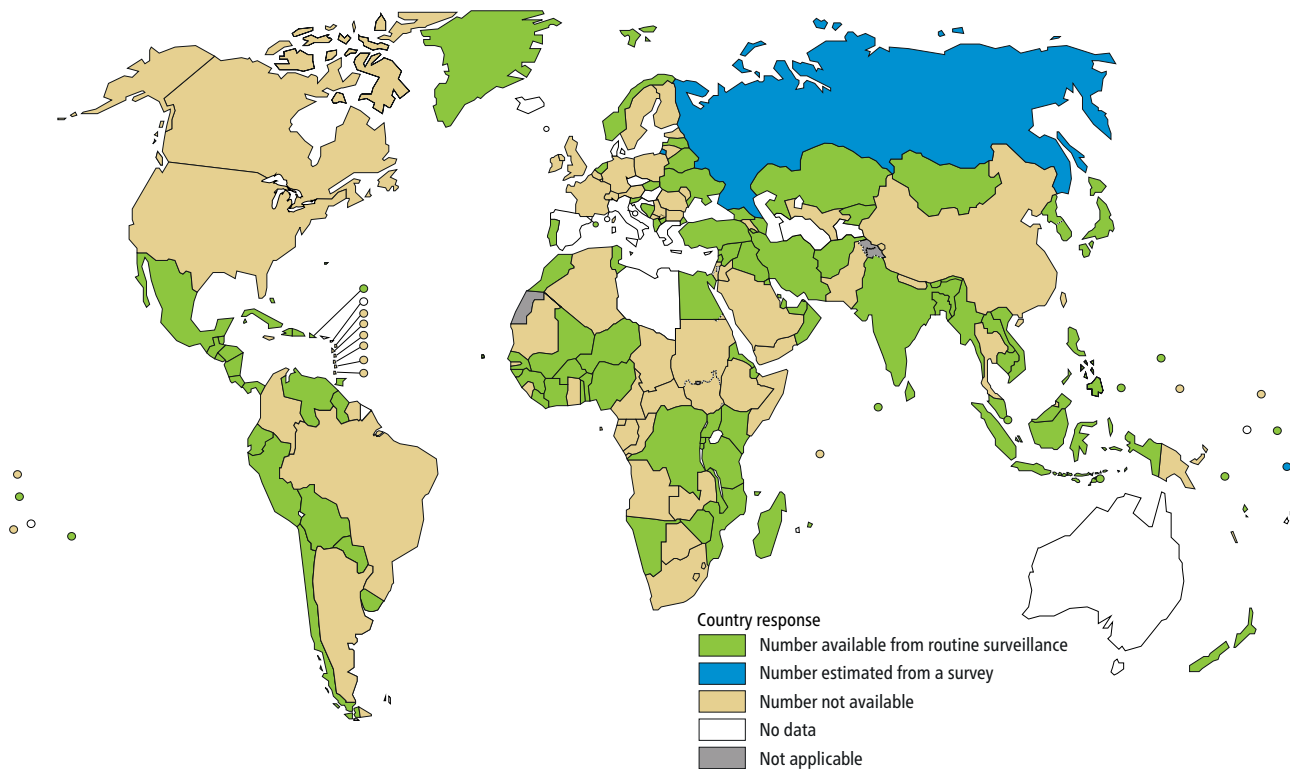
**TABLE 5.1**

**Summary of monitoring and evaluation indicators recommended by WHO for the programmatic management of LTBI**

CORE GLOBAL AND NATIONAL INDICATORS	CORE NATIONAL INDICATORS	OPTIONAL INDICATORS
<p>1) Proportion of children less than 5 years old who are household TB contacts (according to national guidelines) who have completed TB investigations.</p> <p>2) Proportion of children under 5 years old who are household TB contacts (according to national guidelines) who are eligible for starting on TB preventive therapy that have started treatment.</p> <p>3) Proportion of eligible people living with HIV newly enrolled in HIV care, started on TB preventive therapy.</p>	<p>4) Proportion of eligible individuals from at risk populations (according to national guidelines) tested for latent TB infection.</p> <p>5) Proportion of individuals from at risk populations (according to national guidelines) with a positive latent TB test who are eligible for starting TB preventive therapy that have started treatment.</p> <p>6) Proportion of individuals from at risk populations (according to national guidelines) with a positive latent TB test who have started on TB preventive therapy that have completed the course.</p> <p>7) Proportion of eligible people living with HIV who completed a course of TB preventive therapy.</p> <p>8) Proportion of children less than 5 years old who are household TB contacts (according to national guidelines) who have completed a course of TB preventive therapy.</p>	<p>9) TB incidence rate among risk populations (as defined by national guidelines).</p>

**FIG. 5.1**

**Availability of data on the number of children aged <5 years who were household contacts of bacteriologically confirmed pulmonary TB cases and were started on TB preventive treatment, 2016**



**TABLE 5.2**

**TB preventive treatment in 2016 for people living with HIV and children under 5 years of age who were household contacts of a bacteriologically confirmed pulmonary TB case, 23 high TB or TB/HIV burden countries that reported data,<sup>a</sup> WHO regions and globally**

	NUMBER OF PEOPLE LIVING WITH HIV NEWLY ENROLLED IN CARE IN 2016 (A)	PEOPLE NEWLY ENROLLED IN HIV CARE WHO WERE STARTED ON TB PREVENTIVE TREATMENT IN 2016		ESTIMATED NUMBER OF CHILD HOUSEHOLD CONTACTS UNDER 5 YEARS OF AGE ELIGIBLE FOR TB PREVENTIVE TREATMENT, IN 2016 (C) <sup>b</sup>	CHILDREN UNDER 5 YEARS OF AGE WHO WERE STARTED ON TB PREVENTIVE TREATMENT IN 2016	
		NUMBER (B)	COVERAGE, % (B*100÷A)		NUMBER (D)	COVERAGE, % (D*100÷C)
Bangladesh			–	49 000 (45 000–53 000)	8 537	17 (16–19)
Cambodia	3 193	631	20	5 200 (4 800–5 700)	1 877	36 (33–39)
DPR Korea			–	11 000 (9 900–12 000)	11 707 <sup>c</sup>	–
DR Congo			–	75 000 (68 000–82 000)	4 725	6.3 (5.8–6.9)
Ethiopia	36 761	19 244	52	28 000 (26 000–31 000)		–
Guinea-Bissau			–	2 100 (1 900–2 300)	94	4.5 (4.1–4.9)
India	174 125	8 135	4.7	360 000 (330 000–390 000)	6 637	1.9 (1.7–2)
Indonesia	36 294	877	2.4	65 000 (60 000–71 000)	948	1.5 (1.3–1.6)
Liberia	4 528	390	8.6	2 100 (1 900–2 300)	92	4.4 (4.0–4.8)
Malawi	145 117	72 446	50	4 700 (4 200–5 100)	2 351	50 (46–55)
Mozambique	315 712	162 646	52	20 000 (18 000–21 000)	19 634	100 (91–100)
Myanmar	34 765	1 018	2.9	17 000 (15 000–18 000)	317	1.9 (1.8–2.1)
Namibia			–	3 100 (2 900–3 400)	810	26 (24–28)
Nigeria	216 293	62 781	29	47 000 (43 000–51 000)	8 562	18 (17–20)
Philippines	5 966	2 938	49	55 000 (51 000–60 000)	2 777	5 (4.6–5.5)
Russian Federation	21 153	19 611	93	1 700 (1 100–2 300)	9 850 <sup>d</sup>	–
Sierra Leone	17 843	3 609	20	9 100 (8 300–9 900)		–
South Africa	751 620	385 932	51	46 000 (42 000–50 000)		–
Swaziland	138 016	21 320	15	1 300 (1 200–1 400)		–
Uganda			–	21 000 (19 000–23 000)	1 094	5.2 (4.8–5.7)
UR Tanzania	49 351	4 202	8.5	20 000 (19 000–22 000)	6 309	31 (28–34)
Viet Nam	13 593	3 474	26	16 000 (14 000–17 000)	3 038	19 (18–21)
Zimbabwe	168 968	123 846	73	8 200 (7 500–8 900)	5 177	63 (58–69)
<b>Africa</b>	<b>1 862 671</b>	<b>859 727</b>	<b>46</b>	<b>460 000 (450 000–470 000)</b>	<b>74 348</b>	<b>16 (16–17)</b>
<b>The Americas</b>	<b>65 485</b>	<b>20 067</b>	<b>31</b>	<b>24 000 (22 000–25 000)</b>	<b>16 219</b>	<b>68 (64–72)</b>
<b>Eastern Mediterranean</b>	<b>6 419</b>	<b>1 015</b>	<b>16</b>	<b>150 000 (140 000–160 000)</b>	<b>24 127</b>	<b>16 (15–17)</b>
<b>Europe</b>	<b>51 501</b>	<b>36 086</b>	<b>70</b>	<b>14 000 (13 000–14 000)</b>	<b>7 404</b>	<b>55 (52–58)</b>
<b>South-East Asia</b>	<b>245 425</b>	<b>10 055</b>	<b>4.1</b>	<b>510 000 (480 000–550 000)</b>	<b>30 071</b>	<b>5.8 (5.5–6.2)</b>
<b>Western Pacific</b>	<b>32 181</b>	<b>13 319</b>	<b>41</b>	<b>95 000 (89 000–100 000)</b>	<b>9 571</b>	<b>10 (9.5–11)</b>
<b>GLOBAL</b>	<b>2 263 682</b>	<b>940 269</b>	<b>42</b>	<b>1 260 000 (1 220 000–1 300 000)</b>	<b>161 740</b>	<b>13 (12–13)</b>

Blank cells indicate data not reported.

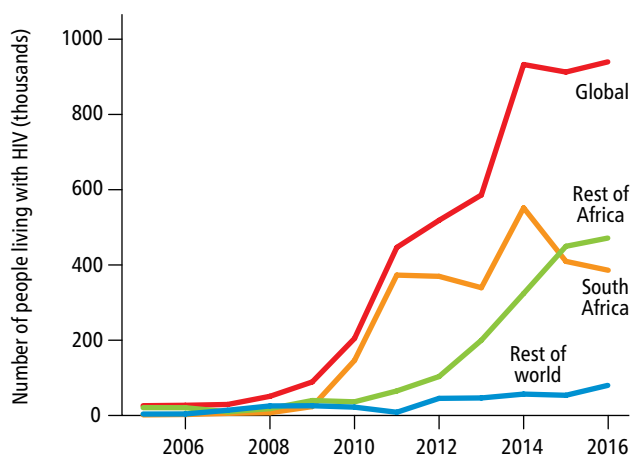
<sup>a</sup> There were 15 other countries in the list of high TB or TB/HIV burden countries that did not report data for either risk group. These were Angola, Botswana, Brazil, Central African Republic, Chad, China, Congo, Ghana, Guinea-Bissau, Kenya, Lesotho, Pakistan, Papua New Guinea, Thailand, and Zambia.

<sup>b</sup> This is the estimated number of children under 5 years of age who were household contacts of a notified bacteriologically confirmed pulmonary TB case, and eligible for TB preventive treatment, 2016. Estimates are shown to two significant figures for numbers below 1 million, and to three significant figures for numbers above 1 million.

<sup>c</sup> This number includes contacts aged 5–7 years. Therefore, the estimated coverage was not calculated.

<sup>d</sup> This number includes contacts other than household contacts. Therefore, estimated coverage was not calculated. The number was also not included in the regional and global figures.

**FIG. 5.2**  
**Provision of TB preventive treatment to people living with HIV, 2005–2016**



subsequently levelled off. In 2016, a total of 60 countries (representing 70% of the estimated global burden of HIV-associated TB) reported providing preventive TB treatment to people newly enrolled in HIV care, compared with 57 countries in 2015.

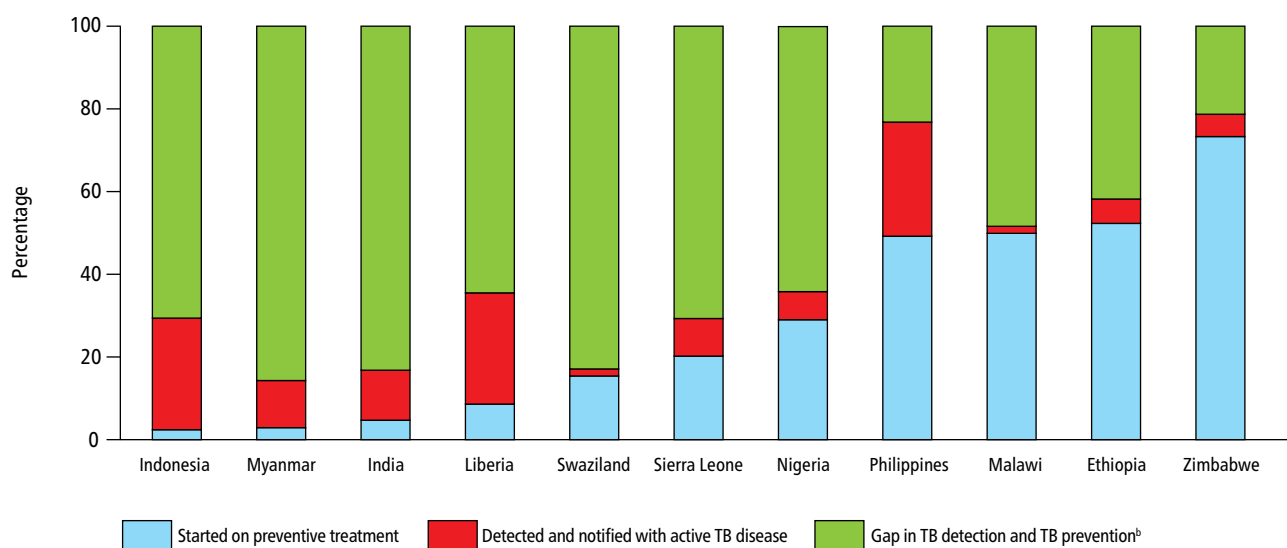
As in previous years, South Africa accounted for the largest proportion (41%) of the global total in 2016 (Fig. 5.2), followed by Mozambique, Zimbabwe and Malawi (Table 5.2). Large absolute increases compared with 2015 numbers were

reported in Zimbabwe (+85 357), Mozambique (+32 226) and Nigeria (+21 926). Two of the 30 high TB/HIV burden countries, India and Liberia, reported data for the first time. In Kenya, data on the number of people newly enrolled in HIV care who were started on TB preventive treatment in 2016 were not available. However, TB preventive treatment was provided to a total of 390 298 people living with HIV in 2016. Combined with data reported by other countries, this means that the global total of people living with HIV who were started on TB preventive treatment in 2016 was at least 1.3 million.

Despite progress in some countries, much remains to be done. For example, of the 30 high TB/HIV burden countries, 18 did not report any provision of TB preventive treatment in 2016; and in the 12 countries that provided data, coverage among people newly enrolled in HIV care varied considerably, from 2.4% in Indonesia to 73% in Zimbabwe (Table 5.2). Fig. 5.3 shows gaps in the provision of TB preventive treatment to people living with HIV for selected high TB burden countries or high TB/HIV burden countries.

Accelerating progress in the global and national response to HIV-associated TB is one of the eight thematic tracks at the WHO Ministerial Conference on Ending TB in the SDG Era, to be held in November 2017. This theme will include a specific focus on ending TB deaths among people living with HIV, including through wider use of TB preventive treatment. It is hoped that the conference will galvanize greater political commitment, and in turn expedite the scale-up of key interventions for HIV-associated TB, including TB preventive treatment.

**FIG. 5.3**  
**Gaps in TB preventive treatment for people who were newly enrolled in HIV care in 2016, selected countries<sup>a</sup>**



<sup>a</sup> The selected countries are high TB or TB/HIV burden countries that reported on all three of the following: the number of people newly enrolled in HIV care; the number of TB cases detected among people newly enrolled on HIV care; and the number of people newly enrolled on HIV care who were started on TB preventive treatment. In high TB burden countries, testing for LTBI is not a requirement for initiation of TB preventive treatment, such that all those without active TB disease are eligible for TB preventive treatment.

<sup>b</sup> The gap represents people living with HIV who should have undergone complete evaluation for TB disease or TB preventive treatment.

**TABLE 5.3**

**Provision of TB preventive treatment to other at-risk populations in 2016, for selected low TB burden countries for which data could be reported**

	NUMBER OF INDIVIDUALS AMONG AT RISK POPULATIONS ELIGIBLE AND STARTED ON TB PREVENTIVE TREATMENT									
	AT-RISK POPULATIONS FOR WHICH THERE IS A STRONG RECOMMENDATION TO PROVIDE PREVENTIVE THERAPY					AT-RISK POPULATIONS FOR WHICH THERE IS A CONDITIONAL RECOMMENDATION TO PROVIDE PREVENTIVE THERAPY				
	CHILDREN AGED 5 YEARS OR OLDER AND ADULT CONTACTS OF TB CASES	PATIENTS INITIATING ANTI-TNF TREATMENT	PATIENTS RECEIVING DIALYSIS	PATIENTS PREPARING FOR ORGAN OR HAEMATOLOGICAL TRANSPLANTATION	PATIENTS WITH SILICOSIS	IMMIGRANTS FROM HIGH TB BURDEN COUNTRIES	HEALTH WORKERS	PRISONERS	HOMELESS PEOPLE	ILLCIT DRUG USERS
France	2750/5500 <sup>a</sup>						186/397 <sup>b</sup>	18/108 <sup>b</sup>	177/300 <sup>b</sup>	
Japan	4 802					455	1859		20	
Netherlands	686/867	60/66	17/19	4/4	0/0	88/107	31/42			
Portugal	1250		9		3	229	389	33	68 <sup>c</sup>	87
Republic of Korea	2133/3192						1508/3128	111/230		
Slovakia	350/550	158/352		28/64	1/2	2/2	15/120	15/15	6/36	0/2

Blank cells indicate data not reported.

<sup>a</sup> The denominator is an estimate based on extrapolation from data reported in 2015.

<sup>b</sup> Data are limited to individuals identified through contact tracing.

<sup>c</sup> This number includes 64 people in community housing.

**5.1.3 Other at-risk populations**

Data on provision of TB preventive treatment to other at-risk populations were reported by six countries: France, Japan, the Netherlands, Portugal, Republic of Korea and Slovakia (Table 5.3). These countries reported providing preventive treatment to children aged 5 years or more and to adult contacts. Coverage was more than 50% in the four countries that reported denominators (i.e. data on the number of people eligible). Data for clinical risk groups – such as patients starting anti-tumour necrosis factor (TNF) therapy and those preparing for organ transplantation – were reported by the Netherlands, Portugal and Slovakia.

**5.1.4 Facilitating collection and analysis of data on TB preventive treatment**

Routine collection of data about TB preventive treatment remains challenging, particularly data for clinical risk groups. Reasons include the fact that notification of LTBI is not mandatory in most countries; the existence of multiple paper-based registers; fragmentation of monitoring and evaluation systems among multiple service providers; and a large, unregulated private health sector in some countries. To facilitate faster and more complete data collection, WHO has developed a mobile phone application (app) to record and report case-based data on TB preventive treatment (Box 5.1).

**5.2 TB infection control**

TB infection control is one of the components of Pillar 2 of the End TB Strategy (Chapter 2); it is also one of the collaborative TB/HIV activities that falls under Pillar 1. The risk of TB transmission is high in health-care and other congregate settings. This puts health-care workers at greater risk of TB infection and disease, and nosocomial outbreaks of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB)

among people living with HIV have been documented in the literature.<sup>1,2</sup>

TB infection control should be part of national infection prevention and control policy. Thus, TB and HIV programmes at national and subnational level should provide managerial direction to implement TB infection control measures. In health-care facilities and congregate settings, a comprehensive set of infection control measures – comprising administrative, environmental and personal protection measures – should be implemented.<sup>3</sup> Periodic assessment of TB infection control in health-care facilities is essential to ensure that appropriate measures are in place.<sup>4</sup>

In the latest revision of WHO guidance on monitoring and evaluation of collaborative TB/HIV activities,<sup>5</sup> the risk of TB among health-care workers relative to the risk in the general adult population is one of the global indicators recommended to measure the impact of TB infection control activities in health-care facilities. If effective TB infection control measures are in place, the relative risk of TB in health-care workers compared with the general adult population should be close to 1.

<sup>1</sup> Gandhi NR, Weissman D, Moodley P, Ramathal M, Elson I, Kreiswirth BN et al. Nosocomial transmission of extensively drug-resistant tuberculosis in a rural hospital in South Africa. *J Infect Dis.* 2013;207(1):9–17.

<sup>2</sup> Moro ML, Gori A, Errante I, Infuso A, Franzetti F, Sodano L et al. An outbreak of multidrug-resistant tuberculosis involving HIV-infected patients of two hospitals in Milan, Italy. *AIDS.* 1998;12(9):1095–1102.

<sup>3</sup> World Health Organization. WHO policy on TB infection control in health-care facilities. Geneva: WHO; 2009 ([http://apps.who.int/iris/bitstream/10665/44148/1/9789241598323\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44148/1/9789241598323_eng.pdf), accessed 31 August 2016).

<sup>4</sup> World Health Organization. Checklist for periodic evaluation of TB infection control in health-care facilities. Geneva: WHO; 2015 ([http://www.who.int/tb/areas-of-work/preventive-care/checklist\\_for\\_periodic\\_evaluation\\_of\\_tb\\_infection\\_control\\_in\\_health\\_facilities.pdf](http://www.who.int/tb/areas-of-work/preventive-care/checklist_for_periodic_evaluation_of_tb_infection_control_in_health_facilities.pdf), accessed 13 July 2017).

<sup>5</sup> World Health Organization. A guide to monitoring and evaluation for collaborative TB/HIV activities: 2015 revision. Geneva: WHO; 2015 (<http://www.who.int/tb/publications/monitoring-evaluation-collaborative-tb-hiv/en/>, accessed 31 August 2016).

## BOX 5.1

### A mobile application for case-based recording and reporting for LTBI

Coverage of contact investigation and treatment of LTBI among child contacts and people living with HIV are both in the 10 indicators listed as highest priority for monitoring implementation of the End TB Strategy. However, systematic monitoring and evaluation of the programmatic management of LTBI remains weak in many countries. The establishment of monitoring systems is particularly challenging when multiple health-care service providers are involved.

A global consultation on LTBI convened by WHO in 2016 recognized the potential role of digital health in facilitating implementation of the programmatic management of LTBI, and the associated monitoring and evaluation.

After the consultation, a mobile phone application to facilitate monitoring and evaluation of programmatic management of LTBI according to international standards was developed by WHO, with support from the European Respiratory Society.

The application uses DHIS2 software and can be integrated into existing national electronic surveillance systems. It is designed to help health-care workers to collect client variables (e.g. demographic, clinical and treatment outcome variables) required to monitor indicators for TB preventive treatment. The application generates unique identifiers (based on the demographic data) that allow



case-based recording and reporting. If required, data can be entered offline and synchronized to the central database later.

Using an online dashboard, users can track indicators in real time. Indicators are disaggregated by risk groups at national, subnational and facility levels. The dashboard also provides geospatial data and allows users to visualize the location of clients on a map. This facilitates the

provision of preventive treatment and follow-up visits, particularly for household contacts.

The application is freely downloadable from the WHO website<sup>a</sup> and can be adapted to meet country-specific contexts, such as the availability of national unique identifiers, the existence of a DHIS2 system, and the presence of different risk groups. WHO is planning to start field-testing of the application to investigate access and acceptability in several settings later in 2017.

<sup>a</sup> [http://www.who.int/tb/areas-of-work/preventive-care/ltbi/ltbi\\_app/en/](http://www.who.int/tb/areas-of-work/preventive-care/ltbi/ltbi_app/en/) (accessed 9 October 2017)

In 2016, 8144 TB cases among health-care workers were reported from 60 countries; China accounted for 39% of these cases and Brazil for 13%. The notification rate among health-care workers could be calculated for 54 of the 60 countries; it ranged from zero to 701 cases per 100 000 population, with the highest rate observed in Mozambique.

The notification rate among the general adult population in each country was calculated based on the number of notified TB cases in adults and the estimated size of the adult populations from the United Nations population division (2017 revision). The ratios of the TB notification rate among health-care workers to the rate in the general adult population are shown in Fig. 5.4. The ratio was above two in seven countries (Burkina Faso, Colombia, Dominican Republic, Georgia, Lithuania, Mexico and the Bolivarian Republic of Venezuela). In five high TB/HIV burden countries for which the ratio could be calculated, the ratio was between 1 and 2 in two countries (Botswana and Mozambique) and below 1 in three countries (Angola, China and Namibia).

### 5.3 TB vaccination

There is a clear need for a vaccine that is more effective than the BCG vaccine, in particular to reduce the risk of infection with *M. tuberculosis* and the risk of progression from

infection to active TB disease in adults. Although there are 12 candidates in the TB vaccine pipeline, a new TB vaccine is not expected in the near future (Chapter 8).

BCG vaccination has been shown to prevent disseminated disease; this category includes TB meningitis and miliary TB, which are associated with high mortality in infants and young children. Currently, WHO recommends that, in countries with a high TB burden, a single dose of the BCG vaccine should be provided to all infants as soon as possible after birth as part of childhood immunization programmes. In countries with low TB incidence rates, provision of the BCG vaccine may be limited to neonates and infants in recognized high-risk groups, or to older children who are skin-test negative for TB infection.

Fig. 5.5 summarizes national policies on BCG vaccination.<sup>1</sup> Among 178 countries for which data were collected, 153 recommended universal BCG vaccination; the remaining countries had policies of selective vaccination for at-risk individuals in high-risk groups.

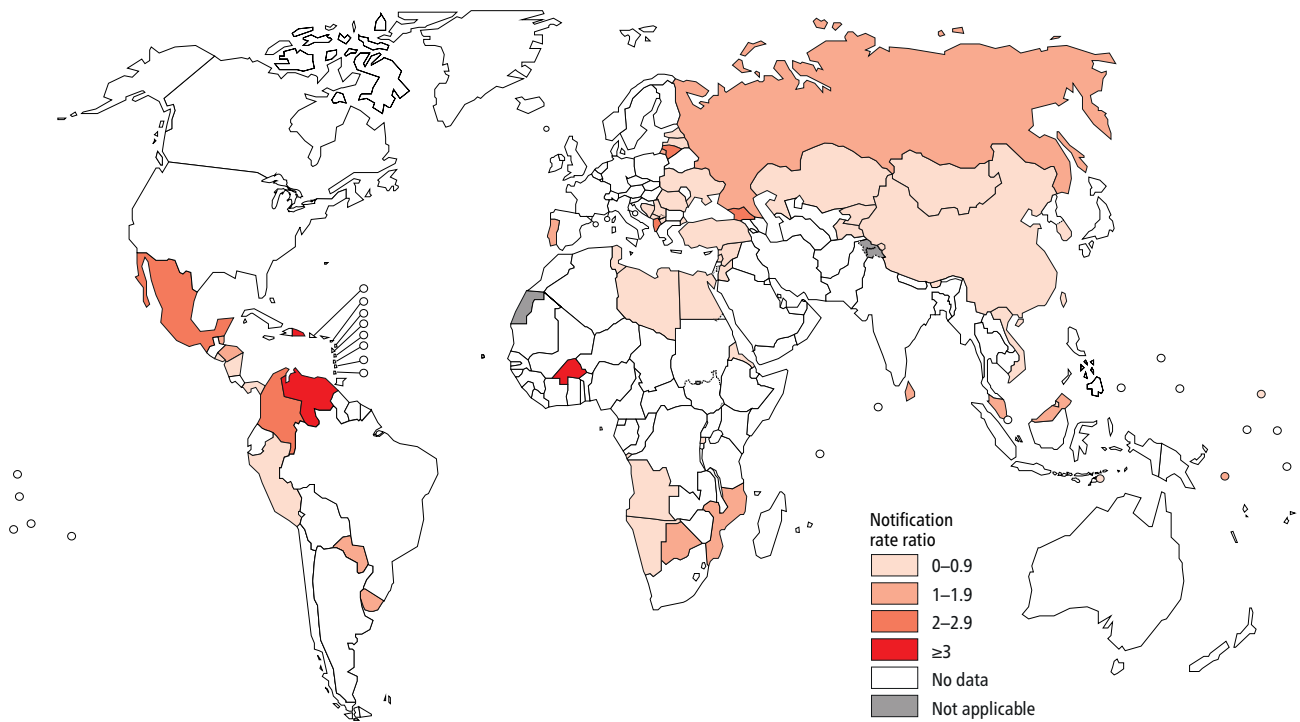
The latest data on BCG coverage<sup>2</sup> (for 2016) are shown in

<sup>1</sup> The BCG world atlas 2nd Edition. <http://www.bcgatlas.org/index.php>, accessed 25 July 2017.

<sup>2</sup> [http://apps.who.int/immunization\\_monitoring/globalsummary/timeseries/tscoveragebcg.html](http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tscoveragebcg.html), accessed 25 July 2017.

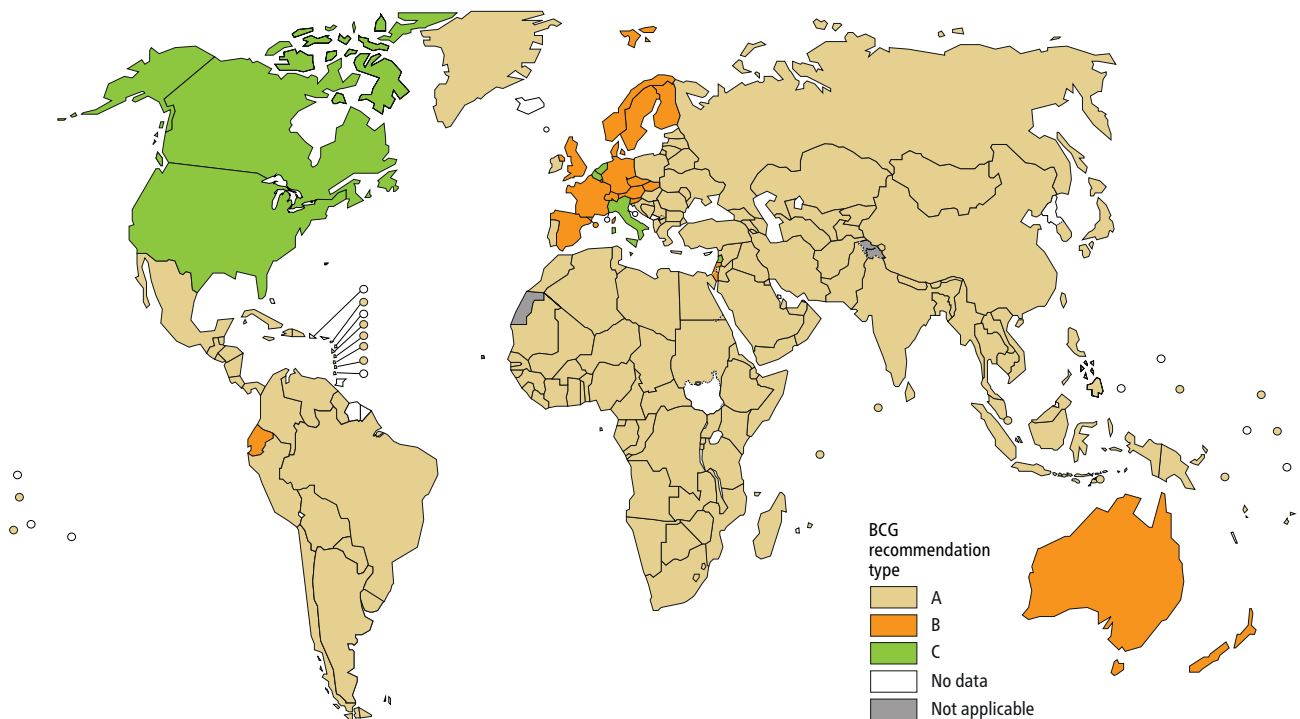
**FIG. 5.4**

**Notification rate ratio of TB among healthcare workers compared with the general adult population, 2016**



**FIG. 5.5**

**BCG vaccination policy by country**



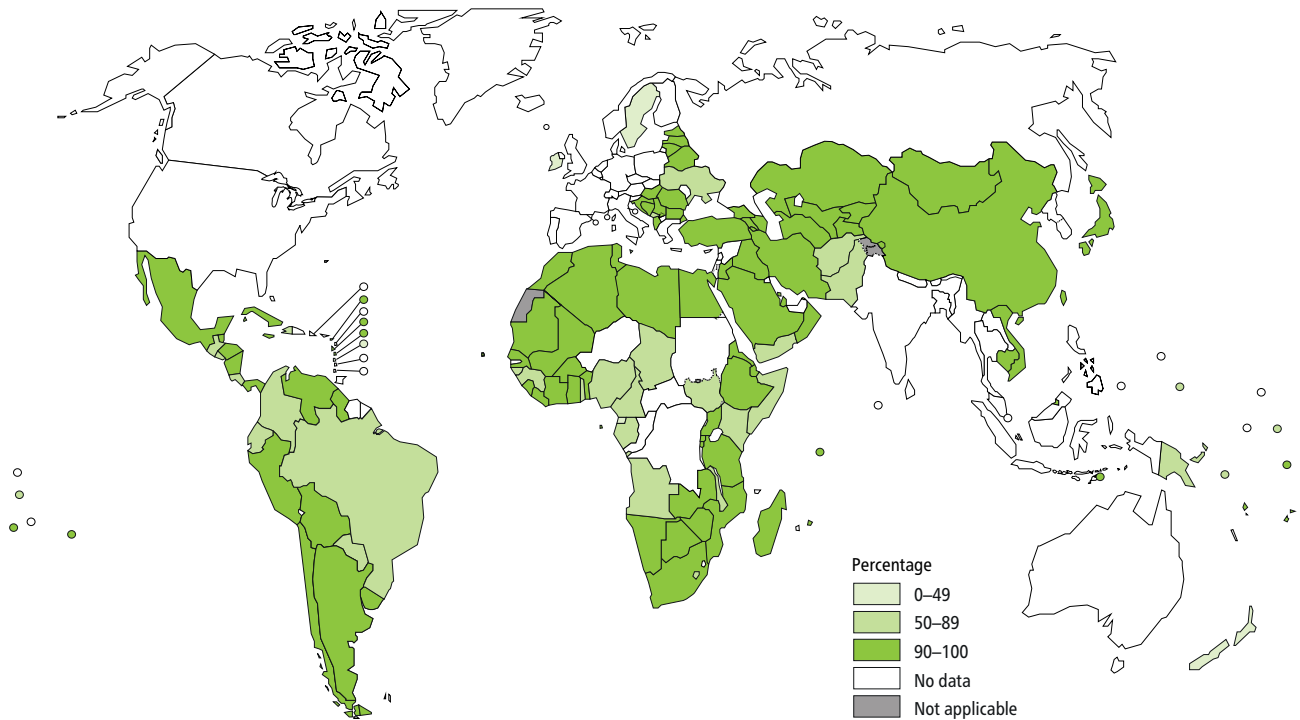
- A. The country currently has a universal BCG vaccination programme.
- B. The country used to recommend BCG vaccination for everyone, but currently does not.
- C. The country recommends BCG vaccination only for specific groups.

Source: The BCG World Atlas 2nd Edition. <http://www.bcgatlas.org/index.php>, accessed 25 July 2017.



**FIG. 5.6**

**Coverage of BCG vaccination, 2016<sup>a</sup>**



<sup>a</sup> The target population of BCG coverage varies depending on national policy, but is typically for the number of live births in the year of reporting.

Source: [http://apps.who.int/immunization\\_monitoring/globalsummary/timeseries/tscveragebcg.html](http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tscveragebcg.html), accessed 25 July 2017.

**Fig. 5.6.** In the 154 countries that reported data, 111 reported coverage of more than 90%. Among the 30 high TB burden countries, coverage ranged from 58% in Angola and Nigeria to 99% in Cambodia, China, Mozambique, the United Republic of Tanzania and Zambia, and 12 reported coverage of at least 90%. In addition to Angola and Nigeria, coverage was below 80% in two other high TB burden countries: Lesotho and Papua New Guinea.



**Patients queue at a hospital pharmacy in Zomba, Malawi**

SIMON RAWLES / ALAMY STOCK PHOTO

## CHAPTER 6.

# Financing for TB prevention, diagnosis and treatment

### KEY FACTS AND MESSAGES

The Stop TB Partnership's *Global Plan to End TB, 2016–2020*<sup>a</sup> (the Global Plan) estimates that, in low- and middle-income countries, US\$ 52 billion is required over 5 years to implement interventions that are currently available. The amount required for 2017 is US\$ 9.2 billion, which increases to US\$ 12.3 billion in 2020. Most of this funding is for diagnosis and treatment of drug-susceptible tuberculosis (TB) (e.g. US\$ 7.0 billion in 2017), but the amount for diagnosis and treatment of multidrug-resistant TB (MDR-TB) increases from US\$ 2.0 billion in 2017 to US\$ 3.6 billion by 2020; the remainder is for TB/HIV interventions. From 2016 to 2020, a further US\$ 6.3 billion is needed for high-income countries, and an additional US\$ 9.0 billion is needed for TB research and development.

Based on data reported to WHO by 118 low- and middle-income countries with 97% of the world's notified TB cases, US\$ 6.9 billion is available for TB prevention, diagnosis and treatment in 2017. Although an increase from previous years, this figure still represents a shortfall of US\$ 2.3 billion compared with the estimated requirement for this group of countries in the Global Plan. Increased domestic and international donor commitments are needed to close the funding gaps.

Of the total US\$ 6.9 billion available in 118 low- and middle-income countries in 2017, US\$ 5.8 billion (84%) is from domestic sources. However, this aggregate figure is strongly influenced by the BRICS group of countries (Brazil, the Russian Federation, India, China and South Africa). BRICS accounted for 46% of the available funding for TB in 2017 (and 48% of the world's notified TB cases), with 95% (range 89%–100%) of their funding coming from domestic sources. In other countries with a high TB burden, international donor funding remains crucial, accounting for 48% of the funding available in the 25 high TB burden countries outside BRICS (which have 38% of the world's notified TB cases) and for 56% of funding in low-income countries.

In India, the country with the largest burden of TB disease, a marked increase occurred in the TB-specific budget and the domestic funding for this budget in 2017. This followed high-level (Prime Ministerial) political commitment to an ambitious goal of ending TB by 2025 and the development of a new national strategic plan for TB 2017–2025. The budget in 2017 is US\$ 525 million (almost double the 2016 budget of US\$ 280 million), and is fully funded, including US\$ 387 million (74%) from domestic sources (triple the 2016 amount of US\$ 124 million).

International donor funding reported by national TB programmes amounts to US\$ 1.1 billion in 2017. The single largest source (80% of the total) is the Global Fund to Fight AIDS, Tuberculosis and Malaria. The largest bilateral donor is the United States government, which also provides about one-third of the contributions received by the Global Fund.

International donor funding for TB falls far short of the US\$ 2.6 billion annual requirement included in the Global Plan, and remains much less than donor contributions for HIV and malaria. The latest data from the Organisation for Economic Co-operation and Development (OECD) creditor reporting system, which are for 2015, show disbursement totals of US\$ 6.2 billion for HIV, US\$ 1.8 billion for malaria and US\$ 0.8 billion for TB. To provide some context for these amounts, the latest estimates (for 2015) of the burden of disease in terms of disability-adjusted life years (DALYs) lost due to illness and death are 67 million for HIV/AIDS, 56 million for malaria and 40 million for TB.

The median cost per patient treated in 2016 was US\$ 1253 for drug-susceptible TB and US\$ 9529 for MDR-TB.

Health financing data from national health accounts provide important insights into the current status of progress towards universal health coverage, as discussed in [Chapter 7](#).

<sup>a</sup> The Global Plan to End TB, 2016–2020. Geneva: Stop TB Partnership; 2015 (<http://www.stoptb.org/global/plan/>, accessed 14 July 2017).

Progress in tuberculosis (TB) prevention, diagnosis and treatment requires adequate funding sustained over many years. WHO began annual monitoring of funding for TB in 2002, with findings published in global TB reports and peer-reviewed publications.<sup>1</sup>

This chapter has four main sections. It starts with a summary of the most up-to-date estimates of the financial resources required to achieve the 2020 milestones of the End TB Strategy (Section 6.1). It then presents and discusses trends in funding for TB prevention, diagnosis and treatment by category of expenditure and source of funding for the period 2006–2017, both globally and for major country groupings (Section 6.2). More detailed country-specific data for 2017 are also presented for the 30 high TB burden countries. The third section analyses funding gaps reported by national TB programmes (NTPs) to WHO, with breakdowns by category of expenditure and country group (Section 6.3). The final section provides the latest estimates (for 2016) of the unit costs of treatment for drug-susceptible TB and multidrug-resistant TB (MDR-TB) (Section 6.4).

As highlighted in the previous two editions of the *Global tuberculosis report*,<sup>2,3</sup> analysis of health financing data can provide important insights into progress towards universal health coverage (UHC), which is necessary to achieve the End TB Strategy milestones set for 2020 and 2025 (Chapter 2). Measurement of costs faced by TB patients and their households is also required to assess progress towards one of the three high-level indicators of the End TB Strategy; that is, the percentage of TB patients and their households who face catastrophic costs as a result of TB disease. The 2020 milestone of zero set for this indicator requires progress in terms of both UHC and social protection (included under Pillar 2 of the End TB Strategy). These two topics – analysis of health financing data, and measurement of costs faced by TB patients and their households – are discussed in Chapter 7.

Further country-specific data on TB financing can be found in finance profiles that are available online.<sup>4</sup>

## 6.1 Estimates of funding required to achieve the 2020 milestones of the End TB Strategy

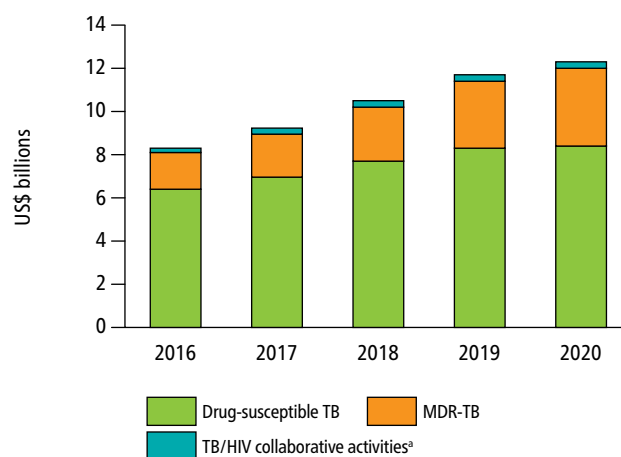
The 2020 milestones of the End TB Strategy are a 35% reduction in TB deaths compared with deaths in 2015, a 20% reduction in the TB incidence rate compared with 2015, and that no TB patients and their households face catastrophic

costs as a consequence of TB disease (Chapter 2). Estimates of the funding required to achieve these milestones have been set out in the Stop TB Partnership's *Global Plan to End TB, 2016–2020* (the Global Plan).<sup>5</sup> Worldwide, the total amount required for implementation of TB prevention, diagnostic and treatment interventions is US\$ 58 billion for the period 2016–2020, rising from US\$ 9.5 billion in 2016 to US\$ 14 billion in 2020.<sup>2</sup> An additional US\$ 9.0 billion is needed for global TB research and development in the same period.<sup>6</sup>

Of the US\$ 58 billion required over 5 years (excluding research and development), an estimated US\$ 52 billion is required in low- and middle-income countries, growing from US\$ 8.3 billion in 2016 to US\$ 12 billion in 2020 (Fig. 6.1). In 2017, an estimated total of US\$ 9.2 billion is required: US\$ 7.0 billion (75%) for diagnosis and treatment of drug-susceptible TB, US\$ 2.0 billion for drug-resistant TB<sup>7</sup> and the remainder for TB/HIV interventions. The amount for TB/HIV interventions is comparatively small because it does not include the funding needed for antiretroviral therapy for HIV-positive TB patients; this figure is instead included in estimates of funding required for HIV, published by UNAIDS.<sup>8</sup>

In the Global Plan, estimates of the funding that could be mobilized from domestic and international donor sources

**FIG. 6.1**  
Estimates of funding required for TB prevention, diagnosis and treatment in low- and middle-income countries in the Global Plan to End TB 2016–2020



<sup>a</sup> Funding estimates for TB/HIV exclude the cost of antiretroviral therapy (ART) for TB patients living with HIV. Such costs are included in global estimates of the funding required for HIV, published by UNAIDS.

Source: Data from Stop TB Partnership Global Plan to End TB 2016–2020.

<sup>1</sup> The most recent publication is: Floyd K, Fitzpatrick C, Pantoja A, Raviglione M. Domestic and donor financing for tuberculosis care and control in low-income and middle-income countries: an analysis of trends, 2002–11, and requirements to meet 2015 targets. *Lancet Glob Health*. 2013;1(2):e105–115 (<http://www.ncbi.nlm.nih.gov/pubmed/25104145>, accessed 14 July 2017).

<sup>2</sup> World Health Organization. *Global tuberculosis report 2015*. Geneva: WHO; 2015 ([http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf), accessed 14 July 2017).

<sup>3</sup> World Health Organization. *Global tuberculosis report 2016*. Geneva: WHO; 2016 (<http://apps.who.int/iris/bitstream/10665/250441/1/9789241565394-eng.pdf>, accessed 14 July 2017).

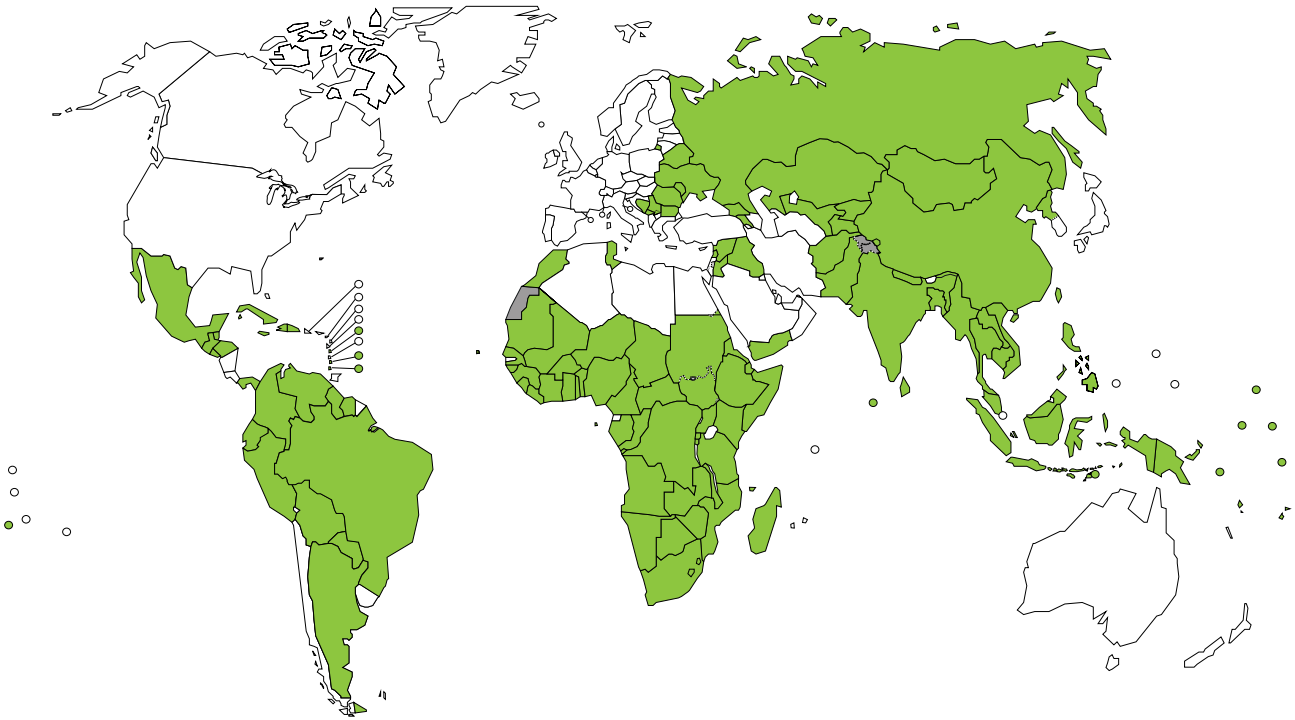
<sup>4</sup> [www.who.int/tb/data](http://www.who.int/tb/data)

<sup>5</sup> The Global Plan to End TB, 2016–2020. Geneva: Stop TB Partnership; 2015 (<http://www.stoptb.org/global/plan/>, accessed 14 July 2017).

<sup>6</sup> Funding for TB research and development, which is monitored by the Treatment Action Group, is discussed further in Chapter 8.

<sup>7</sup> The burden of drug-resistant TB (in terms of cases per year) is not projected to increase between 2016 and 2020. Increased funding is required to close detection and treatment gaps (see also Chapter 4).

<sup>8</sup> World Health Organization. *Global tuberculosis report 2016*. Geneva: WHO; 2016 ([http://www.who.int/tb/publications/global\\_report/archive/en/](http://www.who.int/tb/publications/global_report/archive/en/), accessed 20 July 2017).

**FIG 6.2****The 118 low- and middle-income countries included in analyses of TB financing, 2006–2017<sup>a</sup>**

<sup>a</sup> Countries were included in trend analyses if at least three years of high-quality finance data were available in the period 2006–2017.

were restricted to countries eligible to apply to the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund).<sup>1</sup> For eligible countries, the funding required over 5 years amounted to US\$ 29 billion. Of this total, it was estimated that about US\$ 16 billion could be mobilized from domestic sources, and that the remainder (an average of US\$ 2.6 billion per year) would need to be provided by international donors.

The Global Plan did not attempt to assess the broader investments required to increase the overall coverage and quality of health-care services or to remove financial barriers to accessing care. Such investments are needed for many essential preventive, treatment and care interventions, not only for TB. Progress on these fronts is critical, as explained in [Chapter 2](#) and as reflected in Pillar 2 of the End TB Strategy. The costings in the Global Plan can thus be seen as the financial resources required for Pillars 1 and 3 of the End TB Strategy. Recent estimates of the funding required in low- and middle-income countries to achieve UHC by 2030 are presented and discussed in [Chapter 7](#).

## 6.2 TB funding, overall and by category of expenditure and source of funding, 2006–2017

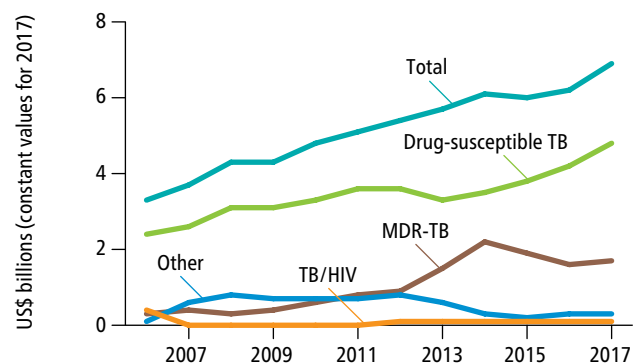
Data reported by NTPs to WHO since 2006 were used to analyse funding trends for 2006–2017 in 118 low- and middle-

income countries ([Fig. 6.2](#)). These countries accounted for 97% of the global number of TB cases notified in 2016. The methods used to collect, review and analyse financial data are summarized in [Box 6.1](#).

In these 118 low- and middle-income countries, funding for TB prevention, diagnosis and treatment reached US\$ 6.9 billion in 2017, up from US\$ 6.3 billion in 2016 and more than double the US\$ 3.3 billion that was available in 2006 ([Fig. 6.3](#); all figures are in constant 2017 dollars). Despite this growth in funding, amounts fall short of what is needed. The shortfall

**FIG. 6.3**

**Funding for TB prevention, diagnosis and treatment in total and by category of expenditure, 2006–2017, 118 countries with 97% of reported cases**



<sup>1</sup> Countries not eligible to apply to the Global Fund include Brazil, China, the Russian Federation and about half of the other 52 countries classified as upper middle income.

## BOX 6.1

### Methods used to compile, validate and analyse financial data reported to WHO

WHO began monitoring government and international donor financing for TB in 2002. All data are stored in the WHO global TB database. The standard methods used to compile, review, validate and analyse these data have been described in detail elsewhere;<sup>a,b</sup> this box provides a summary.

Each year, WHO asks all NTPs in low- and middle-income countries to report:

- the funding they estimate will be needed for TB prevention, diagnosis and treatment in their current fiscal year, by category of expenditure and source of funding; and
- expenditures for the most recently completed fiscal year, also by category of expenditure and source of funding.

In the 2017 round of global TB data collection, the fiscal years were 2016 and 2017. Consistency in categories of expenditure used to report TB budget and expenditure data has been maintained as far as possible to enable monitoring of trends. For low- and middle-income countries, the categories of expenditure for drug-susceptible TB used in the 2017 round of global TB data collection were:

- laboratory infrastructure, equipment and supplies;
- NTP staff at central and subnational levels (e.g. NTP managers and provincial or district TB coordinators);
- first-line drugs;
- programme costs (e.g. management and supervision activities, training, policy development, meetings, purchase of office equipment and vehicles, recording and reporting of notifications and treatment outcomes, advocacy and communication, public-private mix activities and community engagement); and
- operational research, including surveys.

For MDR-TB, two expenditure categories were used: second-line drugs and programme costs specifically related to MDR-TB. Starting in 2015, a separate category for patient support was included, linked to the emphasis on financial and social protection in the End TB Strategy. There is also a separate category for collaborative TB/HIV activities (this excludes any budget items financed by HIV programmes, such as antiretroviral therapy for TB patients living with HIV, and TB preventive treatment for people newly enrolled in HIV care). A breakdown of the total amount of available funding is requested in four categories: domestic funding excluding loans; external loans, also considered domestic funding; the Global Fund; and grant financing from sources other than the Global Fund.

As in previous years, in 2017 all high-income countries were asked to report funding requirements and expenditures in total, without any breakdown by category of expenditure or source of funding. However, only a few countries reported financing data and therefore data for high-income countries are not featured in [Chapter 6](#).

As in previous years, in 2017 all countries (irrespective of income level) were asked to report on the use of

inpatient and outpatient care for treatment of people with drug-susceptible TB and MDR-TB on a per-patient basis (i.e. the average number of days spent in hospital, and the average number of outpatient visits to a health facility). These data can be based on actual use of services (preferable where available), or on the expected use of services based on the typical approach used to deliver treatment (which may be defined in national policy documents). They are combined with other data to estimate the financial resources used for TB treatment that are not reflected in NTP-reported budgets and expenditures (further details are provided below).

The core methods used to review and validate data have remained consistent since 2002. They include:

- **routine checks for plausibility and consistency, including validation checks that are built into the online reporting system** – examples of validation checks are checks for implausibly large year-to-year changes (e.g. in total reported funding by source and by category of expenditure), or implausibly high or low values of funding for drugs relative to the number of TB patients (that differ substantially from prices quoted by the Global TB Drug Facility);
- **discussions with country respondents to resolve queries;** and
- **triangulation with other data sources** – such sources include estimates of unit costs from independent economic evaluations<sup>c,d</sup> and funding applications submitted to the Global Fund;<sup>e</sup> comprehensive budgets for national strategic plans for TB are an essential requirement for funding applications to the Global Fund. Further details about the comparisons with other data sources are available from WHO upon request.

In review and validation of data, particular attention has always been given to the high TB burden countries.

Since 2014, an extra question about the average cost of drugs per patient treated has been asked, to allow reviewers to better assess the validity of budgets reported for first-line and second-line drugs, and to identify whether reported budgets include funding for buffer stocks.

In 2017, specific efforts to improve the quality of financial data reported to WHO included discussions with NTP staff at the June 2017 meeting of WHO's Strategic and Technical Advisory Group for TB and an associated summit in which NTP managers from the 30 high TB burden countries participated; discussions with NTP staff during workshops on TB modelling; and individual and customized follow-up with in-country staff involved in the development of national strategic plans.

Usually, TB funding reported by NTPs does not include the financial costs associated with the inpatient and outpatient care required during TB treatment. Since many detailed costing studies in a wide range of countries show that these costs can account for a large share of the cost of treating someone with TB, WHO analyses of TB financing have always included estimates of the

funding required for both inpatient and outpatient care. These costs have been estimated from a provider perspective only, and do not include the costs faced by TB patients and their households. Increasing attention is now being given to costs faced by TB patients and their households, as discussed in [Chapter 7](#).

WHO estimates the funding used to provide inpatient and outpatient care for TB patients by multiplying the number of outpatient visits and days of inpatient care per patient (reported by NTPs each year) by the cost per bed day and per clinic visit available from the WHO CHOosing Interventions that are Cost-Effective (WHO-CHOICE) database,<sup>f</sup> and then by the reported number of TB patients notified or projected to be notified. These estimates are done separately for drug-susceptible TB and MDR-TB. In 2017, costs per bed day and per clinic visit were estimated using the CHOICE regression model and the latest data available from the World Bank. For four countries (India, South Africa, Thailand and Viet Nam), WHO-CHOICE estimates were replaced with estimates of unit costs obtained directly from national health account data, or from recent studies and discussions with experts supporting the costing of national strategic plans.

Where possible, estimates are compared with hospital and clinic expenditure data for drug-susceptible and MDR-TB that are being tracked through the System of Health Accounts (SHA).<sup>g</sup> In 2017, SHA data were available for 27 countries for one or two years, including six high burden countries (Cambodia, Democratic Republic of the Congo, Namibia, the Philippines, Sierra Leone and United Republic of Tanzania).<sup>h</sup> After review, the SHA data were used in preference to estimates based on reported use and unit costs estimates from WHO-CHOICE. The WHO Health Governance and Financing Department has initiated a process to assess the validity of the latest results from the new SHA, including disease-specific results.

Expanded implementation of SHA and validation against existing disease-specific tracking systems may facilitate more comprehensive reporting of domestic funding for TB, especially reporting of the contributions from subnational administrative levels that are not always known or compiled at the national level. Although much of this contribution is probably for delivery of inpatient and outpatient care (which is included in current WHO estimates of domestic funding for TB, as explained above), reporting of funding from these levels (including TB-specific budgets) is a particular challenge in large countries with decentralized systems for TB treatment (e.g. Indonesia, Nigeria and South Africa).

- <sup>a</sup> Floyd K, Pantoja A, Dye C. Financing tuberculosis control: the role of a global financial monitoring system. *Bull World Health Organ.* 2007;85(5):334–340 (<http://www.ncbi.nlm.nih.gov/pubmed/17639216>, accessed 29 July 2016).
- <sup>b</sup> Floyd K, Fitzpatrick C, Pantoja A, Raviglione M. Domestic and donor financing for tuberculosis care and control in low-income and middle-income countries: an analysis of trends, 2002–11, and requirements to meet 2015 targets. *Lancet Glob Health.* 2013;1(2):e105–115 (<http://www.ncbi.nlm.nih.gov/pubmed/25104145>, accessed 28 July 2016).
- <sup>c</sup> Global Health Cost Consortium unit cost study data repository, accessed 13 July 2017 (<http://ghcosting.org/pages/data/ucsr/app/index>).
- <sup>d</sup> Laurence YV, Griffiths UK, Vassall A. Costs to health services and the patient of treating tuberculosis: a systematic literature review. *Pharmacoeconomics.* 2015;33(9):939–955 (<http://www.ncbi.nlm.nih.gov/pubmed/25939501>, accessed 29 July 2016).
- <sup>e</sup> Global Fund Data and the Open Data Protocol <http://web-api.theglobalfund.org/odata/>, accessed May 2017 and country financial gap analysis materials approved for funding in the first rounds of New Funding Model.
- <sup>f</sup> Cost effectiveness and strategic planning (WHO-CHOICE): health service delivery costs. Geneva: World Health Organization; 2008 ([http://www.who.int/choice/cost-effectiveness/inputs/health\\_service/en/](http://www.who.int/choice/cost-effectiveness/inputs/health_service/en/), accessed 13 July 2017).
- <sup>g</sup> OECD/Eurostat/WHO. A system of health accounts. OECD Publishing; 2011 (<http://www.who.int/health-accounts/methodology/sha2011.pdf>, accessed 29 July 2016).
- <sup>h</sup> Health accounts. Geneva: World Health Organization; data shared by WHO Health Governance and Financing Department on 11 July 2017.

compared with the Global Plan estimate ([Section 6.1](#)) is US\$ 2.3 billion in 2017 (US\$ 6.9 billion available compared with an estimated requirement of US\$ 9.2 billion).

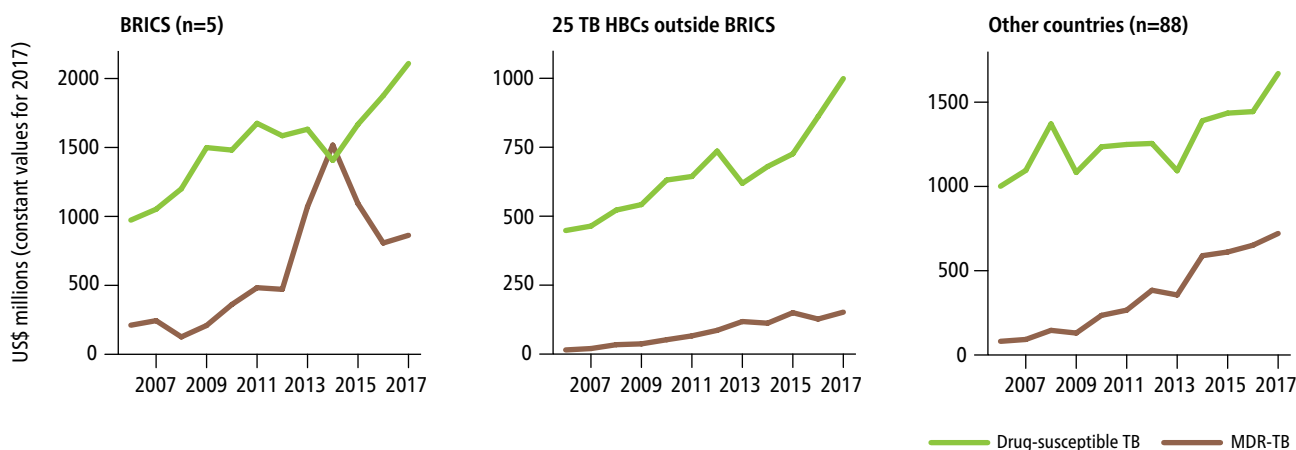
Of the total US\$ 6.9 billion available in 2017, US\$ 4.8 billion (73%) is for the diagnosis and treatment of drug-susceptible TB. This is US\$ 2.1 billion less than the requirement estimated in the Global Plan.

Funding for MDR-TB reached US\$ 1.7 billion in 2017; the annual amount increased steadily from 2006 to 2014, declined from 2014 to 2016, and then slightly increased from 2016 to 2017 ([Fig. 6.3](#)). This aggregate trend reflects the pattern in the BRICS group of countries (Brazil, Russian Federation, India, China and South Africa) ([Fig. 6.4](#)), where a downturn after 2014 is explained by decreasing funding in the Russian Federation (2014–2017) and South Africa (2013–2016). Funding in other countries has been increasing ([Fig. 6.4](#)). The shortfall between the funding available in 2017 and the requirement of US\$ 2.0 billion in 2017 estimated in the Global Plan is comparatively small (US\$ 0.3 billion). However, funding for diagnosis and treatment of MDR-TB needs to increase

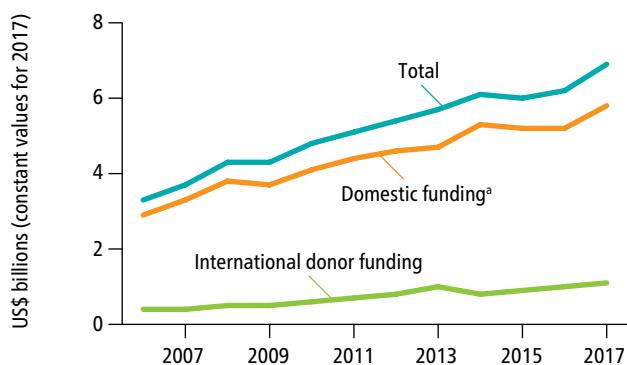
substantially. This is evident from large and persistent gaps in detection and treatment of MDR-TB, both globally and in most countries with a high burden of MDR-TB (for details, see [Chapter 4](#)). It is also evident from the Global Plan, in which the annual funding required for MDR-TB reaches US\$ 3.6 billion in 2020, more than double the amount of US\$ 1.7 billion available in 2017.

Overall, most funding during the period 2006–2016 has been provided from domestic sources, and this remains the case in 2017 ([Fig. 6.5](#)).<sup>1</sup> Thus, in 2017, US\$ 5.8 billion (84%) of the total funding of US\$ 6.9 billion for TB is from domestic sources. However, aggregated figures for the 118 low- and

<sup>1</sup> Domestic funding includes both funding for TB-specific budgets and funding for inpatient and outpatient care (usually funded through more general budget lines), as also explained in [Box 6.1](#). In [Fig. 6.5](#) and [Fig. 6.6](#), it is assumed that funding for inpatient and outpatient care is funded domestically and not by international donors. This is justified on the basis that most (93%) of the funding estimated to be used for inpatient and outpatient care for TB patients is accounted for by middle-income countries, where international donor funding for such components of care is unlikely (such support is more likely to occur in low-income countries, via general budget support to the health sector).

**FIG. 6.4****Funding for drug-susceptible TB and MDR-TB, 2006–2017, by country group<sup>a</sup>**

<sup>a</sup> BRICS accounted for 48% of the world's notified TB cases (2016). The 25 high TB burden countries outside BRICS accounted for 38% of the world's notified TB cases (2016), and the remainder (11%) were in other countries.

**FIG. 6.5****Funding for TB prevention, diagnosis and treatment by funding source, 2006–2017, 118 countries with 97% of reported TB cases**

<sup>a</sup> Domestic funding includes TB-specific budgets and the estimated resources used for inpatient and outpatient care (see Box 6.1). 93% of the funding of US\$ 3 billion for inpatient and outpatient care in 2017 is accounted for by middle-income countries; such countries do not typically receive international donor funding for inpatient and outpatient care services.

middle-income countries conceal substantial variation among countries in the share of funding from domestic and international sources (Fig. 6.6). While domestic funding dominates in eight of the nine (not mutually exclusive) country groups shown in Fig. 6.6, including BRICS where domestic funding accounts for 95% of total funding in 2017 (range 89%–100% among the five countries), international donor funding exceeds funding from domestic sources in low-income countries (56% of the total in 2017) and is similar to levels of domestic funding in the 25 high TB burden countries outside BRICS (48% of the total in 2017).<sup>1</sup>

<sup>1</sup> The list of 30 high TB burden countries being used by WHO during the period 2016–2020 is explained in Chapter 2. The countries are those listed in Fig. 6.7, Table 6.1 and Table 6.2.

International donor funding reported by NTPs to WHO amounts to US\$ 1.1 billion in 2017. Of this, most (80%) was provided by the Global Fund. However, because funding reported by NTPs to WHO does not capture all international donor funding for TB,<sup>2</sup> a complementary analysis based on donor reports to the Organisation for Economic Co-operation and Development (OECD) is provided in Box 6.2.<sup>3</sup>

The importance of international donor funding in high TB burden countries is particularly evident when considering only the TB-specific budgets included in national strategic plans for TB (Fig. 6.7, Table 6.1, Table 6.2). In 23 of the 30 high TB burden countries, more than 80% of funding for the TB-specific budgets included in national strategic plans for TB is from international donors in 2017.

Both Fig. 6.7 and recent developments in India illustrate the potential to increase domestic funding in some high TB burden countries. In the group of nine low-income high TB burden countries, the proportion of the reported TB budget funded from domestic sources in 2017 ranges from 0.3% in Zimbabwe to 24% in Liberia. In the group of 15 lower-middle-income high TB burden countries the proportion ranges from 6.8% in Bangladesh to 88% in Congo. In the group of six upper-middle-income countries, the proportion ranges from 30% in Namibia to 100% in the Russian Federation.

In India, the country with the largest burden of TB disease (Chapter 3), there was a marked increase in both the TB-specific budget and the domestic funding for this budget in 2017. This increase followed high-level (Prime Ministerial) political commitment to an ambitious goal of ending TB by 2025, and the development of a new national strategic plan for TB 2017–2025 that aims to accelerate progress towards

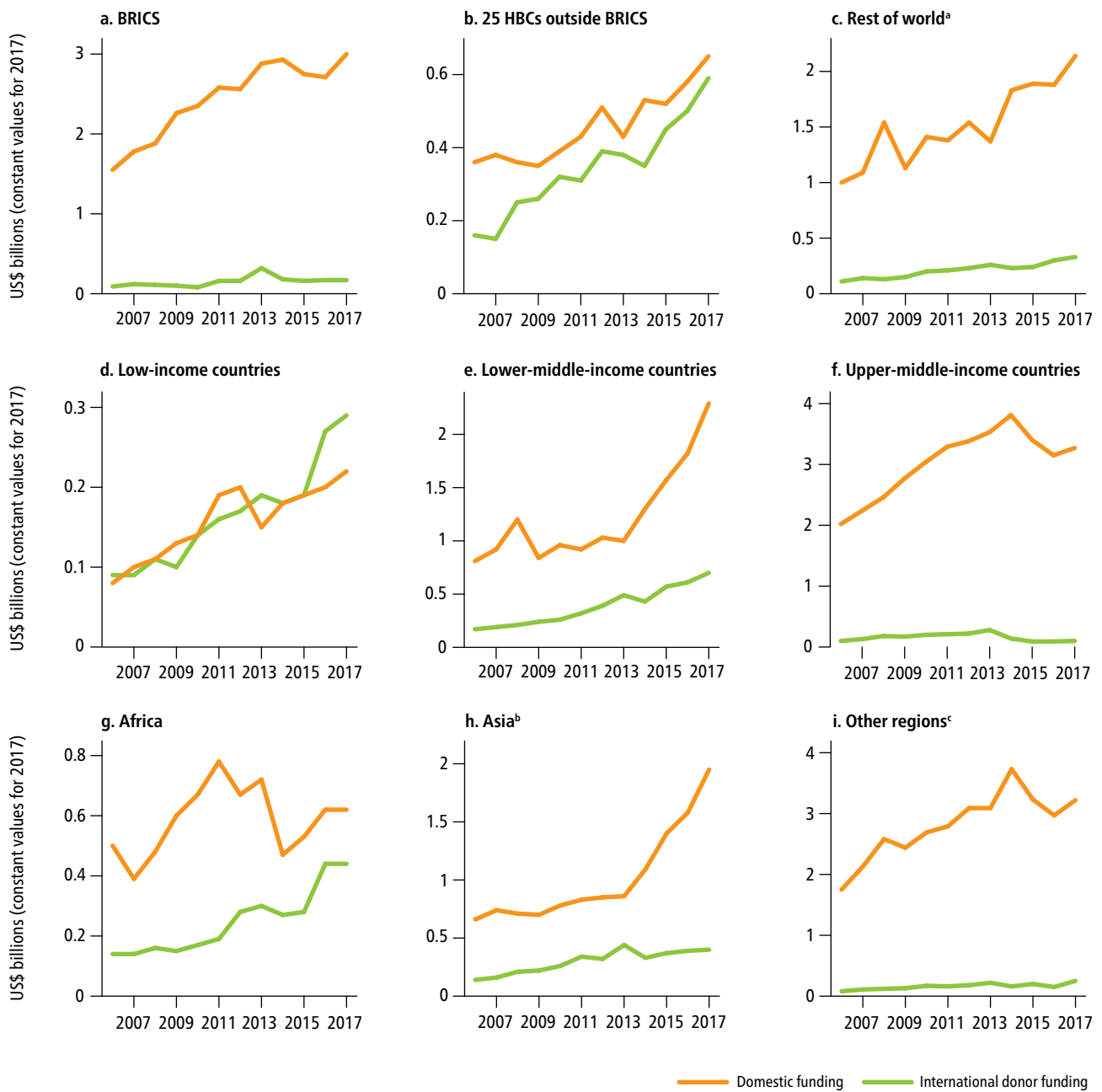
<sup>2</sup> Donor funding is also provided to entities other than NTPs, including international and national governmental and nongovernmental organizations.

<sup>3</sup> Out-of-pocket expenditures are also not included in the financing data reported by NTPs. These are discussed in more detail in Chapter 7.



**FIG. 6.6**

**Funding for TB prevention, diagnosis and treatment from domestic sources and international donors, 2006–2017, 9 country groups**



<sup>a</sup> Rest of the world includes 88 countries that are not in the list of 30 high TB burden countries.

<sup>b</sup> Asia includes the WHO regions of South-East Asia and the Western Pacific.

<sup>c</sup> Other regions consist of three WHO regions: the Eastern Mediterranean Region, the European Region, and the Region of the Americas.

## BOX 6.2 International donor funding for TB prevention, diagnosis and treatment, based on donor reports to the OECD

Not all international donor funding that is provided for TB prevention, diagnosis and treatment is channelled through NTPs. The creditor reporting system (CRS) of the OECD is the most comprehensive source of information about international donor funding. Funding data (both commitments and disbursements) are provided by 31 multilateral donor organizations, the 26 countries that are members of the OECD's Development Assistance Committee, and a further two non-committee members (Kuwait and the United Arab Emirates).

Disbursement data include both direct transfers to countries and the provision of goods and services, such as in-kind transfers or technical assistance. Data on gross disbursements<sup>a</sup> for TB (code 12263: Tuberculosis control) received by non-OECD countries during 2006–2015 were analysed. Funding for TB that flows from one OECD member to an institution or government within the OECD, such as grants from the United States (US) National Institutes for Health flowing to the United Kingdom, is not captured in the CRS. Also, government contributions to multilateral organizations are not attributed to the government of origin, only to the multilateral organization.<sup>b</sup>

**FIG. B6.2.1**  
International donor funding for TB prevention, diagnosis and treatment by source, 2006–2015

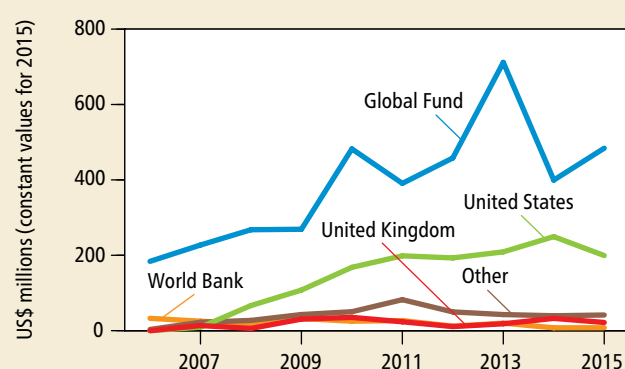
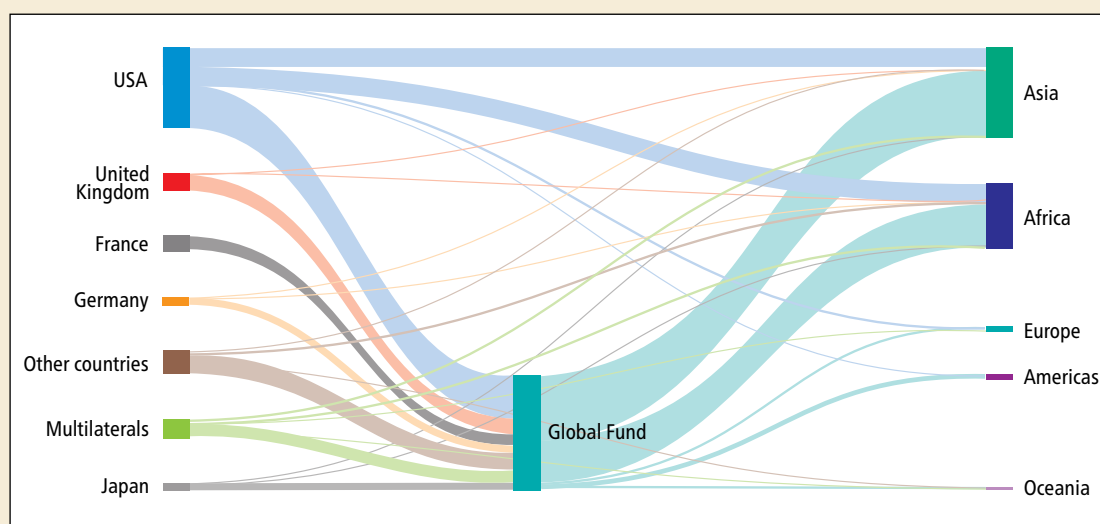


Fig. B6.2.1 shows trends in international donor funding between 2006 and 2015, from five major sources. The total from all sources in 2015 was US\$ 754 million, increased from US\$ 220 million in 2006. In 2015, 64% of international TB donor funding was provided by the Global Fund (US\$ 484 million); the second largest contributor was the US government<sup>c</sup> (26%, US\$ 199 million). Given that about one third of the contributions to the Global Fund are from the US government, about 47% of international donor funding for TB globally originated from the US government in 2015. The remaining funding came from the United Kingdom (3%), the World Bank (1%), and other sources (6%), within which the largest contributing country was Belgium.

From 2006 to 2015, the Global Fund was consistently the largest provider of international donor funding, but a marked drop occurred from a peak of US\$ 712 million in 2013 to US\$ 399 million in 2014, followed by a recovery to US\$ 484 million in 2015. This pattern may reflect the transition to a new funding model that started in 2013, and some associated delays in approving and disbursing funds. Disbursements from the US government steadily increased from 2004 to 2014, peaking at US\$ 249 million in 2014 and then declining in 2015 to US\$ 199 million.<sup>c</sup>

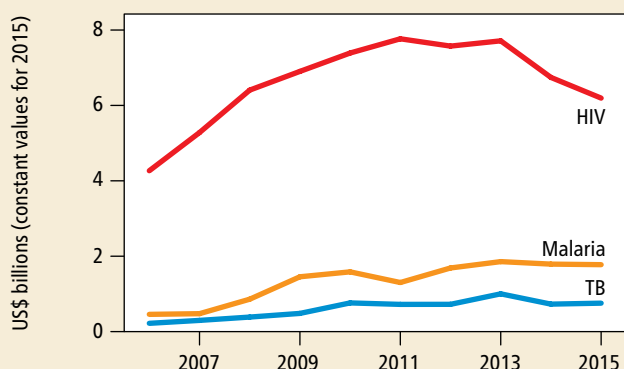
Fig. B6.2.2 shows the flow of TB funding in 2015. Almost half of all funding from the US was given bilaterally, primarily to non-OECD countries in Asia and Africa. France, Germany, Japan and the United Kingdom also provided funding streams directly to countries in addition to their disbursements to the Global Fund. In 2015, Asia received the largest share of TB

**FIG. B6.2.2**  
International donor funding flows for TB prevention, diagnosis and treatment to non-OECD countries, 2015



**FIG. B6.2.3**

### International donor funding for TB, HIV and malaria, 2006–2015



funding (50%), followed by Africa (36%). **Fig. B6.2.3** shows that international funding for TB is less than half that for malaria and approximately one eighth that for HIV. The disability-adjusted life years (DALYs) lost due to illness and death for these three diseases are 67 million for HIV/AIDS, 56 million for malaria and 40 million for TB.<sup>d</sup>

<sup>a</sup> As opposed to commitments, which may not materialize.

<sup>b</sup> An important example is funding from the Global Fund to non-OECD countries, which is attributed to the Global Fund and not to the governments or other entities that contribute to the Global Fund.

<sup>c</sup> Disbursements from the US government captured in the OECD database are lower than official allocations. In 2015, the official allocation for TB was US\$ 242 million and there was additional funding of US\$ 132 million for TB/HIV via the President's Emergency Plan for AIDS Relief (PEPFAR).

<sup>d</sup> Source: <http://ghdx.healthdata.org/gbd-results-tool>, accessed on 13 July 17.

this goal. **Fig. 6.8** shows that the budget in 2017 is US\$ 525 million (almost double the budget of US\$ 280 million in 2016). The budget is fully funded, including US\$ 387 million (74%) from domestic sources (triple the amount of US\$ 124 million in 2016).

### 6.3 Funding gaps reported by national TB programmes, 2006–2017

Despite growth in funding from domestic and international donor sources, many NTPs continue to be unable to mobilize all the funding required for full implementation of their national strategic plans (**Fig. 6.7**, **Fig. 6.9**, **Table 6.1**). Funding gaps (i.e. the difference between assessments by NTPs of funding needs for TB prevention, diagnosis and treatment, and the actual amount of funds mobilized) have persisted, and in 2017 they amounted to a reported total of US\$ 0.9 billion. This is less than half of the gap of US\$ 2.3 billion that exists between the US\$ 9.2 billion estimated to be needed in low- and middle-income countries in 2017 according to the Global Plan (**Section 6.1**) and the US\$ 6.9 billion available in 2017 (**Section 6.2**). The difference can be explained by the fact that, in many countries, national strategic plans for TB are less ambitious than the targets set in the Global Plan (**Section 6.1**).

Of the US\$ 0.9 billion funding gap reported by NTPs in 2017, US\$ 0.75 billion (81%) is for drug-susceptible TB and US\$ 0.18 billion (19%) is for MDR-TB. Relative to total funding needs, the funding gap is larger for drug-susceptible TB than for MDR-TB (not shown).

Lower-middle-income countries account for the largest reported funding gap (US\$ 626 million) in 2017 (**Fig. 6.9**). In 2017, the largest funding gaps among low-income countries were for high TB burden countries: the United Republic of Tanzania (US\$ 40 million), Ethiopia (US\$ 36 million), the

Democratic Republic of the Congo (US\$ 28 million) and the Democratic People's Republic of Korea (US\$ 13 million) (**Table 6.1**). Funding gaps were relatively small in upper-middle-income countries in 2017 (US\$ 97 million), and have fallen in recent years. This trend is mostly explained by large reductions in the funding gaps reported by China, Kazakhstan and the Russian Federation, which reported funding gaps in 2006–2011 but negligible or zero gaps thereafter.

Geographically, half of the total reported funding gap in 2017 is accounted for by countries in the WHO African Region (US\$ 502 million), with Nigeria reporting the largest gap (US\$ 215 million). Most of the remaining gap was reported in the South-East Asia Region, primarily by Indonesia (US\$ 98 million) and Bangladesh (US\$ 36 million) (**Fig. 6.9**).

### 6.4 Unit costs of treatment for drug-susceptible TB and multidrug-resistant TB, 2016

The cost per patient treated in 2016 for drug-susceptible TB and MDR-TB was estimated for 111 and 80 countries, respectively.<sup>1</sup> All countries in the lists of high TB burden countries and high MDR-TB burden countries were included in the analyses.<sup>2</sup> Unit cost estimates are shown in **Fig. 6.10** and **Fig. 6.11**, and analytical methods are summarized in **Box 6.3**.

#### 6.4.1 Drug-susceptible TB

The median cost per patient treated for drug-susceptible TB in 2016 was US\$ 1253 (**Fig. 6.10**).<sup>3</sup> In general, about 60% of this

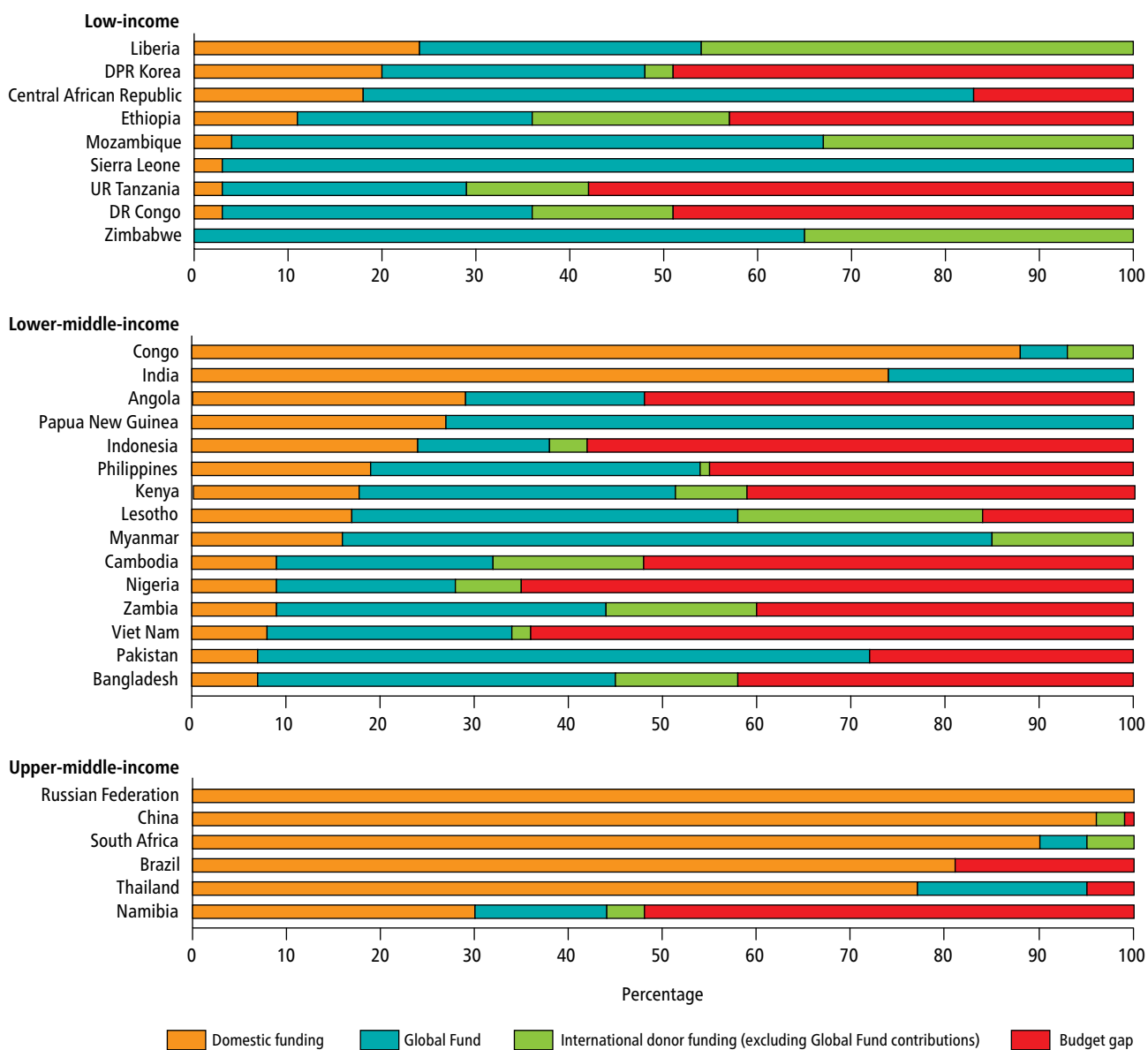
<sup>1</sup> Analysis for drug-susceptible TB was limited to countries that notified at least 100 TB cases in 2016. For MDR-TB, estimates were restricted to countries that reported at least 10 patients on second-line treatment for MDR-TB.

<sup>2</sup> For further details about both lists, see **Chapter 2**.

<sup>3</sup> Median values are cited rather than means because of extreme values for a few countries.

**FIG. 6.7**

**Sources of funding and funding gaps for the TB-specific budgets included in national strategic plans for TB in 2017, 30 high TB burden countries**



**TABLE 6.1**

**Reported budget, available funding for this budget from domestic and international donor sources, funding gap and share of budget in national strategic plan for TB provided by domestic and international donor funding, 30 high TB burden countries, 2017 (current US\$ millions)**

	BUDGET IN NATIONAL STRATEGIC PLAN FOR TB	DOMESTIC FUNDING (A)	INTERNATIONAL DONOR FUNDING (B)	SHARE OF AVAILABLE FUNDING (A+B) PROVIDED FROM DOMESTIC SOURCES (%)	SHARE OF AVAILABLE FUNDING (A+B) PROVIDED BY INTERNATIONAL DONORS (%)	FUNDING GAP <sup>c</sup>
Angola	14	3.9	2.6	60%	40%	7.2
Bangladesh <sup>a</sup>	85	5.8	43	12%	88%	36
Brazil	67	55	<0.1	100%	0%	12
Cambodia	37	3.5	14	20%	80%	19
Central African Republic	1.6	0.3	1.0	21%	79%	0.3
China	384	369	11	97%	3%	4.0
Congo	2.2	2.0	0.3	88%	12%	0
DPR Korea	27	5.6	8.3	40%	60%	13
DR Congo	57	1.5	27	5%	95%	28
Ethiopia	84	10	38	20%	80%	37
India	525	387	138	74%	26%	0
Indonesia	185	53	34	61%	39%	98
Kenya <sup>a</sup>	62	11	26	30%	70%	26
Lesotho	4.7	0.8	3.2	20%	80%	0.8
Liberia	1.7	0.4	1.3	24%	76%	0
Mozambique	32	1.4	30	4%	96%	0
Myanmar	78	13	65	16%	84%	0.1
Namibia	56	17	10	62%	38%	29
Nigeria	336	31	90	26%	74%	215
Pakistan	108	7.5	71	10%	90%	30
Papua New Guinea	11	2.9	7.9	27%	73%	0
Philippines	104	20	55	27%	73%	29
Russian Federation	1 175	1 175	0	100%	0%	0
Sierra Leone	6.9	0.2	6.8	3%	97%	0
South Africa	244	220	24	90%	10%	0
Thailand <sup>b</sup>	20	15	3.4	81%	19%	1.1
UR Tanzania	70	1.9	27	6%	94%	41
Viet Nam	70	5.9	20	23%	77%	44
Zambia	14	1.2	7.0	14%	86%	5.4
Zimbabwe	18	<0.1	18	0%	100%	0
<b>30 high TB burden countries</b>	<b>3 881</b>	<b>2 420</b>	<b>784</b>	<b>76%</b>	<b>24%</b>	<b>677</b>

Blank cells indicate data not reported.

– indicates values that cannot be calculated.

<sup>a</sup> In 2017, the budget reported by Bangladesh is for the calendar year (as opposed to the fiscal year).

<sup>b</sup> In 2017, the budget reported by Thailand was for the central level only.

<sup>c</sup> The funding gap reflects the anticipated gap for the year at the time a country reported data to WHO in the 2017 round of global TB data collection. Totals are computed prior to rounding.

**TABLE 6.2**

**Reported budget in National Strategic Plan for TB, by intervention area and estimated cost of inpatient and outpatient care for drug-susceptible (DS-TB) and MDR-TB, 30 high TB burden countries, 2017 (current US\$ millions)**

	BUDGET IN NATIONAL STRATEGIC PLAN FOR TB				ADDITIONAL RESOURCES REQUIRED FOR INPATIENT AND OUTPATIENT CARE		TOTAL RESOURCES REQUIRED FOR TB CARE
	TOTAL	DS-TB	MDR-TB	TB/HIV	DS-TB	MDR-TB	
Angola	14	11	2.3	0.3	63	2.6	79
Bangladesh <sup>a</sup>	85	77	8.3	0.3	1.8	1.0	88
Brazil	67	54	11	2.0	48	2.3	117
Cambodia	37	34	2.3	0.9	27	0.5	64
Central African Republic	1.6	1.2	<0.1	0.4	0.7	<0.1	2.3
China <sup>b</sup>	384	356	28	0	–	–	384
Congo	2.2	2.2	<0.1	<0.1	1.5	<0.1	3.7
DPR Korea	27	24	3.3	0.1	42	5.8	75
DR Congo	57	42	11	4.2	15	1.5	74
Ethiopia	84	59	18	7.6	12	0.3	97
India	525	421	97	6.6	579	114	1 217
Indonesia	185	158	20	7.7	44	9.9	239
Kenya	62	53	4.1	4.7	12	0.6	75
Lesotho	4.7	2.8	1.7	0.2	0.3	0.0	5.0
Liberia	1.7	1.2	0.3	0.2	0.3	0.4	2.4
Mozambique	32	20	6.6	4.6	6.8	0.3	39
Myanmar	78	59	15	4.0	3.1	0.6	82
Namibia	56	48	1.2	7.2	5.2	10	71
Nigeria	336	223	100	13	13	4.8	354
Pakistan	108	99	8.3	0.7	4.8	0.3	113
Papua New Guinea	11	7.6	2.9	0.3	1.7	2.4	15
Philippines	104	92	11	0.8	87	7.4	199
Russian Federation <sup>b,c</sup>	1 175	590	550	35	–	–	1 175
Sierra Leone	6.9	6.2	0.3	0.4	20	0.9	28
South Africa	244	203	30	11	16	36	297
Thailand <sup>d</sup>	20	19	0.2	<0.1	4.2	0.2	24
UR Tanzania	70	57	7.0	6.3	2.9	0.3	73
Viet Nam	70	55	13	1.7	22	2.6	95
Zambia	14	10	1.7	1.6	2.6	0.8	17
Zimbabwe	18	14	3.2	0.3	3.7	0.2	22
<b>30 high TB burden countries</b>	<b>3 881</b>	<b>2 800</b>	<b>958</b>	<b>122</b>	<b>1 039</b>	<b>205</b>	<b>5 125</b>

– indicates values that cannot be calculated. Totals are computed prior to rounding.

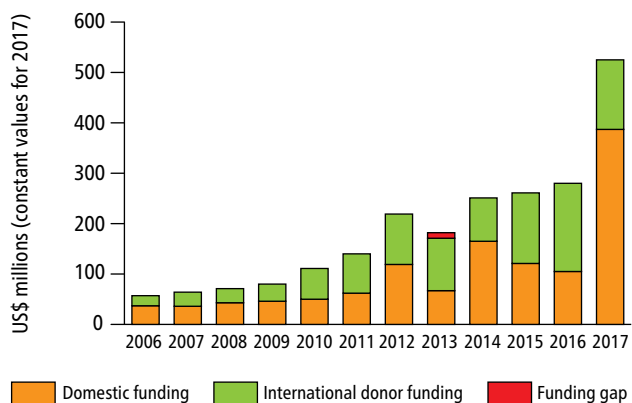
<sup>a</sup> In 2017, the budget reported by Bangladesh is for the calendar year (as opposed to the fiscal year).

<sup>b</sup> No amounts for the additional resources required for inpatient and outpatient care are shown for China and the Russian Federation because the NTP budgets reported by those countries include all budgets for inpatient and outpatient care.

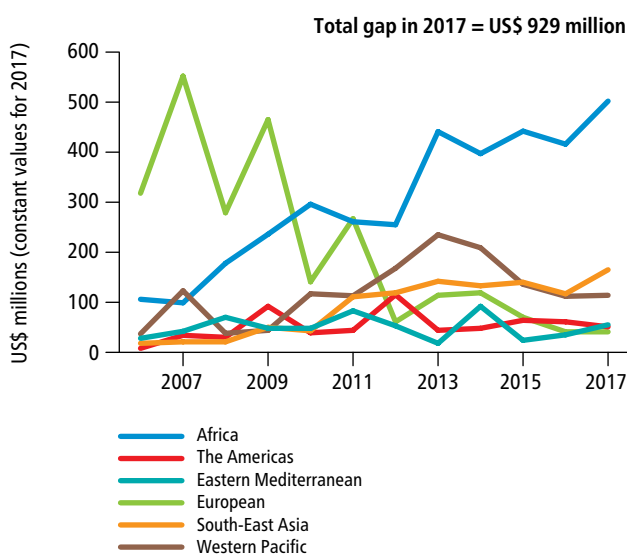
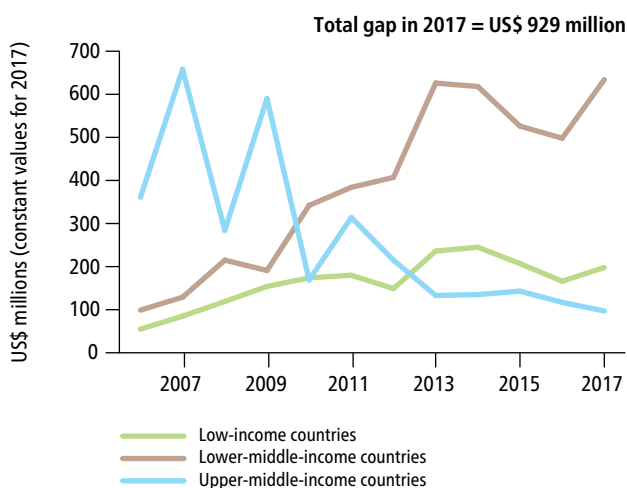
<sup>c</sup> The total budgets reported for staff and infrastructure costs were allocated to DS-TB (52%) and MDR-TB (48%) by WHO, based on the reported proportion of beddays used by patients with DS-TB and MDR-TB, respectively.

<sup>d</sup> In 2017, the budget reported by Thailand was for the central level only.

**FIG. 6.8**  
National budget for TB and sources of funding in India, 2006–2017



**FIG. 6.9**  
Reported funding gaps for TB by income group and by WHO region, 2006–2017



cost was accounted for by reported NTP expenditures, with the remainder being inpatient and outpatient care. There was a positive relationship between the cost per patient treated and gross domestic product (GDP) per capita, and a negative relationship with the size of the patient case-load (indicating economies of scale, e.g. in China and India). In 29 of the 30 high TB burden countries included in the analysis, the cost per patient treated for drug-susceptible TB was less than GDP per capita; the exception was Sierra Leone.

The cost per patient treated was typically higher in countries in the WHO European Region. Eastern Europe and Central Asia (EECA) countries have relatively high costs owing to extensive use of hospitalization for patients in the intensive phase of treatment, with hospital admissions averaging 62 days per person. High programme costs relative to a smaller pool of patients also help to explain comparatively high per-patient costs in some countries (e.g. Bosnia and Herzegovina). However, some EECA countries have markedly reduced their reliance on hospitalization and have changed the model of care for patients with drug-susceptible TB. From 2014 to 2016, five of the 12 EECA countries reduced the number of bed days per patient treated for drug-susceptible TB: Armenia (10%), Azerbaijan (47%), Georgia (38%), Kyrgyzstan (33%) and the Russian Federation (66%).

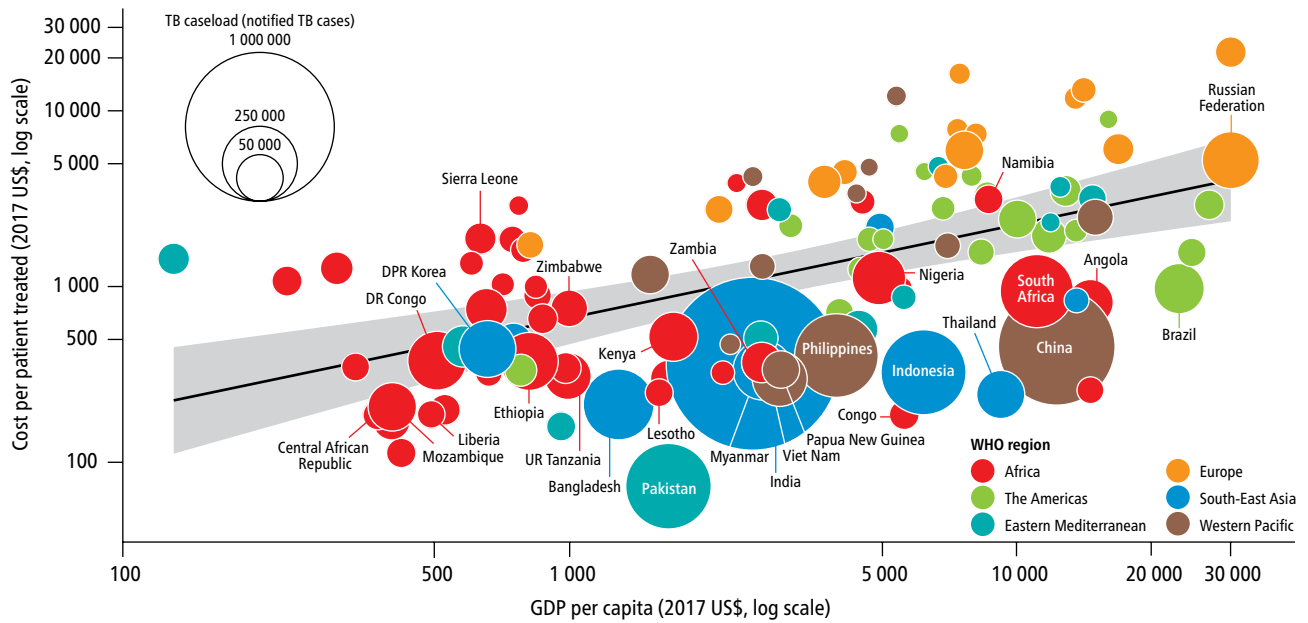
#### 6.4.2 Multidrug-resistant TB

For MDR-TB, the median cost per patient treated was US\$ 9529 in 2016 (Fig. 6.11). As with drug-susceptible TB, the cost per patient treated was positively correlated with GDP per capita. New shortened regimens of 9–12 months cost about US\$ 1000 per person. These regimens have been recommended since 2016 by WHO for patients (other than pregnant women) with rifampicin-resistant or MDR pulmonary TB who do not have resistance to second-line drugs.<sup>1</sup> The uptake of such regimens should contribute to a decrease in the unit cost of treatment for MDR-TB in future.

<sup>1</sup> For further details about this recommendation, see Chapter 1.

**FIG. 6.10**

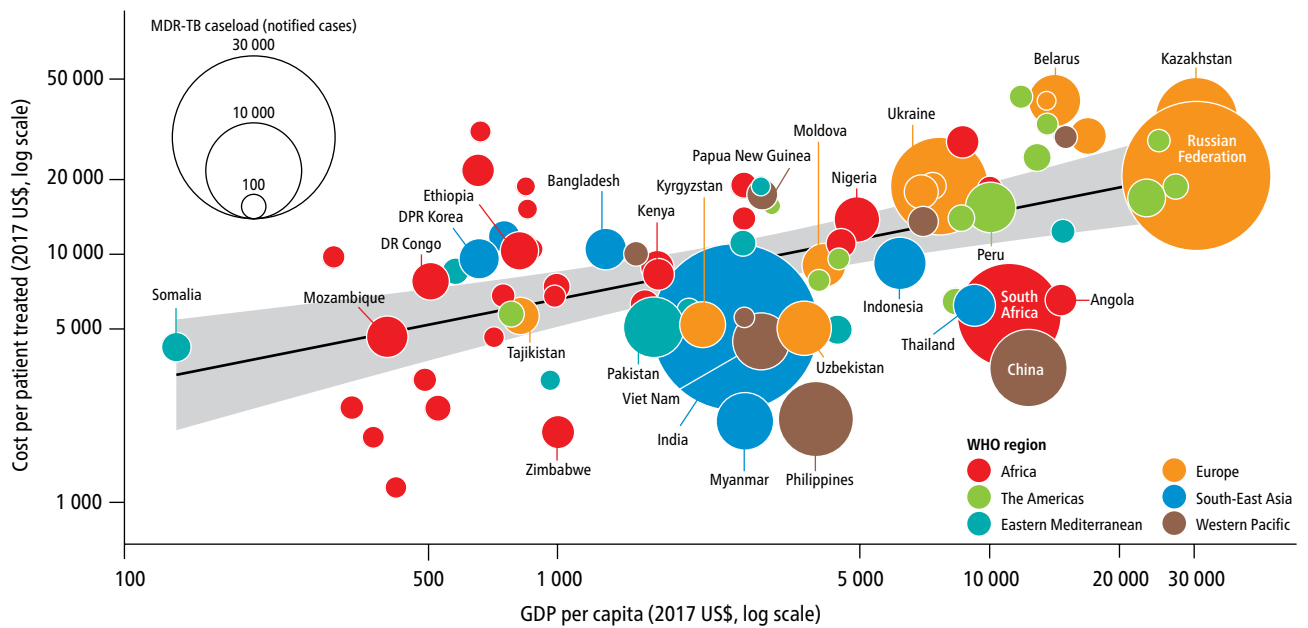
**Estimated cost per patient treated for drug-susceptible TB in 111 countries, 2016<sup>a</sup>**



<sup>a</sup> Limited to countries with at least 100 patients on first-line treatment in 2016.

**FIG. 6.11**

**Estimated cost per patient treated for MDR-TB in 80 countries, 2016<sup>a</sup>**



<sup>a</sup> Limited to countries with at least 20 patients on second-line treatment in 2016.



**BOX 6.3****Methods used to estimate the cost per patient treated for drug-susceptible TB and MDR-TB**

Two main data sources were used to estimate the cost per patient treated for drug-susceptible TB and MDR-TB. The first was the validated expenditure data reported by NTPs that are stored in the WHO global TB database. The second was country-specific estimates of the unit costs of bed days and outpatient visits, available from the WHO-CHOICE model<sup>a</sup> and associated database (managed by the WHO Health Governance and Financing Department). In the few instances in which no expenditure data were reported, information about the total funding available or reported drug expenditure per patient treated was used as a proxy for expenditures.

Costs were calculated separately for drug-susceptible TB and MDR-TB. In each case, the numerator was the total estimated cost of treatment, which has two main parts: the national expenditures reported by the NTP, and the costs associated with the use of health services for TB patients.

As explained in **Box 6.1**, the NTP expenditures of countries are reported annually to WHO using the online WHO global TB data collection system, and are then reviewed and validated. Categories of expenditure considered as costs for MDR-TB were second-line drugs and all other inputs or activities implemented for the programmatic management of MDR-TB. All other categories (except collaborative TB/HIV activities) were assumed to be for drug-susceptible TB. An exception was made for the Russian Federation: expenditures for staff and infrastructure were allocated

by WHO to drug-susceptible TB (52%) and MDR-TB (48%), based on the proportion of bed days used for these two categories of patients.

For most countries, the total costs associated with use of inpatient and outpatient care were calculated using information about the typical number of days of inpatient care and outpatient visits required on a per-patient basis during treatment (reported separately for drug-susceptible TB and MDR-TB by NTPs) combined with WHO-CHOICE unit cost estimates, multiplied by the number of patients treated in a given year (based on notification data; see **Chapter 4**). For 27 countries (including six high burden countries, see **Box 6.1**), TB inpatient and outpatient expenditures available from national health accounts<sup>b</sup> were used instead of the estimated cost from this ingredients-based approach.

Unit costs were then calculated as the sum of 2016 NTP expenditures and total costs for use of inpatient and outpatient care, divided by the reported number of patients treated. Again, this calculation was carried out separately for drug-susceptible TB and MDR-TB.

<sup>a</sup> Cost effectiveness and strategic planning (WHO-CHOICE): health service delivery costs. Geneva: World Health Organization; 2008 ([http://www.who.int/choice/cost-effectiveness/inputs/health\\_service/en/](http://www.who.int/choice/cost-effectiveness/inputs/health_service/en/), accessed 13 July 2017).

<sup>b</sup> Health accounts. Geneva: World Health Organization; data shared by WHO Health Governance and Financing Department on 11 July 2017.



## Urbanization in Rio de Janeiro, Brazil

MIHAI ANDRITOIU / ALAMY STOCK PHOTO

## CHAPTER 7.

# Universal health coverage, social protection and social determinants

### ■ KEY FACTS AND MESSAGES ■

Achieving the tuberculosis (TB) targets and milestones of the Sustainable Development Goals (SDGs) and End TB Strategy requires provision of TB care and prevention within the broader context of universal health coverage (UHC) and multisectoral action to address the social and economic determinants and consequences of TB.

In 2017, WHO published estimates of the funding required for progress towards UHC in low- and middle-income countries during the period 2016–2030 and compared these with projections of total health expenditures. Overall, these estimates and projections suggest that most middle-income countries can mobilize the resources required to make progress towards UHC and reach other SDG-related health targets by 2030, but that low-income countries are unlikely to have the resources to do so. Improved revenue generation and management of public expenditures as well as increased public health budgets are needed.

In most high TB burden countries, out-of-pocket expenditures account for a high proportion (>30%) of total health expenditures. Increasing the share of financing that is derived from compulsory prepaid sources and pooled to spread risk across the population is critical to reduce the financial hardships arising from out-of-pocket expenditures and enable access to care. In addition, funds must then be directed to priority services and populations through the mechanisms used to pay providers.

Results from surveys of costs faced by TB patients and their households reveal a high economic and financial burden due to TB disease. Some of the main cost drivers could be reduced or eliminated through improved models of care, while others require use of new tools and social support. Most high TB burden countries have national policies that provide the foundation for expanding social protection, including cash transfer programmes for some poor and vulnerable populations; finding ways to link TB patients into these schemes is important.

WHO has developed a TB-SDG monitoring framework of 14 indicators that are associated with TB incidence, under seven SDGs. Examples include levels of poverty, income inequality, housing quality, undernourishment, coverage of social protection programmes, coverage of essential health services, HIV prevalence, smoking and diabetes. Monitoring of these indicators can be used to identify key influences on the TB epidemic at national level and inform the multisectoral actions required to end the TB epidemic. Analysis of these indicators for the 30 high TB burden countries shows that most have major challenges ahead to reach SDG targets.

Of the 10.4 million incident cases of TB globally in 2016, an estimated 1.9 million were attributable to undernourishment, 1.0 million to HIV infection, 0.8 million to smoking and 0.8 million to diabetes.

The End TB Strategy and the Sustainable Development Goals (SDGs) include a common aim: to end the global TB epidemic. Specific targets set in the End TB Strategy include a 90% reduction in TB deaths and an 80% reduction in TB incidence (new cases per year) by 2030, compared with 2015; more immediate milestones for 2020 are reductions of 35% and 20%, respectively. As highlighted elsewhere in this report, in particular in [Chapter 2](#), achieving these targets requires provision of TB care and prevention within the broader context of universal health coverage (UHC), multisectoral action to address the social and economic determinants and consequences of TB, and a technological breakthrough by 2025 so that incidence can fall faster than rates achieved historically.

This chapter has three major sections. The first provides an overview of estimates of the resources required for progress towards UHC and achievement of other SDG-related health targets during the period 2016–2030, published by WHO in 2017. The second section summarises recent data for indicators related to UHC, including levels of out-of-pocket (OOP) expenditures on health and costs borne by TB patients and their households as a result of TB disease. Implications for improving financing, TB care delivery, and social protection measures that could help to alleviate these burdens, and examples of efforts to better plan for the financing and policy changes needed at country level to reach UHC, are discussed. The third section includes estimates of the share of the global TB burden in 2016 that can be attributed to five major determinants of the TB epidemic (undernutrition, HIV infection, alcohol misuse, smoking and diabetes), and an assessment of the latest status of these and other indicators associated with TB incidence in the 30 high TB burden countries based on the TB-SDG monitoring framework defined in [Chapter 2](#).

## 7.1 UHC financing prospects, 2016–2030

SDG Target 3.8 is to “Achieve UHC, including financial risk protection, access to quality essential healthcare services and access to safe, effective, quality and affordable essential medicines and vaccines” ([Chapter 2](#)).<sup>1</sup> UHC means that all people and communities can use the promotive, preventive, curative, rehabilitative and palliative health services they need, of sufficient quality to be effective, while also ensuring that the use of these services does not expose the user to financial hardship.

In 2017, WHO published estimates of the resources needed during the period 2016–2030 to make progress towards UHC and reach other SDG-related health targets,<sup>2</sup> and compared

these with projected total health expenditures in the same time period. Referred to in shorthand as the *WHO SDG Health Price Tag*,<sup>3</sup> the estimates are for 67 low- and middle-income countries that account for 75% of the world’s population and focus on the additional (or incremental) resources needed compared with levels in 2014. Two scenarios were considered for resource needs (termed “progress” and “ambitious”) and two scenarios (referred to as “moderate” and “optimistic”) were also considered for total health expenditures.

Key findings include:

- In the “ambitious” scenario for resource needs (based on achievement of 2030 SDG targets), the additional investment (compared with 2014) required per year grows from US\$ 134 billion in 2016 to US\$ 371 billion (equivalent to an extra US\$ 58 per person) in 2030.
- Most of the increased investment required (75% of the total) is for expanding and strengthening the health workforce and health services infrastructure (including buildings and medical equipment) to reach recommended benchmarks. The remainder is for specific priorities, including TB. The largest share of investments needed for specific diseases or programmes is accounted for by noncommunicable diseases (NCDs).
- Overall, health expenditure is projected to be sufficient to cover “ambitious” scenario investment needs in middle-income countries. However, there is uneven capacity to mobilize additional resources and some countries are expected to face gaps, especially in the first few years. In the period 2026–2030, an average of five out of the 39 middle-income countries included in the analysis are predicted to face funding gaps.
- Overall, projected health expenditure is not sufficient to cover investment needs in low-income countries.
- Improved revenue generation and management of public expenditures as well as increased public health budgets are needed, in both low and middle-income countries.

Further analyses based on the *WHO SDG Health Price Tag*, focusing on comparisons of total (as opposed to incremental) investment needs with projections of total health expenditures, are shown in [Fig. 7.1](#), [Fig. 7.2](#) and [Fig. 7.3](#). These illustrate the same key messages in terms of the extent to which the resources needed to achieve UHC and other SDG-related health targets can be mobilized in low and middle-income countries. In addition, they indicate that total funding needs as a percentage of gross domestic product (GDP) would rise from 5.6% in 2014 to 7.5% by 2030 across all 67 countries ([Fig 7.2](#)), with a much greater increase needed in low-income countries (from an average of 6% in 2014 to around 12% by 2024). By 2030, total average health spending would need

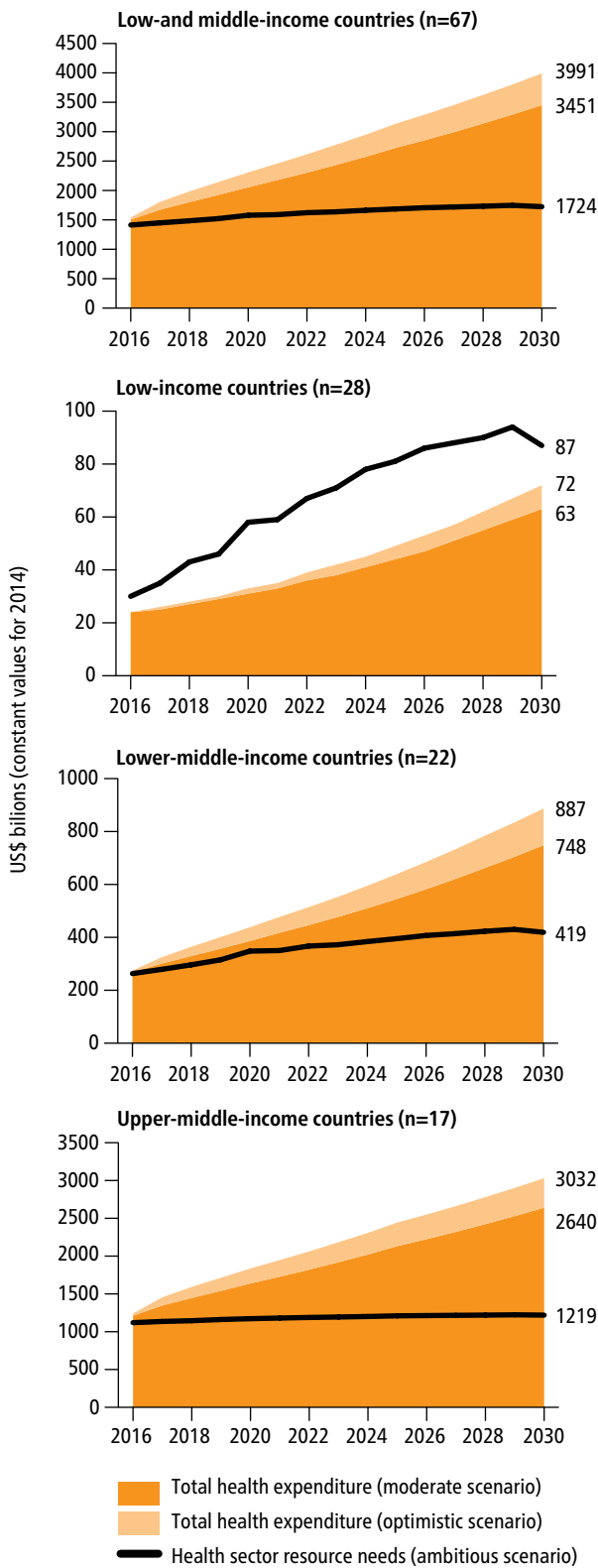
<sup>1</sup> Two indicators have been defined for Target 3.8. The first is the coverage of essential health services; this is a composite indicator that includes TB treatment coverage as one of 16 tracer indicators. The second is the proportion of the population with large household expenditures on health as a share of total household expenditure or income. Methods to calculate the first indicator are under development. WHO will publish data related to these UHC indicators on UHC day 2017 (in December); these data will be available at <http://apps.who.int/gho/cabinet/uhc.jsp>

<sup>2</sup> One of these is the target of ending the TB epidemic, which is included as part of SDG Target 3.3.

<sup>3</sup> Stenberg K, Hanssen O, Tan-Torres Edejer T et al. Financing transformative health systems towards achievement of the health Sustainable Development Goals: a model for projected resource needs in 67 low-income and middle-income countries. (published online July 17) *Lancet Glob Health*. 2017; [http://dx.doi.org/10.1016/S2214-109X\(17\)30263-2](http://dx.doi.org/10.1016/S2214-109X(17)30263-2)

**FIG. 7.1**

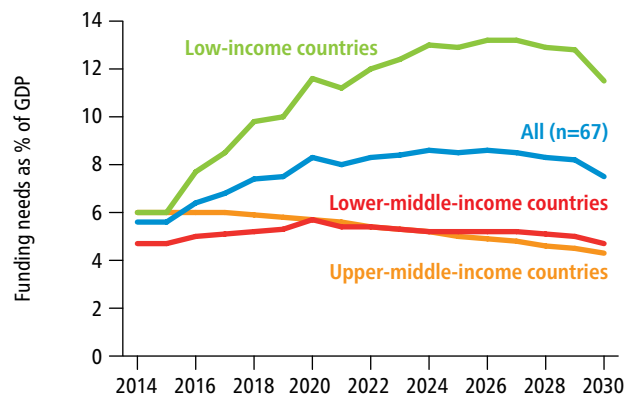
**Funding needs to progressively expand services towards UHC and reach other SDG health targets in 67 low-and middle-income countries compared with projected total health expenditures, 2016–2030**



Source: Data from Stenberg K, Hanssen O, Tan-Torres Edejer T et al. Financing transformative health systems towards achievement of the health Sustainable Development Goals: a model for projected resource needs in 67 low-income and middle-income countries. Lancet Global Health 2017; 5: e875–87.

**FIG. 7.2**

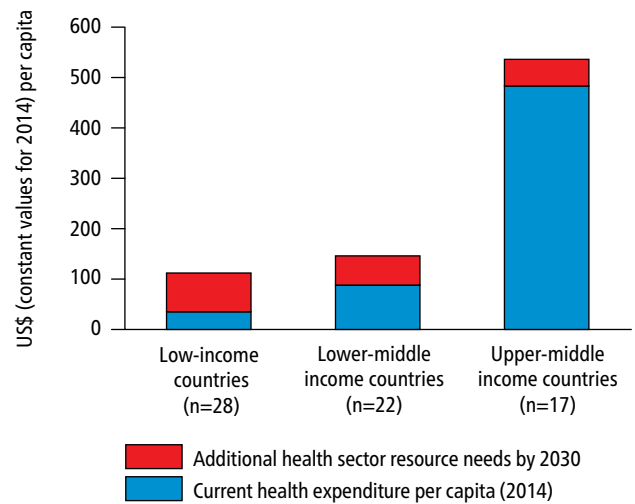
**Funding needs (as a percentage of projected GDP) to progressively expand services towards UHC and reach other SDG health targets in 67 low-and middle-income countries, 2016–2030**



Source: Data from Stenberg K, Hanssen O, Tan-Torres Edejer T et al. Financing transformative health systems towards achievement of the health Sustainable Development Goals: a model for projected resource needs in 67 low-income and middle-income countries. Lancet Global Health 2017; 5: e875–87.

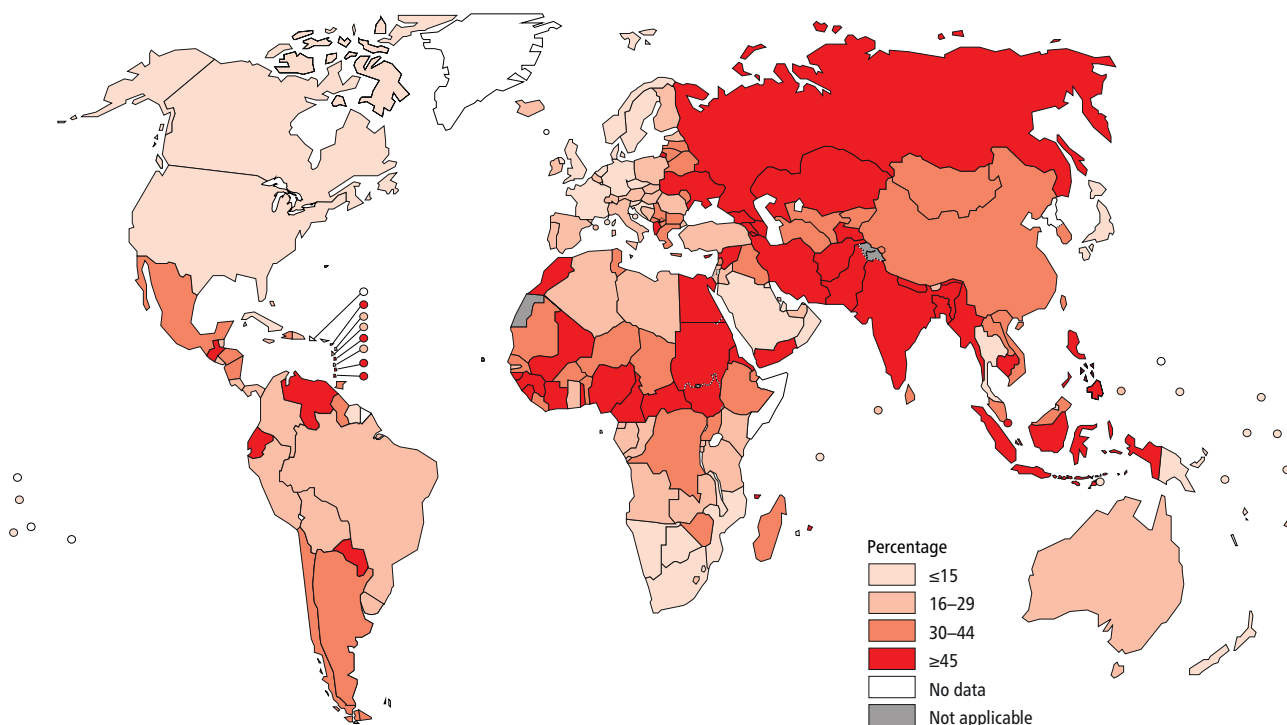
**FIG. 7.3**

**Funding needs (per capita) to progressively expand services towards UHC and reach other SDG health targets by 2030, by country income group<sup>a</sup>**



<sup>a</sup> Income groups are defined as of July 2016. Per person health costs are reported as population-weighted mean values per income group per year.

Source: Data from Stenberg K, Hanssen O, Tan-Torres Edejer T et al. Financing transformative health systems towards achievement of the health Sustainable Development Goals: a model for projected resource needs in 67 low-income and middle-income countries. Lancet Global Health 2017; 5: e875–87.

**FIG. 7.4****Out-of-pocket expenditure as a percentage of total health expenditure, 2014<sup>a</sup>**

<sup>a</sup> Data for 2015 will be available in December 2017.

Source: Data extracted from WHO's Global Health Expenditure Database (<http://apps.who.int/nha/database/Home/Index/en>).

to increase to US\$ 112 per capita in low-income countries, US\$ 146 per capita in lower-middle-income countries and US\$ 536 per capita in upper-middle income countries (Fig. 7.3).

## 7.2 Reducing financial hardship and increasing social protection

### 7.2.1 Out-of-pocket expenditures and financial hardship

UHC requires that people can access needed services without suffering financial hardship. The percentage of total health expenditure accounted for by OOP expenditure provides a proxy measure of the extent to which financial protection is in place.

In 2014,<sup>1</sup> OOP expenditures were less than 15% of total health spending in 44 of the 190 countries for which data were available, including high TB burden countries such as Namibia, South Africa and Thailand (Fig. 7.4). However, there were 46 countries in which OOP expenditures accounted for at least 45% of total health expenditures. This included 11 high TB burden countries: Bangladesh, Cambodia, Central African Republic, India, Indonesia, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation and Sierra Leone.

<sup>1</sup> The latest year for which data are available; WHO will report on updated data in December 2017.

### 7.2.2 National surveys of costs faced by TB patients and their households

As introduced in the *Global TB report 2016*, WHO aims to annually report on results from national surveys of costs faced by TB patients and their households. These surveys have two primary objectives:

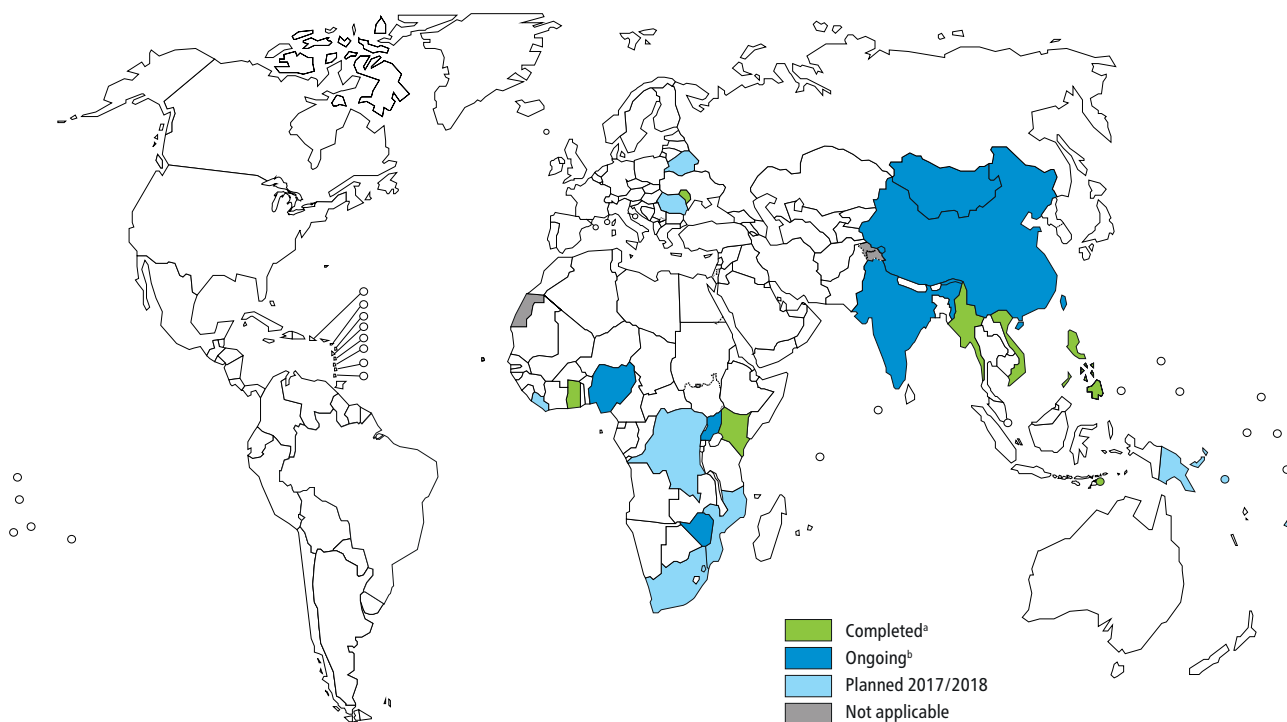
- to document the magnitude and main drivers of different types of costs incurred by TB patients (and their households), in order to guide policies to reduce financial barriers to accessing care and minimize the adverse socioeconomic impact of TB; and
- to determine the baseline and periodically measure the percentage of TB patients (and their households) treated in the national TB programme (NTP) network who incur catastrophic total costs due to TB. This information is needed to monitor progress towards one of the three high-level indicators of the End TB Strategy for which targets and milestones have been set (Chapter 2).

The distinction between the indicator of catastrophic total costs due to TB disease and the broader indicator of catastrophic expenditures on health is explained in Box 7.1.

WHO recommends conducting a baseline survey by 2020 at the latest. Findings are needed to inform the improved design or implementation of care and to assess whether the

**FIG. 7.5**

**National surveys of costs faced by TB patients and their households: progress and plans as of August 2017**



<sup>a</sup> At least field work has been completed.

<sup>b</sup> Subnational surveys are ongoing in Bolivia (Cochabamba) and Brazil (Sao Paulo).

**BOX 7.1**

**The difference between “catastrophic total costs” for TB patients and their households, and catastrophic expenditures on health**

It is important to distinguish the indicator of catastrophic total costs due to TB from the indicator of catastrophic expenditures on health being used within the SDG monitoring framework and in regional frameworks for UHC. The latter is a population-based indicator that measures the share of the population incurring “catastrophic expenditures” on health, with a threshold defined based on household ability to pay. Expenditures are defined as direct expenditures on medical care. The TB-specific indicator incorporates not only direct medical payments for diagnosis and treatment but also direct non-medical payments (such as for transportation and lodging) and indirect costs (such as lost income). The TB-specific indicator is also restricted to a particular population: diagnosed TB patients treated by providers that are part of NTP networks.

2020 milestone of the End TB Strategy (that no TB patients and their households should face catastrophic total costs due to TB) is achieved.<sup>1</sup> Social protection programmes are one mechanism that can help to mitigate costs.

WHO developed a draft protocol and survey instrument for the conduct of these nationally-representative and

health-facility-based surveys in 2016.<sup>2</sup> By early 2018, a WHO handbook for conducting these surveys will be available, and will include an updated protocol. This handbook builds on lessons learned from surveys implemented 2015–2017 and

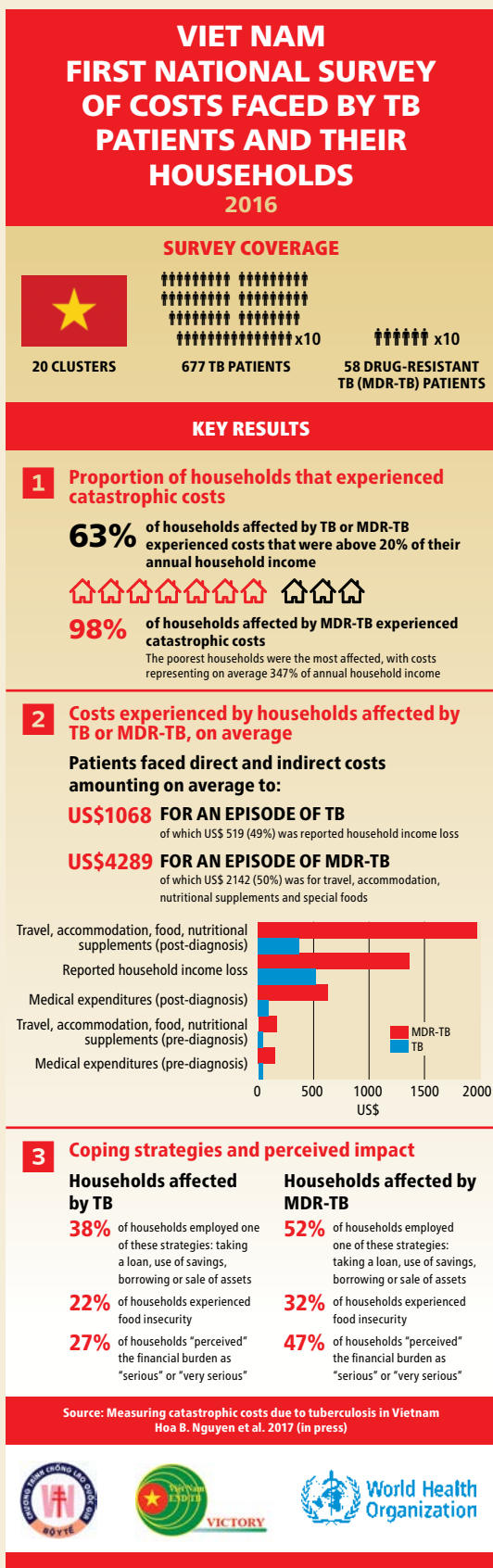
<sup>1</sup> This target is in line with policy efforts to move health systems closer to UHC, because access to TB prevention and care requires that general barriers to accessing health care are addressed.

<sup>2</sup> World Health Organization. Protocol for survey to determine direct and indirect costs due to TB and to estimate proportion of TB-affected households experiencing catastrophic costs due to TB: field testing version. Geneva: WHO; 2015 ([http://www.who.int/tb/advisory\\_bodies/impact\\_measurement\\_taskforce/meetings/tf6\\_background\\_5a\\_patient\\_cost\\_surveys\\_protocol.pdf](http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/tf6_background_5a_patient_cost_surveys_protocol.pdf), accessed 2 August 2017).

**BOX 7.2**

## Measuring costs faced by TB patients and their households in Viet Nam

From July to October 2016, the NTP in Viet Nam worked with the Viet Nam Integrated Center for TB and Respiratory Research (VICTORY), a Vietnamese research network, to conduct the first national survey of costs faced by TB patients and their households. Viet Nam is a lower-middle-income country and is one of the 30 high TB burden countries. This was the second national survey in which the WHO-recommended protocol was applied, following a survey in Myanmar in 2016.



The cross-sectional public-facility-based survey involved 735 patients with either drug-susceptible or MDR-TB who were receiving treatment in health facilities across 20 clusters. The instrument included questions on costs, time losses, coping measures and asset ownership. Total costs were expressed as a percentage of annual household income, and if they exceeded 20% of household income the household was classified as "experiencing catastrophic total costs".

Survey results (see infographic) suggested that, in Viet Nam, an estimated 63% of TB-affected households and 98% of the households of patients with MDR-TB experienced total costs that were catastrophic. On average, the cost was US\$ 1068 for an episode of drug-susceptible TB and US\$ 4289 per episode of MDR-TB. The most important cost drivers were reported income losses and non-medical costs after diagnosis. Significant predictors for experiencing catastrophic costs were being in the poorest or less poor household wealth quintiles.

Using the results of this baseline survey, Viet Nam's NTP has defined a roadmap (2017–2020) involving non-health actors to address access barriers and an operational research plan. A commitment to periodically monitor TB patient costs has also been made. Subsequently, a stakeholders' meeting to review survey results and refine the elements of the roadmap and the monitoring and evaluation framework was held. Participants included representatives from the social protection department of the Ministry of Labour-Invalids and Social Affairs (MOLISA); the Ministry of Health (MoH) departments of planning and finance, medical services administration, international cooperation and health strategy; the Farmer's Union; the Women's Union; WHO; VICTORY; former TB patients; and local and international research institutions.

The roadmap aims to enable policy guidance and interventions to reduce and compensate for costs faced by TB patients and their households. It includes the development and costing of a package of ambulatory TB services to be explored for inclusion in the new National health insurance (NHI) scheme, and advocating for donor support for TB-specific patient social support. Other elements are the launch of a charity fund for TB patients that can be used for purchasing of health insurance cards for the poor; providing travel vouchers, food packages or cash; and developing a roadmap for how the MoH can collaborate with MOLISA to:

- scale up and adapt for TB patients the existing mechanism to purchase health insurance cards for the poor;
- enable access to other social protection schemes and adapt them to the needs of TB patients;
- assess additional financial and human resource needs;
- train health service staff in social protection practices, and social service staff in TB issues; and
- monitor and evaluate initiatives.

A MOLISA pilot on social protection for MDR-TB patients will be assessed. MOLISA will also be engaged to assess and strengthen current regulations for workers' protection, and to use existing and new research platforms to test new approaches to reduce patient costs.



advice provided by a WHO TB Patient Cost Task Force. The *Global TB report 2016* included results from the first national survey using the WHO protocol, which was conducted in Myanmar (2015–2016).

The status of survey planning and implementation as of August 2017 is shown in **Fig. 7.5**. Seven surveys had been completed, in Ghana, Kenya, Myanmar, the Philippines, Republic of Moldova, Timor Leste and Viet Nam, with results in the process of being analysed, reviewed by national stakeholders and prepared for publication. Six surveys were ongoing and ten are scheduled to start later in 2017 or in 2018. It is anticipated that several additional countries will start planning surveys in 2018.

A profile of the survey conducted in Viet Nam in 2016 is provided in **Box 7.2**. The findings are similar to those in Myanmar, demonstrating that a high proportion of TB patients are experiencing catastrophic total costs as a result of TB (using a threshold of costs representing more than 20% of household income<sup>1</sup>). The findings also suggest that people with multidrug-resistant TB (MDR-TB) face a particularly serious burden, and that some of these costs could be reduced through improved (more patient-centred) models of care and adoption of new tools, while others indicate a need for social assistance and other forms of social protection.

### 7.2.3 Establishing or strengthening national social protection schemes

TB patient cost surveys and related studies show that TB patients and their households can face debilitating and often catastrophic total costs due to TB disease, related to indirect costs such as income loss, direct medical costs, transport or food costs. The second pillar of the End TB Strategy (bold policies and systems) includes the pursuit of social protection for TB patients and their households. In addition, WHO guidance on the treatment of drug-susceptible and drug-resistant TB highlights evidence that economic and social support is associated with improved treatment results.

The *Global TB report 2016* and the WHO guide to implementing the End TB Strategy<sup>2</sup> included examples (e.g. in Brazil, India and the Philippines) of general social protection systems, including cash transfer programmes for poor and vulnerable populations. In these countries and many others, TB-specific social support projects are in place to assist patients, for example by providing food, cash, vouchers, or other economic or psycho-social support. Both publications also signaled the need to explore more efficient, systematic and possibly more sustainable approaches through establishment of linkages with existing social assistance efforts.

In part stimulated by the adoption of the International Labour Organization (ILO) recommendation on social protec-

tion floors in 2012,<sup>3</sup> and collaboration with other institutions including the World Bank, WHO and the United Nations Children's Fund (UNICEF), many low and middle-income countries have started to expand their social protection systems, with a focus on basic services, social assistance or social insurance, and labour programmes, and with particular attention to the needs of low-income populations.

Based on available documentation compiled by the WHO Global TB Programme for policy briefs on social protection systems in high TB burden countries,<sup>4</sup> **Table 7.1** shows the basic components of social protection policy and cash transfer schemes that exist in the 30 high TB burden countries. The focus is on three major elements of social protection schemes that may be of substantial relevance to efforts to improve social protection for TB patients and households specifically: the existence of overall policy, strategy or legislative frameworks; a register of target populations or beneficiaries; and some level of coverage of cash transfers for specific poor or vulnerable populations or disabled persons.

Of the 30 high TB burden countries, 26 have a policy document, strategy or relevant legislation for social protection, and most have some form of cash transfer system. Data on coverage levels are not easy to obtain, but coverage in many countries remains low and fragmented.<sup>5</sup> Nevertheless, these initiatives are increasingly backed by domestic policies, they are managed by administrative authorities or agencies, they have some operational experience and financing, and they are likely more systematic than most TB-specific social support projects. They also indicate collaboration between ministries of health and social protection agencies. Stakeholder workshops to discuss the results from surveys of costs faced by TB patients and their households offer an opportunity to engage across ministries and with nongovernmental partners on ways to provide social protection for TB patients, as well as to define research that may be required to inform these efforts.

### 7.2.4 Improving patient access through tailored provider payment mechanisms

Increasing the share of financing that is derived from compulsory prepaid sources and pooled to spread risk across the population is critical to reduce the financial hardships arising from out-of-pocket expenditures and enable access to care. However, increasing such pooled funding alone is not sufficient; the funds must then be directed to priority services and populations through the mechanisms used to pay providers.

The *Global TB report 2016* provided examples of compulsory prepayment and pooling to spread risk within the

<sup>1</sup> Further explanation and justification of this threshold is provided in the forthcoming WHO handbook on surveys of costs faced by TB patients and their households.

<sup>2</sup> World Health Organization. Implementing the End TB Strategy: the essentials (WHO/HTM/TB/2015.31). Geneva: WHO; 2015 ([http://www.who.int/tb/publications/2015/end\\_tb\\_essential.pdf?ua=1](http://www.who.int/tb/publications/2015/end_tb_essential.pdf?ua=1)).

<sup>3</sup> International Labour Organization. R202 – Social Protection Floors Recommendation, 2012 (no. 202), Adoption: Geneva, 101st ILC session (14 June 2012).

<sup>4</sup> WHO. Global TB Programme Country Social Protection Briefs ([www.who.int/tb/areasofwork/socialprotection/en](http://www.who.int/tb/areasofwork/socialprotection/en)).

<sup>5</sup> See World Health Organization. Report from the first consultation of the Health and Social Protection Action Research & Knowledge Sharing (SPARKS) Network (WHO/HTM/TB/ 2017.10). 2017 (<http://www.who.int/tb/publications/sparksreport/en/>).

## BOX 7.3 ■ Provider payment for TB care under PhilHealth, the Philippines NHI programme<sup>a,b,c</sup>

PhilHealth, the Philippines' NHI programme, has made important contributions to health service delivery, including for TB. The benefit package for TB care (referred to within PhilHealth as the DOTS package) includes reimbursement for elements of TB care delivery (such as follow-up testing once TB patients are diagnosed, consultation services and health education and counselling during treatment) delivered by accredited providers and TB drugs are provided by the NTP. PhilHealth reimburses health facilities and providers for providing TB services with a case-based payment mechanism, comprising a flat-rate payment for new and retreatment cases of drug-susceptible pulmonary and extra-pulmonary TB in children and adults. Reimbursement is provided in two payments – an initial payment after the accredited facility has finished provision of the intensive phase of TB treatment (2 months); and a second payment at the end of the continuation phase (4 months). To be eligible for TB benefits, a PhilHealth member must have TB disease based on the diagnostic criteria defined by the NTP and the care must be managed by an accredited TB care facility. The patient must be an active PhilHealth member, meaning that the person is registered, with qualifying contributions.

Managing the benefit package through PhilHealth has required strengthening processes in areas such as accreditation, administration of TB care benefits, regulation and coordination, patient information and private sector engagement.

Despite substantial achievements, measures still need to be taken, in particular, to streamline the care and accreditation process and, as a consequence, increase the number of accredited TB care centres accessible to patients and the number of patients using the PhilHealth TB benefits. Sometimes, there are also difficulties in enabling reimbursement of providers, because payments made to local government units are not always then passed along to the facilities or providers that had provided the services. Furthermore, MDR-TB treatment is not yet included in the benefits package, which is a significant limitation, given that the Philippines is a high MDR-TB burden country. Work is underway to resolve each of these challenges.

<sup>a</sup> USAID TB CARE II Project Synthesis report: inclusion of TB in national insurance programs. United States Agency for International Development (USAID); 2013 (<http://tbcare2.org/sites/tbcare2.org/files/Synthesis%20Report%20on%20Country%20%20Assessments%20on%20TB%20Insurance%20Study%20TB%20CARE%20II%20Final.pdf>, accessed 2 August 2017).

<sup>b</sup> Picazo OF, Gilbert V, Ulep T, et al. A critical analysis of PhilHealth. Discussion paper series. 2015–54. Philippine Institute for Development Studies; 2015. Revised guidelines for the PhilHealth outpatient anti-tuberculosis directly-observed treatment short-course (DOTS) benefit package. PhilHealth Circular, 2014.

<sup>c</sup> Kaiser K, Bredekamp C, Iglesias R. Sin tax reform in the Philippines: transforming public finance, health, and governance for more inclusive development. World Bank Publications. 2016.

health financing systems of several countries that are considered pathfinders in Asia, including those in Indonesia, the Philippines and Thailand. It also commented on related opportunities and challenges for TB care and prevention. One concern in these countries is how public and especially private providers receive payments for services. The private sector dominates health-care provision even in many low-income communities; there can be considerable spending on services that are largely free in the public sector, but are more easily accessible or of perceived higher quality. In such contexts, provider payment systems that include private providers may enable greater access without financial burdens for the users. However, the way providers are enrolled or accredited and then paid can affect the coverage and quality of care, as well as how much users, including TB patients, benefit from low-cost or free care. Therefore, the design and management of provider payment arrangements, as well as benefit packages for TB patients, can affect care and costs. Typically, financing systems that include these mechanisms involve a distinct agency responsible for implementing provider payments, such as a National Health Insurance (NHI) Fund. In such contexts, ensuring that services for TB patients are paid and

care coordinated effectively depends on collaboration among the insurance agency, general health services, public and private providers, and TB programmes within the Ministry of Health.

The PhilHealth NHI Fund in the Philippines was one of the examples profiled in last year's report. An up-to-date summary of TB care provider payment arrangements in place under PhilHealth is provided in [Box 7.3](#).

### 7.3 Addressing broader determinants of the TB epidemic

The influence of various social and economic determinants on the TB epidemic has been long recognized. For example, TB incidence and mortality started to decline in western Europe well before effective drug treatments became available, and the fastest historic rates of decline in TB incidence at national level occurred in the same part of the world during the 1950s and 1960s, when the availability of effective treatments coincided with rapid social and economic development. The links between TB and poverty, social protection, the prevalence of undernutrition, diabetes, HIV, alcohol use, smoking, indoor air pollution and income per capita have been analysed,

**TABLE 7.1**
**Social protection policy and cash transfer schemes in 30 high TB burden countries**

Yes <input checked="" type="checkbox"/> Not identified <input type="checkbox"/>	STRATEGY/POLICY <sup>a</sup>	REGISTRY <sup>b</sup>	TARGETING <sup>c</sup>	
			POOR AND VULNERABLE	DISABLED
Angola	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bangladesh	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Brazil	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Cambodia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Central African Republic	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
China	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
DR Congo	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Congo	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
DPR Korea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ethiopia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
India	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Indonesia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Kenya	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Lesotho	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Liberia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Mozambique	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Myanmar	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Namibia	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Nigeria	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Pakistan	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Papua New Guinea	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Philippines	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Russian Federation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Sierra Leone	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
South Africa	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Thailand	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
UR Tanzania	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Viet Nam	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Zambia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Zimbabwe	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

<sup>a</sup> Strategy/policy indicates whether a national strategy, and/or policy/legislative framework for social protection was identified.

<sup>b</sup> Registry indicates whether a social and/or beneficiary registry system for social assistance programmes is in place.

<sup>c</sup> Targeting indicates whether there are any identified non-contributory cash transfer schemes specifically for poor and vulnerable groups and the disabled. Poor and vulnerable groups include transfers to individuals and households based on socio-economic criteria and may include children, the elderly, poor people with disabilities, and those facing food insecurity; disabled refers to persons having a disability regardless of socio-economic status.

Sources: WHO Global TB Programme Country Social Protection Briefs ([www.who.int/tb/areasofwork/socialprotection/en](http://www.who.int/tb/areasofwork/socialprotection/en)); additional information on registries: The state of social safety nets 2015 (<http://documents.worldbank.org/curated/en/415491467994645020/The-state-of-social-safety-nets-2015>); Social registries for social assistance and beyond: a guidance note & assessment tool (<http://documents.worldbank.org/curated/en/698441502095248081/pdf/117971-REVISED-PUBLIC-Discussion-paper-1704.pdf>).

**TABLE 7.2****TB cases attributable to selected risk factors**

RISK FACTOR	RELATIVE RISK <sup>a</sup>	EXPOSED (MILLIONS IN 2015)	GLOBAL POPULATION ATTRIBUTABLE FRACTION (%)	ATTRIBUTABLE TB CASES (MILLIONS IN 2015)
Undernourishment	3.1 – 3.3	734	18	1.9
HIV infection	22	36	9.4	1.0
Smoking	1.6 – 2.5	1047	7.9	0.83
Diabetes	2.3 – 4.3	460	7.5	0.79
Harmful use of alcohol	1.9 – 4.6	407	4.7	0.49

<sup>a</sup> Source: Lönnroth K, Castro KG, Chakaya JM et al. Tuberculosis control and elimination 2010–50: cure, care, and social development. *Lancet*. 2010 May 22;375(9728):1814–29. The relative risk for HIV infection is based on data from UNAIDS and estimates from this Global TB report.

reviewed or summarized in recent publications (further details are provided in [Chapter 2](#)).<sup>1,2,3,4</sup>

[Table 7.2](#) shows new WHO estimates of the number of incident TB cases that were attributable to selected risk factors. Undernutrition is responsible for nearly twice as many TB cases as HIV, due to the large size of the population affected. A reduction in the risk of developing TB among people latently infected with TB – including by combating these and other risk factors – will be essential to achieve the End TB Strategy milestones and targets. These findings reinforce the grounds for inclusion of social protection, poverty alleviation and action on other determinants of TB under the “bold policies and systems” pillar of the End TB Strategy.

As explained in [Chapter 2](#), in 2017 WHO has developed a TB-SDG monitoring framework that focuses attention on 14 indicators (under seven SDGs) that are associated with TB incidence. Monitoring of these indicators can be used to identify key influences on the TB epidemic at national level and inform the multisectoral actions required to end the TB epidemic.

For SDG 3, the seven indicators selected for monitoring are:

- coverage of essential health services;
- percentage of total health expenditures that are out-of-pocket;
- health expenditure per capita;
- HIV prevalence;
- prevalence of smoking;

- prevalence of diabetes; and
- prevalence of alcohol use disorder.

For SDGs 1, 2, 7, 8, 10 and 11, the seven indicators selected for monitoring are:

- proportion of the population living below the international poverty line;
- proportion of the population covered by social protection floors/systems;
- prevalence of undernourishment;
- proportion of the population with primary reliance on clean fuels and technology;
- GDP per capita;
- Gini index for income inequality;<sup>5</sup> and
- proportion of the urban population living in slums.

Collection and reporting of data for the 14 indicators does not require any additional data collection and reporting efforts by NTPs. Nor does it require data collection and reporting efforts that go beyond those to which countries have already committed in the context of the SDGs. Data are available from global databases, primarily those maintained by the UN, WHO, the World Bank and UNAIDS (for further details, see [Annex 1](#)).

The most recent data for five of the seven SDG 3 (health) indicators are shown for the 30 high TB burden countries in [Table 7.3](#).<sup>6</sup> For all of the indicators shown, a lower level is more desirable.<sup>7</sup>

The most recent data for six of the seven selected SDG indicators beyond SDG 3 are shown in [Fig. 7.6](#), this time for the 23 high TB burden countries for which data for all six indicators were available.<sup>8</sup> In this figure, the outer edge of the hexagon (100) is the ideal value for each indicator. Therefore,

<sup>1</sup> Lönnroth K, Jaramillo E, Williams B, Dye C, Raviglione M. Tuberculosis: the role of risk factors and social determinants. In: Blas E & Kurup A (eds.), *Equity, social determinants and public health programmes*, WHO. 2010 ([http://apps.who.int/iris/bitstream/10665/44289/1/9789241563970\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44289/1/9789241563970_eng.pdf), accessed 2 August 2017).

<sup>2</sup> Lönnroth K, Castro KG, Chakaya JM, Chauhan LS, Floyd K, Glaziou P et al. Tuberculosis control and elimination 2010–50: cure, care, and social development. *Lancet*. 2010;375(9728):1814–1829 (<http://www.sciencedirect.com/science/article/pii/S0140673610604837?via%3Dihub>, accessed 2 August 2017).

<sup>3</sup> Lienhardt C, Glaziou P, Uplekar M, Lönnroth K, Getahun H, Raviglione M. Global tuberculosis control: lessons learnt and future prospects. *Nat Rev Microbiol*. 2012;10(6):407–416 (<https://www.nature.com/nrmicro/journal/v10/n6/full/nrmicro2797.html>, accessed 2 August 2017).

<sup>4</sup> Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Soc Sci Med*. 2009;68(12):2240–2246 (<http://www.sciencedirect.com/science/article/pii/S0277953609002111>, accessed 2 August 2017).

<sup>5</sup> The index can take values between 0 and 1, with 0 representing perfect equality and 1 representing perfect inequality.

<sup>6</sup> Coverage of health services is not included because methods to calculate this indicator are in development; health expenditure per capita is also not shown, but data are included in [Annex 2](#).

<sup>7</sup> The composite indicator of coverage for essential health services was excluded because WHO has not yet published its recommendations for definition and measurement of the indicator.

<sup>8</sup> GDP per capita is not included because it is the only indicator that is not measured on a scale of 0–100. However, the latest value and recent trends in this indicator are shown in the country profiles in [Annex 2](#).

**TABLE 7.3**
**Status of selected SDG 3 indicators, 30 high TB burden countries, latest available year<sup>a</sup>**

COUNTRY	OUT-OF-POCKET HEALTH EXPENDITURE (% OF TOTAL EXPENDITURE ON HEALTH) <sup>b</sup>	HIV PREVALENCE (% OF POPULATION AGED 15–49 YEARS)	SMOKING PREVALENCE (% OF MALE POPULATION AGED ≥15 YEARS)	SMOKING PREVALENCE (% OF FEMALE POPULATION AGED ≥15 YEARS)	DIABETES PREVALENCE (% OF POPULATION AGED ≥18 YEARS)	ALCOHOL USE DISORDERS, 12 MONTH PREVALENCE (% OF POPULATION AGED ≥15 YEARS)
Angola	24	2.2	–	–	4.1	4.9
Bangladesh	67	0.10	40	0.70	8.3	0.80
Brazil	25	0.60	19	11	10	5.6
Cambodia	74	0.60	44	2.8	3.0	4.4
Central African Republic	46	3.7	–	–	6.3	3.1
China	32	–	48	1.8	9.8	4.8
Congo	18	–	43	1.7	6.9	1.7
DPR Korea	–	–	–	–	4.4	2.9
DR Congo	39	0.80	–	–	6.4	4.1
Ethiopia	32	–	8.9	0.50	3.4	2.1
India	62	–	20	1.9	9.3	2.6
Indonesia	47	0.50	76	3.6	6.5	0.80
Kenya	26	5.9	25	2.1	2.4	3.2
Lesotho	16	23	55	0.40	3.9	4.2
Liberia	31	1.1	28	2.4	2.3	4.2
Mozambique	9	11	31	5.9	2.6	2.6
Myanmar	51	0.80	32	6.4	6.8	1.5
Namibia	7	13	39	11	4.2	5.1
Nigeria	72	3.1	17	1.1	2.3	2.1
Pakistan	56	0.10	42	3.0	8.1	0.30
Papua New Guinea	10	0.80	–	–	15	4.6
Philippines	54	0.10	43	8.5	6.9	4.6
Russian Federation	46	–	59	23	9.2	17
Sierra Leone	61	1.3	60	12	2.2	2.7
South Africa	6	19	31	6.5	7.6	5.6
Thailand	12	1.1	41	2.3	7.1	5.0
UR Tanzania	23	4.7	28	3.8	4.1	5.5
Viet Nam	37	0.50	47	1.3	6.0	4.7
Zambia	30	13	27	4.6	4.1	4.4
Zimbabwe	36	15	31	2.1	3.9	5.2

<sup>a</sup> Data sources: SDG indicators database, The World Bank, World Health Organization (see [Annex 1, Table A1.2](#)). Missing values indicate data not available in these data sources.

<sup>b</sup> Out of pocket expenditure is any direct outlay by households, including gratuities and in-kind payments, to health practitioners and suppliers of pharmaceuticals, therapeutic appliances, and other goods and services whose primary intent is to contribute to the restoration or enhancement of the health status of individuals or population groups. It is a part of private health expenditure.

better performance corresponds to a larger shaded-in region. To achieve this, the indicators “proportion of the urban population living in slums” and “proportion of the population living below the international poverty line” were inverted.

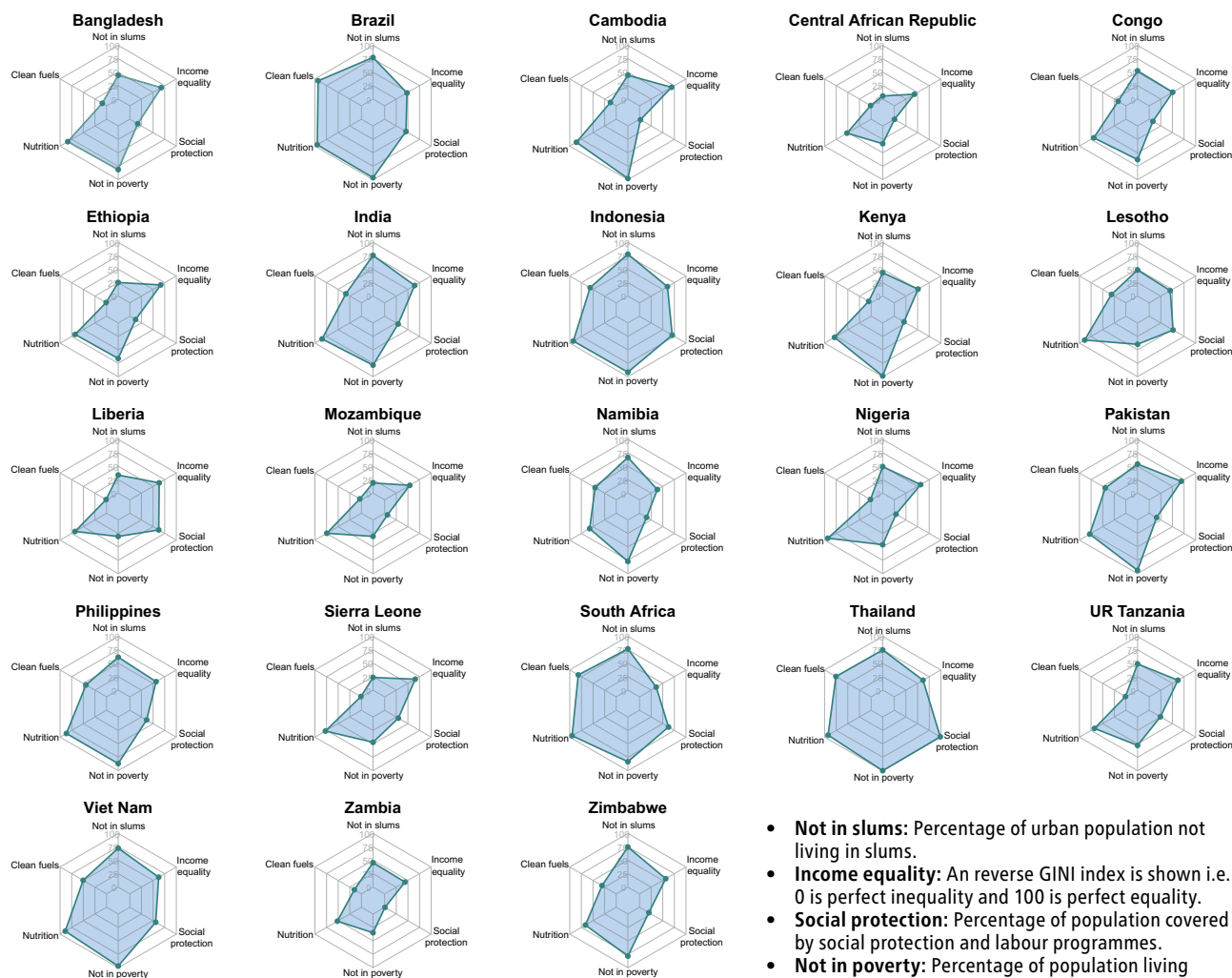
**Table 7.3** and **Fig. 7.6** show that many high TB burden countries, especially those in the low-income category, still face significant challenges to achieve a range of TB-related SDG targets. It is also important to highlight that values for poor populations and vulnerable groups most at risk of developing TB are likely to be worse than national averages. Examples of high TB burden countries doing relatively well

in terms of at least some of the indicators include Brazil, Indonesia, South Africa, Thailand and Viet Nam.

Monitoring of all 14 indicators should stimulate more exploration of the factors affecting progress, interrelationships between indicators and resulting actions needed. This is one of the reasons why the country profiles for high TB burden countries contained in **Annex 2** include, for the first time in 2017, a full page showing the status of and recent trends in indicators included in the TB-SDG monitoring framework.

**FIG. 7.6**

**Status of selected SDG indicators beyond SDG 3 in selected high TB burden countries, latest available year<sup>a</sup>**



- **Not in slums:** Percentage of urban population not living in slums.
- **Income equality:** An reverse GINI index is shown i.e. 0 is perfect inequality and 100 is perfect equality.
- **Social protection:** Percentage of population covered by social protection and labour programmes.
- **Not in poverty:** Percentage of population living above the international poverty line.
- **Nutrition:** Percentage of population not undernourished.
- **Clean fuels:** Percentage of population with access to clean fuels and technologies for cooking.

<sup>a</sup> Data are shown for the high TB burden countries that had at least one data point for all six indicators (23 of the 30 countries). Source: World Bank Sustainable Development Goals Database (<http://datatopics.worldbank.org/sdgs/>).





**A child receives her daily TB medication in New Delhi, India**

ANDREW AITCHISON / ALAMY STOCK PHOTO



## CHAPTER 8.

# TB research and development

### KEY FACTS AND MESSAGES

“Intensified research and innovation” is the third pillar of the End TB Strategy.

The diagnostic pipeline is relatively stagnant. Few technologies emerged in 2017 and several have not demonstrated adequate performance in field evaluation studies.

The next-generation Xpert® MTB/RIF Ultra cartridge has been found to have significantly better performance (increased sensitivity) than the Xpert MTB/RIF cartridge for the detection of *Mycobacterium tuberculosis*. Following review of the evidence by an expert group, WHO recommendations for the use of Xpert MTB/RIF as the initial diagnostic test for all adults and children with signs and symptoms of TB, and for the testing of selected extrapulmonary specimens (cerebrospinal fluid, lymph nodes and tissue specimens) now also apply to the Ultra cartridge.

The development and evaluation of the GeneXpert Omni® instrument, which is intended as a close-to-care platform that uses either Xpert MTB/RIF or Xpert Ultra cartridges, has been delayed. Field evaluations are scheduled to start in 2018.

There are 17 drugs in Phase I, II or III trials for the treatment of drug-susceptible TB, multidrug-resistant TB (MDR-TB) or latent TB infection (LTBI). These drugs include eight new compounds: delpazolid,

GSK-3036556, OPC-167832, PBTZ169, pretomanid, Q203, SQ109 and sutezolid. Two other drugs, bedaquiline and delamanid, have already received accelerated or conditional regulatory approval based on Phase IIb results. The seven repurposed drugs that are undergoing further testing are clofazimine, linezolid, levofloxacin, moxifloxacin, nitazoxanide, rifampicin (high dose) and rifapentine.

Various combination regimens with new and/or repurposed drugs are in Phase II or Phase III trials.

There are 12 vaccine candidates in clinical trials: nine in Phase II or Phase III, and three in Phase I. They include candidates to prevent the development of TB, and candidates to help improve the outcomes of treatment for TB disease.

WHO continues to promote TB research, based on the Global Action Framework for TB Research that was published in 2015. Particular attention has been given to the development of national TB research networks. Countries that used the framework in 2016–2017 included India, Indonesia, Swaziland and Thailand.

A substantial increase in funding for TB research and development will be needed to achieve the targets set in the End TB Strategy and Sustainable Development Goals.

“Intensified research and innovation” is one of the three pillars of the WHO End TB Strategy.<sup>1</sup> The two main components of this pillar are “discovery, development and rapid uptake of new tools, interventions and strategies” and “research to optimize implementation and impact, and promote innovations” (Chapter 2). Both components are fundamental to achieving the global TB targets set in the End TB Strategy and the Sustainable Development Goals (SDGs). The 2030 targets are a 90% reduction in the TB incidence rate and an 80% reduction in the number of TB deaths compared with levels in 2015; such reductions can only be achieved if there is a major technological breakthrough by 2025, so that the rate at which TB incidence falls can be dramatically accelerated compared with historic levels (Chapter 2). A substantial increase in investment in TB research and development will be needed to achieve such a breakthrough. The Stop TB Partnership’s *Global Plan to End TB, 2016–2020*<sup>2</sup> estimates that about US\$ 2 billion per year is needed

<sup>1</sup> 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/](http://www.who.int/tb/post2015_strategy/en/), accessed 8 August 2016).

<sup>2</sup> The global plan to end TB, 2016–2020. Geneva: Stop TB Partnership; 2015 (<http://www.stoptb.org/global/plan/>, accessed 28 July 2016).

## BOX 8.1 Advancing TB research in the context of the WHO Ministerial Conference on Ending TB in the Era of the SDGs

TB research and development is one of the major topics of the WHO Global Ministerial Conference on Ending TB in the Era of the SDGs, which will be held in the Russian Federation in November 2017. There will be a panel discussion on scientific research and innovations, covering issues such as how to address the persistently large funding gaps for TB research and development, the need for a multisectoral and multidisciplinary

approach to research, how to build institutional capacity at global and national levels, engagement of communities and how to reduce regulatory barriers that affect the speed of uptake of tools. Commitments made in the Ministerial Declaration at the end of the conference will then be taken forward in the lead-up to the United Nations General Assembly high-level meeting on TB in 2018.

during the period 2016–2020, but funding between 2005 and 2015 never exceeded US\$ 0.7 billion per year.<sup>1,2</sup> The urgent need for increased financing for TB research will be one of the topics discussed at the 2017 WHO Global Ministerial Conference on Ending TB in the Era of the SDGs (Box 8.1).

This chapter is not intended as an exhaustive overview of current or recently completed TB research. As in previous global TB reports, it focuses on providing an overview of progress in the development of new TB diagnostics (Section 8.1), drugs (Section 8.2) and vaccines (Section 8.3). This includes presentation and description of the status of the pipelines as of August 2017, based on recent publications, communications with the secretariats of the relevant working groups of the Stop TB Partnership, and discussions with other stakeholders. The last part of the chapter (Section 8.4) discusses the role of multisectoral and multidisciplinary research in optimizing the implementation and impact of available tools and approaches, linked to the WHO Global Action Framework for TB Research that was published in 2015.<sup>3</sup>

### 8.1 New diagnostics for TB

This section starts by providing an overview of the TB diagnostics pipeline, with particular attention to developments in 2017. It then describes diagnostic tests, products and methods related to the detection of TB disease and drug resistance that were reviewed by WHO in 2017, or that are scheduled for evaluation in 2018. Finally, it discusses tests for identification of latent TB infection (LTBI), with particular attention to tests to predict progression from TB infection to active TB disease.

#### 8.1.1 An overview of the diagnostics pipeline

Research and development of new diagnostics for TB appears to be stalling. Only a few technologies successfully emerged from the pipeline in 2017. Rapid and robust point-of-care diagnostics, technologies to reliably detect LTBI and accurate biomarker tests to monitor treatment response remain elusive. This reflects serious underinvestment (especially in basic science) as well as persistent scientific and technical challenges that affect the development of new TB diagnostics.

An overview of the pipeline for TB diagnostics in August 2017 is shown in Fig. 8.1. The list of technologies is not necessarily complete, but does reflect technologies that have been documented in recent reports published by the Treatment Action Group<sup>4</sup> and Unitaid.<sup>5</sup> Technologies under development include tests to detect TB, to detect drug resistance among confirmed TB cases, and to detect TB and drug resistance simultaneously. The pipeline remains similar to the one published in the 2016 edition of the *Global TB report* and highlights the urgent need for new technologies to minimize barriers to health care access, ensure quality testing for difficult-to-diagnose groups, expand the spectrum of drug-susceptibility testing, and reduce costs of diagnostic platforms and their maintenance.

Data on the performance of Cepheid's close-to-care platform – GeneXpert Omni® (Omni) – were expected to be available for WHO evaluation in 2017. Omni is described by the manufacturer as a small, light and durable instrument designed for simultaneous testing for TB and rifampicin-resistant TB using either Xpert® MTB/RIF cartridges or the next-generation Xpert MTB/RIF Ultra cartridges. It is aimed at facilitating wider access to rapid molecular testing for TB and rifampicin resistance in decentralized settings, aided by specific features such as built-in batteries and use of cartridges that incorporate a near-field communication chip to allow cellular transfer of data. The development of Omni

<sup>1</sup> Treatment Action Group (2015). 2015 report on tuberculosis research funding trends, 2005–2014: a decade of data. New York: Treatment Action Group (<http://www.treatmentactiongroup.org/tbrd2015>, accessed 8 August 2017).

<sup>2</sup> The global plan to stop TB, 2011–2015. Geneva: Stop TB Partnership; 2010 (<http://www.who.int/tb/publications/tb-global-plan/en/>, accessed 20 July 2017).

<sup>3</sup> World Health Organization. A global action framework for TB research in support of the third pillar of WHO's End TB Strategy. Geneva: World Health Organization; 2015 (<http://www.who.int/tb/publications/global-framework-research/en/>, accessed 8 August 2017).

<sup>4</sup> Lessem E. The tuberculosis diagnostics pipeline. Treatment Action Group; 2017 (<http://www.pipelinerreport.org/sites/default/files/2017-Pipeline-Report-TB-Diagnostics.pdf>, accessed 16 August 2017).

<sup>5</sup> Unitaid. Tuberculosis – diagnostic technology landscape, 5th edition. Geneva: World Health Organization; 2017 (<https://unitaid.eu/assets/2017-Unitaid-TB-Diagnostics-Technology-Landscape.pdf>, accessed 16 August 2017).

**FIG. 8.1****An overview of progress in the development of TB diagnostics, August 2017<sup>a</sup>**

TECHNOLOGIES IN DEVELOPMENT	TECHNOLOGIES ENDORSED BY WHO	SCHEDULED FOR WHO EVALUATION IN 2018/19
<p><b>Molecular detection of TB and drug resistance</b></p> <ul style="list-style-type: none"> <li>■ Gendrive MTB/RIF ID, Epistem, UK</li> <li>■ Xpert XDR-TB cartridge, Cepheid, USA</li> <li>■ TruArray MDR-TB, Akkoni, USA</li> <li>■ INFINITIMTB Assay, AutoGenomics, USA</li> <li>■ FluoroType XDR-TB assay, Hain Lifescience, Germany</li> <li>■ MeltPro TB assay, Zeesan Biotech, China</li> <li>■ QuantuMDx, POC, UK</li> </ul>	<p><b>Molecular detection of TB and drug resistance</b></p> <ul style="list-style-type: none"> <li>■ Xpert MTB/RIF Ultra for detection of TB and rifampicin resistance in pulmonary, extra-pulmonary and paediatric samples, Cepheid, USA</li> <li>■ Line probe assays for the detection of <i>Mycobacterium tuberculosis</i> (MTB), isoniazid and rifampicin resistance in acid-fast bacilli smear positive sputum or MTB cultures (FL-LPA), Hain Lifescience, Germany and Nipro, Japan</li> <li>■ Line probe assays for the detection of resistance to fluoroquinolones and second-line injectable agents (SL-LPA), Hain Lifescience, Germany</li> <li>■ TB LAMP for detection of TB, Eiken, Japan</li> </ul> <p><b>Nonmolecular technologies</b></p> <ul style="list-style-type: none"> <li>■ Alere Determine TB-LAM, Alere, USA (TB detection in people seriously ill with HIV)</li> <li>■ Interferon gamma release assay (IGRAs) for the diagnosis of latent TB infection (LTBI) Oxford Immunotec, UK, Qiagen, USA</li> </ul> <p><b>Culture-based technologies</b></p> <ul style="list-style-type: none"> <li>■ Commercial liquid culture systems and rapid speciation</li> <li>■ Culture-based phenotypic DST using 1% critical proportion in LJ,7H10,7H11 and MGIT media.</li> </ul> <p><b>Microscopy</b></p> <ul style="list-style-type: none"> <li>■ Light and light-emitting diode microscopy (diagnosis and treatment monitoring)</li> </ul>	<p><b>Molecular detection of TB and drug resistance</b></p> <ul style="list-style-type: none"> <li>■ Molecular technologies for genotypic drug resistance testing (including sequencing technologies)</li> <li>■ FluoroType MTBDR, Hain Lifescience, Germany</li> <li>■ m2000 RealTime MTB System, Abbott, USA</li> <li>■ BD Max MDR-TB, Becton Dickinson, USA</li> <li>■ GeneXpert Omni, Cepheid, USA</li> </ul> <p><b>Radiology</b></p> <ul style="list-style-type: none"> <li>■ Chest X-ray</li> <li>■ Computer aided detection (CAD)</li> </ul>
<p><b>ON THE MARKET (EVIDENCE FOR USE NOT SUBMITTED TO WHO FOR EVALUATION)</b></p> <p><b>Molecular detection of TB and drug resistance</b></p> <ul style="list-style-type: none"> <li>■ iCubate System, iCubate, USA</li> <li>■ Genechip, TB drug resistance array, Capital Bio, China</li> <li>■ EasyNAT TB Diagnostic kit, Ustar Biotechnologies, China</li> <li>■ Truelab/Truenat MTB, Molbio/bigtec Diagnostics, India</li> </ul>		

<sup>a</sup> This is not an exhaustive list of technologies in development but includes all those described in the TAG Tuberculosis Diagnostics Pipeline Report 2017. Lessem E. The Tuberculosis Diagnostic Pipeline. New York. Treatment Action Group 2016 (<http://www.pipelinerreport.org/sites/default/files/2017-Pipeline-Report-TB-Diagnostics.pdf>).

has, however, been delayed. Field evaluations are expected to start in 2018.

Several manufacturers are developing centralized testing platforms suitable for high laboratory throughput. In principle, these should have similar performance to Xpert assays, but with higher throughput and potentially a lower unit cost (per sample tested). Performance data for these platforms have not yet been submitted to WHO for formal review, but examples include:

- The RealTime platform, developed by Abbott. This is already widely used in central laboratories for HIV-1 viral load testing. Assays called RealTime MTB (for detection of TB disease) and RealTime MTB RIF/INH (for detection of resistance to rifampicin and isoniazid) have been developed.
- FluoroType MTBDR, launched by Hain Lifescience in early 2017. This platform detects TB and resistance to rifampicin and isoniazid simultaneously, directly from sputum specimens. The technology is fully automated, from DNA extraction to amplification and detection.
- Platforms being developed by Becton Dickinson and Roche, which are expected to be ready for field evaluation studies in 2018.

The pipeline also includes three commercial technologies intended for use at lower levels of diagnostic systems (as opposed to reference level): Epistem Genedrive (Epistem, United Kingdom); EasyNAT (Ustar Biotechnologies, China); and Molbio TrueNAT (Molbio, India. Performance data for these tests remain limited, and to date only the Epistem Genedrive has undergone a multicentre evaluation in different epidemiological settings. Evidence about the performance of these technologies from well-designed validation studies is needed to enable WHO to review and assess their performance.

### 8.1.2 TB diagnostic tests, products and methods reviewed by WHO in 2017

In 2017, WHO reviewed the next-generation Xpert MTB/RIF Ultra cartridge, critical concentrations for performing drug-susceptibility testing (DST) using phenotypic methods, and products for transporting specimens that could potentially improve the detection of *Mycobacterium tuberculosis* using culture-based and molecular methods. The main outcomes of these reviews are discussed below.

### Xpert® MTB/RIF Ultra cartridge

The Ultra cartridge showed significantly better performance (increased sensitivity) than the current Xpert MTB/RIF cartridge in detecting *M. tuberculosis* in specimens with low numbers of bacilli. This was particularly the case for smear-negative, culture-positive specimens (e.g. those from people living with HIV), extrapulmonary specimens (notably cerebrospinal fluid) and specimens from children. However, the increased sensitivity has been offset by a decrease in specificity, possibly due to the well-described limitations of the reference standard (culture) used as the comparator for both versions of the Xpert cartridge. This reduced specificity may lead to false-positive results for TB disease (compared with culture), with the Ultra assay detecting TB bacilli that are not replicating. The accuracy of the Ultra assay in detecting rifampicin resistance was similar to that of the Xpert cartridge.

Following review of the latest evidence,<sup>1</sup> WHO recommendations for the use of Xpert MTB/RIF<sup>2</sup> as the initial diagnostic test for all adults and children with signs and symptoms of TB, and for the testing of selected extrapulmonary specimens (cerebrospinal fluid, lymph nodes and tissue specimens) now also apply to the Ultra assay.

### Products for transportation of samples

Detection of *M. tuberculosis* and testing for drug resistance are fundamental for accurate diagnosis and treatment of TB. However, they are often hampered by difficulties in transporting and storing samples between remote locations and reference laboratories. Products for transportation of samples that improve the recovery and detection of *M. tuberculosis* and reduce culture contamination rates in the laboratory are highly desirable, as are products that can improve the detection of *M. tuberculosis* using molecular tools.

Four commercial transport products were assessed by WHO in 2017:

- OMNIgene•SPUTUM (DNA Genotek, Ottawa, Canada);
- PrimeStore Molecular Transport Medium (Longhorn Vaccines and Diagnostics, San Antonio, United States of America [USA]);
- FTA card (Whatman, GE Healthcare Life Sciences, Pittsburgh, USA); and
- GENO•CARD (Hain Lifescience GmbH, Nehren, Germany).

The OMNIgene•SPUTUM) product was designed to retain the viability of culture specimens; the other three aim to

improve the molecular yield of specimens without needing to preserve their viability for culture. When compared with untreated specimens transported under ambient conditions, there was insufficient evidence that any of the existing commercial transport products improved the performance of TB diagnostics, largely as a result of poorly-designed studies and significant heterogeneity in the data. Full details are available in the meeting report.<sup>3</sup>

### Critical concentrations for culture-based drug-susceptibility testing

DST is essential to guide the choice of appropriate treatment for a patient, to confirm whether resistance has emerged when a patient does not have a satisfactory response to treatment, and for surveillance of resistance to anti-TB drugs. Culture-based phenotypic DST is the current reference method for *M. tuberculosis*, and relies on the testing of so-called critical concentrations of drugs, i.e. the lowest concentration of an anti-TB drug that will inhibit the growth of at least 95% of wild-type strains of *M. tuberculosis*.

In 2017, WHO commissioned a systematic review of studies on culture-based DST results for second-line anti-TB drugs. The main outcomes were changes to the critical concentrations for the fluoroquinolones and the establishment of interim critical concentrations for bedaquiline and delamanid.<sup>4</sup>

### 8.1.3 TB diagnostic tests, products and methods that may be evaluated by WHO in 2018

In 2018, there may be sufficient data for WHO to review the performance of centralized high-throughput testing platforms, the use of molecular sequencing as a reference standard for DST, and tests for extensively drug-resistant TB (XDR-TB).<sup>5</sup>

#### Centralized high-throughput testing platforms

If sufficient evidence becomes available, the centralized high-throughput testing platforms described in [Section 8.1.1](#) could be evaluated in 2018. WHO and FIND have developed a two-step evaluation process for this purpose. The first step includes verification of the accuracy of the assays in detecting *M. tuberculosis* as well as resistance to rifampicin and isoniazid, based on an external evaluation of a standardized panel of strains, conducted independently of the manufacturers at one or more WHO TB supranational reference laboratories (SRLs). The second step is evaluation of the clinical validity of the assays, based on testing of the platforms in two or three reference laboratories in high TB burden settings, and

<sup>1</sup> World Health Organization. WHO meeting report of a technical expert consultation: non-inferiority analysis of Xpert MTB/RIF Ultra compared to Xpert MTB/RIF (WHO/HTM/TB/2017.04). Geneva: World Health Organization; 2017 (<http://www.who.int/tb/publications/2017/XpertUltra/en/>, accessed 16 August 2017).

<sup>2</sup> World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children – policy update (WHO/HTM/TB/2013.16) Geneva: World Health Organization; 2013 ([http://apps.who.int/iris/bitstream/10665/112472/1/9789241506335\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/112472/1/9789241506335_eng.pdf?ua=1), accessed 16 August 2017).

<sup>3</sup> World Health Organization. Technical Expert Group meeting report: Sample transport products and a target product profile (TPP) for solutions that improve the recovery of mycobacteria with culture (WHO/HTM/TB/2017.19). Geneva: World Health Organization; 2017.

<sup>4</sup> World Health Organization. WHO meeting report of a technical expert consultation: critical concentrations for TB medicines (WHO/HTM/TB/2017.22). Geneva: World Health Organization; 2017.

<sup>5</sup> XDR-TB is defined as MDR-TB plus resistance to at least one fluoroquinolone and a second-line injectable.

comparing results with the reference standards of culture, phenotypic DST and molecular sequencing, as well as with Xpert MTB/RIF.

### **Molecular sequencing as a reference standard for drug-susceptibility testing**

Drug resistance in the *M. tuberculosis* complex may be exclusively due to mutations affecting the bacterial genome. In 2018, WHO expects to assess evidence about the accuracy of genotypic DST compared with current phenotypic reference standards, and to develop a related list of priority mutations (so-called high-confidence mutations) to aid in test development. WHO will also consider whether the combination of genotypic DST and informed interpretation of the mutations can replace phenotypic DST, at least for certain key drugs such as rifampicin and pyrazinamide.

### **Tests for XDR-TB**

Molecular line probe assays (LPAs) for second-line anti-TB drugs are currently the only rapid molecular tests recommended by WHO to detect whether patients with confirmed multidrug-resistant (MDR) or rifampicin-resistant TB have XDR-TB.<sup>1</sup> However, LPAs require sophisticated laboratory infrastructure and equipment that is normally only available in centralized laboratories.

Hain Lifescience is developing a real-time assay for the detection of resistance to second-line injectable agents and fluoroquinolones, using the new Fluorotype platform. Cepheid plans to develop an XDR-TB cartridge to detect resistance to isoniazid, injectable agents and fluoroquinolones as an alternative to LPAs. If sufficient data become available, WHO will evaluate these tests using the same two-step approach described above for centralized high-throughput testing platforms.

### **8.1.4 Tests for the identification of LTBI**

Identifying and effectively treating or vaccinating people with LTBI who have no signs and symptoms of TB disease will be necessary to achieve the 2030 and 2035 targets of the End TB Strategy.

The tests that are currently available for the identification of LTBI are the tuberculin skin test (TST) and interferon gamma release assays (IGRAs). These tests indirectly measure TB infection by detecting memory T-cell response, signifying the presence of host sensitization to *M. tuberculosis* antigens.<sup>2</sup> Test results show only whether or not an individual has been exposed to *M. tuberculosis*, and are poor predictors of whether

the individual will progress to active TB disease in the future.<sup>3</sup> Without being able to predict who is most likely to develop disease, a large number of people would need to be treated to prevent one case of active TB. This is a major barrier to scaling up existing treatment for LTBI.

In 2017, an expert meeting was held to develop consensus around a target product profile (TPP) for a test that would accurately measure the progression of LTBI to active disease. The meeting was convened by WHO, on behalf of the New Diagnostics Working Group of the Stop TB Partnership. Participants defined the key specifications of the required product, including its intended use, performance and operational characteristics, and pricing; they also established a framework for future evaluation of any new tests that are developed. Further details are available in the meeting report.<sup>4</sup>

## **8.2 New drugs and drug regimens to treat TB**

The pipeline for new anti-TB drugs in August 2017 is shown in Fig. 8.2. There are 17 drugs in Phase I, II or III trials. These include eight new compounds: delpazolid, GSK-3036656, OPC-167832, PBTZ169, pretomanid, Q203, SQ109 and sutezolid. Two other drugs, bedaquiline and delamanid, have already received accelerated or conditional regulatory approval based on Phase IIb results and are now in Phase III trials. The seven repurposed drugs that are undergoing further testing are clofazimine, linezolid, levofloxacin, moxifloxacin, nitazoxanide, rifampicin (high dose) and rifapentine. These 17 drugs are described in more detail in Section 8.2.1 and Section 8.2.2. New TB drug regimens are also being tested, and these are described in Section 8.2.3.

### **8.2.1 New compounds**

#### **Bedaquiline**

WHO issued interim policy guidance on the use of bedaquiline for treatment of patients with MDR-TB in 2013, based on Phase IIb trial results.<sup>5</sup> There was a conditional recommendation to use bedaquiline to strengthen the longer treatment regimens for MDR-TB that are recommended by WHO. Following the availability of more evidence about the use of bedaquiline, WHO convened a Guideline Development Group in 2016. The main outcome of this review was to maintain the same conditional recommendation, until a new systematic review

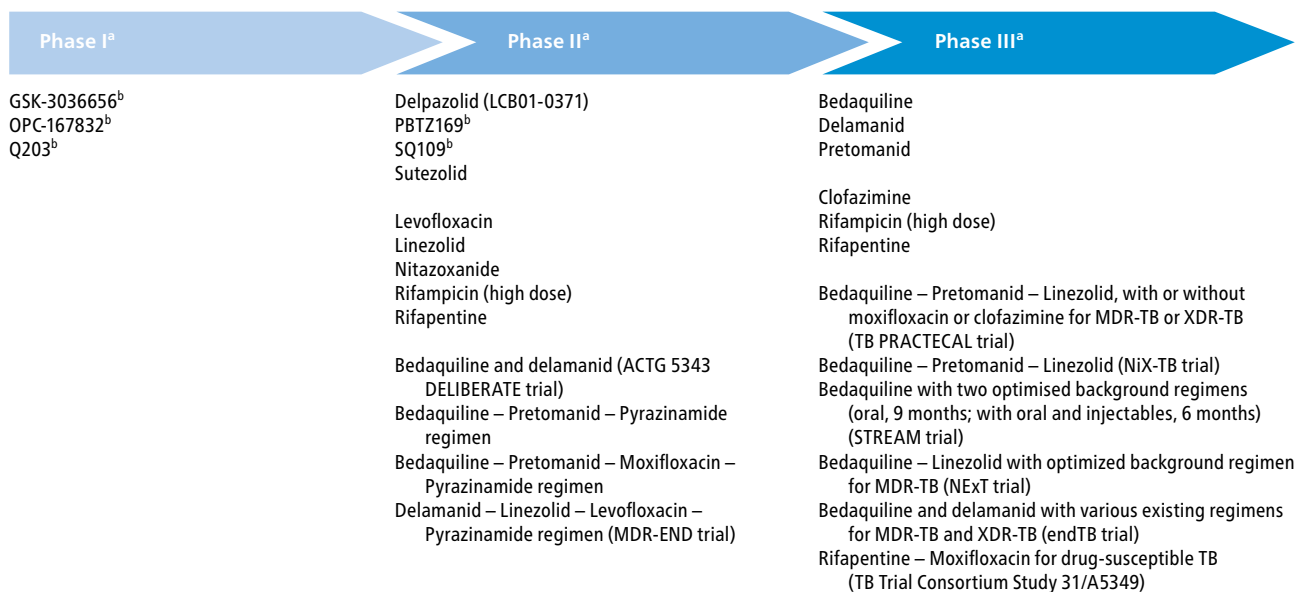
<sup>1</sup> The use of molecular line probe assays for the detection of resistance to second-line anti-tuberculosis drugs. Policy guidance. WHO/HTM/TB/2016.07. Geneva: World Health Organization. (<http://www.who.int/tb/publications/lpa-mdr-diagnostics/en/>, accessed 8 August 2017)

<sup>2</sup> Implementing tuberculosis diagnostics. Policy framework. WHO/HTM/TB/2015.11. Geneva: World Health Organization, 2015. ([http://apps.who.int/iris/bitstream/10665/162712/1/9789241508612\\_eng.pdf?ua=1&ua=1](http://apps.who.int/iris/bitstream/10665/162712/1/9789241508612_eng.pdf?ua=1&ua=1), accessed 8 August 2017).

<sup>3</sup> Matteelli A, Sulis G, Capone S, D'Ambrosio L, Migliori GB, Getahun H. Tuberculosis elimination and the challenge of latent tuberculosis. *Presse Med.* 2017;46(2 Pt 2):e13-e21 (<http://www.sciencedirect.com/science/article/pii/S0755498217300556?via%3Dihub>, accessed 16 August 2017).

<sup>4</sup> World Health Organization. Consensus meeting report: development of a target product profile and framework for evaluation for a test of progression from tuberculosis infection to active disease (WHO/HTM/TB/2017.18). Geneva: World Health Organization; 2017.

<sup>5</sup> World Health Organization. The use of bedaquiline in the treatment of multidrug-resistant tuberculosis: interim policy guidance (WHO/HTM/TB/2013.6). Geneva: WHO; 2013 ([http://apps.who.int/iris/bitstream/10665/84879/1/9789241505482\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/84879/1/9789241505482_eng.pdf), accessed 8 August 2017).

**FIG. 8.2****The global development pipeline for new anti-TB drugs and regimens, August 2017**

<sup>a</sup> New drug compounds are listed first, followed by repurposed drugs and then by regimens.

<sup>b</sup> New chemical class.

Source: Adapted from the Stop TB Partnership Working Group on New TB Drugs pipeline. More information on these products and other ongoing projects can be found at <http://newtbdrugs.org>

of evidence is warranted or results from the Phase III clinical trial become available.<sup>1</sup>

The safety and efficacy of bedaquiline as part of short MDR-TB regimens (i.e. 6 and 9 months duration), compared with the updated current standard of care recommended by WHO (i.e. a shortened regimen) is being investigated in the second stage of the Phase III STREAM trial. Recruitment started in March 2016,<sup>2</sup> and the first results are expected in 2020. A study on the use of bedaquiline to treat children with MDR-TB is being implemented in the Philippines, the Russian Federation and South Africa. Bedaquiline is also being used in trials of all-oral treatment regimens (Section 8.2.3), and investigation of its use in treatment of drug-susceptible TB has started.

### Delamanid

The follow-up stage of a Phase III trial of the safety and efficacy of delamanid as an addition to an optimized background regimen for the treatment of adults with MDR-TB was recently completed. Final results are expected by early 2018.

The use of delamanid in addition to an optimized background regimen to treat children with MDR-TB is being investigated in Phase I and II trials. Following the results of two trials in cohorts of children and adolescents with MDR-

TB aged 6–17 years, WHO's interim guidance on the use of delamanid was updated to include recommendations for its use in this age group.<sup>3</sup>

As with bedaquiline, delamanid is being used in trials of all-oral treatment regimens (Section 8.2.3). Studies of its use in the prevention of drug-resistant TB among contacts of people with MDR-TB are planned.

### Delpazolid (LCB01-0371)

Delpazolid is a new oxazolidinone developed by LegoChem BioSciences. It entered a Phase II trial in the Republic of Korea in 2017.

### GSK-3036656

GSK-3036656 is a new oxaborole compound developed by GlaxoSmithKline. A Phase I trial started in March 2017.

### OPC-167832

OPC-167832 is a carbostyryl developed by Otsuka that is bactericidal against both growing and intracellular bacilli. A single ascending dose study will be completed in late 2017. A multiple ascending dose/early bactericidal activity (EBA) study of OPC-167832 alone and in combination with delamanid is planned for 2018.

<sup>1</sup> Report of the Guideline Development Group Meeting on the use of bedaquiline in the treatment of multidrug-resistant tuberculosis, 2016 revision (WHO/HTM/TB/2017.01). Geneva, WHO, 2017. <http://apps.who.int/iris/bitstream/10665/254712/1/WHO-HTM-TB-2017.01-eng.pdf>

<sup>2</sup> Moodley R, Godec TR, Team ST. Short-course treatment for multidrug-resistant tuberculosis: the STREAM trials. *Eur Respir Rev.* 2016;25(139):29–35 (<http://err.ersjournals.com/content/25/139/29.long>, accessed 16 August 2017).

<sup>3</sup> World Health Organization. The use of delamanid in the treatment of multidrug-resistant tuberculosis in children and adolescents: Interim policy guidance (WHO/HTM/TB/2016.14). Geneva: WHO; 2016. ([http://who.int/tb/publications/Delamanid\\_interim\\_policy/en/](http://who.int/tb/publications/Delamanid_interim_policy/en/), accessed 16 August 2017)

### **PBTZ169**

PBTZ169 is a benzothiazinone developed by the Swiss Federal Institute of Technology (Lausanne) and Innovative Medicines for Tuberculosis (iM4TB). A Phase I trial has been completed; results are not yet published. A Phase II trial has started in the Russian Federation.

### **Pretomanid**

Pretomanid is a nitroimidazole that is being developed by the TB Alliance (the Global Alliance for TB Drug Development).<sup>1</sup> It is currently being tested as part of combination regimens for the treatment of both drug-susceptible and drug-resistant TB, including XDR-TB (Section 8.2.3).

### **Q203**

Q203 is an imidazopyridine that has been developed by Qurient (Republic of Korea).<sup>2</sup> Single doses of various sizes are being tested in two Phase I trials.

### **SQ109**

SQ109 is a drug discovered by scientists at Sequella Inc. (USA) and the US National Institutes of Health. A Phase IIb/III trial in which the drug was added to a standard regimen for MDR-TB has been completed in seven clinical centres in the Russian Federation; positive results in terms of safety, efficacy and tolerability were reported in a press release in March 2017. A Phase II trial is being implemented in the USA.

### **Sutezolid**

Sutezolid (PNU-100480) is an oxazolidinone and an analogue of linezolid. Results from an EBA study presented in 2012 showed a significant reduction in colony-forming unit counts compared with the baseline level after 14 days of treatment. In January 2017, the Medicines Patent Pool announced that it has signed a licence with Johns Hopkins University to facilitate the clinical development of sutezolid in combination with other drugs. On World TB Day 2017, the TB Alliance and the Medicines Patent Pool announced a licensing agreement for the clinical development of sutezolid.

## **8.2.2 Approved drugs being tested for new purposes**

### **Clofazimine**

Clofazimine is a riminophenazine that is used to treat leprosy. Its use in MDR-TB treatment is being explored in preclinical models of TB infection, to better understand its anti-TB effects. Novartis, the company that manufactures the drug, has withdrawn support for Phase II trials; however, clofazimine continues to be tested as part of treatment regimens for MDR-TB that are in Phase III trials.

### **Levofloxacin**

Levofloxacin is being tested in the Phase II Opti-Q study. This is investigating the best dose of levofloxacin to use for treatment of MDR-TB in adults with smear- and culture-positive pulmonary TB. Four doses are being tested (11, 14, 17, 20 mg/kg) as part of an optimized background regimen. The trial is being implemented in Peru and South Africa and is scheduled for completion in late 2017.

### **Linezolid**

Linezolid is an oxazolidinone with potent activity against TB. It has been widely used in the treatment of drug-resistant TB and there is good evidence that it improves culture conversion and cure rates when added to treatment regimens. Since the medicine has a narrow therapeutic window, and the optimal dosing strategy remains unknown, the TB Alliance is implementing a Phase II trial to evaluate mycobactericidal activity, safety, tolerability, and pharmacokinetics of 5 doses of linezolid in adults with pulmonary TB.

### **Moxifloxacin**

Moxifloxacin is included in several trials of new regimens for treatment of both drug susceptible and drug-resistant TB (Section 8.2.3).

### **Nitazoxanide**

Nitazoxanide is an anti-parasitic drug. Its activity against *M. tuberculosis* is being tested in a Phase II trial in Haiti.

### **Rifampicin (high dose)**

Findings from the multi-arm, multi-stage TB (MAMS-TB) trial of the PanACEA consortium were published in 2017.<sup>3</sup> These showed that 35 mg/kg of rifampicin given over 12 weeks was safe, and shortened the time to stable culture conversion from 62 to 48 days. The other trial arms, which included various combinations of 10 mg/kg or 20 mg/kg of rifampicin, moxifloxacin and SQ109, did not achieve significant improvements compared with the control arm. When all the data are taken into consideration, the trial suggests that a 35 mg/kg dose of rifampicin given for 12 weeks is likely to improve treatment outcomes. This trial is the first multi-arm adaptive trial design to be successfully implemented in multiple sites in countries with a high burden of TB. It may help to pave the way for accelerated testing of new TB treatment regimens at reduced cost.

### **Rifapentine**

The effectiveness of rifapentine in the treatment of drug-susceptible TB is being studied in three trials. The TB Trial Consortium (TBTC) Study 31/A5349, which is investigating

<sup>1</sup> <https://www.tballiance.org/>

<sup>2</sup> Pethe K, Bifani P, Jang J, Kang S, Park S, Ahn S et al. Discovery of Q203, a potent clinical candidate for the treatment of tuberculosis. *Nat Med*. 2013;19(9):1157–1160.

<sup>3</sup> Boeree MJ, Heinrich N, Aarnoutse R, Diacon AH, Dawson R, Rehal S et al. High-dose rifampicin, moxifloxacin, and SQ109 for treating tuberculosis: a multi-arm, multi-stage randomised controlled trial. *Lancet Infect Dis*. 2017;17(1):39–49 (<https://http://www.sciencedirect.com/science/article/pii/S1473309916302742?via%3Dihub>, accessed 16 August 2017).

the use of rifapentine with or without moxifloxacin to shorten the treatment of drug-susceptible pulmonary TB to 4 months, started in 2016. TBTC Study 35, a Phase II study of the pharmacokinetics of new water-dispersible paediatric formulations of rifapentine, is scheduled to start in two sites in South Africa in 2018. TBTC Study 37 is a Phase III trial of the safety and efficacy of 6 weeks of daily rifapentine for the treatment of LTBI in HIV-negative people in settings with a low burden of TB. It is being compared with a locally available 3–4 month rifamycin-based regimen.

### 8.2.3 New regimens for the treatment of drug-susceptible or drug-resistant TB

New combinations of drugs are being tested in Phase II or Phase III trials.

#### **ACTG A5343 DELIBERATE**

The ACTG A5343 DELIBERATE trial is testing the cardiotoxicity of regimens containing delamanid and bedaquiline alone and in combination in pharmacokinetic and drug-drug interaction studies. The trial is sponsored by NIH/NIAID.

#### **endTB**

The endTB trial started in 2017, to compare several regimens for treatment of MDR-TB or XDR-TB with the current longer regimen recommended by WHO. The regimens being tested include bedaquiline or delamanid (or both), moxifloxacin or levofloxacin, and pyrazinamide plus linezolid or clofazimine (or both), in various combinations.

#### **MDR-END**

The MDR-END trial is investigating a 9–12 month regimen of delamanid, linezolid, levofloxacin and pyrazinamide for treatment of MDR-TB among TB patients without resistance to fluoroquinolones.

#### **NeXT**

The NeXT trial is testing a 6–9 month injection-free regimen of bedaquiline, ethionamide or high-dose isoniazid, linezolid, levofloxacin and pyrazinamide for patients with MDR-TB, compared with the short regimen of 12 months recommended by WHO. Recruitment started in South Africa in 2016.

#### **NiX-TB and ZeNix**

The NiX-TB trial is investigating the safety and efficacy of a 6-month combination of bedaquiline, pretomanid and linezolid (all oral agents) in patients with XDR-TB and treatment-intolerant MDR-TB. It is being implemented by the TB Alliance in South Africa. The primary endpoint is bacteriological failure (relapse or clinical failure) 6 months after completion of treatment. A cure rate of 87% has been reported for the first 15 patients. A follow-on trial called ZeNix will explore lower doses and shorter durations of linezolid to minimize toxicity.

The TB Alliance is also in the process of implementing a Phase IIc trial of bedaquiline, pretomanid, moxifloxacin and pyrazinamide (BPamZ), with a primary endpoint of culture conversion at 2 months. A previous Phase IIb study of this BPamZ regimen showed almost 100% culture conversion at 2 months in patients with MDR-TB.

In combination, these two regimens could potentially treat all patients with active TB with oral drugs only, within a maximum of 6 months.

#### **STREAM**

The STREAM stage 1 trial is comparing a 9-month regimen for MDR-TB with longer regimens of 18–24 months.<sup>1</sup> Patients with rifampicin-resistant pulmonary TB and no evidence of resistance to fluoroquinolones or kanamycin are eligible. The trial is being implemented in Ethiopia, Mongolia, South Africa and Viet Nam, and final results are expected in 2018.

#### **TB-PRACTECAL**

The TB-PRACTECAL trial is a Phase II/III trial to evaluate the safety and efficacy of 6-month regimens that contain bedaquiline, pretomanid and linezolid, with or without moxifloxacin or clofazimine, for the treatment of adults with MDR-TB or XDR-TB. It is being implemented in Belarus, South Africa and Uzbekistan.

## 8.3 New vaccines to prevent TB

The BCG vaccine, first used in the 1920s, remains the only licensed vaccine for preventing TB. Despite high coverage of BCG vaccination as part of childhood immunization programmes (Chapter 5), the slow decline in TB incidence globally highlights the need for a much more effective vaccine that provides protection against all forms of TB in all age groups.

The status of the pipeline for new TB vaccines in August 2017, including the names of vaccine developers, is shown in **Fig. 8.3**. There are 12 vaccines in Phase I, II or III trials. Their main characteristics are summarized below.

### 8.3.1 Phase I trials

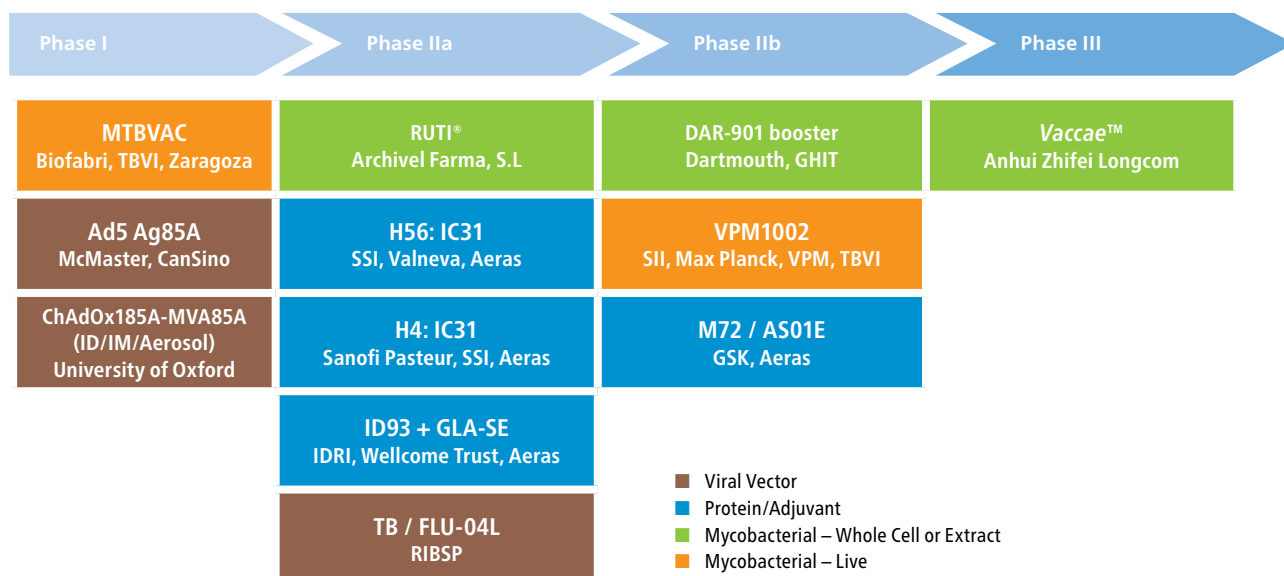
There are three vaccine candidates in Phase I trials.

#### **Ad5 Ag85A**

Ad5 Ag85A is an adenovirus serotype 5 vector expressing Ag85A. It has been evaluated for safety and immunogenicity in both BCG-naïve and previously BCG-immunized healthy volunteers in Canada. Overall, intramuscular administration was found to be safe, well tolerated and immunogenic in both

<sup>1</sup> Nunn AJ, Rusen ID, Van Deun A, Torrea G, Phillips PP, Chiang CY et al. Evaluation of a standardized treatment regimen of anti-tuberculosis drugs for patients with multi-drug-resistant tuberculosis (STREAM): study protocol for a randomized controlled trial. *Trials*. 2014;15:353 (<https://trialsjournal.biomedcentral.com/articles/10.1186/1745-6215-15-353>, accessed 16 August 2017).



**FIG. 8.3****The global development pipeline for new TB vaccines, August 2017<sup>a</sup>**

<sup>a</sup> Information was self-reported by vaccine sponsors, and the Stop TB Partnership Working Group on New TB Vaccines helped to coordinate their feedback.

trial groups, with more potent immunogenicity observed in volunteers who had been previously vaccinated with BCG. A safety and immunogenicity study of aerosol administration in BCG-vaccinated healthy volunteers has started.

#### **ChAdOx185A – MVA85A (ID/IM/Aerosol)**

ChAdOx185A is a simian adenovirus and MVA85A is a recombinant pox virus – both express antigen 85A. These candidates are being developed with the overall aim of generating a joint-heterologous prime-boost regimen delivered through both systemic and mucosal routes.

A Phase I trial of intramuscular administration of ChAdOx185A in BCG-vaccinated adults in the United Kingdom, both alone and as part of a prime-boost strategy with MVA85A, has been completed. Phase I trials of aerosol administration of ChAdOx185A in BCG-vaccinated adults are scheduled to start in late 2017. Two studies of aerosol administration of MVA85A in BCG-vaccinated individuals have been completed and a further study in people with LTBI is being implemented.

#### **MTBVAC**

MTBVAC is a live strain of *M. tuberculosis*, attenuated via deletions of the *phoP* and *fadD26* genes. The primary target population is neonates (as a BCG replacement vaccine); the secondary target population is adolescents and adults (as a booster vaccine). A Phase Ib trial in neonates is due to be completed at the end of 2017. Phase IIa trials in both target populations are expected to start in 2018.

### **8.3.2 Phase II and Phase III clinical trials**

There are currently nine vaccines in Phase II or Phase III trials.

#### **DAR-901 booster**

DAR-901 is a whole-cell, heat-inactivated, nontuberculous mycobacterial vaccine. It represents a new scalable manufacturing method for SRL172, a candidate vaccine which showed some efficacy among adults living with HIV in a Phase II/III trial in the United Republic of Tanzania. It is now being tested in a Phase IIb prevention of (established) infection trial among BCG-primed adolescents, also in the United Republic of Tanzania. The trial is scheduled for completion in 2018.

#### **H4:IC31**

H4:IC31 is a BCG booster vaccine that contains a fusion protein of Ag85B and TB10.4, formulated with IC31 adjuvant. It is being tested in a pre-proof-of-concept Phase II trial of prevention of (established) infection among IGRA-negative, HIV-negative adolescents at high risk of acquiring *M. tuberculosis* infection. It is also in a Phase I/II trial in infants.

#### **H56:IC31**

H56:IC31 is an adjuvanted subunit vaccine that combines three *M. tuberculosis* antigens (Ag85B, ESAT-6 and Rv2660c) with the IC31 adjuvant. Three Phase I or I/IIa trials of safety and immunogenicity have been completed. Two of these were in HIV-negative, BCG-vaccinated adults with and without LTBI and without a history or any evidence of TB disease. The other was in HIV-negative pulmonary TB patients who had recently completed treatment. The trials showed that the vaccine had an acceptable safety profile and was immunogenic at

## BOX 8.2 ■ The WHO Global Action Framework for TB Research: progress in 2016–2017

### Country level

WHO has developed a toolkit to support countries to develop a national research plan.<sup>a</sup> This includes an emphasis on the development or strengthening of national TB research networks to drive efforts in TB research, increasing national investment in health research, and multisectoral collaboration. Countries that adopted this approach in 2016–2017 included India, Indonesia, Swaziland and Thailand.

### Global level

The Task Force on Global TB Research was established in 2016, to advise WHO on how to support the global TB research community to extend its reach and impact. WHO subsequently convened a TB Research Funders' Forum to promote discussion among funding agencies, national TB programme managers, advocates and public–private partnerships on how to invigorate impact-oriented research at country level. WHO continues to promote TB research by convening stakeholders to share knowledge, contributing to the development of a consensus-based agenda that addresses priorities in high TB burden countries, and facilitating the development and maintenance of regional and global TB research networks.

<sup>a</sup> World Health Organization. A toolkit for developing a national TB research plan, in support of the third pillar of the End TB Strategy. Geneva: World Health Organization; 2016 ([http://www.who.int/tb/publications/TB\\_research\\_toolkit/en/](http://www.who.int/tb/publications/TB_research_toolkit/en/), accessed 20 July 2017).

all studied doses. Analysis of a Phase Ib trial evaluating the safety and immunogenicity of H4:IC31, H56:IC31 and BCG revaccination in adolescents is underway.

### ID93 + GLA-SE

The ID93 + GLA-SE vaccine comprises four *M. tuberculosis* antigens associated with virulence (Rv2608, Rv3619 and Rv3620) or latency (Rv1813), and the adjuvant GLA-SE. A Phase IIa trial in HIV-negative TB patients that have recently completed treatment for pulmonary TB disease was recently completed in South Africa, in preparation for a Phase IIb trial that will investigate prevention of recurrence of disease in the same population.

### M72/AS01E

M72/AS01E is a subunit vaccine that pairs two *M. tuberculosis* antigens (32A and 39A) with an adjuvant (AS01E). It is being tested in a Phase IIb efficacy trial in HIV-negative adults infected with *M. tuberculosis* in Kenya, South Africa and Zambia. The primary endpoint is the number of incident cases of active pulmonary TB disease not associated with HIV infection. Secondary endpoints include safety and immunogenicity.

### RUTI®

RUTI® is a non-live, polyantigenic vaccine based on cell-wall fragmented *M. tuberculosis* bacteria. It is intended as a therapeutic vaccine, to be used in conjunction with a short intensive antibiotic treatment. A Phase I study in healthy volunteers and a Phase II study in people with LTBI have demonstrated a good safety profile and found the vaccine to be immunogenic at all studied doses. The main target for RUTI is MDR-TB, and a Phase IIa study in patients with MDR-TB is being implemented.

### TB/FLU-04L

TB/FLU-04L is a mucosal vectored vaccine based on an attenuated replication-deficient influenza virus vector expressing antigens Ag85A and ESAT-6. It was designed as a prophylactic boost vaccine for infants, adolescents and adults. A Phase IIa trial in people with LTBI is being implemented.

### Vaccae™

Vaccae™ vaccine is a specified lysate that has been licensed by the China Food and Drug Administration as an immunotherapeutic agent to help shorten TB treatment for patients with drug-susceptible TB. A Phase III trial to assess its efficacy and safety in preventing TB disease in people with LTBI is being implemented. It is the largest TB vaccine trial undertaken in the past decade, involving 10 000 people aged 15–65 years. The trial is scheduled to be completed in 2018.

### VPM1002

VPM1002 is a live recombinant vaccine. A Phase II trial is being implemented in South Africa to assess the safety and immunogenicity of the vaccine in HIV-exposed and unexposed neonates and the preparations for a subsequent Phase III trial are underway. A Phase II/III trial for prevention of TB recurrence in adults is expected to start before the end of 2017 in India.

## 8.4 Multisectoral and multidisciplinary approach to TB research

The second component of the research pillar of the End TB Strategy is “to optimize implementation and impact, and promote innovations”. This requires a multisectoral and multidisciplinary approach. The WHO Global Action Framework for TB Research (GAF), published in 2015, was

developed to support such an approach.<sup>1</sup> It has two main components: promoting TB research at country level to find ways to address local barriers; and catalysing research at global level through advocacy, knowledge sharing, research prioritization, and support to international networks for research and capacity-building. Examples of ways in which WHO has built on the GAF in 2016–2017 at global and country levels are provided in **Box 8.2**.

A good recent example of an international network that is promoting multisectoral and multidisciplinary research to address a top priority of the End TB Strategy is the Social Protection Action Research & Knowledge Sharing (SPARKS) Network. This has been established by the Karolinska Institute in Sweden, the London School of Hygiene & Tropical Medicine in the United Kingdom, and WHO. SPARKS aims to catalyse and champion research on social protection, and the use of findings to inform multisectoral policy and action. The network will be used to share knowledge and to facilitate collaboration among research institutions, public health practitioners, international organizations and civil society. At the first SPARKS consultation, held in 2016, a three-phase plan for collaboration was developed, with a focus on collaborative research involving national TB programmes, academic institutions and other partners.<sup>2</sup> One of the participating countries is Brazil (**Box 8.3**).

A second example of an international initiative to improve TB prevention and care services is the Global Task Force on Digital Health for TB. This was established by WHO in 2015, in collaboration with the European Respiratory Society. The task force aims to enhance TB prevention and care through the use of electronic health (e-health) and mobile health (m-health) technologies. The main focus to date has been the development of TPPs for nine priority digital health concepts and products related to patient care, surveillance, programme management and e-learning at country level.<sup>3</sup> It is hoped that the TPPs will motivate innovators to invest time and resources in ventures aligned with the End TB Strategy. Digital health innovations will need to be evaluated in a variety of geographic, social and economic contexts and in specific subpopulations to generate the evidence needed to inform global guidance, as well as adaptation and use at country level. Such evaluation and application will involve both the health sector and the field of information and communication technology.

<sup>1</sup> World Health Organization. A global action framework for TB research in support of the third pillar of WHO's End TB Strategy. Geneva: World Health Organization; 2015 (<http://www.who.int/tb/publications/global-framework-research/en/>, accessed 8 August 2017).

<sup>2</sup> World Health Organization. Report from the first consultation of the Health and Social Protection Action Research & Knowledge Sharing (SPARKS) Network (WHO/HTM/TB/2017.10). 2017 (<http://www.who.int/tb/publications/sparksreport/en/>, accessed 16 August 2017).

<sup>3</sup> Falzon D, Timimi H, Kurosinski P, Migliori GB, Van Gemert W, Denkinger C et al. Digital health for the End TB Strategy: developing priority products and making them work. *Eur Respir J*. 2016;48(1):29–45 (<http://erj.ersjournals.com/content/48/1/29.long>, accessed 16 August 2017).

### BOX 8.3

## Mainstreaming a multisectoral research agenda in Brazil

In April 2017, the national TB programme in Brazil organized a workshop on social protection and TB research. Participants included national researchers from the Brazilian Tuberculosis Research Network (Rede TB), advocates, staff from the national TB programme, implementing partners, stakeholders from outside the health sector and funding agencies. The focus was on ways to optimize TB care delivery for the poorest and most vulnerable populations in Brazil, by leveraging the existing national social protection platform. Research priorities that were identified included obtaining a better understanding of the impact of socioeconomic and demographic factors on TB outcomes, identifying how such factors contribute to operational and implementation gaps in the programmatic management of TB, and designing targeted interventions that will address these barriers to care, and will improve patient health and socioeconomic outcomes.