

GLOBAL TUBERCULOSIS REPORT

2020



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Message

from the WHO Director-General



Two years ago, the nations of the world gathered for the first United Nations (UN) high-level meeting on tuberculosis (TB). Heads of State and other leaders made bold commitments to accelerate the response to end the world's top infectious disease killer. Those commitments have offered hope for ending the death and

suffering of millions worldwide who are struggling with TB – a preventable and treatable disease.

This year's World Health Organization (WHO) global TB report comes at a critical time. The report provides an opportunity to reflect on progress made in the fight against TB, but also to highlight the risks that threaten to erode the gains we have made.

There is good news. The number of people treated for TB has grown since the UN high level meeting, with over 14 million people reached with TB care in 2018 and 2019. The number of people provided with TB preventive treatment has quadrupled since 2015, from 1 million in 2015 to over 4 million in 2019.

These are impressive achievements that we must celebrate. However, equitable access to quality and timely diagnosis, prevention, treatment and care remains a challenge. Accelerated action worldwide is urgently needed if we are to meet our targets by 2022.

The COVID-19 pandemic threatens to unwind the gains made over recent years. The impact of the pandemic on TB services has been severe. Data collated by WHO from high TB burden countries show sharp drops in TB notifications in 2020. Our modelling suggests that a 50% drop in TB case detection over 3 months could result in 400 000 additional TB deaths this year alone. In response, WHO is working closely with our partners and civil society to support countries in maintaining continuity of essential health services, including for TB.

COVID-19 is demonstrating that health is not only an outcome of development: it is also a prerequisite for social, economic and political stability. Although the pandemic is a setback to our efforts to achieve the Sustainable Development Goals, we cannot allow it to become an excuse for not achieving those goals. Instead, we must use it as motivation.

We are all accountable for delivering on the commitments we have made. But none of us can meet those commitments alone. We can only do it together. We need all hands-on-deck. That's why WHO has developed the Global Strategy for TB Research and Innovation and the Multisectoral Accountability Framework for TB. WHO has also updated its TB policies and guidelines, and is supporting countries to adapt and use these tools to translate commitments into actions and to monitor, report and review progress, while engaging leaders, relevant sectors, civil society and other stakeholders.

We're encouraged to see high-level leadership on multisectoral accountability in several countries, including India, Indonesia, Pakistan, the Philippines, the Russian Federation and Viet Nam. In all, 86 countries have reported that a national multisectoral accountability mechanism for high-level review is in place.

But ending TB is not just a job for governments. Everyone has a role to play, from those in the corridors of power to those in the villages and streets where people live and die with TB.

To make sure everyone's voice is heard, WHO established the WHO Civil Society Taskforce on TB two years ago, following the highly successful Global Ministerial Conference on Ending TB in Moscow. When we listen to the voices of people and communities affected by TB, we are reminded that ending TB is not just about ensuring access to health services. It's also about defending human rights. As you know, TB is deeply rooted in populations where human rights and dignity are threatened. While anyone can fall ill with TB, the disease takes the heaviest toll on the most vulnerable. That is why efforts to end TB must go hand-in-hand with other efforts to reduce inequalities, eliminate extreme poverty, ensure social protection and achieve universal health coverage.

COVID-19 has taken so much from us. But nothing can take away our shared vision to end TB.

Together, we will make that vision a reality.

A handwritten signature in black ink, which appears to read 'Tedros Adhanom Ghebreyesus'. The signature is written in a cursive, flowing style.

Dr Tedros Adhanom Ghebreyesus
Director-General
World Health Organization

Foreword



This year, we are at the half-way mark for efforts to reach the 2022 targets committed to by Heads of State at the historic United Nations (UN) high-level meeting on tuberculosis (TB) in 2018. The 2020 World Health Organization (WHO) global TB report showcases the progress made towards ending

the TB epidemic, and puts in stark perspective the current and potential impact of the COVID-19 pandemic, in eroding the hard-won gains of recent years.

TB remains the world's most deadly infectious disease; it claims more than a million lives each year and affects millions more, with enormous impacts on families and communities. The report highlights the fact that TB incidence and deaths are falling, but not fast enough to reach global TB targets.

Globally, the annual number of people reported to have accessed TB treatment has grown from about 6 million in 2015, to 7 million in 2018 and 7.1 million in 2019. Access to TB preventive treatment has also increased, from 1 million in 2015, to 2.2 million in 2018 and 4.1 million in 2019. There is an urgent need to bolster these increases, to reach the 2022 targets on quality care and preventive treatment that were set in the political declaration of the UN high-level meeting. The political declaration targets are aligned with those of WHO's End TB Strategy and the WHO Director-General's flagship initiative 'Find. Treat. All. #EndTB', which is being implemented in collaboration with the Stop TB Partnership and the Global Fund to Fight AIDS, Tuberculosis and Malaria. We need to close gaps and reach the 2.9 million people with TB who are still not accessing quality care, including those with drug-resistant TB. We also need to intensify prevention efforts, and address funding gaps that impede progress in the TB response and in research.

The good news is that the WHO European Region is on track to reach the 2020 milestones of the End TB Strategy, and the African Region is making good progress towards these milestones.

Putting the spotlight on the impact of the COVID-19 pandemic on TB, this report includes data collected by WHO's Global TB Programme that show sharp drops in TB case notifications in several high TB burden countries

in 2020. WHO modelling and analysis of the pandemic's impact on TB mortality indicate that a 50% drop in the detection of TB cases over 3 months will lead to almost 400 000 more people dying from TB. We need to work together and do our best to save these lives.

The report includes an assessment of universal health coverage (UHC), social determinants and multisectoral action. TB impedes development; at the same time, poverty, vulnerability and other social factors fuel TB. Success depends on action across sectors; thus, it is crucial to implement WHO's multisectoral accountability framework on TB. In 2019 and 2020, WHO worked with high TB burden countries to develop or strengthen accountability mechanisms. Examples include joint reviews of national TB programmes with independent and civil society representatives, as well as support for high-level collaboration and review mechanisms, broad stakeholder forums, and head-of-state or government initiatives. In addition, WHO has worked with high TB burden countries to strengthen the engagement of civil society and youth, to galvanize the TB response.

All these efforts are being led under the umbrella of UHC and WHO's General Programme of Work, to ensure that no one is left behind.

This year's WHO global TB report comes in tandem with the UN Secretary-General's 2020 progress report on TB; the latter was prepared with support from WHO, as requested in the UN political declaration on TB. The overarching message of both reports is clear. High-level commitments have galvanized global, regional and national progress towards ending TB, but we need urgent and more ambitious investments and actions to put the world on track to reach the targets, especially in the context of the COVID-19 pandemic.

We need to stand in solidarity. Any slackening of commitment and action will impede efforts to save millions of lives. I believe that, together, we can and will make a difference. It's time for action. It's time to End TB.

A handwritten signature in black ink, appearing to read 'Tereza Kasaeva'.

Dr Tereza Kasaeva
Director, WHO Global TB Programme
World Health Organization

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Nazis Arefin Saki, Anuj Bhattachan, Ratna Bhattarai, Mizaya Cader, Choe Kum Song, Rada Dukpa, Abdul Hameed, Fathaath Hassan, Herath Hemantha, Md. Shamiul Islam, Dushani Jayawardana, Phalin Kamolwat, Ahmadul Hasan Khan, Constantino Lopes, Endang Lukitosari, Sanjay Kumar Mattoo, Imran Pambudi, Jamyang Pema, Kuldeep Singh Sachdeva, Cho Cho San, Sharad Kumar Sharma, Wilawan Somsong, Sulistyo SKM M.Epid, Janaka Thilakarathna, Zaw Tun.

WHO Western Pacific Region

Hjh Anie Haryani Hj Abd Rahman, Zirwatul Adilah Aziz, Sandy Ahoia, Paul Aia, Mohammad Fathi Alikhan, Samantha Anuntak, Uranchimeg Borgil, Amy Bright, Sarah Brown, Risa Bukbuk, Stacey Cain, Chi Kuen Chan, Kwok Chiu Chang, Thilaka Chinnayah, Phonenaly Chittamany, Chou Kuok Hei, Clément Couteaux, Alice Cuenca, Jeffery Lawrence Cutter, Enkhmandakh Danjaad, Pascale Domingue, Jack Ekiek Mayleen, Jenny Eveni, Apinelu Puafitu Faaalo, Ludovic Floury, Louise Fonua, Saipale Fuimaono, Sam Fullman, Anna Marie Celina Garfin, Donna Mae Gaviola, James Hofscneider, Laurence Holding, Edna Iavro, Mohd Ihsani bin Mahmood, Noel Itogo, Mike Kama, Seiya Kato, Lisa Kawatsu, Kim Jinsun, Phonesavanh Kommanivanh, Christine Lifuka Alopua, Leo Lim, Liza Lopez, Shepherd Machechera, Mao Tan Eang, Chima Mbakwem, Mei Jian, Serafi Moa, Binh Hoa Nguyen, Nguyen Viet Nhung, Nou Chanly, Connie Olikong, Marcelina Rabauliman, Asmah Binti Razali, Bereka Reiher, Shim Eunhye, Jane Short, Phitsada Siphanthong, Edwina Tangaroa, Annie Teannaki, Tieng Sivanna, Kazuhiro Uchimura, Tereapii Uka, Frank Underwood, Lalomilo Varea, Du Xin, Zhang Hui, Zhao Yanlin.

Abbreviations

AIDS	acquired immunodeficiency syndrome	MDG	Millennium Development Goal
ART	antiretroviral therapy	MDR	multidrug-resistant
BCG	bacille Calmette-Guérin	MDR/RR-TB	multidrug-resistant TB or rifampicin-resistant TB
BPamZ	bedaquiline, pretomanid, moxifloxacin and pyrazinamide	MDR-TB	multidrug-resistant TB
BRICS	Brazil, Russian Federation, India, China and South Africa	M:F	male to female (ratio)
CAD	computer-aided detection	MIC	minimum inhibitory concentration
CB	clinical breakpoint	MTBC	<i>Mycobacterium tuberculosis</i> complex
CC	critical concentration	NAAT	nucleic-acid amplification tests
CCM	country coordination mechanism	NGS	next-generation sequencing
CDC	Centers for Disease Control and Prevention (United States)	NIAID	National Institute of Allergy and Infectious Diseases
CFR	case fatality ratio	NIH	National Institutes of Health
CHW	community health worker	NSP	national strategic plan
CI	confidence interval	NTP	national TB programme
COR	correlate of risk	ODA	official development assistance
CORTIS	Correlate of Risk Targeted Intervention Study	OECD	Organisation for Economic Co-operation and Development
CRS	creditor reporting system	PanACEA	Pan-African Consortium for the Evaluation of Antituberculosis Antibiotics
CV	community volunteer	PBMC	peripheral blood mononuclear cell
CXR	chest X-ray	PCR	polymerase chain reaction
DAC	Development Assistance Committee (OECD)	pDST	phenotypic drug-susceptibility testing
DALY	disability-adjusted life year	PEPFAR	President's Emergency Plan for AIDS Relief
DNA	deoxyribonucleic acid	P:N	prevalence to notification (ratio)
DST	drug-susceptibility testing	PPD	purified protein derivative
DTG	dolutegravir	PPM	public-public and public-private mix
EDCTP	European & Developing Countries Clinical Trials Partnership	RNA	ribonucleic acid
EECA	Eastern Europe and Central Asia	RR-TB	rifampicin-resistant TB
ELISA	enzyme-linked immunosorbent assay	SANAC	South Africa National AIDS Council
ELISPOT	enzyme-linked immunosorbent spot assay	SCI	service coverage index
FDA	United States Food and Drug Administration	SDG	Sustainable Development Goal
FIND	Foundation for Innovative New Diagnostics	SDR	systematic drug reaction
Gates MRI	Bill & Melinda Gates Medical Research Institute	SRL	Supranational Reference Laboratory
GDG	guideline development group	STREAM	Standardised Treatment Regimen of Anti-TB Drugs for Patients with MDR-TB
GDP	gross domestic product	TAG	Treatment Action Group
Global Fund	The Global Fund to Fight AIDS, Tuberculosis and Malaria	TB	tuberculosis
GTB	Global TB Programme	TB Alliance	Global Alliance for TB Drug Development
HIV	human immunodeficiency virus	TBTC	TB Trial Consortium
HP	isoniazid and rifapentine	TDR	Special Programme for Research and Training in Tropical Diseases
ICD-10	International Classification of Diseases (10th edition)	tRNA	transfer ribonucleic acid
IFN	interferon	TST	tuberculin skin test
IGRA	interferon gamma release assay	TU	tuberculin units
IHME	Institute for Health Metrics and Evaluation	UHC	universal health coverage
IPT	isoniazid preventive treatment	UN	United Nations
IR	implementation research	UNAIDS	Joint United Nations Programme on HIV/AIDS
IU	international units	US	United States
LF-LAM	lateral flow lipoarabinomannan assay	USA	United States of America
MAF-TB	multisectoral accountability framework for TB	USAID	United States Agency for International Development
MAMS-TB	Multi-Arm, Multi-Stage TB	VR	vital registration
		WHO	World Health Organization



TB outreach to a "floating" neighborhood near Port Moresby, Papua New Guinea.

John Rae Photography

Executive Summary

Background

Tuberculosis (TB) is a communicable disease that is a major cause of ill health, one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV/AIDS). TB is caused by the bacillus *Mycobacterium tuberculosis*, which is spread when people who are sick with TB expel bacteria into the air; for example, by coughing. The disease typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB). About a quarter of the world's population is infected with *M. tuberculosis*.¹

TB can affect anyone anywhere, but most people who develop the disease are adults, there are more cases among men than women, and 30 high TB burden countries account for almost 90% of those who fall sick with TB each year. TB is a disease of poverty, and economic distress, vulnerability, marginalization, stigma and discrimination are often faced by people affected by TB.

TB is curable and preventable. About 85% of people who develop TB disease can be successfully treated with a 6-month drug regimen; treatment has the additional benefit of curtailing onward transmission of infection. Since 2000, TB treatment has averted more than 60 million deaths, although with access still falling short of universal health coverage (UHC), many millions have also missed out on diagnosis and care. Preventive treatment is available for people with TB infection. The number of people developing infection and disease (and thus the number of deaths) can also be reduced through multisectoral action to address TB determinants such as poverty, undernutrition, HIV infection, smoking and diabetes.

Research breakthroughs (e.g. a new vaccine) are needed to rapidly reduce TB incidence worldwide to the levels already achieved in low-burden countries, where TB is often regarded as a disease of the past.

This report

The World Health Organization (WHO) has published a global TB report every year since 1997. The purpose of the report is to provide a comprehensive and up-to-date assessment of the status of the TB epidemic, and of progress in the response to the epidemic – at global, regional and country levels – in the context of global commitments and strategies. The report is based primarily on data gathered by WHO in annual rounds of data collection. In 2020, data were reported by 198 countries and territories that accounted for more than 99% of the world's population and estimated number of TB cases.²

The 2020 edition complements and expands on the United Nations (UN) Secretary-General's 2020 progress report on TB, which was prepared with WHO support as requested in the political declaration of the UN high-level meeting on TB in 2018.³

In recognition of the enormous health, social and economic impacts of the COVID-19 pandemic, the report includes a provisional assessment of how the pandemic will affect the TB epidemic, people with TB and progress towards global TB targets.

Global commitments and strategy to end TB

In 2014 and 2015, all Member States of WHO and the UN committed to ending the TB epidemic, through their adoption of WHO's End TB Strategy and the UN Sustainable Development Goals (SDGs). The strategy and SDGs include milestones and targets for large reductions in TB incidence, TB deaths and costs faced by TB patients and their households (**Table E.1**).

Efforts to step up political commitment to the fight against TB intensified in 2017 and 2018.

A WHO global ministerial conference on TB was organized in November 2017. The outcome was the Moscow Declaration to End TB, which was welcomed by all Member States at the World Health Assembly in May 2018.

In September 2018, the UN General Assembly held its first-ever high-level meeting on TB, attended by heads of state and government as well as other leaders. The outcome was a political declaration in which commitments to the SDGs and End TB Strategy were reaffirmed and new ones added. Global targets for the funding to be mobilized for TB prevention, care and research, and for the number of people to be treated for TB infection and disease, were set for the first time (**Table E.1**).⁴

Status of the TB epidemic

Globally, an estimated 10.0 million (range, 8.9–11.0 million)⁵ people fell ill with TB in 2019, a number that has been declining very slowly in recent years.

There were an estimated 1.2 million (range, 1.1–1.3 million) TB deaths among HIV-negative people in 2019 (a reduction from 1.7 million in 2000), and an additional 208 000 deaths (range, 177 000–242 000)⁶ among HIV-positive people (a reduction from 678 000 in 2000).

Men (aged ≥15 years) accounted for 56% of the people who developed TB in 2019; women accounted for 32% and children (aged <15 years) for 12%. Among all those affected, 8.2% were people living with HIV.

TABLE E.1

Global TB targets set in the SDGs, the End TB Strategy and the political declaration of the UN high-level meeting on TB, for the period up to the SDG deadline of 2030

SDG Target 3.3	By 2030, end the epidemics of AIDS, TB, malaria and neglected tropical diseases, and combat hepatitis, water-borne diseases and other communicable diseases
WHO End TB Strategy	80% reduction in the TB incidence rate (new and relapse cases per 100 000 population per year) by 2030, compared with 2015 <i>2020 milestone: 20% reduction; 2025 milestone: 50% reduction</i>
	90% reduction in the annual number of TB deaths by 2030, compared with 2015 <i>2020 milestone: 35% reduction; 2025 milestone: 75% reduction</i>
	No households affected by TB face catastrophic costs by 2020
UN high-level meeting on TB, 2018	40 million people treated for TB from 2018 to 2022, including: <ul style="list-style-type: none"> • 3.5 million children • 1.5 million people with drug-resistant TB, including 115 000 children
	At least 30 million people provided with TB preventive treatment from 2018 to 2022, including: <ul style="list-style-type: none"> • 6 million people living with HIV • 4 million children under 5 years of age and 20 million people in other age groups, who are household contacts of people affected by TB
	Funding of at least US\$ 13 billion per year for universal access to TB prevention, diagnosis, treatment and care by 2022
	Funding of at least US\$ 2 billion per year for TB research from 2018 to 2022

AIDS: acquired immunodeficiency syndrome; HIV: human immunodeficiency virus; SDG: Sustainable Development Goal; TB: tuberculosis; UN: United Nations.

Geographically, most people who developed TB in 2019 were in the WHO regions of South-East Asia (44%), Africa (25%) and the Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8.2%), the Americas (2.9%) and Europe (2.5%). Eight countries accounted for two thirds of the global total: India (26%), Indonesia (8.5%), China (8.4%), the Philippines (6.0%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%) and South Africa (3.6%). The other 22 other countries in WHO’s list of 30 high TB burden countries accounted for 21% of the global total.⁷

The TB incidence rate at national level varies from less than 5 to more than 500 new and relapse cases per 100 000 population per year. In 2019, 54 countries had a low incidence of TB (<10 cases per 100 000 population per year), mostly in the WHO Region of the Americas and European Region, plus a few countries in the Eastern Mediterranean and Western Pacific regions. These countries are well placed to target TB elimination.

Drug-resistant TB continues to be a public health threat. Worldwide in 2019, close to half a million people developed rifampicin-resistant TB (RR-TB),⁸ of which 78% had multidrug-resistant TB (MDR-TB).⁹ The three countries with the largest share of the global burden were India (27%), China (14%) and the Russian Federation (8%). Globally in 2019, 3.3% of new TB cases and 17.7% of previously treated cases had MDR/RR-TB. The highest proportions (>50% in previously treated cases) were in countries of the former Soviet Union.

Progress towards the 2020 milestones of the End TB Strategy

At the end of 2019, the world as a whole, most WHO regions and many high TB burden countries were not on track to reach the 2020 milestones of the End TB Strategy.

Globally, the TB incidence rate is falling, but not fast enough to reach the 2020 milestone of a 20% reduction between 2015 and 2020 (Fig. E.1a). The cumulative reduction from 2015 to 2019 was 9% (from 142 to 130 new cases per 100 000 population), including a reduction of 2.3% between 2018 and 2019.

More positively, the WHO European Region has almost reached the 2020 milestone, with a reduction of 19% in the TB incidence rate between 2015 and 2019, and the African Region has made good progress, with a reduction of 16%.¹⁰ A total of 78 countries are on track to reach the 2020 milestone, including seven high TB burden countries that have already reached it (Cambodia, Ethiopia, Kenya, Namibia, the Russian Federation, South Africa and the United Republic of Tanzania) and three other high TB burden countries that are on course to do so (Lesotho, Myanmar and Zimbabwe).

The annual number of TB deaths is falling globally, but not fast enough to reach the 2020 milestone of a 35% reduction between 2015 and 2020 (Fig E.1a).¹¹ The cumulative reduction between 2015 and 2019 was 14%, less than halfway towards the milestone.

The good news is that the WHO European Region is on track to reach the 2020 milestone, with a 31% reduction in TB deaths from 2015 to 2019, and the African Region has made good progress, achieving a reduction of 19%.¹² A total of 46 countries are on track to reach the 2020 milestone, including seven high TB burden countries that have already reached it (Bangladesh, Kenya, Mozambique, Myanmar, the Russian Federation, Sierra Leone and the United Republic of Tanzania) and one other high TB burden country that is on course to do so (Viet Nam).

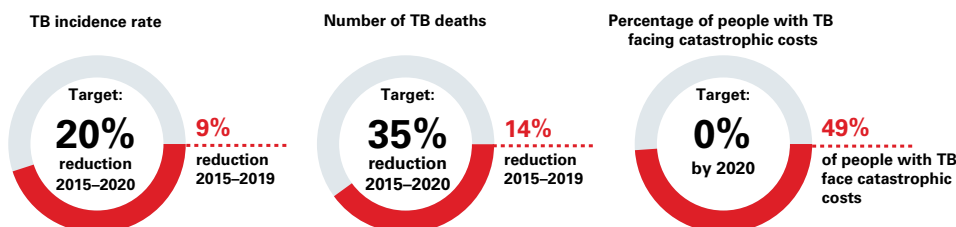
Since 2015, a total of 17 countries (including 10 high TB burden countries) have completed a national survey of costs faced by TB patients and their households. On aver-

FIG. E.1

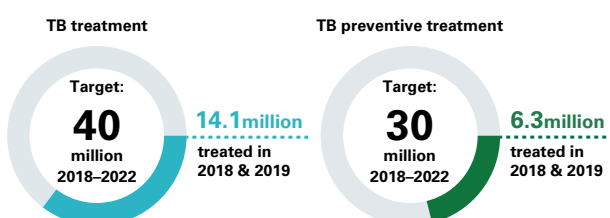
Overview of progress towards global TB targets

The centre of each circle shows the target, the colour coding illustrates the progress made and the text to the right of each circle quantifies the status of progress (by the end of 2019, except for funding).

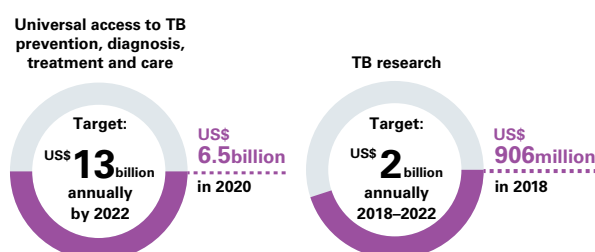
a) SDGs and End TB Strategy: targets for reductions in the TB incidence rate, TB deaths and catastrophic costs



b) UN high-level meeting on TB: targets for the number of people provided with TB treatment and TB preventive treatment



c) UN high-level meeting on TB: targets for increased funding



age, 49% of people with TB and their households faced catastrophic costs (defined as total costs¹³ equivalent to >20% of annual household income), with values at country level of 19–83% (Fig E.1a). For people with drug-resistant TB, the figure was higher still, at 80%, with values at country level of 67–100%. Survey results are being used to inform approaches to health financing, service delivery and social protection that will reduce these costs.

A further 9 surveys are underway in 2020 and 31 are planned for 2020–2021.

Progress towards the global TB targets set at the UN high-level meeting on TB

Progress is lagging behind what is needed to reach the global targets set at the UN high-level meeting on TB (Fig. E.1b and Fig. E.1c):

- ▶ 14.1 million people were treated for TB in 2018 and 2019, 35% of the 5-year (2018–2022) target of 40 million.
- ▶ 6.3 million people were started on TB preventive treatment in 2018 and 2019, 21% of the 5-year target of 30 million.
- ▶ Funding for TB prevention, diagnosis, treatment and care was US\$ 6.5 billion in 2020, 50% of the target of at least US\$ 13 billion per year by 2022.
- ▶ Funding for TB research was US\$ 906 million in 2018, less than half of the target of US\$ 2 billion per year 2018–2022.¹⁴

Progress towards the subtargets for TB treatment in 2018 and 2019 was slower than progress overall:

- ▶ 1.04 million children were treated for TB, 30% of the 5-year target of 3.5 million.
- ▶ 333 304 people were treated for MDR/RR-TB, 22% the 5-year target of 1.5 million.
- ▶ 8986 children were treated for MDR/RR-TB, 8% of the 5-year target of 115 000.

For TB preventive treatment, the subtarget for people living with HIV is on track to be achieved ahead of schedule in 2020, while progress towards the subtargets for household contacts of people with TB falls far short of what is needed. In 2018 and 2019, the numbers provided with TB preventive treatment were:

- ▶ 5.3 million people living with HIV, 88% of the 5-year target of 6.0 million.
- ▶ 782 952 children aged under 5 years who were household contacts of people with TB, 20% of the 5-year target of 4 million.
- ▶ 179 051 people in older age groups who were household contacts of people with TB, <1% of the 5-year target of 20 million.

The COVID-19 pandemic and TB – impact and implications

The COVID-19 pandemic threatens to reverse recent progress in reducing the global burden of TB disease.

The global number of TB deaths could increase by around 0.2–0.4 million in 2020 alone, if health services are disrupted to the extent that the number of people with TB who are detected and treated falls by 25–50% over a period of 3 months (Fig. E.2). In India, Indonesia, the Philippines and South Africa, four countries that account for 44% of global TB cases, there were large drops in the reported number of people diagnosed with TB between January and June 2020 (Fig. E.3). Compared with the same 6-month period in 2019, overall reductions in India, Indonesia and the Philippines were in the range 25–30%.

The economic impact of the pandemic is predicted to worsen at least two of the key determinants of TB incidence: GDP per capita and undernutrition (Fig E.4). Modelling has suggested that the number of people developing TB could increase by more than 1 million per year in the period 2020–2025. The impact on livelihoods resulting from lost income or unemployment could also increase the percentage of people with TB and their households facing catastrophic costs.

In line with WHO guidance, actions that countries have reported taking to mitigate impacts on essential TB services include expanded use of digital technologies for remote advice and support (108 countries including 21 high TB burden countries) and reducing the need for visits to health facilities by giving preference to home-based treatment and providing TB patients with a one-month supply of drugs (100 countries including 25 high TB burden countries).

Negative impacts on essential TB services include the reallocation of human, financial and other resources from TB to the COVID-19 response. Many countries have reported the use of GeneXpert machines for COVID-19 testing instead of diagnostic testing for TB (43 countries including 13 high TB burden countries), reassignment of staff in national TB programmes to COVID-19 related duties (85 countries including 20 high TB burden countries), and reallocation of budgets (52 countries including 14 high TB burden countries). Smaller but still considerable numbers of countries reported reducing the number of health facilities providing inpatient and outpatient care for people with TB (35 and 32 countries, respectively). In many countries, data collection and reporting have also been affected.

FIG. E.2

Estimated impact of the COVID-19 pandemic on the global number of TB deaths in 2020, for different combinations of decreases in case detection and the duration of these decreases

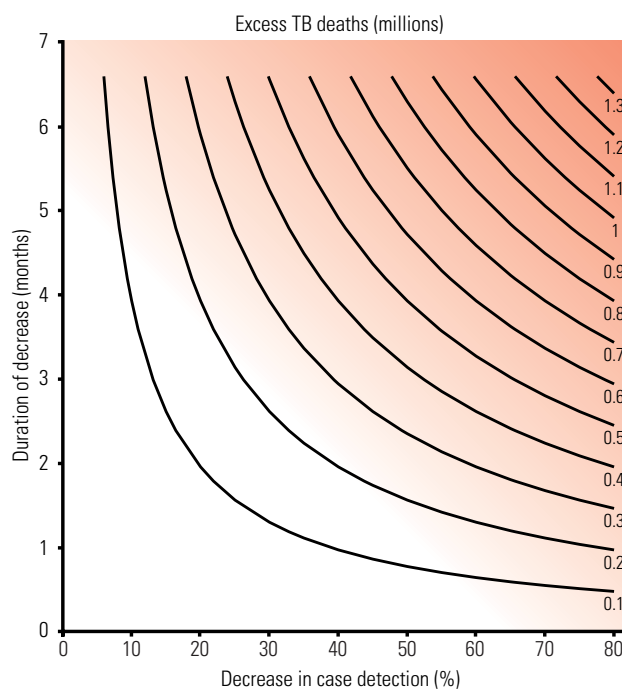


FIG. E.3

Trends in monthly notifications of people diagnosed with TB in four high TB burden countries, January–June 2020

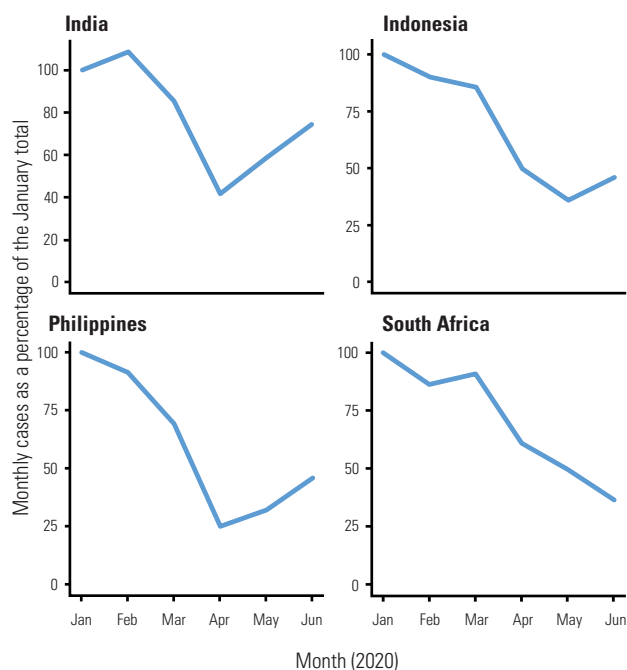
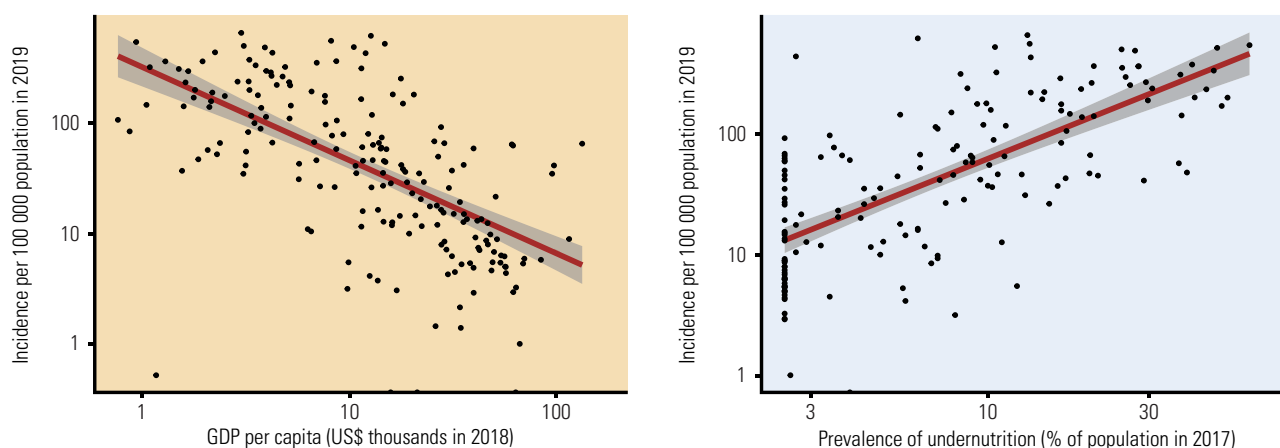


FIG. E.4

The relationship between GDP per capita and the prevalence of undernutrition, and TB incidence per 100 000 population



TB diagnosis and treatment

Globally, 7.1 million people with TB were reported to have been newly diagnosed and notified in 2019, up from 7.0 million in 2018 and a large increase from 6.4 million in 2017 and 5.7–5.8 million annually in the period 2009–2012.

Many countries have increased the number of people newly diagnosed with TB since 2013. The biggest contributors to the global increase were India and Indonesia, the two countries that rank first and second worldwide in terms of estimated incident cases per year.¹⁵ In India, notifications of people newly diagnosed with TB rose from 1.2 million to 2.2 million between 2013 and 2019 (+74%). In Indonesia, the number rose from 331 703 in 2015 to 562 049 in 2019 (+69%).

Despite increases in TB notifications, there was still a large gap (2.9 million) between the number of people newly diagnosed and reported and the 10 million people estimated to have developed TB in 2019. This gap is due to a combination of underreporting of people diagnosed with TB and underdiagnosis (if people with TB cannot access health care or are not diagnosed when they do).

Five countries accounted for more than half of the global gap: India (17%), Nigeria (11%), Indonesia (10%), Pakistan (8%) and the Philippines (7%). In these countries especially, intensified efforts are required to reduce underreporting and improve access to diagnosis and treatment.

As countries intensify efforts to improve TB diagnosis and treatment and close gaps between incidence and notifications, the proportion of notified cases that are bacteriologically confirmed needs to be monitored, to ensure that people are correctly diagnosed and started on the most effective treatment regimen as early as possible. The aim should be to increase bacteriological confirmation by scaling up the use of WHO-recommended diagnostics

(e.g. rapid molecular tests) as the initial diagnostic test for TB. In 2019, 57% of pulmonary cases were bacteriologically confirmed, a slight increase from 55% in 2018. In high-income countries with widespread access to the most sensitive diagnostic tests, about 80% of pulmonary TB cases are bacteriologically confirmed.

The percentage of notified TB patients who had a documented HIV test result in 2019 was 69%, up from 64% in 2018. In the WHO African Region, where the burden of HIV-associated TB is highest, 86% of TB patients had a documented HIV test result. A total of 456 426 people with TB coinfecting with HIV were reported, of whom 88% were on antiretroviral therapy.

The treatment success rate for people newly enrolled on treatment in 2018 was 85%.

Drug-resistant TB: diagnosis and treatment

In accordance with WHO guidelines, detection of MDR/RR-TB requires bacteriological confirmation of TB and testing for drug resistance using rapid molecular tests, culture methods or sequencing technologies. Treatment requires a course of second-line drugs for at least 9 months and up to 20 months, supported by counselling and monitoring for adverse events. WHO recommends expanded access to all-oral regimens.

There was some progress in testing, detection and treatment of MDR/RR-TB between 2018 and 2019. Globally in 2019, 61% of people with bacteriologically confirmed TB were tested for rifampicin resistance, up from 51% in 2017 and 7% in 2012.¹⁶ Coverage of testing was 59% for new and 81% for previously treated TB patients. A global total of 206 030 people with MDR/RR-TB were detected and notified in 2019, a 10% increase from 186 883 in 2018, and 177 099 people were enrolled in treatment, up from 156 205 in 2018.

Despite these improvements, the number of people enrolled in treatment in 2019 was equivalent to only 38% of the estimated number of people who developed MDR/RR-TB in 2019. Closing this wide gap requires one or more of the following: improving detection of TB; increasing bacteriological confirmation among those diagnosed with TB; expanding the coverage of testing for drug resistance among those with bacteriologically confirmed TB; and ensuring that all those diagnosed with MDR/RR-TB are enrolled in treatment.

Ten countries accounted for 77% of the global gap between treatment enrolments and the estimated number of new cases of MDR/RR-TB in 2019, and thus will have a strong influence on progress in closing this gap. China and India accounted for 41% of the global gap.¹⁷

The latest treatment outcome data for people with MDR/RR-TB show a global treatment success rate of 57%. Three examples of high MDR-TB burden countries with relatively high TB treatment coverage that have higher treatment success rates for MDR/RR-TB ($\geq 75\%$) are Ethiopia, Kazakhstan and Myanmar.

TB prevention services

The main health care intervention available to reduce the risk of TB infection progressing to active TB disease is TB preventive treatment.¹⁸ Other interventions are TB infection prevention and control; and vaccination of children with the bacille Calmette–Guérin (BCG) vaccine, which can confer protection, especially from severe forms of TB in children.

WHO guidance recommends TB preventive treatment for people living with HIV, household contacts of bacteriologically confirmed pulmonary TB cases and clinical risk groups (e.g. those receiving dialysis). Globally in 2019, TB preventive treatment was provided to 4.1 million people, up from 2.2 million in 2018.

People living with HIV accounted for 85% (3.5 million) of the 2019 total. Of the 3.5 million, three countries – India, the United Republic of Tanzania and South Africa – accounted for 25%, 17% and 14%, respectively.

Numbers of household contacts provided with TB preventive treatment were much smaller: 423 607 in 2018 and 538 396 in 2019. Of these, 81% were children under 5 years (349 796 in 2018 and 433 156 in 2019, equivalent to 27% and 33% of the 1.3 million estimated to be eligible) and 19% were people in older age groups (73 811 in 2018 and 105 240 in 2019). Substantial scale-up will be needed to reach the targets set at the UN high-level meeting on TB. Building synergies with contact tracing efforts related to the COVID-19 pandemic may help.

The COVID-19 pandemic has also highlighted the importance of infection prevention and control in health care facilities and congregate settings, for both health care workers and people seeking care.

In 2019, 153 countries reported providing BCG vaccination as a standard part of childhood immunization programmes, of which 87 reported coverage of $\geq 90\%$.

Financing for TB prevention, diagnosis and treatment

Funding for the provision of TB prevention, diagnostic and treatment services has doubled since 2006 but still falls far short of what is needed (**Fig. E.1c**).

In 121 low- and middle-income countries that reported data (and accounted for 98% of reported TB cases globally), funding is projected to reach US\$ 6.5 billion in 2020. This is higher than estimated expenditures of US\$ 6.0–6.1 billion annually in these countries between 2017 and 2019, but still only 50% of the global target of at least US\$ 13 billion annually by 2022. Moreover, the final amount may be lower due to reallocation of funding for the COVID-19 response.

As in previous years, most of the funding (85%) available in 2020 is from domestic sources. This aggregate figure is strongly influenced by the BRICS group of countries (Brazil, Russian Federation, India, China and South Africa). The BRICS countries account for 57% of the available funding in 2020, and 97% of their funding is from domestic sources.

In other low- and middle-income countries, international donor funding remains crucial, accounting for 44% of the funding available in the 25 high TB burden countries outside BRICS and 57% of the funding available in low-income countries.

International donor funding, as reported by national TB programmes (NTPs), increased from US\$ 0.9 billion in 2019 to US\$ 1.0 billion in 2020. The single largest source (77% of the total in 2020) is the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund). The largest bilateral donor is the US government, which provides almost 50% of total international donor funding for TB, when combined with funds channelled through and allocated by the Global Fund.

Universal health coverage, social determinants and multisectoral action

The End TB Strategy milestones for 2020 and 2025 can only be achieved if TB diagnosis, treatment and prevention services are provided within the context of progress towards UHC, and if there is multisectoral action and accountability to address the broader determinants that influence TB epidemics and their socioeconomic impact.

UHC means that everyone can obtain the health services they need without suffering financial hardship. SDG Target 3.8 is to achieve UHC by 2030; the two indicators to monitor progress are a UHC service coverage index (SCI), and the percentage of the population experiencing household expenditures on health care that are large in relation to household expenditures or income.

The global SCI increased steadily between 2000 and 2017, from 45 (out of 100) in 2000 to 66 in 2017. Improvements were made in all WHO regions and all World Bank income groups. However, values of the SCI in 2017 in the 30 high TB burden countries were mostly in the range of 40–60.

In 2015, at least 930 million people, or 12.7% of the world's population, faced out-of-pocket expenditures on health care that accounted for 10% or more of their household expenditure or income (a threshold used within the SDG framework to define direct expenditures on health in the general population as catastrophic), up from 9.4% in 2010.

Among high TB burden countries, Thailand stands out as having a high SCI of 80 and a low level of catastrophic health expenditures (2% of households). Brazil and China both had a relatively high SCI of 79.

Many new cases of TB are attributable to five risk factors: undernutrition, HIV infection, alcohol use disorders, smoking (especially among men) and diabetes. In 2019, the estimated numbers of cases attributable to these risk factors were 2.2 million, 0.76 million, 0.72 million, 0.70 million and 0.35 million, respectively. In the context of the COVID-19 pandemic, multisectoral action to address these and other determinants of TB and its consequences, including GDP per capita, poverty and social protection, is more important than ever (Fig. E.4).

Following the request to the WHO Director-General at the UN high-level meeting, a multisectoral accountability framework for TB (MAF-TB) was released by WHO in May 2019. The framework has four major components: commitments; actions; monitoring and reporting; and review. These apply at the global/regional level, and at national (including subnational) level.

At global level, actions taken by WHO include: the development of a MAF-TB checklist; high-level missions; the WHO Director-General Initiative Find.Treat. All#EndTB; engagement of civil society (e.g. the WHO Civil Society Task Force on TB) and youth; updating of guidelines and tools; and development and release of a global strategy for TB research and innovation. Global monitoring, reporting and review has been ensured through annual rounds of data collection, the WHO global TB report, TB reports to the World Health Assembly and the UN Secretary-General 2020 progress report on TB.

Countries have started to adapt and use the MAF-TB. In terms of actions in 2020, 25/30 high TB burden countries reported that they had developed or updated a national strategic plan for TB since the UN high-level meeting on TB, with countries reporting the involvement of civil society and affected communities in 29/30. Most high TB burden countries (27/30) reported that they produce an annual TB report. High-level review mechanisms were stated to be in place in 16/30 countries. More

detailed assessments of the status of accountability using the checklist developed by WHO are underway.

TB research and innovation

The SDG and End TB Strategy targets set for 2030 cannot be met without intensified research and innovation. Technological breakthroughs are needed by 2025, so that the annual decline in the global TB incidence rate can be accelerated to an average of 17% per year. Priorities include a vaccine to lower the risk of infection, a vaccine or new drug treatment to cut the risk of TB disease in the approximately 2 billion people already infected, rapid diagnostics for use at the point of care, and simpler, shorter treatments for TB disease.

The diagnostic pipeline appears robust in terms of the number of tests, products or methods in development. Examples include several cartridge-based technologies for the detection of drug resistance; next-generation sequencing (NGS) assays for detecting drug-resistant TB directly from sputum specimens; and newer skin tests and interferon gamma release assays (IGRA) to test for TB infection.

As of August 2020, there were 22 drugs, various combination regimens and 14 vaccine candidates in clinical trials.

Final results from a Phase IIb trial of the M72/AS01_E vaccine candidate showed a 50% (90% CI: 12–71%) point estimate for vaccine efficacy for people with TB infection after 3 years of follow-up. If the findings are confirmed in a Phase III trial, this vaccine could transform global TB prevention efforts. In 2020, the Gates Medical Research Institute obtained a license to develop M72/AS01_E for use in low-income countries.

A Global Strategy for TB Research and Innovation was adopted by all WHO Member States through a World Health Assembly resolution in August 2020. The strategy aims to support countries and relevant stakeholders to translate commitments in the Moscow Declaration and the political declaration of the UN high-level meeting on TB into concrete actions. WHO has also developed a TB/COVID-19 research compendium and launched a toolkit to support expanded use of digital technologies in TB care.

Conclusion

Leaders of all UN Member States have committed to “ending the global TB epidemic” by 2030, backed up by concrete milestones and targets.

Progress is being made. At the end of 2019, global indicators for reductions in TB disease burden, improved access to TB prevention and care and increased financing were all moving in the right direction. The WHO European Region and several high TB burden countries are on track to reach 2020 milestones for reductions in TB cases and deaths. However, agreed milestones and targets are not

on track to be met globally and the COVID-19 pandemic now threatens to stall or reverse the progress that has been achieved. The UN Secretary-General's 2020 progress report on TB urges countries to implement 10 priority recommendations needed to reach targets and reduce the enormous human and societal toll caused by TB (Fig. E.5).

The overarching message of this report and that of the UN Secretary-General's 2020 progress report on TB is the same. High-level commitments have galvanized global, regional and national progress towards ending TB, but urgent and more ambitious investments and actions are required to put the world on track to reach targets, especially in the context of the COVID-19 pandemic.

¹ For these people, the lifetime risk of developing TB disease is about 5–10%.

² WHO's annual rounds of global TB data collection and the annual WHO Global TB Report are key elements of "monitoring and reporting" in the WHO multisectoral accountability framework for TB.

³ The UN Secretary General's report was released in September 2020.

⁴ The treatment targets were built on the WHO Flagship Initiative "Find. Treat. All. #EndTB" and the funding targets were based on the Stop TB Partnership's Global Plan to End TB, 2018–2022.

⁵ Here and elsewhere, "range" in the context of estimates of TB disease burden refers to the 95% uncertainty interval.

⁶ When an HIV-positive person dies from TB disease, the underlying cause is coded as HIV in the International Classification of Diseases system.

⁷ The other 22 countries are Angola, Brazil, Cambodia, Central African Republic, the Congo, the Democratic People's Republic of Korea, the Democratic Republic of the Congo, Ethiopia, Kenya, Lesotho, Liberia, Mozambique, Myanmar, Namibia, Papua New Guinea, the Russian Federation, Sierra Leone, Thailand, the United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe.

⁸ The 95% uncertainty interval is 400 000–535 000.

⁹ MDR-TB is defined as resistance to rifampicin and isoniazid.

¹⁰ Reductions in other WHO regions were 3.5% in the Eastern Mediterranean Region, 8.7% in the South-East Asia Region and 6.1% in the Western Pacific Region. In the WHO Region of the Americas, incidence is slowly increasing, owing to an upward trend in Brazil.

¹¹ Including TB deaths among both HIV-negative and HIV-positive people.

¹² Reductions in other WHO regions were 6.1% in the Americas, 11% in the Eastern Mediterranean, 10% in South-East Asia and 17% in the Western Pacific.

¹³ Calculated as the sum of direct medical expenditures, non-medical expenditures and income losses.

¹⁴ Funding for TB research is monitored by Treatment Action Group; the latest data are from their 2019 report.

¹⁵ Other countries with large relative increases in 2017–2019 are shown in Fig. 5.2.

¹⁶ The numbers cited refer to pulmonary cases.

¹⁷ The other 8 countries were the Democratic Republic of the Congo, Indonesia, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation and Viet Nam.

¹⁸ The drug regimens currently recommended by WHO are explained in Chapter 6.

FIG. E.5

10 priority recommendations of the UN Secretary-General's 2020 progress report on TB for actions needed to accelerate progress towards global TB targets

-  1. Fully activate high-level leadership to urgently reduce TB deaths and drive multisectoral action to end TB
-  2. Urgently increase funding for essential TB services including the health workforce
-  3. Advance universal health coverage to ensure all people with TB have access to affordable quality care, and resolve underreporting challenges
-  4. Address the drug-resistant TB crisis to close persistent gaps in care
-  5. Dramatically scale up provision of preventive treatment for TB
-  6. Promote human rights and combat stigma and discrimination
-  7. Ensure meaningful engagement of civil society, communities and people affected by TB
-  8. Substantially increase investments in TB research to drive technological breakthroughs and the rapid uptake of innovations
-  9. Ensure that TB prevention and care are safeguarded in the context of COVID-19 and other emerging threats
-  10. Request WHO to continue to provide global leadership for the TB response, working in close collaboration with Member States and other stakeholders, including to prepare for a high-level meeting on TB in 2023 that aligns with the high-level meeting of the General Assembly on universal health coverage also to be held in 2023



Doctors reviewing a patient's medication in a rural TB clinic, South Sudan.

John Rae Photography

Chapter 1

Introduction

Tuberculosis (TB) is a communicable disease that is a major cause of ill health, one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV/AIDS). In 2019, about 10 million people developed TB and 1.4 million died.¹ TB is caused by the bacillus *Mycobacterium tuberculosis*, which is spread when people who are sick with TB expel bacteria into the air; for example, by coughing (Box 1.1). The disease typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB).

TB can affect anyone anywhere, but most people who develop the disease (about 90%) are adults; there are more cases among men than women; and of those who fell sick with TB in 2019, 87% were in 30 high TB burden countries. Case rates at national level vary from less than 5 to more than 500 per 100 000 population per year. TB is a disease of poverty, and economic distress, vulnerability, marginalization, stigma and discrimination are often faced by people affected by TB. About a quarter of the world's population is infected with *M. tuberculosis*.

TB is curable and preventable. Most people (about 85%) who develop TB disease can be successfully treated with a 6-month drug regimen; treatment has the additional benefit of curtailing onward transmission of infection. Since 2000, TB treatment has averted more than 60 million deaths, although with access still falling short of universal health coverage (UHC), many millions have also missed out on diagnosis and care. Preventive treatment is available for people with TB infection. The number of people developing infection and disease (and thus the number of deaths) can also be reduced through multisectoral action to address TB determinants such as poverty, undernutrition, HIV infection, diabetes and smoking.

Research breakthroughs (e.g. a new vaccine) are needed to rapidly reduce TB incidence worldwide to the levels already achieved in low-burden countries, where TB is often regarded as a disease of the past.

In 2014 and 2015, all Member States of the World Health Organization (WHO) and the United Nations (UN) committed to ending the TB epidemic, through their adoption of WHO's End TB Strategy and the UN Sustainable Development Goals (SDGs). The strategy and SDGs include milestones and targets for large reductions in TB incidence, TB deaths and costs faced by TB patients and their households, between 2015 and 2035.

Efforts to step up political commitment to the fight against TB intensified in 2017 and 2018.

A WHO global ministerial conference on TB was organized in November 2017. The outcome was the Moscow Declaration to End TB, which was welcomed by all Member States at the World Health Assembly in May 2018. In September 2018, the UN General Assembly held its first-ever high-level meeting on TB, attended by heads of state and government as well as other leaders. The outcome was a political declaration in which commitments to the SDGs and End TB Strategy were reaffirmed and new ones added. Global targets for the funding to be mobilized for TB prevention, care and research, and for the number of people to be treated for TB infection and disease, were set for the first time.

WHO has published a global TB report every year since 1997. The purpose of the report is to provide a comprehensive and up-to-date assessment of the status of the TB epidemic, and of progress in the response to the epidemic – at global, regional and country levels – in the context of global commitments and strategies. The report is based primarily on data gathered by WHO in annual rounds of data collection. In 2020, data were reported by 198 countries and territories that accounted for more than 99% of the world's population and estimated number of TB cases.

The first major chapter of this 2020 report provides a high-level overview of progress made towards global TB targets by the end of 2019. In recognition of the enormous current and predicted health, economic and social impacts of the COVID-19 pandemic, the next chapter discusses the impact of the pandemic on TB. The remaining chapters cover the following topics: estimates of TB disease burden; TB diagnosis and treatment; TB prevention services; financing for TB prevention, diagnosis and treatment; UHC, TB determinants and multisectoral action; and research and innovation (Table 1.1). The annexes explain WHO's lists of high TB burden countries² and how to access both global, regional and country profiles and online datasets.

This WHO report complements and expands on the UN Secretary-General's 2020 progress report on TB, which was prepared with WHO support as requested in the political declaration of the UN high-level meeting. The overarching message is the same: high-level commitments and targets have galvanized global, regional and national progress towards ending TB, but urgent and more ambitious investments and actions are required to put the world on track to reach targets, especially in the context of the COVID-19 pandemic.

¹ This includes 0.2 million deaths among HIV-positive people, which are officially classified as deaths caused by HIV/AIDS.

² The countries in these lists are given particular attention in the report.

Basic facts about tuberculosis

Tuberculosis (TB) is an old disease – studies of human skeletons show that it has affected humans for thousands of years.^a Its cause remained unknown until 24 March 1882, when Dr Robert Koch announced his discovery of the bacillus responsible, subsequently named *Mycobacterium tuberculosis*.^b The disease is spread when people who are sick with TB expel bacteria into the air (e.g. by coughing). TB typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB).

A relatively small proportion (5–10%) of the approximately 2 billion people infected with *M. tuberculosis* worldwide will develop TB disease during their lifetime. However, the probability of developing TB disease is much higher among people living with HIV, and among people affected by risk factors such as undernutrition, diabetes, smoking and alcohol consumption.

Diagnostic tests for TB disease include sputum smear microscopy (developed more than 100 years ago), rapid molecular tests (first endorsed by WHO in 2010) and culture-based methods – the latter take up to 8 weeks to provide results but remain the reference standard. Today, TB that is resistant to first-line and second-line anti-TB drugs can be detected using rapid tests, culture methods and sequencing technologies.

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.^c

Effective drug treatments were first developed in the 1940s. The currently recommended treatment for cases of drug-susceptible TB disease 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. For people with drug-susceptible TB, treatment success rates of at least 85% are regularly reported to WHO by its 194 Member States. Treatment for people with rifampicin-resistant TB (RR-TB) and multidrug-resistant TB (MDR-TB)^d is longer, and requires drugs that are more expensive (≥US\$ 1000 per person) and more toxic. The latest data reported to WHO show a treatment success rate for MDR-TB of 57% globally.

Recommended options for TB preventive treatment include: a weekly dose of rifapentine and isoniazid for 3 months (3HP), a daily dose of rifampicin plus isoniazid for 3 months (3HR), a daily dose of rifapentine plus isoniazid for 1 month (1HP), a daily dose of rifampicin for 4 months (4R), and a daily dose of isoniazid for 6 months (6H) or longer.

The only licensed vaccine for prevention of TB disease is the bacille Calmette-Guérin (BCG) vaccine. The BCG vaccine was developed almost 100 years ago, prevents severe forms of TB in children and is widely used. There is currently no vaccine that is effective in preventing TB disease in adults, either before or after exposure to TB infection, although results from a Phase II trial of the M72/AS01E candidate are promising.^e

^a Hershkovitz I, Donoghue HD, Minnikin DE, May H, Lee OY, Feldman M, et al. Tuberculosis origin: the Neolithic scenario. *Tuberculosis*. 2015;95 Suppl 1:S122–6 (<https://www.ncbi.nlm.nih.gov/pubmed/25726364>, accessed 16 September 2020).

^b Sakula A. Robert Koch: centenary of the discovery of the tubercle bacillus, 1882. *Thorax*. 1982;37(4):246–51 (<https://www.ncbi.nlm.nih.gov/pubmed/6180494>, accessed 16 September 2020).

^c 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 (<https://www.ncbi.nlm.nih.gov/pubmed/21483732>, accessed 16 September 2020).

^d Defined as resistance to isoniazid and rifampicin, the two most powerful anti-TB drugs.

^e Further details are provided in [Chapter 9](#).

TABLE 1.1
Overview of topics covered in the 2020 report

Chapter	Standard topics (main text)	New or featured ^a topics
2. Progress towards global TB targets – an overview	<ul style="list-style-type: none"> • None – new chapter in 2020 	<ul style="list-style-type: none"> • A synthesis of progress made towards TB targets set in the SDGs, the End TB Strategy and the political declaration at the first UN high-level meeting on TB, by the end of 2019 • The WHO End TB Strategy “at a glance” • 10 priority recommendations of the UN Secretary-General’s 2020 progress report on TB, for actions needed to accelerate progress towards global TB targets
3. The COVID-19 pandemic and TB – impact and implications	<ul style="list-style-type: none"> • None – new chapter in 2020 	<ul style="list-style-type: none"> • An assessment of how the COVID-19 pandemic will affect progress towards global TB targets • Evidence about trends in monthly notifications of TB cases in 2020 from selected high TB burden countries, in the context of disruptions to access to and provision of essential health services • Impacts on TB service delivery and mitigation strategies in 2020, based on data reported by 184 countries • WHO guidance and support for the TB response in the context of the COVID-19 pandemic
4. TB disease burden	<ul style="list-style-type: none"> • TB incidence • TB mortality • Drug-resistant TB • National TB prevalence surveys • Strengthening TB surveillance 	<ul style="list-style-type: none"> • The WHO Global Task Force on TB Impact Measurement • Updates to estimates of TB disease burden in this report and anticipated updates • Global estimates of the burden of isoniazid-resistant TB • Transitioning to continuous surveillance for drug-resistant TB
5. TB diagnosis and treatment	<ul style="list-style-type: none"> • TB case notifications, including disaggregation by age, sex and type/site of disease • Rapid testing for TB • HIV testing for TB patients • Testing for drug resistance and detection of drug-resistant TB • Digital case-based surveillance • Treatment coverage • Treatment outcomes 	<ul style="list-style-type: none"> • Trends in the contribution of public–private and public–public mix (PPM) approaches to TB case notifications • Strengthening data collection for children and adolescents with TB • Global guidance and tools for strengthening routine country health information systems, and the analysis and use of data they produce • Community contributions to TB notifications and treatment support
6. TB prevention services	<ul style="list-style-type: none"> • TB preventive treatment • Infection prevention and control • TB vaccination 	<ul style="list-style-type: none"> • Uptake of shorter rifamycin-containing regimens for TB preventive treatment • New initiatives to improve uptake and scale-up of TB preventive treatment
7. Financing for TB prevention, diagnosis and treatment	<ul style="list-style-type: none"> • Estimates of funding required for TB prevention, diagnosis and treatment • Trends in TB funding, overall and by category of expenditure and source • Funding gaps reported by national TB programmes • Unit costs of treatment for drug-susceptible TB and MDR-TB 	<ul style="list-style-type: none"> • International donor funding for TB prevention, diagnosis and treatment, based on donor reports to the Organisation for Economic Co-operation and Development
8. Universal health coverage, TB determinants and multisectoral action	<ul style="list-style-type: none"> • Global progress towards universal health coverage • National surveys of costs faced by TB patients and their households • Broader determinants of the TB epidemic 	<ul style="list-style-type: none"> • The difference between “catastrophic total costs” for TB patients and their households, and the SDG indicator of catastrophic expenditures on health care • Results from national surveys of costs faced by TB patients and their households in the Democratic Republic of the Congo and Lao People’s Democratic Republic • TB determinants and TB disease burden: potential impact of the COVID-19 pandemic • The WHO multisectoral accountability framework for TB • The WHO Civil Society Task Force on TB • High-level mechanisms and initiatives to end TB at country level
9. TB research and innovation	<ul style="list-style-type: none"> • New diagnostics for TB • New drugs and drug regimens to treat TB disease • New drugs and drug regimens to treat TB infection • New TB vaccines 	<ul style="list-style-type: none"> • A new WHO global strategy for TB research and innovation • Compendium for research on TB and COVID-19 • Expanding the use of digital technologies in TB service delivery: an implementation research toolkit • Roadmap for the research and development of new TB vaccines

^a “Featured” topics are those highlighted in boxes.



TB screening activities in a rural village, Cambodia.

Yoshi Shimizu/WHO

Chapter 2

Progress towards global TB targets – an overview

Global TB targets for the period 2016–2035 have been set as part of the United Nations (UN) Sustainable Development Goals (SDGs), the World Health Organization (WHO) End TB Strategy and the political declaration of the UN high-level meeting on TB held in 2018 (**Table 2.1, Box 2.1**).

The SDGs were adopted by all UN Member States at the UN General Assembly in September 2015, and are for the period 2016–2030 (1). SDG 3 (the overall health goal) includes a target to end the TB epidemic, for which the indicator for measurement of progress is the TB incidence rate (new and relapse cases per 100 000 population per year).

The End TB Strategy (**Box 2.1**) was adopted by all WHO Member States at the World Health Assembly in 2014 (2). It includes targets and milestones for reductions in TB disease burden in the period 2016–2035, measured as the TB incidence rate (new and relapse cases per 100 000 population per year) and the annual number of TB deaths; and a target that no TB-affected households face catastrophic costs by 2020. To achieve the targets and milestones, the strategy has 10 components organized under three pillars, and four underlying principles (**Box 2.1**).

Provision of people-centred TB prevention and care within the broader context of progress towards universal health coverage (UHC; SDG Target 3.8) and multi-sectoral action on broader determinants of TB incidence (e.g. poverty, housing quality, social protection, undernutrition and economic growth, which are included under other SDGs) are necessary to reach the milestones.¹ Technological breakthroughs from TB research are needed to achieve the targets, so that TB incidence can decline at an average rate of 17% per year after 2025 (3).²

The political declaration of the UN high-level meeting on TB held in September 2018 (4) reaffirmed the SDG and End TB Strategy targets. It also established new targets for the numbers of people to be provided with TB treatment and TB preventive treatment during the period 2018–2022, which were derived from and consistent with End TB Strategy milestones; and new targets for the funding to be mobilized between 2018 and 2022, based on the Stop TB Partnership’s Global Plan to End TB (5).

This chapter provides an overview of progress towards global TB targets by the end of 2019.³ It is an expanded version of Section II of the UN Secretary-General’s 2020 progress report on TB (6), which was prepared with WHO support as requested in the political declaration of the UN high-level meeting.

TABLE 2.1

Global TB targets set in the SDGs, the End TB Strategy and the political declaration of the UN high-level meeting on TB, for the period up to the SDG deadline of 2030

SDG Target 3.3	By 2030, end the epidemics of AIDS, TB, malaria and neglected tropical diseases, and combat hepatitis, water-borne diseases and other communicable diseases
WHO End TB Strategy	80% reduction in the TB incidence rate (new and relapse cases per 100 000 population per year) by 2030, compared with 2015 <i>2020 milestone: 20% reduction; 2025 milestone: 50% reduction</i>
	90% reduction in the annual number of TB deaths by 2030, compared with 2015 <i>2020 milestone: 35% reduction; 2025 milestone: 75% reduction</i>
	No households affected by TB face catastrophic costs by 2020
UN high-level meeting on TB, 2018	40 million people treated for TB from 2018 to 2022, including: <ul style="list-style-type: none"> • 3.5 million children • 1.5 million people with drug-resistant TB, including 115 000 children
	At least 30 million people provided with TB preventive treatment from 2018 to 2022, including: <ul style="list-style-type: none"> • 6 million people living with HIV • 4 million children under 5 years of age and 20 million people in other age groups, who are household contacts of people affected by TB
	Funding of at least US\$ 13 billion per year for universal access to TB prevention, diagnosis, treatment and care by 2022
	Funding of at least US\$ 2 billion per year for TB research from 2018 to 2022

AIDS: acquired immunodeficiency syndrome; HIV: human immunodeficiency virus; SDG: Sustainable Development Goal; TB: tuberculosis; UN: United Nations.

¹ See **Chapters 5–8** for further details.

² See **Chapter 9** for further details.

³ Further details are provided in other chapters and the impact of the COVID-19 pandemic is assessed in **Chapter 3**.

BOX 2.1

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 ^a	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 facing 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

^a Targets linked to the Sustainable Development Goals (SDGs).

2.1 TB incidence

Globally, the TB incidence rate is falling, but not fast enough to reach the first milestone of the End TB Strategy; that is, a 20% reduction between 2015 and 2020 (Fig. 2.1). Worldwide, the cumulative reduction from 2015 to 2019 was 9% (from 142 to 130 new cases per 100 000 population), including a reduction of 2.3% between 2018 and 2019.

More positively, the WHO European Region has almost reached the 2020 milestone, with a reduction of 19% between 2015 and 2019, and the African Region has made good progress, with a reduction of 16%. Reductions in other WHO regions were 3.5% in the Eastern Mediterranean Region, 8.7% in the South-East Asia Region and

6.1% in the Western Pacific Region. In the WHO Region of the Americas, incidence is slowly increasing, owing to an upward trend in Brazil.

A total of 78 countries are on track to reach the 2020 milestone. This includes seven high TB burden countries¹ that have already reached it (Cambodia, Ethiopia, Kenya, Namibia, the Russian Federation, South Africa and the United Republic of Tanzania) and three others that are on track (Lesotho, Myanmar and Zimbabwe).

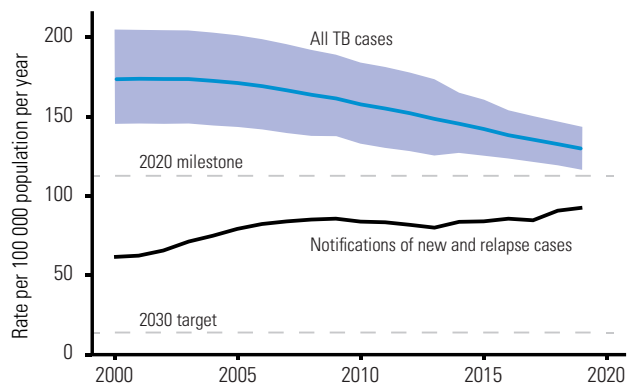
In 2019, 54 countries had a low incidence of TB (<10 cases per 100 000 population per year), mostly in the

¹ In 2015, WHO defined a list of 30 high TB burden countries for the period 2016–2020. It also defined specific lists for multidrug-resistant TB (MDR-TB) and TB/HIV. See Annex 2 for further details.

FIG. 2.1

Global trend in the estimated TB incidence rate (blue), 2000–2019

The blue shaded area is the uncertainty interval. Horizontal dashed lines mark the 2020 milestone and the 2030 target of the End TB Strategy. For comparison, the solid black line shows the number of people with TB who were notified (officially reported) to national authorities.



WHO Region of the Americas and European Region, plus a few countries in the Eastern Mediterranean and Western Pacific regions (Fig. 2.2). These countries are well placed to target TB elimination.

In absolute numbers, about 10.0 million people fell ill with TB in 2019. Of these, 56% were men, 32% were wom-

en and 12% were children (aged <15); overall, 8.2% of people with TB were living with HIV. The 30 high TB burden countries accounted for 87% of global cases; eight of these countries (labelled in Fig. 2.3) accounted for about two thirds of the global total.

2.2 TB deaths

Worldwide, TB is the leading infectious disease killer and one of the top 10 causes of death overall (7). In 2019, it caused 1.4 million deaths, including 208 000 among HIV-positive people.¹

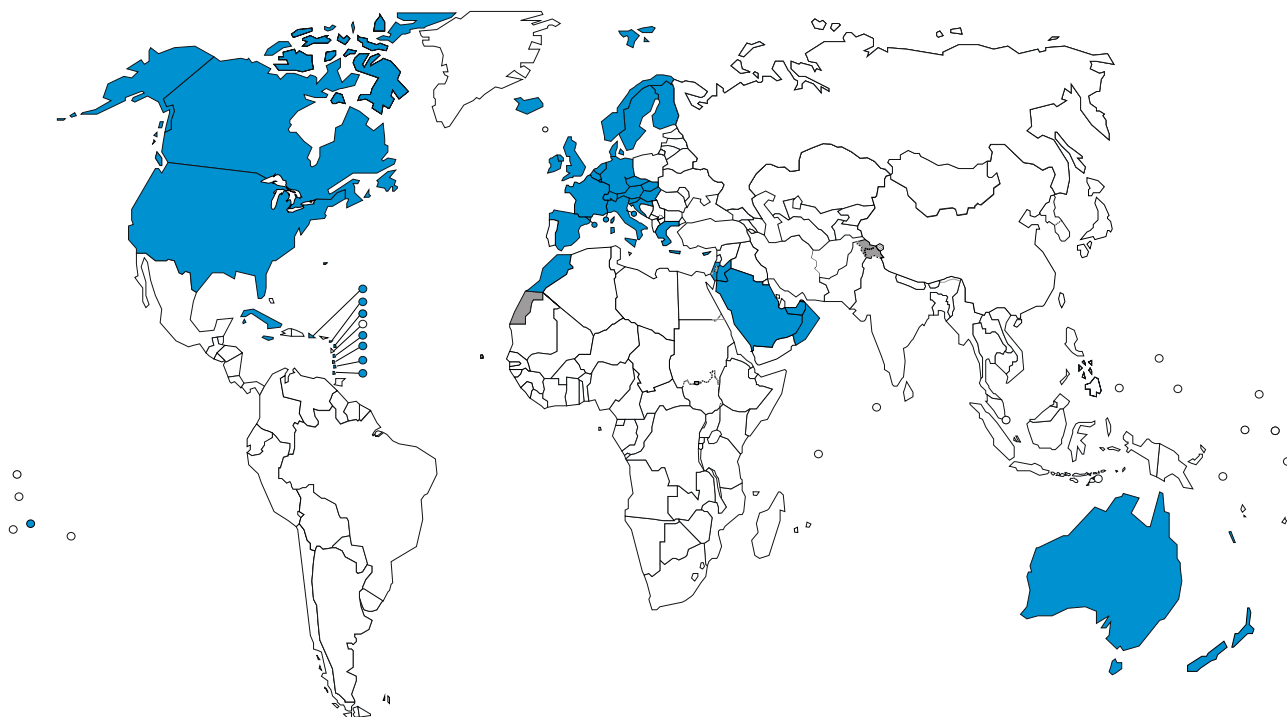
The annual number of TB deaths is falling globally, but not fast enough to reach the first milestone of the End TB Strategy; that is, a 35% reduction between 2015 and 2020 (Fig. 2.4). The cumulative reduction between 2015 and 2019 was only 14%, less than halfway towards the milestone.

The WHO European Region is on track to reach the 2020 milestone, with a 31% reduction from 2015 to 2019, and the African Region has made good progress, achieving a reduction of 19%. Reductions in other WHO regions were 6.1% in the Americas, 11% in the Eastern Mediterranean, 10% in South-East Asia and 17% in the Western Pacific.

A total of 46 countries are on track to reach the 2020 milestone. This includes seven high TB burden countries that have already reached it (Bangladesh, Kenya, Mozambique, Myanmar, the Russian Federation, Sierra Leone and the United Republic of Tanzania) and one other that is on track (Viet Nam).

FIG. 2.2

Countries (in blue) that had an estimated TB incidence rate of less than 10 per 100 000 population in 2019



¹ When an HIV-positive person dies from TB, the underlying cause is coded as HIV in the International Classification of Diseases system.

FIG. 2.3

Countries that had at least 100 000 incident cases of TB in 2019

The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of global cases in 2019, are labelled.

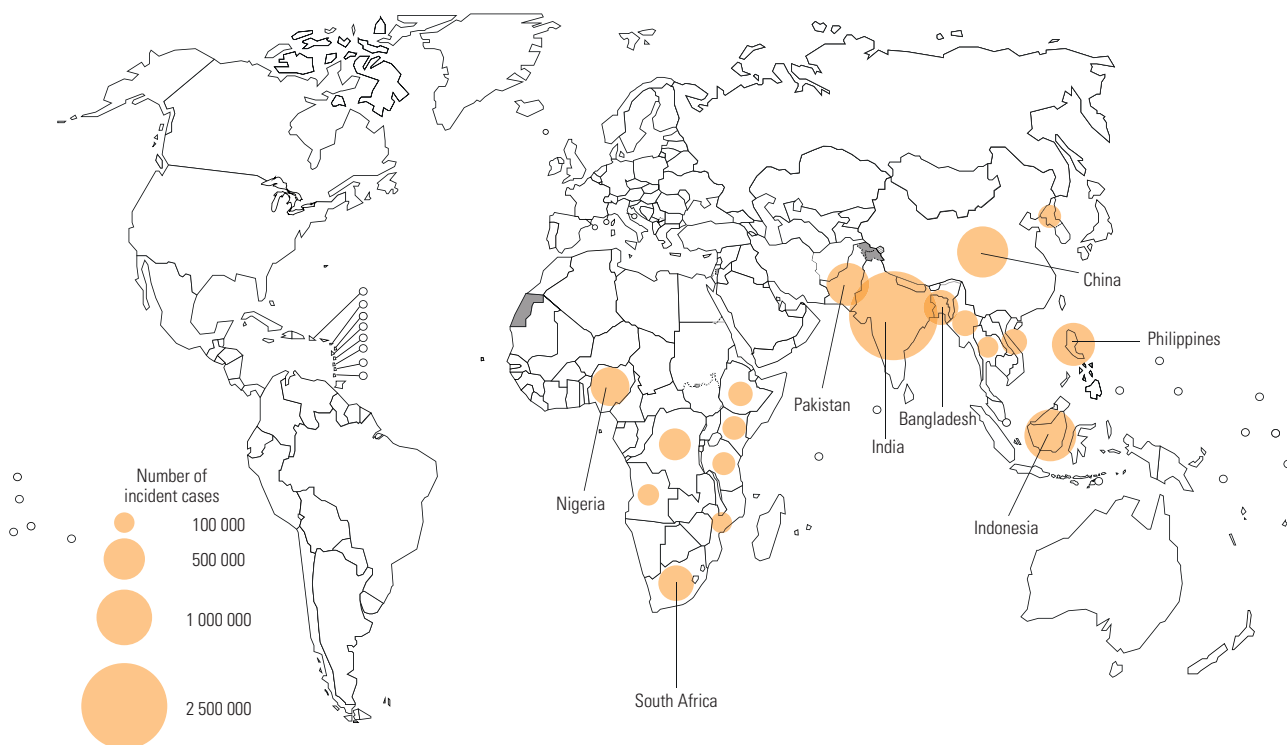
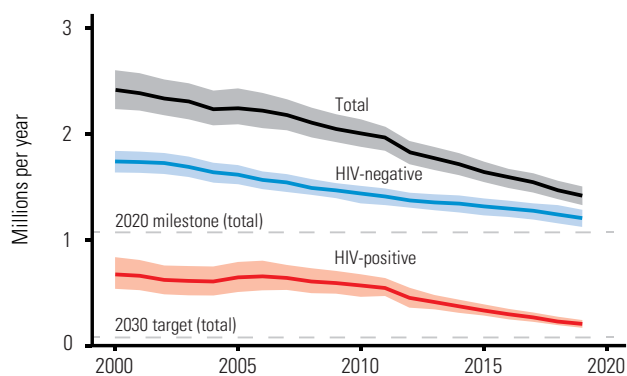


FIG. 2.4

Global trend in the estimated number of TB deaths, 2000–2019

The shaded areas are uncertainty intervals. Horizontal dashed lines mark the 2020 milestone and 2030 target of the End TB Strategy.



2.3 Households affected by TB facing catastrophic costs

Since 2015, a total of 17 countries have completed a national survey of costs faced by TB patients and their households.¹ On average, 49% of people with TB and their households faced catastrophic costs (defined as total costs² equivalent to >20% of annual household income), with a range of 19–83% (Fig. 2.5). For people with drug-resistant TB, the figure was higher still, at 80% (range: 67–100%). No country has yet demonstrated that it has met the target that no TB-affected households face catastrophic costs.

¹ Further details and a discussion of actions needed to reduce these costs are provided in [Chapter 8](#).

² Calculated as the sum of direct medical expenditures, non-medical expenditures and income losses.

2.4 Number of people provided with TB treatment

Globally, the annual number of people reported to have been provided with treatment for TB disease¹ has grown in recent years, from about 6 million in 2015 to 7.0 million in 2018 and 7.1 million in 2019 (Fig. 2.6).

The annual number of people reported to have been provided with treatment for multidrug- or rifampicin-resistant TB (MDR/RR-TB)² disease has also grown, from a global total of 122 726 in 2015 to 156 205 in 2018 and 177 099 in 2019 (Fig. 2.7).³

The cumulative total of 14.1 million people treated for TB in 2018 and 2019 was 35% of the cumulative 5-year (2018–2022) target of 40 million (Fig. 2.8). For children, the combined total was 1.04 million (about 0.5 million in each year), 30% of the way towards the cumulative 5-year target of 3.5 million.

A total of 42 countries, including 13 of the 30 high TB burden countries, reported that the number of people treated for TB increased by 10% or more between 2017 and 2019, while TB incidence in these countries was estimated to have slowly declined. Increases in absolute terms were particularly large in two high TB burden countries, India and Indonesia, at 513 000 people (+31%) and 120 000 people (+27%), respectively. Among the other 30 high TB burden countries, high levels of treatment coverage⁴ (>80%) have already been achieved in Brazil, China and the Russian Federation.

The total number of people treated for MDR/RR-TB in 2018–2019, at 333 304 (Fig. 2.7), was 22% of the way towards the 5-year target of 1.5 million (Fig. 2.8). For children, the total was 8986, less than 10% of the 5-year target of 115 000.

In 70 countries, the number of people reported to have been enrolled in treatment for MDR/RR-TB increased by 10% or more between 2017 and 2019. The five countries with the biggest increases in absolute numbers were (in descending order) India, China, the Russian Federation, Indonesia and Angola. Of the 30 high MDR-TB burden countries, those with the smallest gaps between the estimated number of incident cases of MDR/RR-TB and the number of people enrolled on treatment in 2019 included Azerbaijan, Belarus, Kazakhstan, Peru, Republic of Moldova, the Russian Federation, South Africa and Ukraine.

¹ On the assumption that all people diagnosed with TB who were officially notified to WHO were treated. Additional people whose TB diagnosis was not notified to national authorities and reported to WHO may also have been treated.

² MDR-TB is defined as resistance to rifampicin (RR-TB) and isoniazid, the two most effective first-line anti-TB drugs. WHO recommends a treatment regimen that includes second-line drugs for people with MDR/RR-TB.

³ Additional people whose diagnosis of MDR/RR-TB was not notified to national authorities and reported to WHO may also have been enrolled on treatment.

⁴ That is, the number of people started on treatment divided by the estimated number of incident cases in the same year.

FIG. 2.5

Percentage of people with TB and their households facing catastrophic costs in 17 national surveys completed since 2015

The number in the centre of each circle is the pooled average figure across all surveys; the range is the minimum and maximum values in the 17 countries.

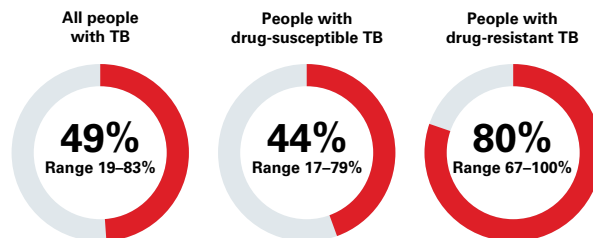


FIG. 2.6

The global number of people reported to have been treated for TB disease, 2015–2019

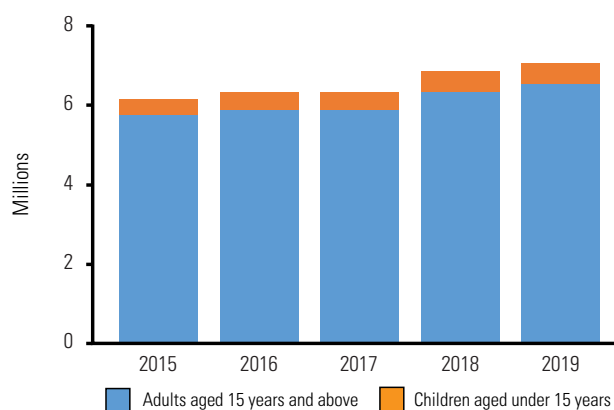


FIG. 2.7

The global number of people reported to have been enrolled on treatment for MDR/RR-TB, 2015–2019

Global data disaggregated by age are not available for the years before 2018.

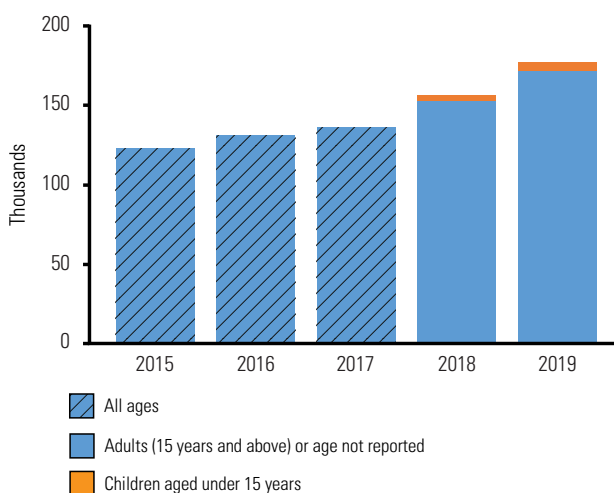
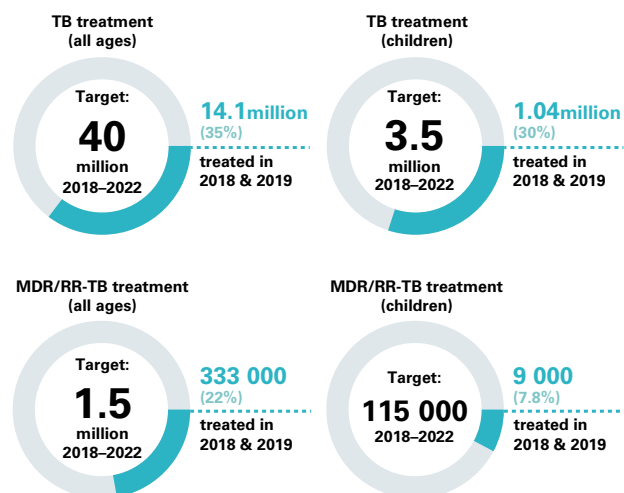


FIG. 2.8

Global progress in the number of people treated for TB in 2018 and 2019 compared with cumulative targets set for 2018–2022 at the UN high-level meeting on TB

The centre of each circle shows the target, the colour coding shows progress made by the end of 2019 and the text to the right of each circle quantifies the status of progress at the end of 2019.



2.5 Number of people provided with TB preventive treatment

WHO recommends TB preventive treatment for people living with HIV, household contacts of those with bacteriologically confirmed pulmonary TB and clinical risk groups (e.g. people receiving dialysis). WHO gathers data for people living with HIV and household contacts.

The number of people provided with TB preventive treatment has increased in recent years, from 1.0 million in 2015 to 2.2 million in 2018 and 4.1 million in 2019 (Fig. 2.9).

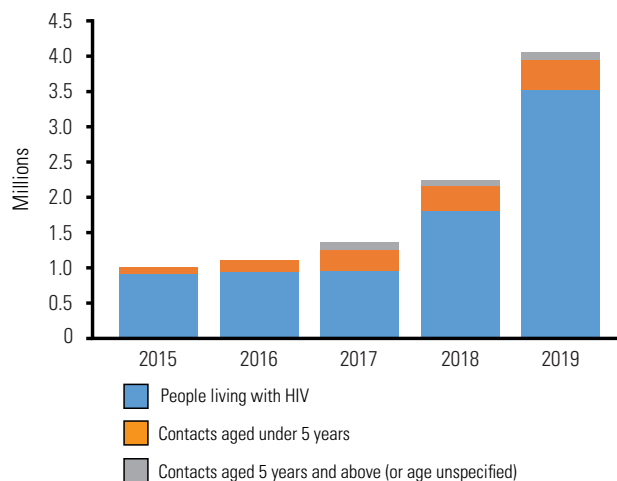
Most of those provided with TB preventive treatment were people living with HIV: 1.8 million in 2018 and 3.5 million in 2019. India and South Africa accounted for 25% and 18% of the combined total for 2018–2019, respectively.

Numbers for household contacts have been much smaller: 423 607 in 2018 and 538 396 in 2019. This included a total of 782 952 children aged under 5 years (349 796 in 2018 and 433 156 in 2019) and 179 051 people in older age groups (73 811 in 2018 and 105 240 in 2019). The WHO Region of the Americas and European Region had the highest coverage of treatment for contacts.

The 6.3 million people started on TB preventive treatment in 2018 and 2019 was 21% of the way towards the 5-year target of 30 million (Fig. 2.10), with progress for household contacts lagging far behind. For people living with HIV, the subtarget of 6 million is on track to be met in 2020.

FIG. 2.9

The global number of people reported to have been provided with TB preventive treatment, 2015–2019



2.6 Funding for universal access to TB prevention, diagnosis, treatment and care

Funding for TB prevention, diagnosis, treatment and care in 121 low- and middle-income countries has reached US\$ 6.5 billion in 2020, up from US\$ 6.1 billion in 2017 and US\$ 5.6 billion in 2015 (Fig. 2.11).¹ Even allowing for the fact that there will have been additional funding in the remaining 14 low- and middle-income countries, and in high-income countries, funding falls far short of the UN high-level meeting target of at least US\$ 13 billion per year by 2022; to reach the target, funding needs to approximately double.

Overall, most funding (85%) comes from domestic sources. However, aggregate figures are strongly influenced by the BRICS group of countries (Brazil, Russian Federation, India, China and South Africa). The BRICS countries account for 57% of available funding in 2020, 97% of which is from domestic sources. In other low- and middle-income countries, international donor funding remains crucial; in 2020, such funding accounted for 44% of the funding available in the 25 high TB burden countries outside BRICS and 57% of funding in low-income countries.

Since 2015, funding from international donors has been about US\$ 1 billion per year, with about 70% of this total coming from the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund).² The recent commitment to replenish this fund means that more than 110

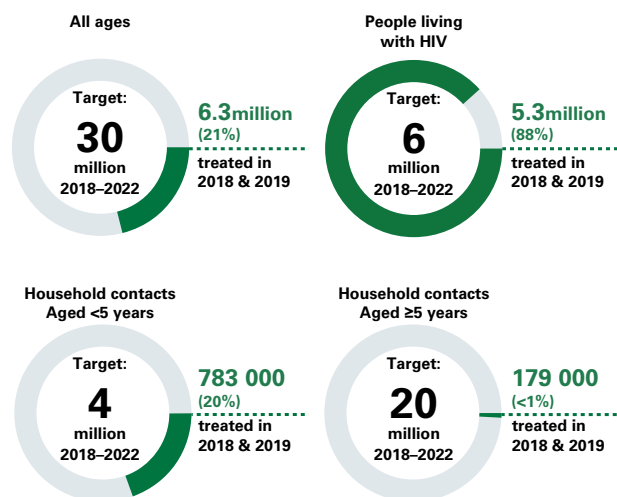
¹ Further details are provided in **Chapter 7**.

² Further details about international donor funding for TB are provided in **Box 7.1** of **Chapter 7**.

FIG. 2.10

Global progress in provision of TB preventive treatment in 2018 and 2019 compared with cumulative targets set for 2018–2022 at the UN high-level meeting on TB

The centre of each circle shows the target, the colour coding shows progress made by the end of 2019 and the text to the right of each circle quantifies the status of progress at the end of 2019.



countries will continue to receive critical financial support, although the share of resources allocated for TB is currently fixed at 18%. The largest bilateral donor is the United States (US) government.

2.7 Funding for TB research

Funding for TB research has grown in recent years; it reached US\$ 906 million in 2018, up from US\$ 772 million in 2017 (Fig. 2.12) (8). However, this amount was less than half of the UN high-level meeting target of US\$ 2 billion per year.

The two largest investors in 2018 were the US government and the Bill & Melinda Gates Foundation, which together accounted for 56% of total funding. The 30 largest funders accounted for 90% of the total. About one third of TB research funding was for drug research, followed by 20% for basic science, 13% for operational research, 12% for vaccines, and 9% each for diagnostics and infrastructure or unspecified research.

2.8 Summary

Progress towards TB targets has been made at global, regional and national levels. However, worldwide, none of the targets is on track to be achieved (Fig. 2.13). Of great concern is the fact that progress made by the end of 2019 could be reversed by the COVID-19 pandemic. This is the subject of the next chapter.

The 10 priority recommendations of the UN Secretary-General’s 2020 progress report on TB for actions needed to accelerate progress towards global TB targets are listed in Box 2.2.

FIG. 2.11

Funding for TB prevention, diagnosis and treatment in low and middle-income countries compared with the global target set at the UN high-level meeting on TB of at least US\$ 13 billion per year by 2022

Data are for 121 low- and middle-income countries that have 98% of the world’s officially reported TB cases.

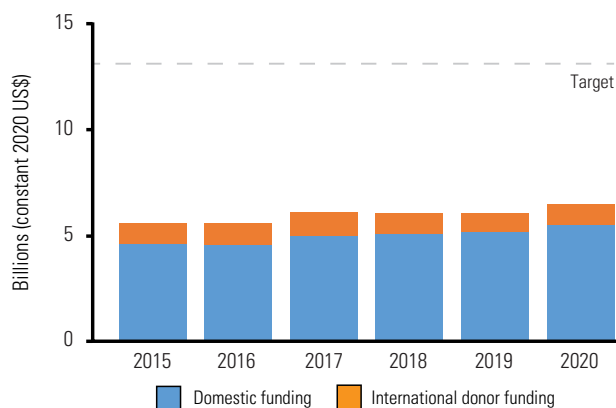
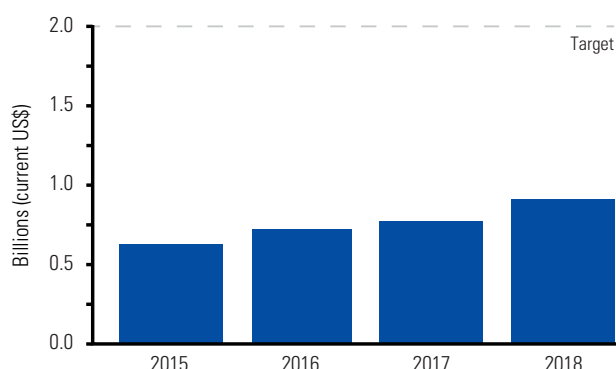


FIG. 2.12

Funding for TB research, 2015–2018



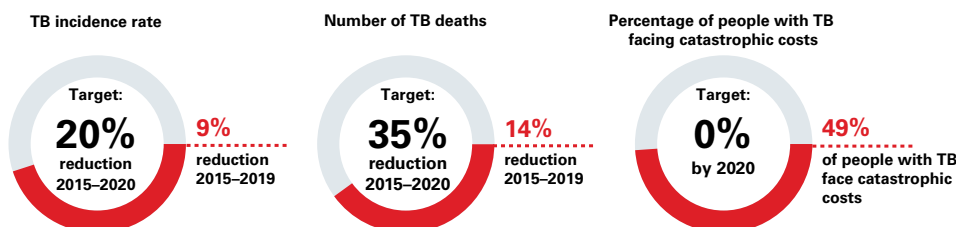
Source: Treatment Action Group, Stop TB Partnership. Tuberculosis research funding trends 2005–2018. New York: Treatment Action Group; 2019 (<https://www.treatmentactiongroup.org/resources/tbrd-report/tbrd-report-2019/>, accessed 22 July 2020).

FIG. 2.13

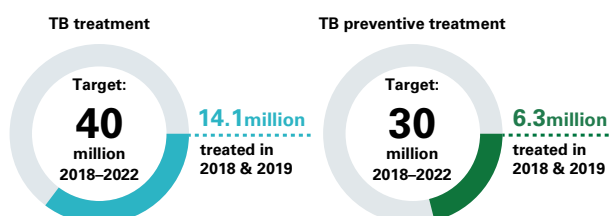
Overview of progress towards global TB targets

The centre of each circle shows the target, the colour coding illustrates the progress made and the text to the right of each circle quantifies the status of progress (by the end of 2019, except for funding).

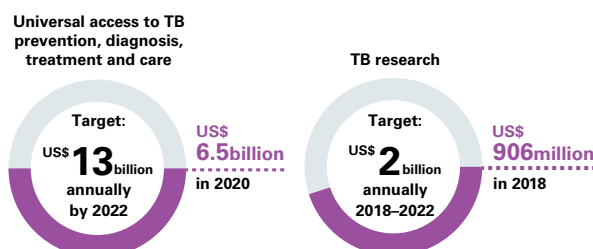
a) SDGs and End TB Strategy: targets for reductions in the TB incidence rate, TB deaths and catastrophic costs



b) UN high-level meeting on TB: targets for the number of people provided with TB treatment and TB preventive treatment



c) UN high-level meeting on TB: targets for increased funding



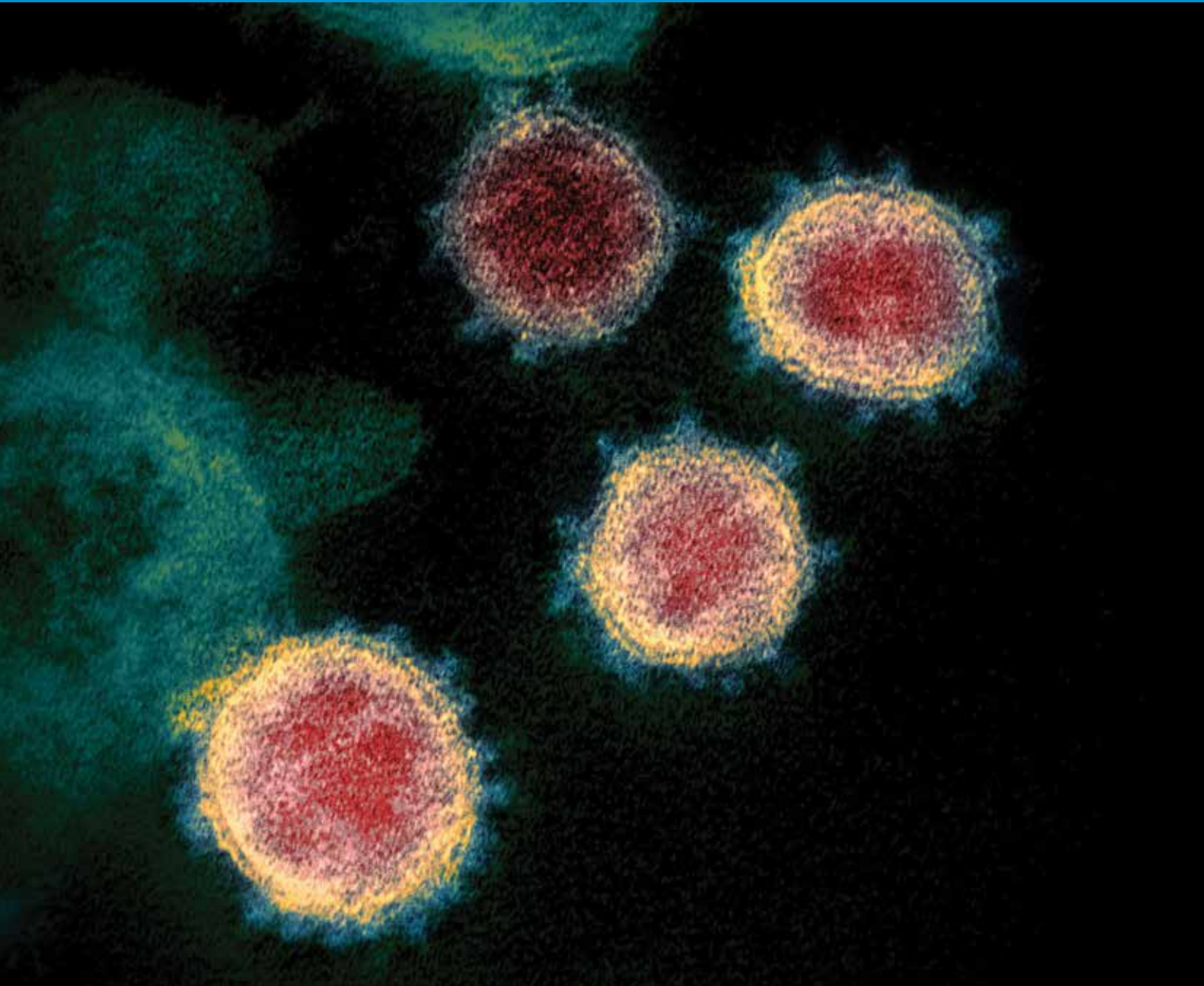
BOX 2.2

10 priority recommendations of the UN Secretary-General's 2020 progress report on TB for actions needed to accelerate progress towards global TB targets

1. Fully activate high-level leadership to urgently reduce TB deaths and drive multisectoral action to end TB
2. Urgently increase funding for essential TB services including for the health workforce
3. Advance universal health coverage to ensure all people with TB have access to affordable quality care and resolve under-reporting challenges
4. Address the drug-resistant TB crisis to close persistent gaps in care
5. Dramatically scale up provision of TB preventive treatment
6. Promote human rights and combat stigma and discrimination
7. Ensure meaningful engagement of civil society, communities and people affected by TB
8. Substantially increase investments in TB research to drive technological breakthroughs and rapid uptake of innovations
9. Ensure that TB prevention and care are safeguarded in the context of the COVID-19 pandemic and other emerging threats
10. Request WHO to continue to provide global leadership for the TB response, working in close collaboration with Member States and other stakeholders, including to prepare for a high-level meeting on TB in 2023

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**SARS-CoV-2 under a scanning
electron microscope.**

BSIP SA / Alamy Stock Photo

Chapter 3

The COVID-19 pandemic and TB – impact and implications

Since the beginning of 2020, the COVID-19 pandemic has caused enormous health, social and economic impacts, which are likely to continue in 2021 and beyond. Even after some of these impacts have been mitigated or contained, there will be medium- and longer-term consequences, including for the tuberculosis (TB) epidemic and response. The pandemic threatens to reverse the progress made towards global TB targets by the end of 2019 (Chapter 2).

This chapter discusses the predicted impact of the COVID-19 pandemic on the global annual number of TB deaths and the global annual number of people developing TB disease in 2020 and beyond, based on modelling; and how the proportion of TB-affected households facing catastrophic costs may be affected. It also summarizes evidence about impacts on access to and delivery of essential TB services and the allocation of human, financial and other resources in 2020, based on data gathered by the World Health Organization (WHO) from national TB programmes (NTPs) as part of the 2020 round of global TB data collection (Chapter 1). The last section summarizes actions taken by the WHO Global TB Programme to support NTPs and identifies the potential for synergies in responding to both TB and COVID-19.

The chapter is an expanded version of Section IV of the UN Secretary-General's 2020 progress report on TB (1), which was prepared with WHO support as requested in the political declaration of the UN high-level meeting on TB held in September 2018 (2).

3.1 Global annual number of TB deaths in 2020 and beyond

Two modelling analyses have reached similar conclusions about the potential impact of the COVID-19 pandemic on global TB deaths (3, 4). They suggest that the annual number could rise to the levels seen in 2015 or even 2012.

The WHO analysis assessed the additional number of TB deaths that could occur globally in 2020 for different combinations of a decrease in case detection (compared with levels before the pandemic) and the number of months for which this decrease occurs (Fig. 3.1). If the number of people with TB detected and treated were to fall by 25–50% over a period of 3 months – a range considered plausible based on data from several high TB burden countries (Fig 3.2, Fig. 3.3) – there could be between 200 000 and 400 000 excess TB deaths in 2020, bringing the total to about 1.6–1.8 million. An increase of 200 000 would take the world back to 2015 levels and an increase of 400 000 to 2012 levels.¹

¹ It is also possible that TB could worsen outcomes in people with COVID-19.

FIG. 3.1

Estimated impact of the COVID-19 pandemic on the global number of TB deaths in 2020, for different combinations of decreases in case detection and the duration of these decreases

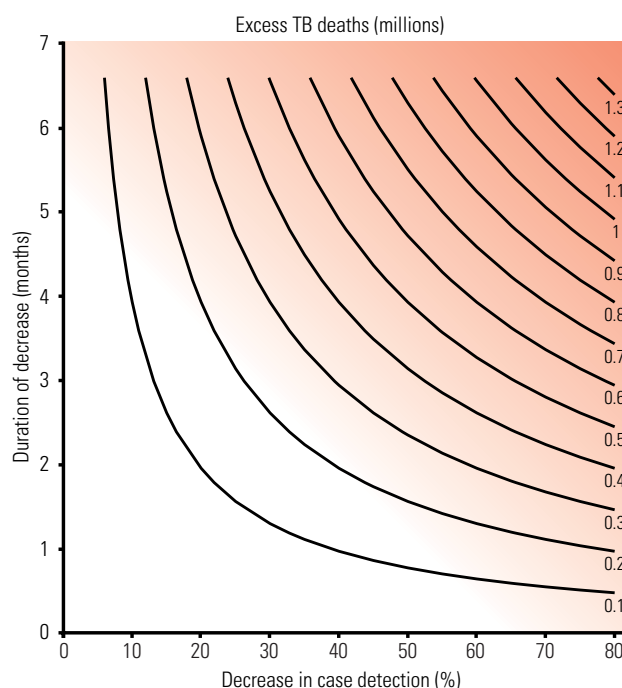
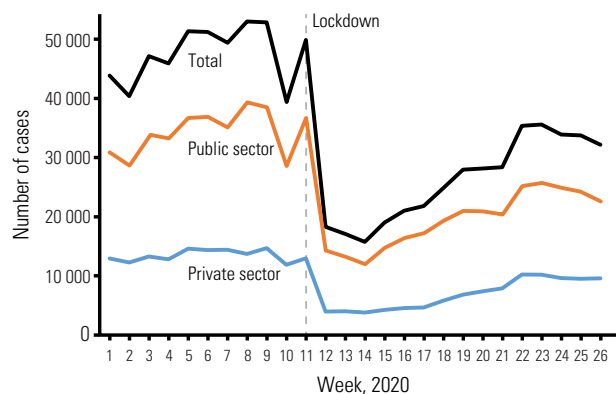


FIG. 3.2

Trends in weekly TB case notifications in India in 2020, before and after lockdown

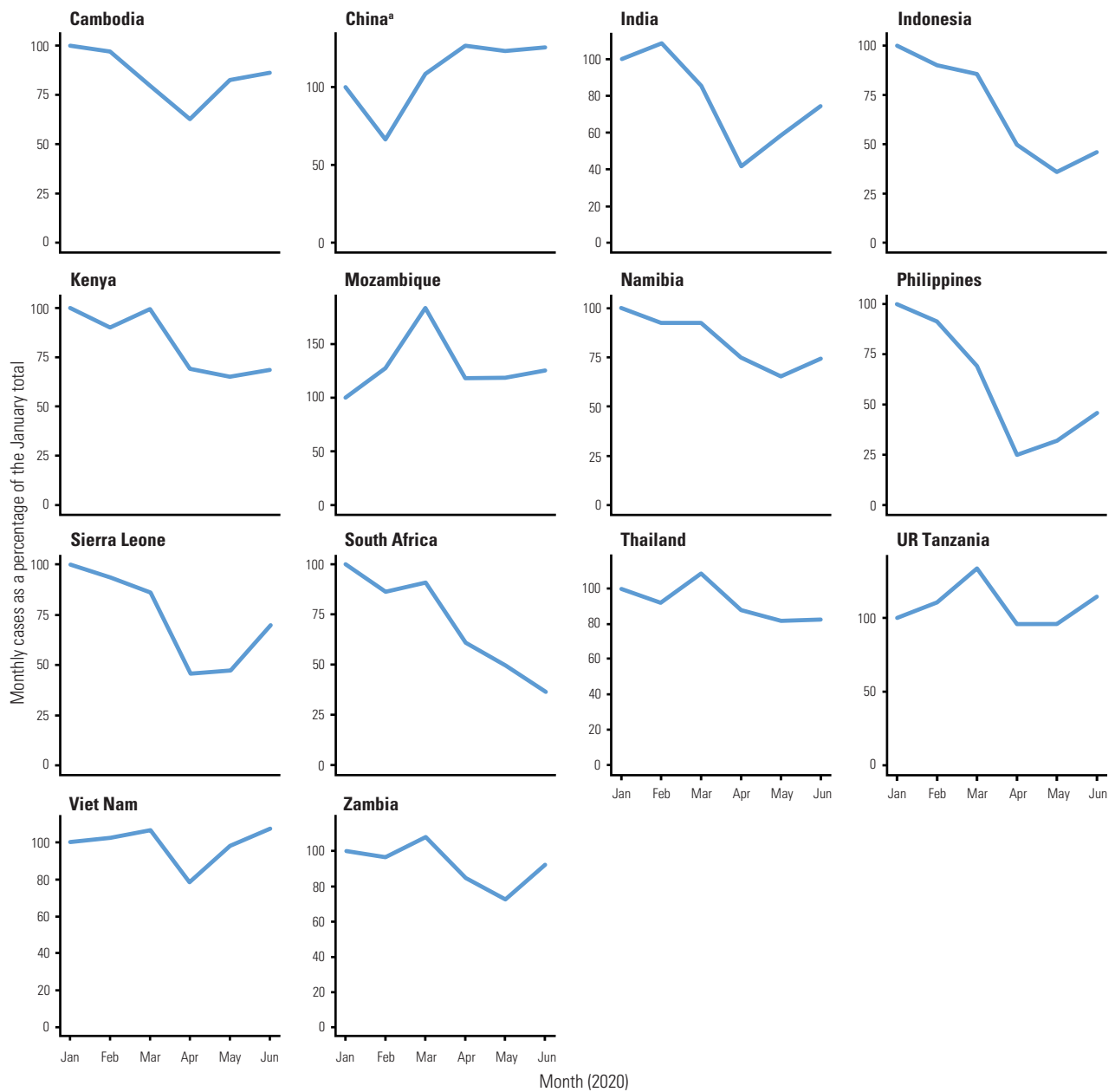


Source: <https://reports.nikshay.in/Reports/TBNotification>, accessed 31 July 2020

FIG. 3.3

Trends in monthly notifications of TB cases from January–June 2020, 14 high TB burden countries

Data are shown for countries that were able to report provisional national numbers for all six months to WHO in August 2020.



^a Data for China were extracted from monthly reports of notifiable diseases published by the National Health Commission. Notifications of TB cases drop every year in January and February, associated with national holidays during the Chinese Spring Festival.

The Stop TB Partnership study – conducted in collaboration with Avenir Health, Imperial College (London, United Kingdom of Great Britain and Northern Ireland) and the United States Agency for International Development (USAID) – suggested that a 3-month lockdown combined with a protracted (10-month) restoration of services could cause an additional 1.4 million TB deaths between 2020 and 2025.

3.2 Global annual number of people developing TB in 2020 and beyond

The COVID-19 pandemic is likely to have a medium-term impact on the number of people who develop TB each year. Although physical distancing¹ policies may help to reduce TB transmission, this effect could be offset by longer durations of infectiousness, increased household exposure to TB infection, worsening treatment outcomes and higher levels of poverty. In the absence of effective mitigation strategies, such as social protection and health insurance,² severe economic contractions and loss of income (particularly among the most vulnerable populations) are likely to worsen some of the factors that determine TB epidemics, especially the prevalence of undernutrition.

The Stop TB Partnership study (4) suggested that the COVID-19 pandemic could cause an additional 6.3 million TB cases globally between 2020 and 2025.

3.3 Access to TB treatment and TB preventive treatment

Extra pressure on health services resulting from the COVID-19 pandemic, combined with impacts on care-seeking behaviour, could slow or reverse progress towards TB treatment and prevention targets set at the UN high-level meeting on TB (2), especially in high TB burden countries.

There is already evidence from several high TB burden countries of large reductions in the monthly number of people with TB being detected and officially reported in 2020, especially in India, Indonesia, the Philippines, Sierra Leone and South Africa (Fig. 3.2, Fig. 3.3).

In India, the weekly and monthly number of TB case notifications fell by more than 50% between the end of March and late April, following the imposition of a national lockdown. Subsequently, there has been some recovery, but as of the end of June, not to pre-March levels. Decreases occurred in both the public and private sector. In Indonesia, monthly notifications fell sharply between March and May, with some signs of a modest recovery in May. Compared with the first six months of 2019, monthly notifications in the first six months of 2020 were approximately 25–30% lower in India, Indonesia and the Philippines.³ In South Africa, monthly notifications fell by more than 50% between March and June. In other high TB burden countries, reductions in 2020 have been small-

er though still considerable (generally in April and May), and there has been some recovery (especially in China, the United Republic of Tanzania and Viet Nam). Continued and timely tracking of trends in weekly or monthly notifications in these and other countries (at least the 30 high TB burden countries) is necessary to understand and rapidly respond to observed impacts.

Plausible explanations for impacts on monthly case notifications include the following: people with chronic conditions or mild symptoms have been discouraged from seeking care to mitigate crowding in health facilities; reductions in the number of health facilities offering TB diagnostic and treatment services; TB staff and molecular diagnostic platforms have been reallocated to the COVID-19 response; the procurement and transportation of medicines and laboratory consumables have been disrupted; restrictions in movement and loss of wages have made it harder for people to travel to health facilities; concerns about stigma, given the similarities in some clinical features of TB (e.g. fever and cough) with those of COVID-19; and delays in recording and reporting of data.

Table 3.1 shows the impacts on approaches to delivery of TB services and mitigation strategies reported by 184 countries in WHO's 2020 round of global TB data collection.⁴

Common actions to mitigate impacts include reducing the frequency of outpatient visits for treatment monitoring or collection of drugs (127 countries including 28 high TB burden countries), allowing TB patients to take a 1-month or more supply of anti-TB drugs home (100 countries including 25 high TB burden countries), allowing TB patients to nominate another household member to collect anti-TB drugs on their behalf (96 countries including 20 high TB burden countries), and expanded use of remote advice and support (108 countries including 21 high TB burden countries).

Negative impacts include the reallocation of human, financial and other resources from TB to the COVID-19 response. Many countries reported the use of GeneXpert machines for COVID-19 testing instead of diagnostic testing for TB (43 countries including 13 high TB burden countries), reassignment of staff in NTPs to COVID-19 related duties (85 countries including 20 high TB burden countries), and reallocation of budgets (52 countries including 14 high TB burden countries). Smaller but still considerable numbers of countries also reported reducing the number of health facilities providing inpatient and outpatient care for people with TB.

Although not documented as part of WHO's 2020 round of global TB data collection, there is evidence that some countries have suspended contact investigation for people with TB and some countries have reported impacts on the provision of TB preventive treatment (5, 6).

¹ Referred to as “social distancing” in many countries.

² These topics are discussed in more detail in Chapter 8.

³ The WHO Regional Office for South-East Asia has published a fuller analysis of impacts in India, Indonesia and other countries in the WHO South-East Asia Region (5).

⁴ This was implemented from April to July 2020.

TABLE 3.1

Impacts on TB services and mitigation strategies reported by 184 NTPs to WHO in April–May 2020

IMPACT OR MITIGATION STRATEGY	NUMBER OF COUNTRIES THAT REPORTED THE IMPACT OR MITIGATION STRATEGY	
	ALL COUNTRIES (N=184)	30 HIGH TB BURDEN COUNTRIES
Impacts on health service availability		
Fewer health facilities providing outpatient care for people with drug-susceptible TB	32	7
Fewer health facilities providing outpatient care for people with multidrug- or rifampicin-resistant (MDR/RR) TB	21	4
Fewer hospitals providing inpatient care for people with drug-susceptible TB	35	9
Fewer hospitals providing inpatient care for people with MDR/RR-TB	33	9
Reduced number of outpatient visits for people with TB	127	28
People with TB asked to self-isolate at home	93	14
Reallocation of TB resources to the COVID-19 response		
Reallocation of NTP staff at national or subnational level	85	20
Reallocation of funding	52	14
Reallocation of GeneXpert machines	43	13
Mitigation strategies to facilitate continued access to treatment		
Providing TB patients with at least a 1-month supply of anti-TB drugs	100	25
Home delivery of anti-TB drugs	77	14
Enabling TB patients to nominate a household member to collect their drugs	96	20
Expanded remote advice and support using digital technologies	108	21

3.4 Funding for the TB response and the proportion of people with TB facing catastrophic costs

In June 2020, the World Bank estimated that global gross domestic product (GDP) will contract by 5.2% in 2020 (7). In many countries, more severe economic contractions have already occurred or are forecast.

Negative impacts on employment opportunities threaten the livelihoods of many millions of people, and those most at risk of developing TB are among the most vulnerable. Half of people affected by TB already face catastrophic costs as a result of the disease (Chapter 2 and Chapter 8). Without strong mitigation measures (including social protection), an even higher proportion of people with TB and their households will be at risk of facing catastrophic costs.

Economic contractions put major pressure on the financial resources that national governments can make available, including for the TB response. There is already evidence from several countries that resources originally allocated for TB (e.g. staff and diagnostic equipment) have been diverted to the COVID-19 response (Table 3.1).

The COVID-19 Response Mechanism of the Global Fund to Fight AIDS, TB and Malaria (the Global Fund) has allocated US\$ 1 billion to help mitigate impacts on TB, HIV and malaria. Countries have begun using this funding; for example, to strengthen laboratory networks and procure additional diagnostics.

3.5 WHO guidance and support for the TB response during the COVID-19 pandemic

Since WHO declared COVID-19 a Public Health Emergency of International Concern (PHEIC) in January 2020, the WHO Global TB Programme has monitored the impact of COVID-19 on TB, and has provided guidance and support to Member States (Fig. 3.4) (8). This has been done in close collaboration with WHO's regional and country offices, civil society and partners, including the Stop TB Partnership and Global Fund. WHO has also created a compendium of research related to TB and COVID-19 (9)¹

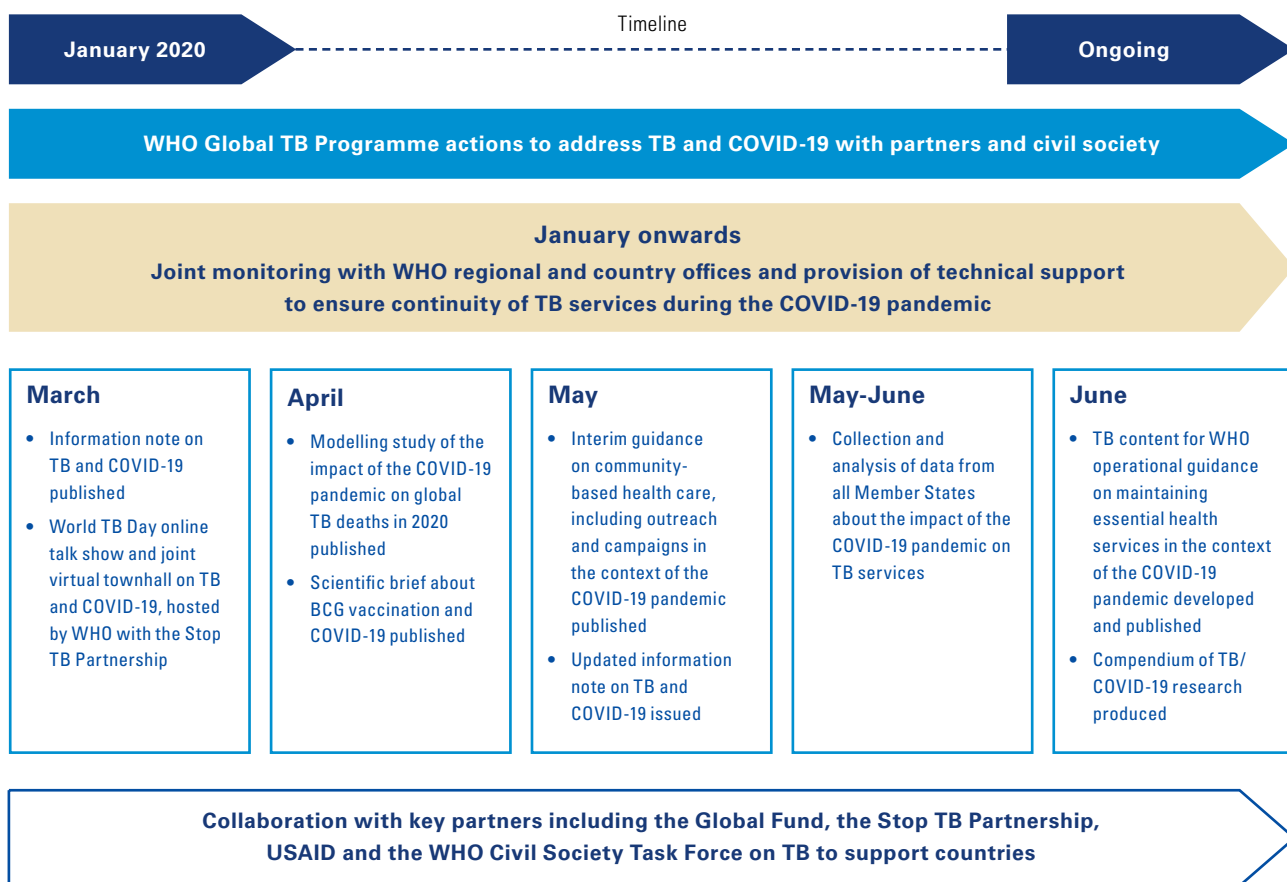
WHO has provided key advice (10–13), including the following:

- ▶ leverage the expertise and experience of NTPs, especially in rapid testing and contact tracing for the COVID-19 response;
- ▶ maximize remote care and support for people with TB by expanding the use of digital technologies;
- ▶ minimize the number of visits to health services that are required during treatment, including through use of WHO-recommended, all-oral TB treatment regimens and community-based care;
- ▶ limit transmission of TB and COVID-19 in congregate settings and health care facilities by ensuring basic infection prevention and control for health staff and patients, cough etiquette, and patient triage;

¹ Further details are provided in Box 9.1 of Chapter 9.

FIG. 3.4

Actions taken by the WHO Global TB Programme in the context of the COVID-19 pandemic since January 2020



- ▶ maintain and scale up TB preventive treatment, including via synergies with contact tracing efforts related to COVID-19;
- ▶ provide simultaneous testing for TB and COVID-19 for individuals when indicated, including by leveraging TB laboratory networks and platforms; and
- ▶ ensure proactive planning and budgeting for both conditions (including for the catch-up phase), procurement of supplies and risk management.

Overall, it is crucial to maintain and strengthen TB services as an essential component of overall progress towards universal health coverage and resilient health systems, and to ensure synergies in the responses to both TB and COVID-19.

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**A patient being assessed
at a TB clinic, Philippines.**

Yoshi Shimizu/WHO

Chapter 4

TB disease burden

Key facts and messages

Tuberculosis (TB) is a major cause of ill health, one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV/AIDS since 2007).

Globally in 2019, an estimated 10.0 million (range, 8.9–11.0 million) people fell ill with TB. There were 1.2 million (range, 1.1–1.3 million) TB deaths among HIV-negative people and an additional 208 000 deaths (range, 177 000–242 000) among HIV-positive people.^a

TB affects people of both sexes and all age groups, but the highest burden is in adult men, who accounted for 56% of all TB cases in 2019; by comparison, adult women accounted for 32% and children for 12%. Among all TB cases, 8.2% were among people living with HIV.

Geographically, in 2019, most TB cases were in the World Health Organization (WHO) regions of South-East Asia (44%), Africa (25%) and the Western Pacific (18%), with smaller shares in the Eastern Mediterranean (8.2%), the Americas (2.9%) and Europe (2.5%). Eight countries accounted for two thirds of the global total: India (26%), Indonesia (8.5%), China (8.4%), the Philippines (6.0%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%) and South Africa (3.6%).

Global targets and milestones for reductions in TB incidence and TB deaths have been set as part of the Sustainable Development Goals (SDGs) and WHO's End TB Strategy. SDG 3 includes a target to end the global TB epidemic by 2030. The End TB Strategy includes targets of a 90% reduction in TB deaths and an 80% reduction in the TB incidence rate (new and relapse cases per

100 000 population per year) between 2015 and 2030; the 2020 milestones are reductions of 35% and 20%, respectively.

Currently, the world as a whole, most WHO regions and many high TB burden countries are not on track to reach the 2020 milestones of the End TB Strategy.

Globally, the reduction in the TB incidence rate between 2015 and 2019 was 9% (from 142 to 130 new and relapse cases per 100 000 population), less than halfway to the 2020 milestone. More positively, the WHO European Region has almost reached the milestone, with a reduction of 19% between 2015 and 2019, and the African Region has made good progress, with a reduction of 16%.

A total of 78 countries are on track to reach the 2020 milestone of a 20% reduction in TB incidence. Among the 30 high TB burden countries, seven have already reached the milestone (Cambodia, Ethiopia, Kenya, Namibia, the Russian Federation, South Africa and the United Republic of Tanzania) and three others are on track to do so (Lesotho, Myanmar and Zimbabwe).

The global reduction in the number of TB deaths between 2015 and 2019 was 14%. The WHO European Region is on track to reach the 2020 milestone, with a 31% reduction from 2015 to 2019, and the African Region has made good progress, achieving a reduction of 19%.

A total of 46 countries are on track to reach the 2020 milestone of a 35% reduction in TB deaths. Among the 30 high TB burden countries, seven

have already reached the milestone (Bangladesh, Kenya, Mozambique, Myanmar, the Russian Federation, Sierra Leone and the United Republic of Tanzania) and one other is on track to do so (Viet Nam).

Faster reductions in TB incidence and deaths require improvements in access to diagnosis and care within the context of progress towards universal health coverage, action on broader determinants of TB incidence (e.g. levels of undernutrition, poverty, smoking and diabetes) and a new treatment or vaccine to substantially lower the risk of developing TB in people who have a latent TB infection.

Globally, the burden of multidrug- or rifampicin-resistant TB (MDR/RR-TB) as a share of the number of TB cases remains stable. In 2019, an estimated 3.3% of new TB cases and 18% of previously treated cases had MDR/RR-TB. In absolute numbers, there were an estimated 465 000 (range, 400 000–535 000) incident cases of rifampicin-resistant TB; 78% had multidrug-resistant TB. India (27%), China (14%) and the Russian Federation (8%) had the largest share of the global burden.

In recent years, sources of data to inform estimates of TB disease burden have improved considerably, particularly from national TB prevalence surveys. National TB notification and vital registration systems require improvements to track TB incidence and mortality reliably.

^a When an HIV-positive person dies from TB disease, the underlying cause is classified as HIV in the International Classification of Diseases system (10th edition).

Global targets and milestones for reductions in the burden of tuberculosis (TB) disease have been set as part of the Sustainable Development Goals (SDGs) and the World Health Organization's (WHO's) End TB Strategy (Chapter 2) (1). SDG 3 includes a target to end the global TB epidemic by 2030, with the TB incidence rate (new and relapse cases 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 the TB incidence rate, compared with 2015 levels. The End TB Strategy also includes targets for 2035 and milestones for 2020 and 2025 (Table 4.1).

TABLE 4.1
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 per year (compared with 2015 baseline)	35%	75%	90%	95%
Percentage reduction in the TB incidence rate (new and relapse cases per 100 000 population per year) (compared with 2015 baseline)	20%	50%	80%	90%

Both progress towards universal health coverage (UHC) and multisectoral actions to address broader social and economic determinants of TB¹ are required to achieve the End TB Strategy milestones. The annual decline in the global TB incidence rate needs to accelerate to 4–5% per year by 2020 and then to 10% per year by 2025. The latter is equivalent to the fastest national declines documented to date (e.g. in countries in western Europe during the 1950s and 1960s), which occurred in the context of progress towards UHC, combined with broader social and economic development. The milestones also depend on reducing the global proportion of people with TB who die from the disease (the case fatality ratio, or CFR) to 10% by 2020 and then to 6.5% by 2025. The latter is comparable to the current level in many high-income countries but is only attainable if all those with TB disease can access high-quality treatment.

To reach the 2030 and 2035 targets, the rate at which TB incidence falls globally needs to accelerate to an average of 17% per year between 2025 and 2035. This is only possible if there are technological breakthroughs that can substantially reduce the risk of developing TB disease among the approximately 1.7 billion people (2) (about one quarter of the world's population) already infected with *Mycobacterium tuberculosis*. Examples include an effective post-exposure vaccine or a short, efficacious and safe treatment for TB infection.²

¹ These are discussed in more detail in Chapter 8.

² The status of the development pipelines for new TB diagnostics, drugs and vaccines in August 2020 is described in Chapter 9.

The first two sections of this chapter present and discuss estimates of TB incidence (Section 4.1) and TB mortality (Section 4.2) at global, regional and country levels for the period 2000–2019, including disaggregation by age and sex. Specific attention is given to the status of progress towards the 2020 milestones of the End TB Strategy; that is, a 35% reduction in the absolute number of TB deaths and a 20% reduction in the TB incidence rate between 2015 and 2020 (Table 4.1).

The burden of drug-resistant TB is of major interest and concern at global, regional and country levels. Section 4.3 provides an overview of the data available to estimate this burden, along with estimates of the number of cases and deaths that occurred in 2019, and an analysis of recent trends in selected countries.

In many high TB burden countries, a national TB prevalence survey currently offers the best method for directly measuring the number of TB cases (and their distribution by age and sex); a repeat survey can be used to assess trends. Section 4.4 describes the latest status of progress in implementing such surveys and provides a synthesis of the main results.

The ultimate goal is that all countries can reliably track their TB epidemics (in terms of TB incidence and mortality), using data from national notification and vital registration (VR) systems that meet standards for quality and coverage. Since 2006, concerted efforts have been made to improve the available data and methods used for estimations, under the umbrella of the WHO Global Task Force on TB Impact Measurement (the Task Force) (Box 4.1). A synopsis of findings and recommendations from systematic assessments of the performance of TB surveillance conducted between January 2016 and August 2020 is provided in Section 4.5.

WHO updates its estimates of the burden of TB disease annually,³ using the latest available data and analytical methods and in accordance with published guidelines.⁴ A summary of the main updates to available data and methods since the 2019 global TB report (3) is provided in Box 4.2. Full details of methods are provided in an online technical appendix.⁵

³ The updates can affect the entire time series back to 2000. Therefore, estimates presented in this chapter for 2000–2019 supersede those of previous reports, and direct comparisons (e.g. between the estimates for 2015 in this report and estimates for 2015 in previous reports) are not appropriate.

⁴ Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER). There is a checklist of 18 best practices that set standards for how health estimates are developed (<http://gather-statement.org/>).

⁵ The online technical appendix is available at <http://www.who.int/tb/data>.

The WHO Global Task Force on TB Impact Measurement

Establishment and progress made, 2006–2015

The WHO Global Task Force on TB Impact Measurement (the Task Force) was established in 2006; the Task Force is convened by the TB Monitoring, Evaluation and Strategic Information unit of WHO's Global TB Programme. The original aim of the Task Force was to ensure a rigorous, robust and consensus-based assessment of whether the 2015 targets for reductions in TB incidence, prevalence and mortality, set in the context of the Millennium Development Goals (MDGs), were achieved at global, regional and country levels. The Task Force pursued three strategic areas of work:

- ▶ strengthening routine surveillance of TB cases (via national notification systems) and TB 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.

The ultimate goal is that all countries can reliably track their TB epidemics (in terms of incidence and mortality) using data from national notification and VR systems that meet standards for quality and coverage.

Work on strengthened surveillance included the development of a TB surveillance checklist of standards and benchmarks (4); guidance on case-based digital recording and reporting (5); and inventory studies to measure underreporting of detected cases (6), with associated support for their implementation. The use of data from VR systems and mortality surveys to produce estimates of the number of TB deaths was also considerably expanded. There was substantial success in the implementation of national TB prevalence surveys (Section 4.4), and a Task Force subgroup undertook two major reviews of methods used to produce TB disease burden estimates, the second of which provided the basis for WHO's final assessment of whether 2015 targets were met (7).

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 updated its mission and strategic areas of work in April 2016, for the period 2016–2020 (8).

The updated mission is as follows:

- ▶ To ensure that assessments of progress towards the 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 of national notification systems for direct measurement of TB incidence,

including drug-resistant TB and HIV-associated TB specifically.

2. Strengthening of national VR systems for direct measurement of TB mortality.
3. Priority studies to measure TB disease burden periodically, including surveys on:
 - a. national TB prevalence;
 - b. drug resistance;
 - c. mortality; and
 - d. costs faced by TB patients and their households.
4. Periodic review of methods used by WHO to estimate the burden of TB disease.
5. Analysis and use of TB surveillance and survey data at country level.

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

Strategic areas of work 1–3 focus 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).

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. The global status of progress in using the WHO TB surveillance checklist to assess the performance of notification and VR systems is shown in Fig. 4.1a; progress in implementing case-based digital surveillance is discussed in Chapter 5; the global status of progress in implementing inventory studies is shown in Fig. 4.1b; the number of countries for which VR data are used to estimate the number of TB deaths is shown in Fig. 4.13; and Section 4.5 provides a synthesis of findings and recommendations from assessments using the TB surveillance checklist that were conducted between January 2016 and August 2020.

Further details about the work of the Task Force are available online (9), and an up-to-date summary is provided in the latest brochure about its work (10).

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

Updates in this report

Estimates of TB incidence and mortality in this report cover the period 2000–2019. Estimates of incidence and mortality disaggregated by age and sex, and for drug-resistant TB, are for 2019.

The main country-specific updates are for estimates of TB incidence in the period 2000–2019 in five countries, following the finalization of results from five national TB prevalence surveys.

1. Estimated TB incidence derived from national TB prevalence surveys

Between November 2019 and July 2020, final results from national TB prevalence surveys in Eswatini, Lesotho, Mozambique, Nepal and South Africa became available. These were used to update estimates of TB incidence, using methods described in the [online technical appendix](#). Compared with previously published incidence estimates, the updated estimates are lower in Mozambique, similar in Lesotho, somewhat higher in Eswatini and South Africa (though with considerable overlap in uncertainty intervals for pre- and post-survey estimates), and higher in Nepal.

For Mozambique, the uncertainty interval for updated estimates of TB incidence is relatively wide. The main reason is the lower-than-anticipated measured level of TB prevalence (compared with that used for calculations of the survey sample size). A second reason is that the survey used a diagnostic algorithm in which Xpert MTB/RIF testing only was performed for all screen-positive individuals, with culture testing used only for those with an Xpert-positive test result. Statistical adjustments to account for the lower sensitivity of Xpert MTB/RIF compared with culture were needed to estimate TB prevalence, which introduced further uncertainty.

2. Drug-resistant TB

As in last year's WHO global TB report (3), the annual incidence of multidrug- or rifampicin-resistant TB

(MDR/RR-TB) was estimated using the following equation:

$$I_{rr} = I[(1-f)p_n((1-r) + r\rho) + fp_r]$$

where I is overall TB incidence, I_{rr} is the incidence of RR-TB, f is the cumulative risk for incident cases to receive a non-relapse retreatment (following failure or return after default), r is the proportion of incident TB cases that are relapses, ρ is the relative risk of MDR/RR-TB in relapse compared with new cases (first episodes) of TB, and p_n and p_r denote the proportions of new and previously treated cases that have MDR/RR-TB.

Although the same equation was used, the parameter values for this year's report are slightly different from those used for last year's report ([Table B4.2.1](#)), reflecting new data on levels of drug resistance, the relative risk of MDR/RR-TB in relapse compared with new TB cases, the proportion of new episodes of TB that were relapse cases and the overall decline in global TB incidence ([Section 4.1.4](#)). These slightly updated values resulted in a slightly lower global estimate of the incidence of MDR/RR-TB.

Between August 2019 and August 2020, new data on levels of drug resistance were reported for many countries:

- ▶ Data from a first-ever national anti-TB drug-resistance survey became available for two countries: Mali and Timor-Leste.
- ▶ Data from a repeat national anti-TB drug-resistance survey became available for two countries: Bangladesh and Malawi.
- ▶ Four countries transitioned from reporting survey data to reporting quality-approved surveillance data: Eritrea, Lao People's Democratic Republic, Lesotho and Syrian Arab Republic.
- ▶ New surveillance data were available for an additional 71 countries.

TABLE B4.2.1.

Parameter values used to estimate the global incidence of MDR/RR-TB in the 2019 and 2020 WHO global TB reports

Parameter	VALUE IN 2019 REPORT	VALUE IN 2020 REPORT	CHANGE (%)
Percentage of new TB cases with MDR/RR-TB	3.36%	3.32%	-1.2%
Percentage of previously treated TB cases with MDR/RR-TB	17.8%	17.7%	-0.6%
Percentage of incident TB cases that were relapses	7.1%	6.8%	-4.3%
Percentage of TB cases that fail treatment or return after default	4.1%	4.3%	5.0%
Risk ratio for MDR/RR-TB (relapse compared with new cases)	4.6	4.2	-8.7%
TB incidence (millions)	10.0	9.96	-0.56%
MDR/RR-TB incidence (thousands)	484	465	-3.9%

BOX 4.2

Among countries estimated to have more than 1000 incident cases of MDR/RR-TB in 2019, changes compared with estimates for 2018 were mostly small. The updated estimate for 2019 was >10% lower than the estimate for 2018 in 10 countries (Bangladesh, Côte d'Ivoire, Kazakhstan, Myanmar, Mozambique, Thailand, Ukraine, Uzbekistan, Zambia and Zimbabwe) and >10% higher in six countries (Ghana, Mongolia, Nepal, Philippines, Tajikistan and South Africa). Reasons for these differences included the availability of revised survey data (Bangladesh, Côte d'Ivoire, Thailand), an updated value for the relative risk of MDR/RR-TB in relapse compared with new cases (Côte d'Ivoire), new surveillance data (Ghana, Kazakhstan, Mongolia, Myanmar, Philippines, Tajikistan, Thailand, Ukraine, Uzbekistan, Zambia, Zimbabwe) and revised estimates of TB incidence (Mozambique, Nepal, South Africa).

Global estimates of the incidence of isoniazid-resistant TB are included for the first time in this report, using methods similar to those applied for rifampicin-resistant TB (RR-TB). The incidence of TB is presented for four possible combinations of isoniazid and rifampicin resistance and susceptibility (Table 4.10). Estimates have been included following a WHO recommendation (issued in 2018) that a modified treatment regimen should be used for people with isoniazid-resistant but rifampicin-susceptible TB. The detection of isoniazid-resistant TB is important to ensure that people receive the most appropriate treatment and to avoid the generation of further resistance.

3. Newly reported data and updated estimates from other agencies

New data on TB mortality were reported to WHO between mid-2019 and mid-2020. Several countries reported historical data that were previously missing, or made corrections to previously reported data. In total, 105 additional country-year data points from the WHO mortality database were retained for analysis compared with last year's report.

Updated estimates of HIV prevalence and mortality were obtained from the Joint United Nations Programme on HIV/AIDS (UNAIDS) in July 2020 (11).

In most instances, resulting changes to TB burden estimates were well within the uncertainty intervals of previously published estimates, and trends were generally consistent.

For 23 countries (shown in Fig. 4.13), estimates of TB mortality among HIV-negative people were based on estimates published by the Institute of Health Metrics and Evaluation (IHME) (12). These estimates use data from national and sample VR systems, and from verbal autopsy surveys. Estimates of TB mortality in South Africa were adjusted by IHME for miscoding of deaths caused by HIV and TB. IHME estimates used in this report were slightly adjusted from those published by IHME, to fit WHO estimates of the total

number of deaths (i.e. the total mortality envelope). The ratio of the median country-year envelope (WHO:IHME) was 1.03 (interquartile range: 0.94–1.11) among 391 data points.

4. Findings from national TB epidemiological reviews

Small adjustments to incidence trajectories were made in a few countries, based on findings from recent national TB epidemiological reviews (e.g. Peru) and extensive discussions with national TB programmes (NTPs) (e.g. Malawi).

5. Estimates of the burden of TB in children

Estimates of the burden of TB in children in 2019 were produced for this report using the same methods as those of last year. Updates were needed because of the use of new notification and mortality data.

Estimation of the burden of TB disease in children remains particularly challenging, owing to the inconsistent quality of notification data for children, particularly in high TB burden countries. Cases among children are often notified based on inconsistent diagnostic criteria (and investigations) for childhood TB disease, leading to instances of overreporting; other cases may be diagnosed in paediatric hospitals and not reported to public health authorities, leading to underreporting; and other cases may not be diagnosed. The scarcity of nationwide population-based survey data results in large uncertainty when TB incidence is disaggregated by age group (reflected in wide uncertainty bounds). This considerably limits their usefulness for activities related to programme planning and evaluation.

Greater priority should be given to the quality of TB notification data for children, as well as the consistency of case definitions and coverage of reporting. Inventory studies specific to childhood TB would help to improve the quality of TB disease burden estimates for children and should be prioritized. Audits of medical records from random samples of childhood cases would provide valuable information on the quality of diagnoses and completeness of prescribed investigations, and should be conducted systematically in countries with a high burden of TB.

6. Incidence of bacteriologically confirmable pulmonary TB

Country-specific estimates of the number of incident cases of pulmonary TB that could be bacteriologically confirmed have been produced. This has been done following growing interest in the use of such estimates in setting targets for the numbers of people with MDR/RR-TB that could be detected using available diagnostic tests, as well as concern about the increasing proportion of notified TB cases that are clinically diagnosed as opposed to bacteriologically confirmed (this topic is discussed in more detail in Chapter 5).

BOX 4.2

Estimates were produced as the product of a) estimated TB incidence b) the observed country-specific proportion of notified cases diagnosed with pulmonary TB and c) the expected proportion of pulmonary cases that could be bacteriologically confirmed if the best tests were used. The [online technical appendix](#) provides further details. Estimates are available on the report's data webpage (<http://www.who.int/tb/data>).

Updates anticipated in the near future

Updates to estimates of disease burden are expected in 2021 for India, following the completion of the country's first-ever national TB prevalence survey. As of August 2020, the survey was on hold due to the COVID-19 pandemic.

The COVID-19 pandemic is likely to affect estimates of incidence and mortality for 2020 in several countries. [Chapter 3](#) discusses the impact and implications of the pandemic, including on incidence, mortality, case finding and notifications, and broader socioeconomic determinants of TB (e.g. poverty, undernutrition and income per capita). [Chapter 8](#) discusses the impact on TB determinants in more depth.

4.1 TB incidence

4.1.1 Methods to estimate TB incidence

TB incidence has never been directly measured at national level because it requires a long-term study that enrolls and follows up with hundreds of thousands of people, which would involve prohibitively 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.

The ultimate goal is to measure TB incidence directly and to monitor trends from TB notifications in all countries. This requires a combination of strong surveillance, good quantification of underreporting (i.e. the number of cases missed by surveillance systems)¹ and UHC. A TB surveillance checklist developed by the Task Force ([Box 4.1](#)) defines the standards that need to be met for notification data to provide a direct measure of TB incidence and for national VR data to provide a direct measure of TB mortality (4).² Between January 2013 and August 2020, 82 countries, including 29 of the 30 high TB burden countries, used this checklist to assess the performance

¹ Inventory studies can be used to measure the number of cases that are diagnosed but not reported. For a guide to inventory studies, see WHO (2019) (6).

² One of the standards is that levels of underreporting of detected TB cases should be minimal.

of their national TB notification and VR systems, and to identify weaknesses that needed to be addressed ([Fig. 4.1](#) and [Table 4.2](#)). Common recommendations have included making or improving the transition from aggregated paper-based recording and reporting of TB cases to digital case-based surveillance, measuring the level of underreporting and taking corrective actions based on findings, and establishing or strengthening VR systems (further details are provided in [Section 4.5](#)).

Methods currently used by WHO to estimate TB incidence can be grouped into four major categories ([Fig. 4.2](#)), as follows:

- ▶ **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 and antiretroviral therapy (ART) on the distribution of disease duration.³ This method is used for 29 countries, of which 28 have national survey data and 1 – India – has a survey in one state. These 29 countries accounted for 66% of the estimated global number of incident cases in 2019.
- ▶ **Notifications adjusted by a standard factor to account for underreporting, overdiagnosis and underdiagnosis.** This method is used for a total of 139 countries: all high-income countries, except Germany, the Netherlands and the United Kingdom of Great Britain and Northern Ireland (United Kingdom); and selected middle-income countries with low levels of underreporting, including Brazil and the Russian Federation. These 140 countries accounted for 6% of the estimated global number of incident cases in 2019.
- ▶ **Results from national inventory studies that measured the level of underreporting of detected TB cases.** This method is used for eight countries: China, Egypt, Germany, Indonesia, Iraq, the Netherlands, the United Kingdom and Yemen. These countries accounted for 17% of the estimated global number of incident cases in 2019.⁴

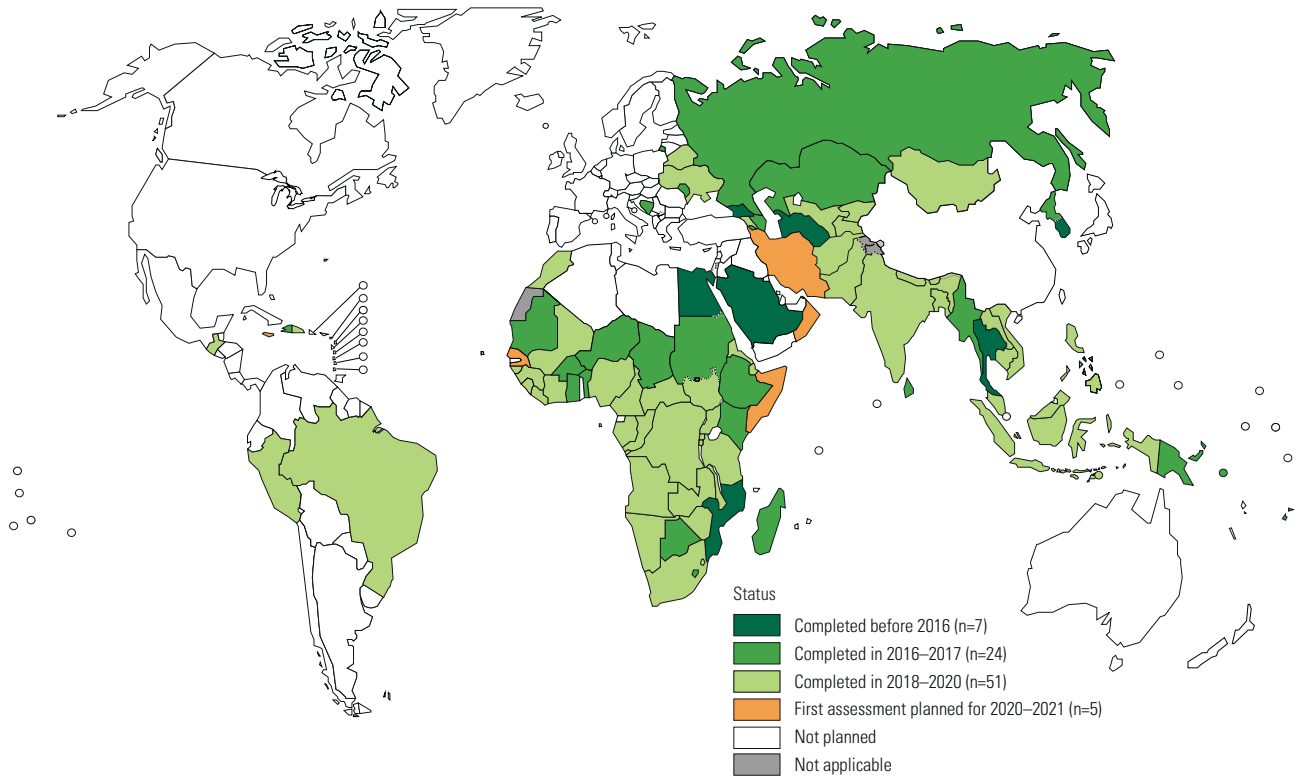
³ Estimation of incidence from prevalence is not straightforward; for example, it requires assumptions about the duration of disease for different case categories. Prevalence surveys focus on bacteriologically confirmed TB in adults; hence, adjustments are needed to include children and extrapulmonary TB.

⁴ The studies in Egypt, Germany, Indonesia, Iraq, the Netherlands, the United Kingdom and Yemen included use of capture-recapture modelling to estimate incidence. This approach is possible if six assumptions are met: all cases are observable; the proportion of mismatches and matching failures in record-linkage is low, which typically requires a large sampling fraction; there is a closed population during the study period (typically 3–6 months); if S represents the number of case lists or data sources available, then at least three data sources are available ($S \geq 3$) and their dependencies are accounted for in the model design, while the full S-way interaction between sources is assumed null; there is homogeneity of within-source observation probabilities across subpopulation groups, such as those defined by socioeconomic and demographic characteristics; and the case definitions across data sources are consistent. Few high TB burden countries are expected to be able to implement inventory studies that will meet these six assumptions to a sufficient degree.

FIG. 4.1

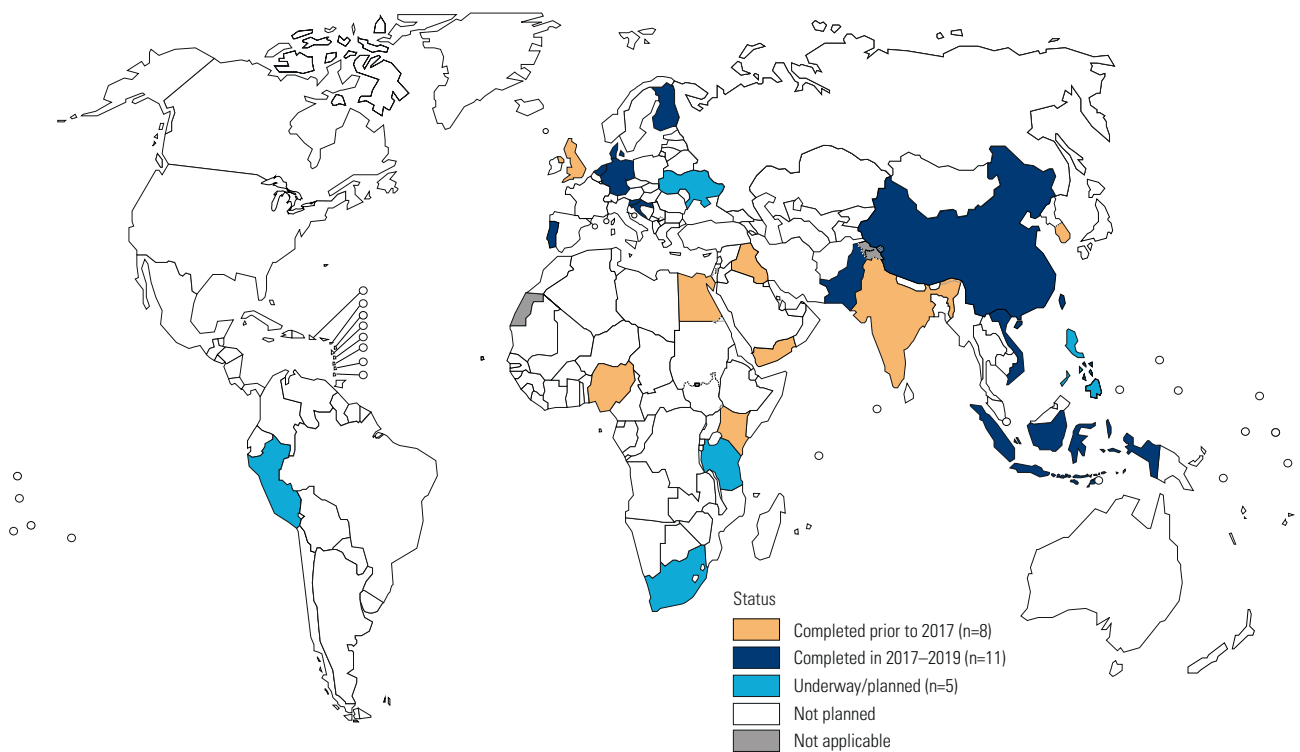
Strengthening national TB surveillance (status in August 2020)

(a) Assessment of the performance of TB surveillance using the WHO checklist of standards and benchmarks since January 2013^a



^a In addition to the five countries planning a first assessment, six countries (Azerbaijan, Egypt, Georgia, Republic of Moldova, Saudi Arabia and Sri Lanka) are planning a repeat assessment in 2020–2021.

(b) National inventory studies of the underreporting of detected TB cases implemented 2000–2019 or planned^a



^a The inventory study in Nigeria was a subnational study based in Lagos.

TABLE 4.2
Sources of data available to inform estimates of TB disease burden in the 30 high TB burden countries, 2000–2019

Blue indicates that a source is available, orange indicates it will be available in the near future, and red indicates that a source is not available.

COUNTRY	NOTIFICATION DATA	STANDARDS AND BENCHMARK ASSESSMENT ^a	NATIONAL INVENTORY STUDY ^b	NATIONAL TB PREVALENCE SURVEY ^c	NATIONAL DRUG RESISTANCE SURVEY OR SURVEILLANCE ^d	NATIONAL VR DATA OR MORTALITY SURVEY ^e
Angola	2000–2019	2016, 2019	-	-	-	-
Bangladesh	2000–2019	2014, 2019	-	2015	2011, 2019	-
Brazil	2000–2019	2018	-	NA	2008	2000–2017
Cambodia	2000–2019	2018	-	2002, 2011	2007, 2018	-
Central African Rep.	2000–2019	2019	-	-	2009	-
China	2000–2019	-	2018	2000, 2010	2007, 2013	2004–2018
Congo	2000–2019	2019	-	-	-	-
DPR Korea	2000–2019	2017	-	2016	2014	-
DR Congo	2000–2019	2017, 2019	-	-	2017	-
Ethiopia	2000–2019	2013, 2016	-	2011	2005, 2018, 2018–	-
India	2000–2019	2019	2016	2019–2021	2016	2000–2014
Indonesia	2000–2019	2017, 2019	2017	2013–2014	2018	2006–2007, 2009–2015
Kenya	2000–2019	2013, 2017	2013	2015	2014	-
Lesotho	2000–2019	2014, 2017	-	2019	2014	-
Liberia	2000–2019	2015, 2019	-	-	-	-
Mozambique	2000–2019	2013	-	2017–2019	2007, 2021	-
Myanmar	2000–2019	2014, 2017	-	2009, 2018	2013, 2018–, 2020	-
Namibia	2000–2019	2016, 2019	-	2017–2018	2008, 2015, 2018–	-
Nigeria	2000–2019	2017, 2020	-	2012	2010	-
Pakistan	2000–2019	2016, 2019	2012, 2017	2011	2013	2006, 2007, 2010
Papua New Guinea	2000–2019	2017	-	-	2014	-
Philippines	2000–2019	2016, 2019	2021	2007, 2016	2012, 2019	2000–2014
Russian Federation	2000–2019	2017	-	NA	2000–	2000–2018
Sierra Leone	2000–2019	2015, 2020	-	-	-	-
South Africa	2000–2019	2015, 2019	2019–2021	2017–2019	2002, 2014	2000–2017
Thailand	2000–2019	2013	-	2012	2012, 2018	2000–2017
UR Tanzania	2000–2019	2013, 2018	2019–2021	2012	2007, 2018	-
Viet Nam	2000–2019	2013, 2019	2017	2007, 2017	2006, 2012, 2018–	-
Zambia	2000–2019	2016, 2020	-	2014	2008, 2018–, 2020	-
Zimbabwe	2000–2019	2016, 2019	-	2014	2016, 2018–	-

NA, not applicable; VR, vital registration

^a The WHO TB surveillance checklist of standards and benchmarks is designed to assess the quality and coverage of notification data (based on 9 core standards), VR data (1 standard) and drug-resistant TB, HIV coinfection and childhood TB (3 supplementary standards). A partial assessment has been done in China. If more than two assessments have been done (Indonesia, Nigeria, Pakistan, Philippines, Zambia and Zimbabwe), the years of the last two only are shown.

^b Studies are currently underway in South Africa and United Republic of Tanzania and are expected to be completed in 2021. A study in the Philippines is scheduled for 2021. Prioritization of TB inventory studies is recommended in countries where a large share of TB care is provided to TB patients outside the existing NTP network.

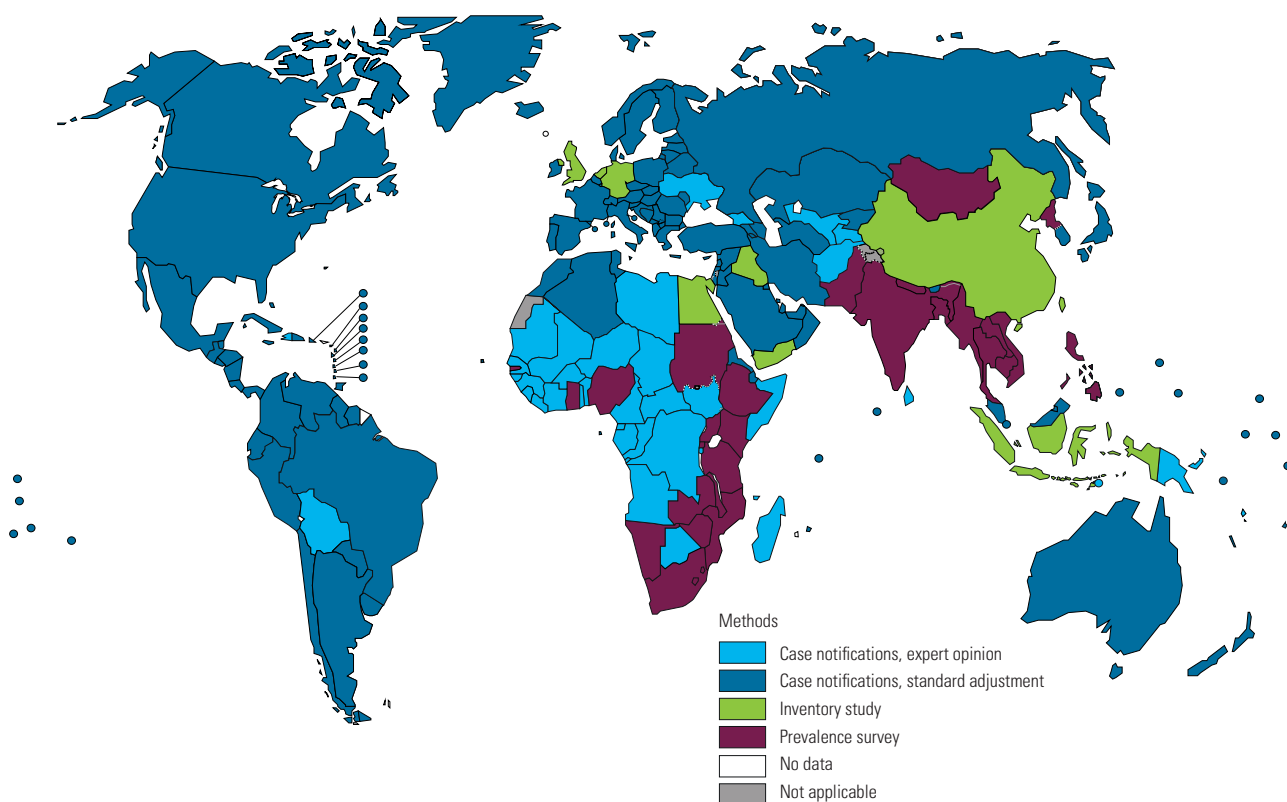
^c A survey is currently underway in India and is expected to be completed in 2021. Brazil and Russian Federation do not meet the following criteria recommended by the WHO Global Task Force on TB Impact Measurement for implementing a national prevalence survey: TB incidence ≥ 150 per 100 000 population per year, no vital registration system and Under-5 mortality rate (probability of dying by age of 5 per 1000 live births) is >10 .

^d The first year of data from continuous surveillance based on routine diagnostic testing is indicated by “–” for Ethiopia, Myanmar, Namibia, Russian Federation, Viet Nam, Zambia and Zimbabwe. The surveys in Brazil, Central African Republic, Democratic People’s Republic of Korea and Papua New Guinea were subnational. If more than two national surveys have been done (Cambodia, Myanmar, Thailand, Philippines, Zambia), the years of the last two only are shown. A survey is currently underway in Myanmar and Zambia, and a survey is planned in Mozambique for 2021.

^e Years of data availability for India, Indonesia, Pakistan and South Africa were provided to WHO by The Institute for Health Metrics and Evaluation (IHME).

FIG. 4.2

Main methods used to estimate TB incidence



► **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, overdiagnosis 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 39 countries, which accounted for 11% of the estimated global number of incident cases in 2019.

Of the four methods, the last one is the least preferred and it is relied on only if none of the other three methods can be used. As explained in **Box 4.1**, the underlying principle for the Task Force, since its establishment in 2006, has been that, as far as possible, estimates of the level of and trends in TB disease burden should be based on direct measurements from routine surveillance and surveys, as opposed to indirect estimates that rely on modelling and expert opinion. Sources of data available to estimate the burden of TB disease in the 30 high TB burden countries are summarized in **Table 4.2**.

Estimates of TB incidence in children (aged <15 years) are based on dynamic modelling (13). Results for the 0–14 year age group (0–4 and 5–14 years) in each country are further disaggregated using outputs from an established deterministic model (13), followed by disaggregation by sex using results from a meta-analysis of the male to female notification ratio (M:F).

Estimates of TB incidence in adults are derived using a two-step method. First, incidence in children is subtracted from incidence in all ages, then the estimates for adults are 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 2007–2019 (**Section 4.4**). Country-specific distributions are used for countries that have implemented a survey; for other countries, the age distribution is predicted using prevalence survey data. Disaggregation by sex is based on actual M:F ratios for countries that have implemented surveys; for other countries, this disaggregation is based on regional M:F ratios from a systematic review and meta-analysis (8).

4.1.2 Estimates of TB incidence in 2019

Globally in 2019, an estimated 10.0 million (range, 8.9–11.0 million) people fell ill with TB,¹ equivalent to 130 cases (range, 116–143) per 100 000 population. Estimates of absolute numbers are shown in **Table 4.3** and estimates of rates per capita are shown in **Table 4.4**.

Most of the estimated number of cases in 2019 occurred in the WHO regions of South-East Asia (44%), Africa (25%) and the Western Pacific (18%); smaller proportions of cases occurred in the WHO regions of the Eastern Mediterranean (8.2%), the Americas (2.9%) and Europe (2.5%).²

¹ Here and elsewhere in the report, “range” refers to the 95% uncertainty interval. If 95% confidence intervals are reported, this is explicitly stated.

² Numbers do not sum to exactly 100, owing to rounding.

TABLE 4.3

Estimated epidemiological burden of TB in 2019 for 30 high TB burden countries, WHO regions and globally

Number in thousands.^a

COUNTRY	POPULATION	TOTAL TB INCIDENCE		HIV-POSITIVE TB INCIDENCE		HIV-NEGATIVE TB MORTALITY		HIV-POSITIVE TB MORTALITY ^b	
		BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Angola	31 800	112	72–160	8.5	5.5–12	17	10–26	2.6	1.7–3.7
Bangladesh	163 000	361	262–474	0.70	0.35–1.2	38	24–56	0.15	0.074–0.26
Brazil	211 000	96	82–111	11	9.2–12	4.9	4.7–5.1	1.8	1.4–2.4
Cambodia	16 500	47	31–68	1.3	0.81–1.8	2.9	1.8–4.2	0.41	0.26–0.59
Central African Rep.	4 750	26	17–37	6.5	4.2–9.3	4.6	2.7–7.0	2.9	1.8–4.2
China	1 430 000	833	717–957	14	12–16	31	28–34	2.2	1.7–2.9
Congo	5 380	20	13–29	5.8	2.9–9.7	2.8	1.6–4.3	2.2	1.1–3.6
DPR Korea ^c	25 700	132	115–150	-	-	-	-	-	-
DR Congo	86 800	278	180–397	30	19–42	43	26–65	9.6	6.2–14
Ethiopia	112 000	157	110–211	10	7.1–14	21	14–31	2.8	1.9–3.8
India ^d	1 370 000	2 640	1 800–3 630	71	49–98	436	404–469	9.5	6.0–14
Indonesia	271 000	845	770–923	19	8.0–35	92	86–98	4.7	1.9–8.8
Kenya	52 600	140	86–208	37	22–54	20	11–30	13	7.8–19
Lesotho	2 130	14	8.6–20	8.6	5.3–13	1.2	0.69–1.9	3.6	2.2–5.3
Liberia	4 940	15	9.8–22	2.2	1.4–3.1	2.8	1.6–4.2	0.86	0.55–1.2
Mozambique	30 400	110	68–162	37	23–55	5.8	3.1–9.3	5.6	3.3–8.6
Myanmar	54 000	174	114–245	14	8.9–19	19	12–29	3.1	2.1–4.4
Namibia	2 490	12	8.7–16	3.9	2.8–5.2	1.4	0.90–2.0	1.3	0.86–1.7
Nigeria	201 000	440	287–625	46	30–66	127	74–195	27	17–40
Pakistan	217 000	570	404–764	5.1	3.4–7.2	42	34–51	1.9	1.3–2.8
Papua New Guinea	8 780	38	31–46	1.5	0.72–2.4	4.1	2.7–5.8	0.31	0.15–0.54
Philippines	108 000	599	336–936	11	4.7–21	27	23–31	0.81	<0.01–4.4
Russian Federation	146 000	73	47–104	17	11–24	8.4	7.9–8.9	1.3	0.56–2.3
Sierra Leone	7 810	23	15–33	3.0	1.9–4.4	2.4	1.4–3.7	0.68	0.43–0.99
South Africa	58 600	360	250–489	209	145–285	22	21–23	36	14–68
Thailand	69 600	105	79–133	10	7.9–13	9.6	7.1–12	1.9	1.4–2.6
UR Tanzania	58 000	137	65–237	33	15–56	20	9.3–35	12	5.7–20
Viet Nam	96 500	170	108–246	5.5	3.5–8.0	9.4	5.9–14	2.0	1.2–2.8
Zambia	17 900	59	39–85	28	18–39	5.9	3.5–9.0	9.5	6.1–14
Zimbabwe	14 600	29	22–38	17	13–23	1.7	1.1–2.4	4.6	3.3–6.2
High TB burden countries	4 880 000	8 610	7 600–9 680	668	585–757	1 040	966–1 120	165	134–198
Africa	1 090 000	2 470	2 190–2 750	595	515–680	378	313–448	169	139–203
The Americas	1 010 000	290	269–311	29	27–32	17	17–18	5.9	5.2–6.6
Eastern Mediterranean	717 000	819	646–1 010	7.9	5.9–10	76	65–87	2.7	2.0–3.6
Europe	930 000	246	215–281	30	23–38	20	20–21	4.2	3.1–5.5
South-East Asia	2 000 000	4 340	3 460–5 320	117	90–147	632	593–671	20	15–26
Western Pacific	1 930 000	1 800	1 480–2 150	36	28–46	84	78–91	6.3	5.2–7.5
Global	7 690 000	9 960	8 940–11 000	815	729–906	1 210	1 130–1 290	208	177–242

Population estimates were obtained from the United Nations 2019 Revision of World Population Prospects as prepared by the Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat. (<https://population.un.org/wpp/>, accessed 22 June 2020)

^a Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

^b Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD-10.

^c WHO estimates of TB incidence among people living with HIV and of TB mortality are not shown for DPR Korea because they had not been approved by national authorities at the time of report publication.

^d Estimates of TB incidence and mortality for India are interim, pending results from the national TB prevalence survey (2020/2021).

TABLE 4.4
Estimated epidemiological burden of TB in 2019 for 30 high TB burden countries, WHO regions and globally

 Rates per 100 000 population.^a

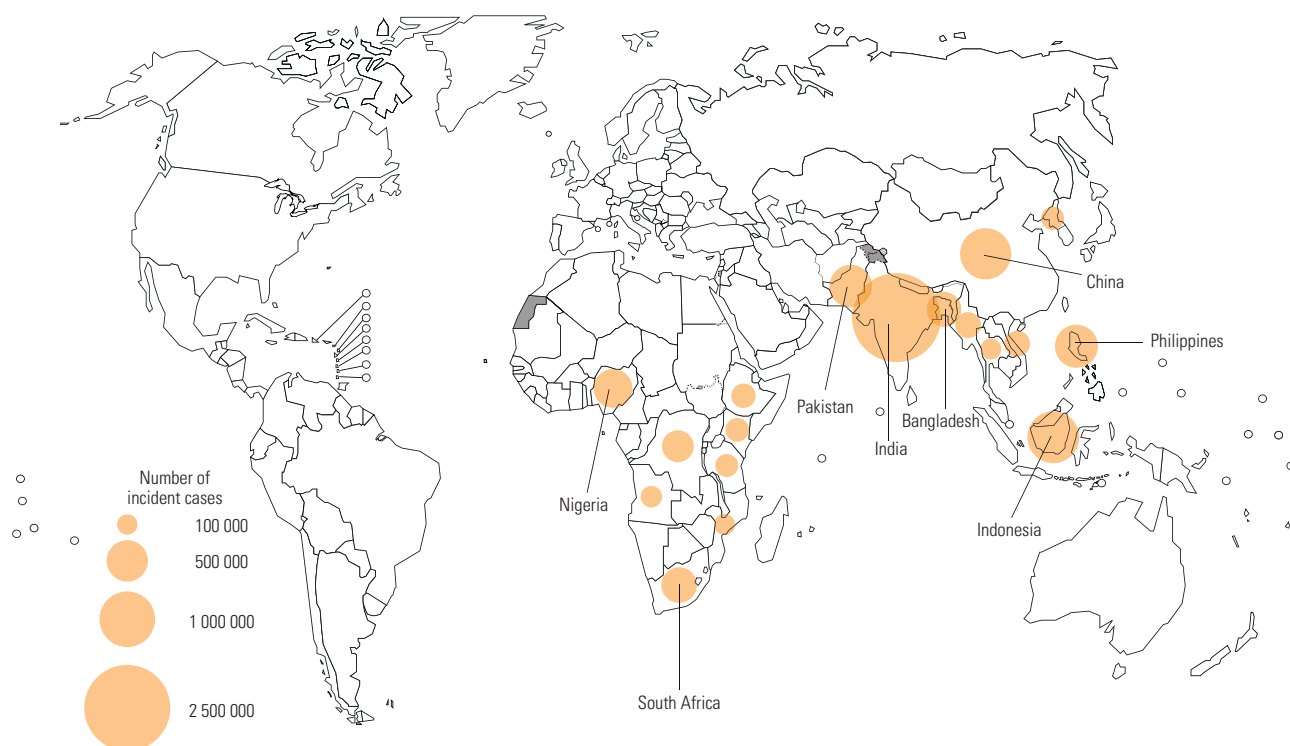
COUNTRY	TOTAL TB INCIDENCE		HIV PREVALENCE AMONG INCIDENT TB CASES (%)		HIV-NEGATIVE TB MORTALITY		HIV-POSITIVE TB MORTALITY ^b	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Angola	351	227–501	7.6	7.4–7.8	53	32–80	8.2	5.4–12
Bangladesh	221	161–291	0.19	0.11–0.30	24	15–34	0.093	0.046–0.16
Brazil	46	39–53	11	11–11	2.3	2.2–2.4	0.87	0.65–1.1
Cambodia	287	186–410	2.7	2.5–2.8	17	11–25	2.5	1.6–3.6
Central African Rep.	540	349–771	25	25–26	98	57–148	61	39–88
China	58	50–67	1.6	1.6–1.7	2.2	2.0–2.4	0.15	0.12–0.20
Congo	373	237–541	29	18–42	52	29–81	40	20–67
DPR Korea ^c	513	446–584	-	-	-	-	-	-
DR Congo	320	207–457	11	11–11	49	29–75	11	7.2–16
Ethiopia	140	98–188	6.5	6.3–6.6	19	12–28	2.5	1.7–3.4
India ^d	193	132–266	2.7	2.7–2.7	32	30–34	0.69	0.44–1.0
Indonesia	312	285–341	2.2	0.95–4.1	34	32–36	1.7	0.71–3.2
Kenya	267	163–396	26	26–26	37	21–58	24	15–36
Lesotho	654	406–959	62	60–63	57	32–88	168	103–248
Liberia	308	199–440	14	14–15	56	33–85	17	11–25
Mozambique	361	223–532	34	34–34	19	10–31	18	11–28
Myanmar	322	212–454	7.8	7.7–8.0	36	21–54	5.8	3.8–8.1
Namibia	486	348–647	32	31–33	57	36–82	50	35–69
Nigeria	219	143–311	11	10–11	63	37–97	14	8.5–20
Pakistan	263	187–353	0.90	0.73–1.1	19	16–24	0.90	0.58–1.3
Papua New Guinea	432	352–521	3.8	2.0–6.3	47	31–66	3.5	1.7–6.1
Philippines	554	311–866	1.9	1.1–3.0	25	22–29	0.75	<0.01–4.0
Russian Federation	50	32–71	23	23–24	5.8	5.4–6.1	0.88	0.38–1.6
Sierra Leone	295	190–422	13	13–14	31	18–47	8.7	5.5–13
South Africa	615	427–835	58	58–58	38	36–40	62	25–115
Thailand	150	114–191	10	9.8–10	14	10–18	2.8	2.0–3.7
UR Tanzania	237	112–408	24	24–24	35	16–61	20	9.8–34
Viet Nam	176	112–255	3.3	3.2–3.4	9.8	6.1–14	2.0	1.3–2.9
Zambia	333	216–474	46	46–47	33	20–50	53	34–76
Zimbabwe	199	147–258	60	59–60	11	7.4–16	31	22–42
High TB burden countries	177	156–198	7.8	6.7–8.9	21	20–23	3.4	2.8–4.1
Africa	226	201–252	24	22–26	35	29–41	16	13–19
The Americas	29	27–31	10	7.8–13	1.7	1.6–1.8	0.58	0.52–0.65
Eastern Mediterranean	114	90–141	0.97	0.41–1.8	11	9.0–12	0.38	0.27–0.50
Europe	26	23–30	12	7.9–18	2.2	2.1–2.3	0.45	0.34–0.59
South-East Asia	217	173–266	2.7	2.0–3.5	32	30–34	1.0	0.75–1.3
Western Pacific	93	77–111	2.0	1.1–3.2	4.4	4.0–4.7	0.33	0.27–0.39
Global	130	116–143	8.2	7.0–9.5	16	15–17	2.7	2.3–3.1

^a Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

^b Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD-10.

^c WHO estimates of TB incidence among people living with HIV and of TB mortality are not shown for DPR Korea because they had not been approved by national authorities at the time of report publication.

^d Estimates of TB incidence and mortality for India are interim, pending results from the national TB prevalence survey (2020/2021).

FIG. 4.3**Estimated TB incidence in 2019, for countries with at least 100 000 incident cases**

The 30 high TB burden countries¹ accounted for 86% of all estimated incident cases worldwide, and eight of these countries accounted for two thirds of the global total: India (26%), Indonesia (8.5%), China (8.4%), the Philippines (6.0%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%) and South Africa (3.6%) (Fig. 4.3 and Table 4.3).

The severity of national TB epidemics, in terms of the annual number of incident TB cases relative to population size (the incidence rate), varied widely among countries in 2019 (Fig. 4.4 and Table 4.4). In 2019, 54 countries had a low incidence of TB (<10 cases per 100 000 population per year), mostly in the WHO Region of the Americas and European Region, plus a few countries in the Eastern Mediterranean and Western Pacific regions.² These countries are well placed to target TB elimination. There were 150–400 cases per 100 000 population in most of the 30 high TB burden countries, and more than 500 cases in the Central African Republic, the Democratic People’s Republic of Korea, Lesotho, the Philippines and South Africa. Among the 30 high TB burden countries, there were three with markedly lower incidence rates per capita – Brazil, China and the Russian Federation – which had best estimates of 46, 58 and 50, respectively.

An estimated 8.2% (range, 7.0–9.5%) of the incident TB cases in 2019 were among people living with HIV (Table 4.3 and Table 4.4). 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. 4.5). Globally, the incidence of TB expressed per 100 person-years with HIV was 2.1% (range, 1.9–2.4%). The risk of developing TB among the 38 million people living with HIV was 18 (range, 15–21) times higher than in the rest of the global population.

An estimated 140 000 (range, 69 800–235 000) new cases of zoonotic TB occurred globally in 2019 (Table 4.5). This estimate is derived from data on *Mycobacterium bovis*, the most common cause of zoonotic TB globally. Given that other mycobacterial species can also cause zoonotic TB, the true burden may be higher.

¹ These countries are listed in Table 4.2, Table 4.3 and Table 4.4. For an explanation of how the list of 30 high TB burden countries was defined, see Annex 2.

² See also Fig. 2.2 in Chapter 2.

FIG. 4.4

Estimated TB incidence rates, 2019

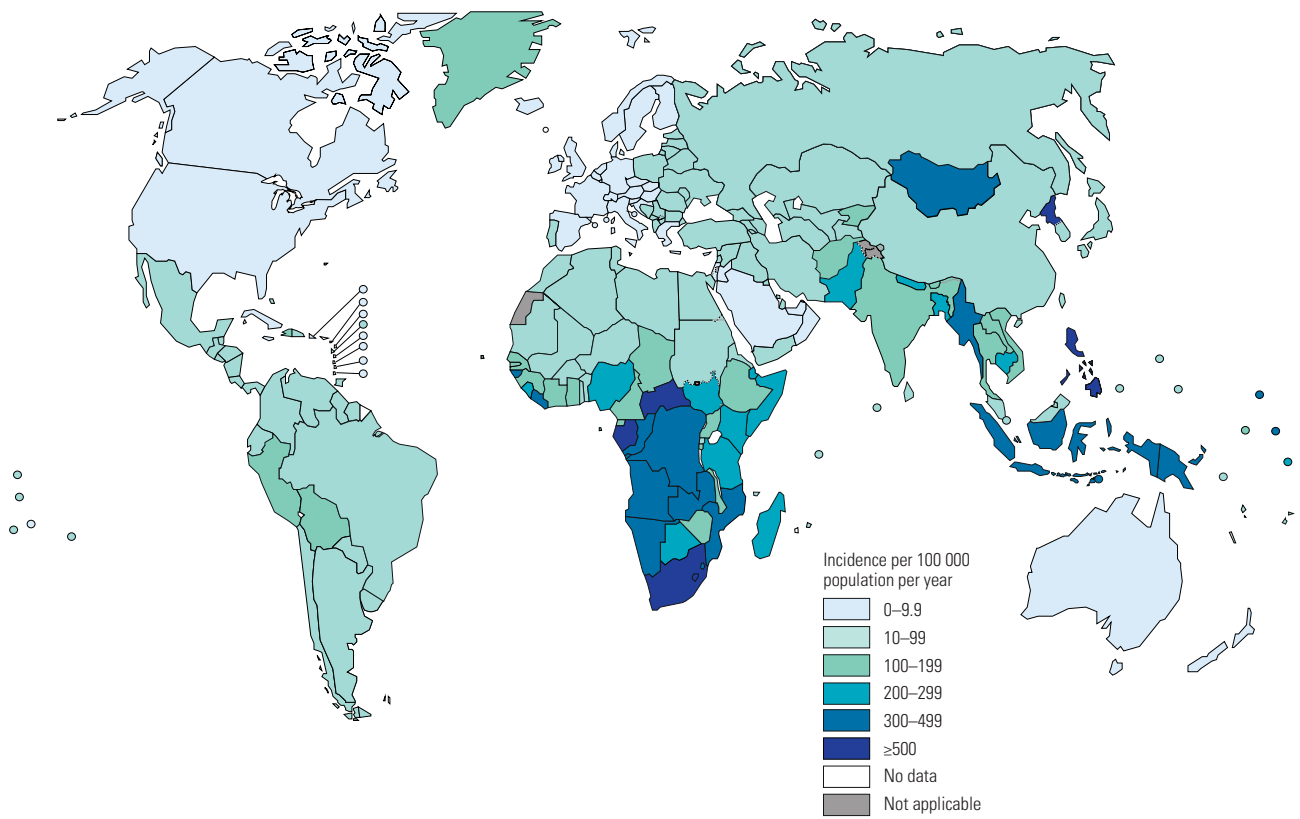


FIG. 4.5

Estimated HIV prevalence in new and relapse TB cases, 2019

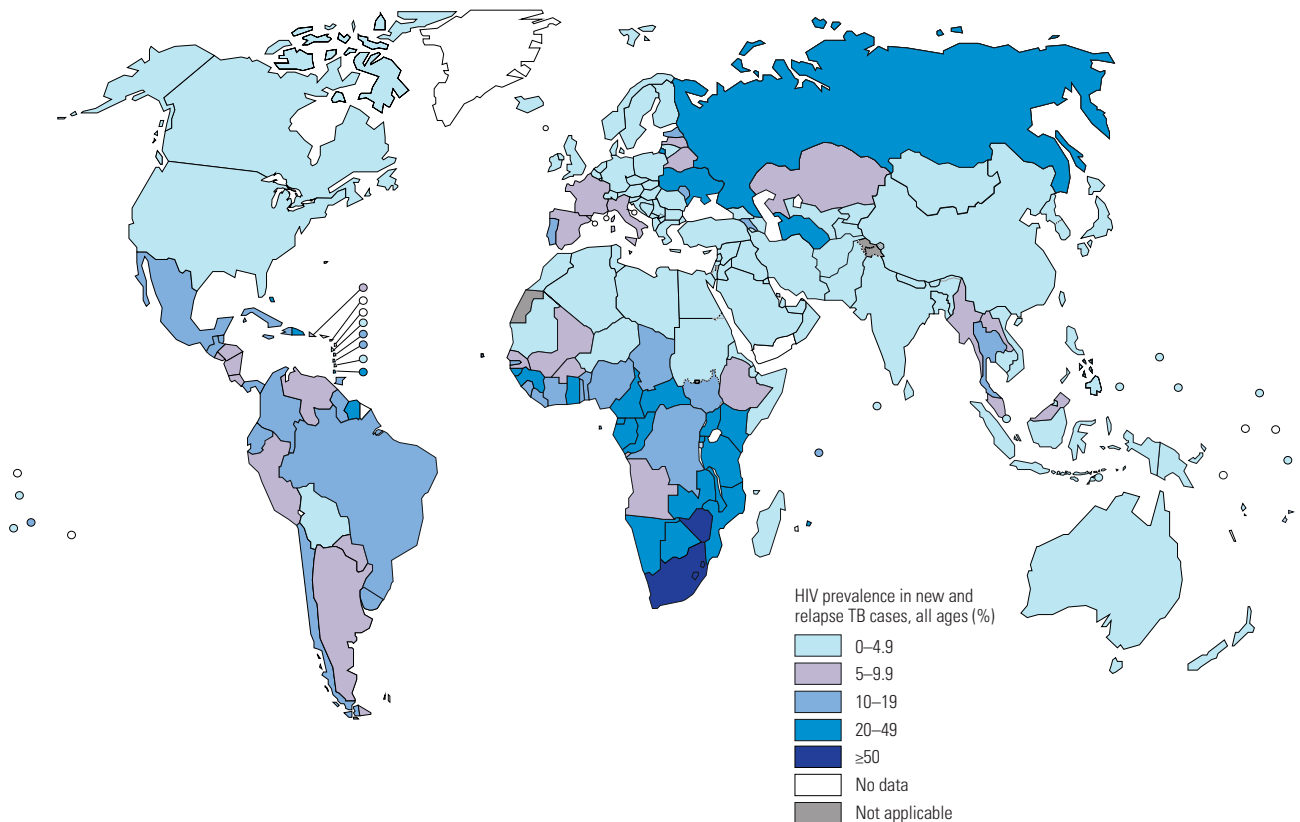


TABLE 4.5

Estimated incidence and mortality due to zoonotic TB for WHO regions and globally, 2019^{a,b}

WHO REGION	NUMBER OF INCIDENT CASES		NUMBER OF DEATHS	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	68 900	18 500–152 000	8 440	2 220–18 700
The Americas	870	236–1 910	42	11–92
Eastern Mediterranean	8 190	2 110–18 300	604	161–1 340
Europe	986	263–2 180	65	18–143
South-East Asia	43 400	11 200–96 900	2 020	548–4 440
Western Pacific	18 000	4 720–40 000	270	73–594
Global	140 000	69 800–235 000	11 400	4 470–21 600

^a Estimates are derived from data on *Mycobacterium bovis*, the most common cause of zoonotic TB globally.

^b Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

4.1.3 TB incidence in 2019 disaggregated by age and sex

Estimates of TB incidence in 2019 disaggregated by age and sex are shown in **Fig. 4.6** (global), **Fig. 4.7** (WHO regions) and **Fig. 4.8** (30 high TB burden countries), and in **Table 4.6**. People in all age groups are affected by TB, but the highest burden is among adult men, who accounted for 56% of all cases in 2019, compared with 32% of cases in adult women and 12% in children.¹ The higher share of TB cases among men is consistent with evidence from prevalence surveys, which show that TB disease affects men more than women, and that gaps in case detection and reporting are higher among men (**Section 4.4**).

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 European and Western Pacific regions. In children, the global M:F ratio was close to 1.

4.1.4 Estimated trends in TB incidence, 2000–2019

Consistent with previous global TB reports, the number of incident cases is falling slowly, in both absolute terms and per capita (**Fig. 4.9**). Globally, the average rate of decline in the TB incidence rate was 1.7% per year in the period 2000–2019, and 2.3% per year in 2018–2019. This is much too slow to reach the End TB Strategy milestone of a 20% reduction between 2015 and 2020 (see right panel of **Fig. 4.9** and left panel of **Fig. 4.10**). The cumulative reduction between 2015 and 2019 was 9%.

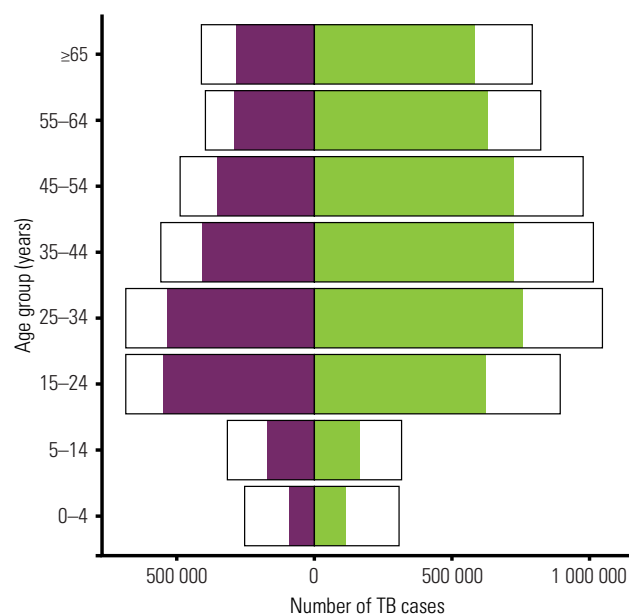
Trends and a comparison of progress with the 2020 milestone of the End TB Strategy are shown for the six WHO regions in **Fig. 4.11** and for the 30 high TB burden countries in **Fig. 4.12**.² Currently, the world as a whole, most WHO regions and many high TB burden countries are not on track to reach the 2020 milestone.

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

² Time series of estimates for all countries are available online. **Annex 1** explains how to access and download them.

FIG. 4.6

Global estimates of TB incidence (black outline) and case notifications disaggregated by age and sex (female in purple; male in green), 2019

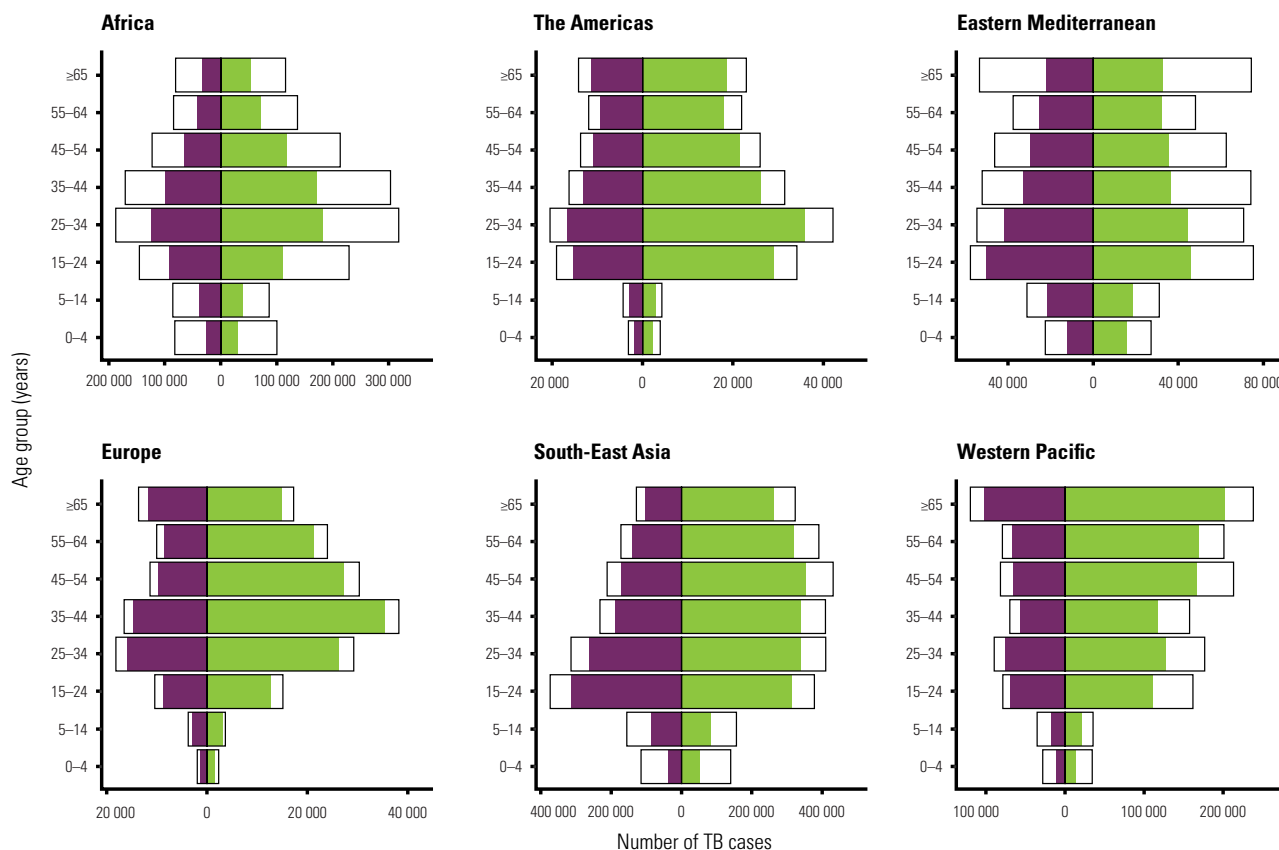


Globally, the reduction in TB incidence between 2015 and 2019 was 9% (from 142 to 130 new cases per 100 000 population), less than halfway to the 2020 milestone.

More positively, the WHO European Region has almost reached the milestone, with a reduction of 19% between 2015 and 2019, and the African Region has made good progress, with a reduction of 16%. The decline in the WHO European Region has been driven in particular by the Russian Federation, where the TB incidence rate has fallen at 5.7% per year in the decade 2010–2019. In the WHO African Region, several countries in southern Africa have achieved impressive reductions of 4–10% per year since 2015, following a peak in the HIV epidemic, and

FIG. 4.7

Regional estimates of TB incidence (black outline) and case notifications disaggregated by age and sex (female in purple; male in green), 2019



the expansion of TB and HIV prevention and care.¹ The incidence of TB expressed per 100 person-years with HIV in the WHO African Region decreased from 5.3% (range, 4.4–6.4%) in 2010 to 3.6% (range, 2.8–3.0%) in 2015 and 2.3% (range, 2.0–2.7%) in 2019. This continuous decline was in large part attributable to the substantial rise in ART coverage in Africa, from an estimated 24% of people living with HIV in 2010 to 51% in 2015 and almost 70% in 2019.

Annual declines in incidence since 2015 have been much slower in the WHO regions of the Eastern Mediterranean (0.9% per year), South-East Asia (2.3% per year) and the Western Pacific (1.5% per year), with cumulative reductions of 3.5%, 8.7% and 6.1%, respectively, for the period 2015–2019. Of concern is the WHO Region of the Americas, where incidence is estimated to be slowly increasing after many years of decline, owing to an upward trend in Brazil during 2016–2019.

A total of 78 countries are on track to reach the milestone of a 20% reduction in TB incidence between 2015 and 2020. Of the 30 high TB burden countries, seven have already reached this milestone (Cambodia, Ethiopia, Kenya, Namibia, the Russian Federation, South Africa and

the United Republic of Tanzania) and three others are on track to do so (Lesotho, Myanmar and Zimbabwe).

Faster reductions in other countries will require improvements in access to TB diagnosis and care within the context of progress towards UHC, action on broader determinants (e.g. levels of undernutrition, poverty, smoking and diabetes), and a new treatment or vaccine to substantially lower the risk of developing TB in people who already have a latent TB infection. These topics are discussed in more detail in [Chapter 8](#) and [Chapter 9](#).

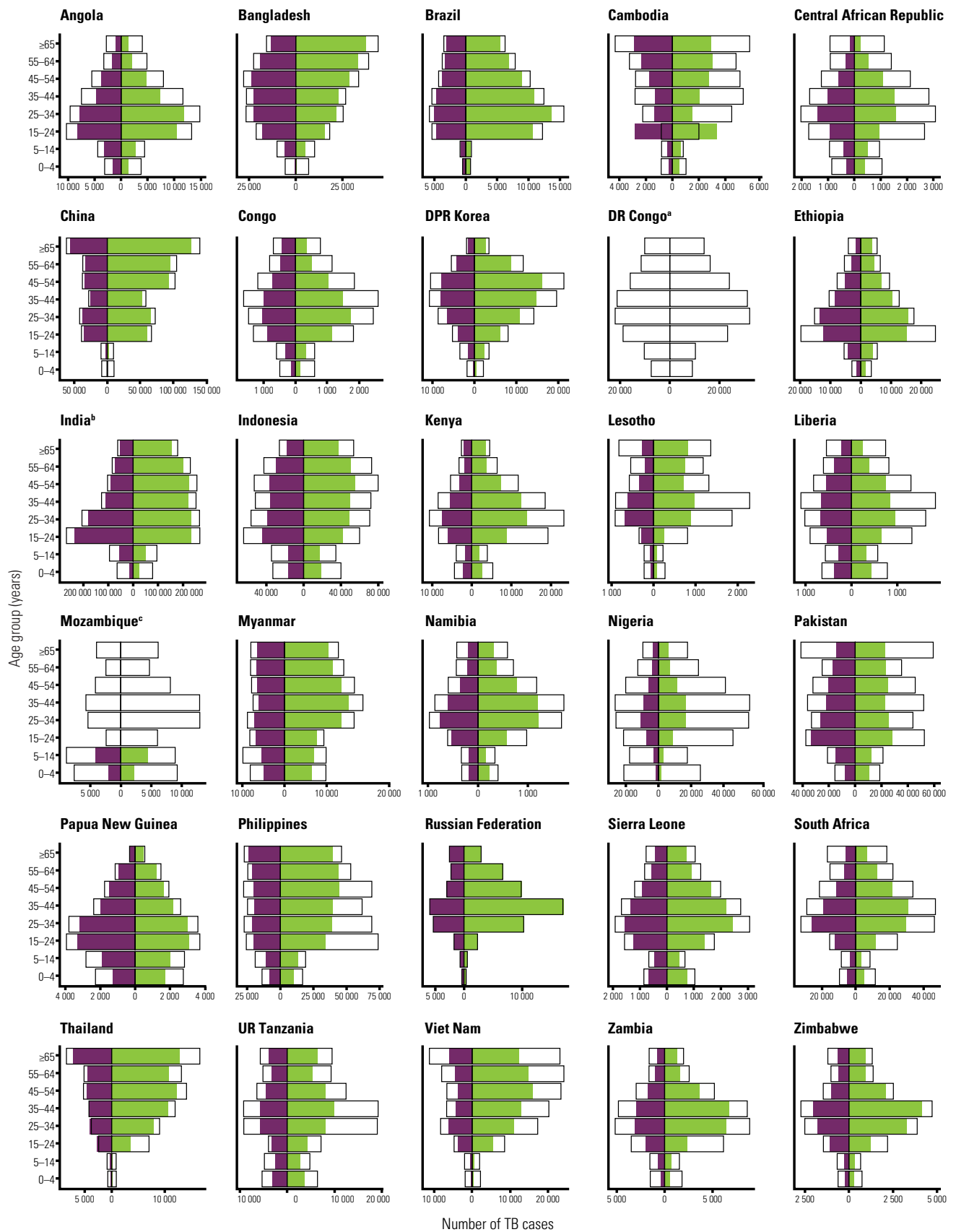
4.2 TB mortality

Deaths from TB among HIV-negative people are classified as TB deaths in the 10th edition of the International Classification of Diseases (ICD-10) (15). When an HIV-positive person dies from TB, the underlying cause is classified as HIV. For consistency with international classifications, this section makes a clear distinction between TB deaths in HIV-negative people and TB deaths in HIV-positive people. The milestones and targets for reductions in TB deaths set in the End TB Strategy are for the combined total of deaths in HIV-positive and HIV-negative people; illustrations of progress towards the 2020 milestone in this chapter are presented accordingly.

¹ Further details are provided in [Box 3.4](#) of the 2018 global TB report (14).

FIG. 4.8

Estimates of TB incidence (black outline) and case notifications disaggregated by age and sex (female in purple; male in green) in the 30 high TB burden countries, 2019



^a Age and sex disaggregated case notifications were not available.

^b Estimates of TB incidence for India are interim, pending results from the national TB prevalence survey (2020/2021).

^c Case notification data disaggregated by age and sex for people aged 15 years and above were not available for Mozambique.

TABLE 4.6

Estimated number of TB cases (in thousands) in children and adults,^a globally and for WHO regions, 2019

WHO REGION	TOTAL		MALE		FEMALE	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	2 460	2 190–2 750	1 500	1 270–1 740	961	810–1 110
The Americas	290	269–311	187	168–205	103	93–114
Eastern Mediterranean	819	646–1 010	464	318–609	356	244–467
Europe	246	215–280	161	132–190	86	70–101
South-East Asia	4 340	3 460–5 320	2 640	1 860–3 420	1 700	1 200–2 210
Western Pacific	1 800	1 480–2 150	1 220	918–1 520	583	439–726
Global	9 960	8 940–11 000	6 170	5 280–7 060	3 790	3 250–4 340

WHO REGION	TOTAL ≥15 YEARS		MALE ≥15 YEARS		FEMALE ≥15 YEARS	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	2 110	1 830–2 380	1 310	1 080–1 550	793	650–935
The Americas	274	253–295	179	160–197	96	86–106
Eastern Mediterranean	707	526–888	405	260–550	302	194–410
Europe	235	202–268	155	125–184	80	65–95
South-East Asia	3 770	2 860–4 690	2 340	1 560–3 130	1 430	953–1 910
Western Pacific	1 670	1 340–2 000	1 150	846–1 450	519	383–656
Global	8 770	7 730–9 800	5 540	4 650–6 440	3 220	2 700–3 740

WHO REGION	TOTAL 0–14 YEARS		MALE 0–14 YEARS		FEMALE 0–14 YEARS	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	355	308–401	186	153–220	168	138–199
The Americas	16	14–17	8.1	7.3–9.0	7.5	6.7–8.3
Eastern Mediterranean	112	83–141	58	37–79	54	34–73
Europe	12	10–13	6.0	4.9–7.1	5.7	4.6–6.8
South-East Asia	567	429–704	296	197–395	271	180–361
Western Pacific	133	107–160	70	51–88	64	47–80
Global	1 190	1 050–1 330	624	524–725	570	478–661

^a Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

FIG. 4.9

Global trends in the estimated number of incident TB cases (left) and the incidence rate (right), 2000–2019

Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone of the End TB Strategy.

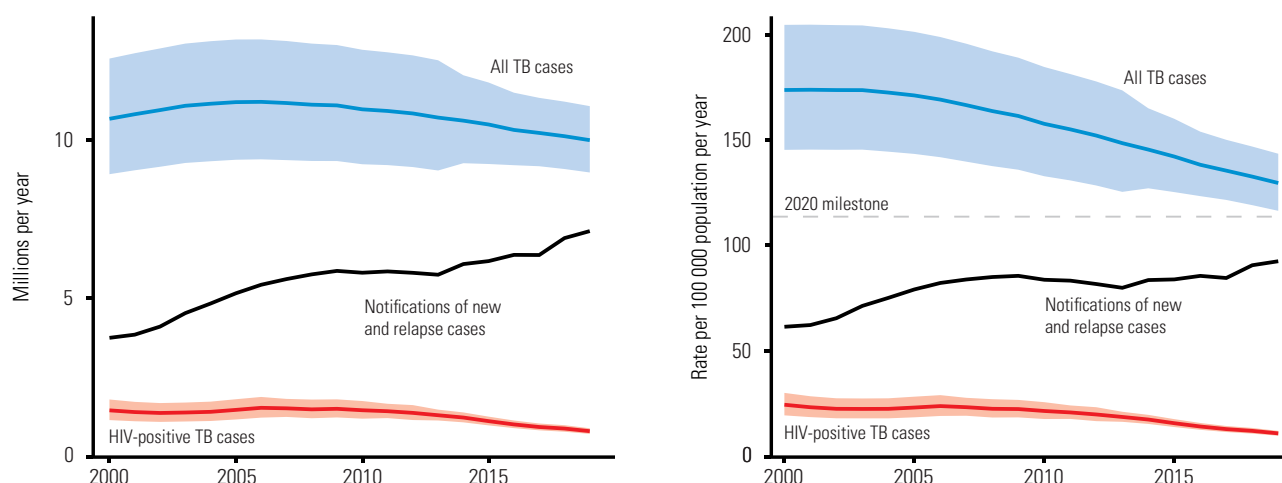


FIG. 4.10

Global trends in the TB incidence rate and the absolute number of TB deaths (solid lines) compared with those required to achieve the 2020 and 2025 milestones of the End TB Strategy (dashed lines)

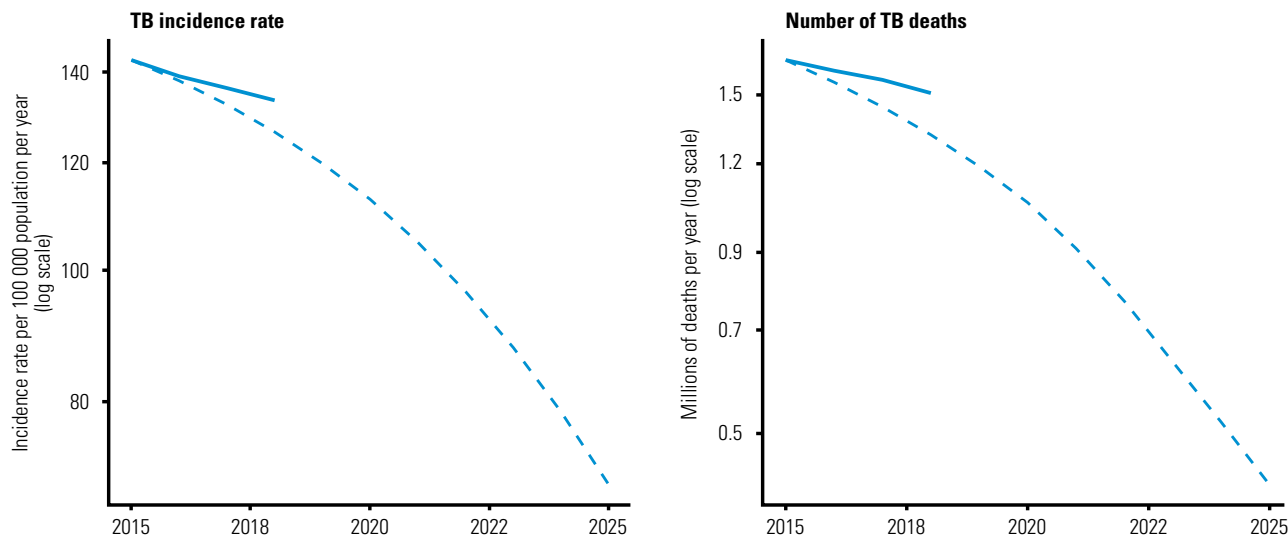


FIG. 4.11

Trends in estimated TB incidence rates by WHO region, 2000–2019

Total TB incidence rates are shown in green and incidence rates of HIV-positive TB are shown in red. The black solid lines show notifications of new and relapse cases for comparison with estimates of the total incidence rate. Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone for incidence of the End TB Strategy.

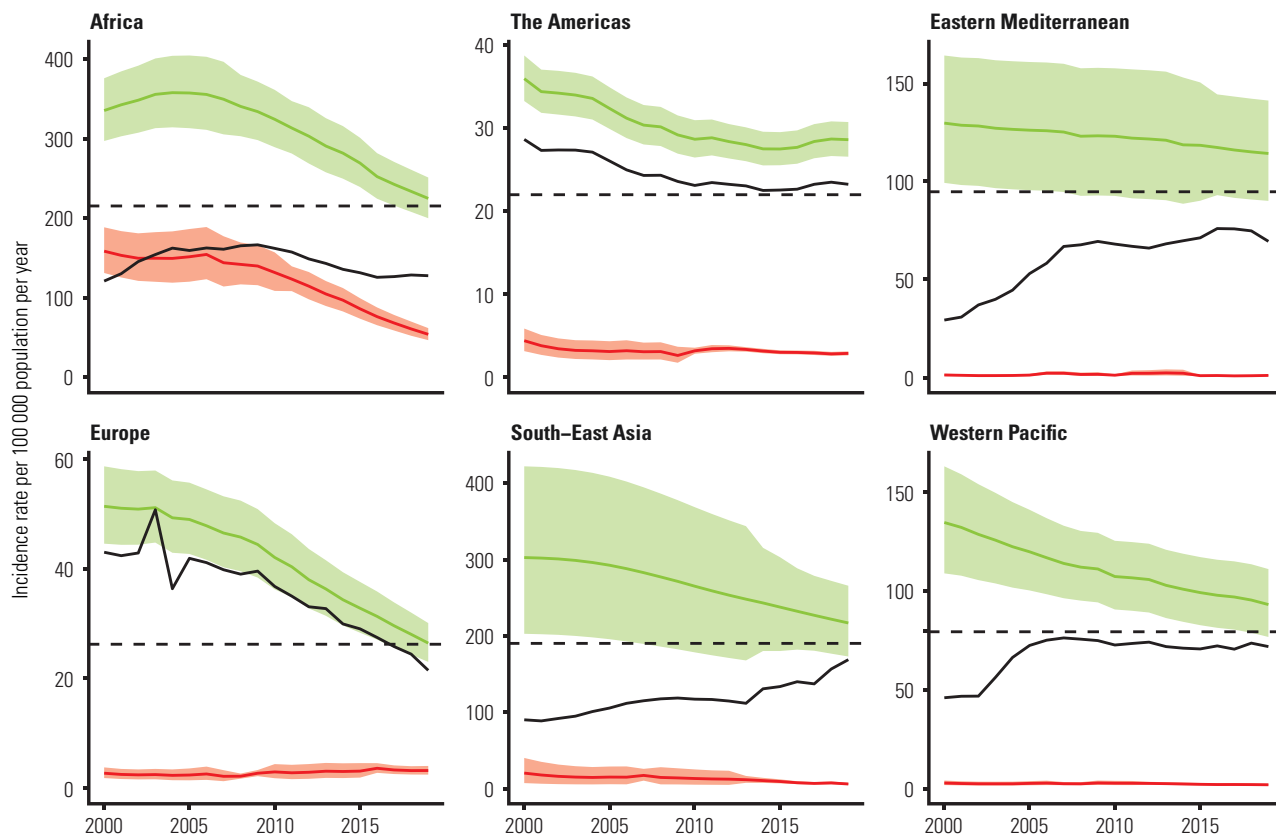
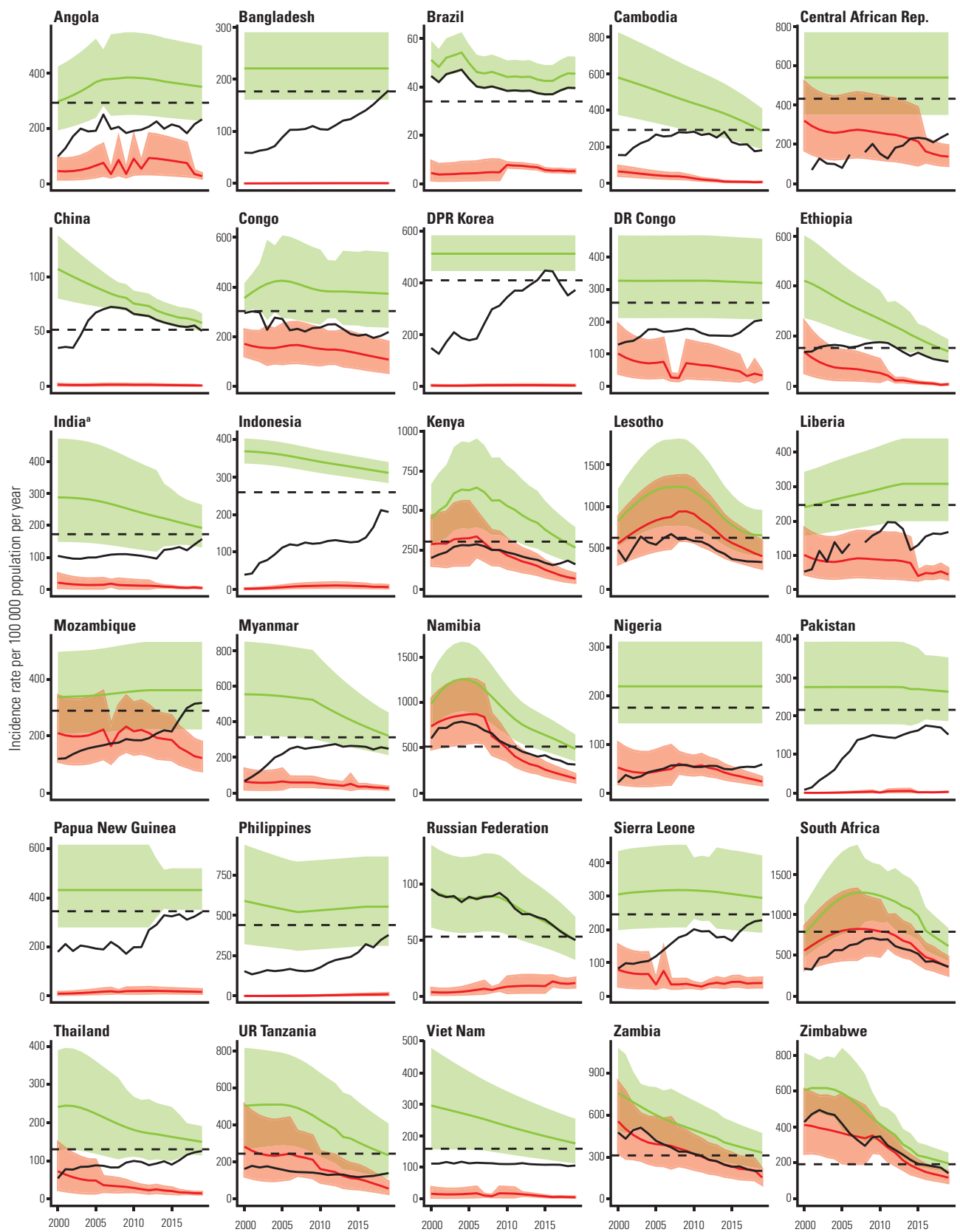


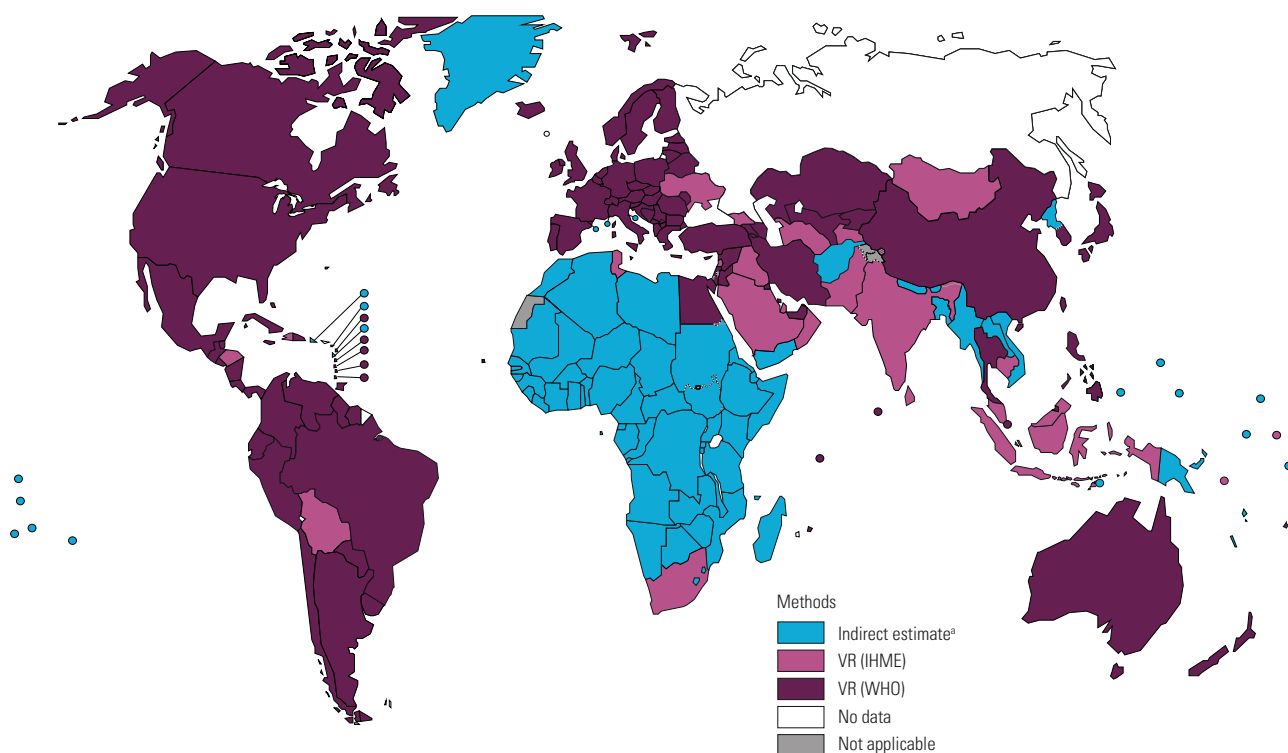
FIG. 4.12

Trends in estimated TB incidence rates in the 30 high TB burden countries, 2000–2019

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 solid lines show notifications of new and relapse cases for comparison with estimates of the total incidence rate. The horizontal dashed line shows the 2020 milestone for incidence of the End TB Strategy.



^a Estimates of TB incidence for India are interim, pending results from the national TB prevalence survey (2020/2021).

FIG. 4.13**Main methods used to estimate TB mortality in HIV-negative people**

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

4.2.1 Methods to estimate TB mortality

TB mortality among HIV-negative people can be measured directly using data from national VR systems, provided that these systems have high coverage, and 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 2019, most countries with a high burden of TB lacked national or sample VR systems, and few had conducted mortality surveys (Table 4.2). In the absence of VR systems or mortality surveys, TB mortality can be estimated as the product of TB incidence and the 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 or recorded. TB deaths among HIV-positive people are estimated by WHO as the product of TB incidence and the CFR, with the latter accounting for the protective effect of ART.

For the current report, VR or mortality survey data were used for 123 countries (Fig. 4.13), which collectively accounted for 60% of the estimated number of TB deaths (among HIV-negative people) globally in 2019. For 21 of these countries, analyses of VR data and resulting esti-

mates of TB deaths published by the Institute of Health Metrics and Evaluation (IHME) were used.¹ The WHO African Region has the greatest need to introduce or strengthen VR systems in which causes of death are classified according to ICD-10.

TB mortality in children is estimated using a previously published approach derived from dynamic modelling (16), and is then disaggregated by sex on the assumption that the pattern is the same as that for incidence. If available, data on TB deaths among adults are 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 cannot be derived from VR data, a CFR is applied to the adult age- and sex-disaggregated incidence. This CFR accounts for differences between HIV-positive and HIV-negative TB cases, and for variation in HIV prevalence by age and sex.

4.2.2 Estimates of TB mortality in 2019

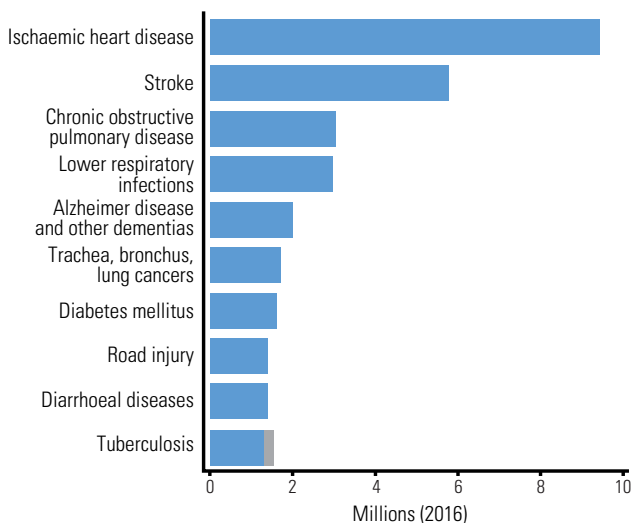
Estimates of the absolute number of deaths caused by TB globally are shown for the six WHO regions and 30 high TB burden countries in Table 4.3. There were an estimated 1.2 million (range, 1.1–1.3 million) deaths from TB among HIV-negative people in 2019 and an additional 208 000 (range, 177 000–242 000) deaths from TB among HIV-positive people.

¹ Downloaded from the GBD results tool (12).

FIG. 4.14

Top causes of death worldwide in 2016^{a,b}

Deaths from TB among HIV-positive people are shown in grey.



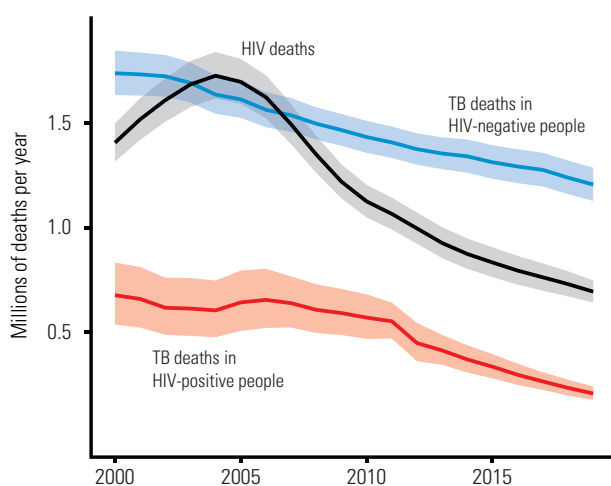
^a This is the latest year for which estimates for all causes are currently available. See WHO estimates, available at <http://apps.who.int/gho/portal> (accessed 13 July 2020) and <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>.

^b Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases.

FIG. 4.16

Global trends in the estimated number of deaths caused by TB and HIV (in millions), 2000–2019^{a,b}

Shaded areas represent uncertainty intervals.



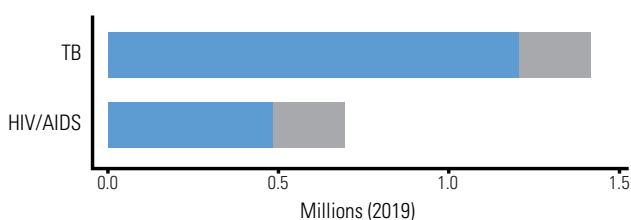
^a For HIV/AIDS, the latest estimates of the number of deaths in 2019 that have been published by UNAIDS are available at <http://www.unaids.org/en/resources/publications/all> (accessed 16 August 2020). For TB, the estimates for 2019 are those published in this report.

^b Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases.

FIG. 4.15

Estimated number of deaths worldwide from TB and HIV/AIDS in 2019^{a,b}

Deaths from TB among HIV-positive people are shown in grey.



^a For HIV/AIDS, the latest estimates of the number of deaths in 2019 that have been published by UNAIDS are available at <http://www.unaids.org/en/> (accessed 16 August 2020). For TB, the estimates for 2019 are those published in this report.

^b Deaths from TB among HIV-positive people are officially classified as deaths caused by HIV/AIDS in the International Classification of Diseases.

TB is the 10th leading cause of death worldwide and, since 2007, it has been the leading cause of death from a single infectious agent, ranking above HIV/AIDS (Fig. 4.14, Fig. 4.15 and Fig. 4.16) (17). 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 2018, the treatment success rate was 85% globally (Chapter 5); and in high-income countries with UHC, the proportion of people who die from TB can be less than 5% (Section 4.2.5).

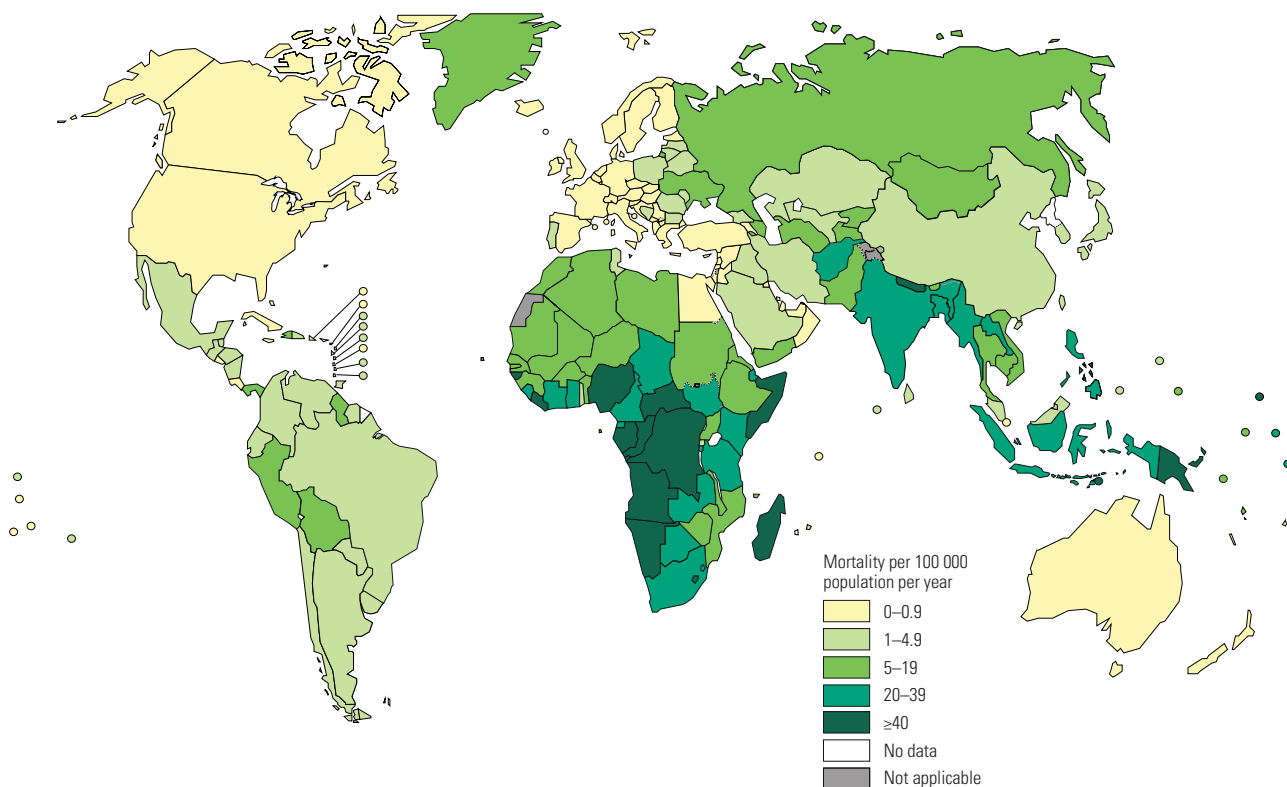
In 2019, about 83% of TB deaths among HIV-negative people occurred in the WHO African and South-East Asia regions; these regions accounted for 85% of the combined total of TB deaths in HIV-negative and HIV-positive people. India accounted for 36% of global TB deaths among HIV-negative people, and for 31% of the combined total number of TB deaths in HIV-negative and HIV-positive people.

Estimates of TB mortality rates (deaths per 100 000 population per year) are shown globally, for the six WHO regions and 30 high TB burden countries, in Table 4.4. Globally, the number of TB deaths among HIV-negative people per 100 000 population was 16 (range, 15–17) in 2019, and 18 (range, 17–20) when TB deaths among HIV-positive people were included. There was considerable variation among countries (Fig. 4.17), 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 two other high TB burden countries (the Democratic People’s Republic of Korea and Papua New Guinea).

Estimates of the number of deaths caused by zoonotic TB are shown in Table 4.5.

FIG. 4.17

Estimated TB mortality rates in HIV-negative people, 2019



4.2.3 TB mortality in 2019 disaggregated by age and sex

Estimates of TB mortality in 2019 disaggregated by age and sex are shown in **Fig. 4.18** (global), **Fig. 4.19** (WHO regions) and **Fig. 4.20** (30 high TB burden countries), and in **Table 4.7**. In **Table 4.7**, 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 (estimates in **Fig 4.18**, **Fig. 4.19** and **Fig. 4.20** are for HIV-negative people only).

Globally in 2019, 53% of the HIV-negative people who died from TB were men, 31% were women and 16% were children (aged <15 years). The higher share for children compared with their estimated share of cases (12%) suggests poorer access to diagnosis and treatment.

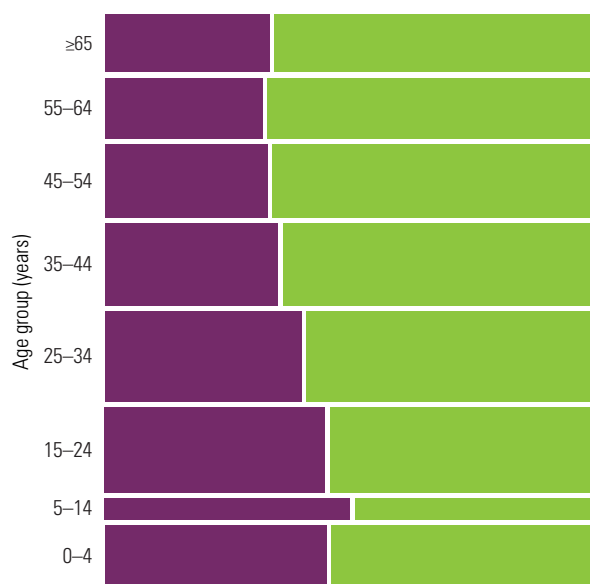
Globally in 2019, 47% of the HIV-positive people who died from TB were men, 36% were women and 17% were children.

4.2.4 Estimated trends in TB mortality, 2000–2019

Global trends in the absolute number of TB deaths in HIV-negative and HIV-positive people and the mortality rate (deaths per 100 000 population per year) are shown in **Fig. 4.21**. The absolute number of TB deaths among HIV-negative people fell 31% between 2000 and 2019, from a best estimate of 1.7 million in 2000 to 1.2 million in 2019, and the mortality rate fell by 45% (including 3.7% between 2018 and 2019). Among HIV-positive people, the

FIG. 4.18

Global distribution of estimated TB mortality in HIV-negative people by age group and sex (female in purple; male in green),^a 2019



^a The total area represents the global number of deaths due to TB and all rectangles are proportional to their share of total TB mortality.

FIG. 4.19

Regional distribution of estimated TB mortality in HIV-negative people by age group and sex (female in purple; male in green),^a 2019



^a The total area represents TB mortality and all rectangles are proportional to their share of total TB mortality by region.

number of TB deaths fell faster, from 678 000 in 2000 to 208 000 in 2019 (a reduction of 69%), and the mortality rate fell by 76% (from 11 to 2.7 per 100 000 population).

Despite this progress, the world is not on track to reach the End TB Strategy milestone of a 35% reduction in the total number of TB deaths between 2015 and 2020 (Fig. 4.10 and Fig. 4.21). The reduction between 2015 and 2019 was only 14%. The total number of deaths can be approximated as the product of two variables: TB incidence and the CFR (the proportion of people with TB who die from the disease). Reaching the 2020 milestone requires the TB incidence rate to be falling at 4–5% per year by 2020 (more than double the current pace of progress) and a CFR of no more than 10% by 2020. The global CFR in 2019 was 14%.

Trends and a comparison of progress with the 2020 milestone of the End TB Strategy are shown for the six WHO regions in Fig. 4.22 and Fig. 4.23, and for the 30 high TB burden countries in Fig. 4.24 and Fig. 4.25.¹

The WHO European Region is on track to reach the 2020 milestone, with a 31% reduction from 2015 to 2019, and the African Region has made good progress, achiev-

ing a reduction of 19%. As with reductions in TB incidence, in the WHO European Region, this progress in reducing the number of TB deaths has been driven by the Russian Federation (where the number of TB deaths has fallen at 10% per year in the decade 2010–2019) and, in the African Region, by expansion of TB and HIV prevention and care (especially ART).

Declines in the number of TB deaths since 2015 have been much slower in the WHO regions of the Americas (1.8% per year), Eastern Mediterranean (2.9% per year), South-East Asia (2.4% per year) and Western Pacific (4.7% per year), with cumulative reductions of 6.1%, 11%, 10% and 17%, respectively, in the period 2015–2019.

A total of 46 countries are on track to reach the 2020 milestone of a 35% reduction in TB deaths. Of the 30 high TB burden countries, seven have already reached this milestone (Bangladesh, Kenya, Mozambique, Myanmar, the Russian Federation, Sierra Leone and the United Republic of Tanzania) and one other country is on track (Viet Nam).

Faster reductions in other countries will require improvements in access to TB diagnosis and care within the broader context of progress towards UHC (to lower the CFR), combined with efforts to accelerate the rate of decline in TB incidence.

¹ Time series of estimates for all countries are available online. Annex 1 and Annex 3 explains how to access them.

FIG. 4.20

Distribution of estimated TB mortality in HIV-negative people in the 30 high TB burden countries by age group and sex (female in purple; male in green),^a 2019



^a The total area represents TB mortality and all rectangles are proportional to their share of total TB mortality by country.

^b Estimates of TB mortality for India are interim, pending results from the national TB prevalence survey (2020/2021).

TABLE 4.7

Estimated number of TB deaths (in thousands) by HIV status in children and adults,^a globally and for WHO regions, 2019

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	377	312–448	32	23–41	28	20–35	201	144–259	116	83–149
The Americas	17	17–18	0.57	0.53–0.61	0.47	0.44–0.51	11	10–12	5.4	5.1–5.8
Eastern Mediterranean	76	65–87	7.3	5.5–9.2	6.4	4.8–8.0	35	27–44	27	20–33
Europe	20	20–21	0.40	0.39–0.42	0.35	0.34–0.36	14	14–15	5.5	5.3–5.8
South-East Asia	632	593–671	52	47–57	45	40–49	334	301–367	201	181–221
Western Pacific	85	78–91	12	10–14	10	9.0–12	42	36–48	20	17–23
Global	1 210	1 130–1 290	104	93–115	90	80–99	638	570–705	375	335–415

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	169	139–203	18	12–23	15	10–20	70	47–92	67	45–88
The Americas	5.9	5.2–6.6	0.080	0.069–0.092	0.070	0.059–0.080	4.5	3.8–5.1	1.3	1.1–1.5
Eastern Mediterranean	2.7	2.0–3.6	0.139	0.081–0.197	0.12	0.070–0.17	1.8	1.1–2.6	0.63	0.37–0.90
Europe	4.2	3.1–5.4	0.012	<0.01–0.016	0.010	<0.01–0.014	3.2	2.1–4.3	0.98	0.64–1.3
South-East Asia	20	15–26	1.1	0.67–1.5	0.94	0.58–1.3	13	8.0–18	4.9	3.0–6.8
Western Pacific	6.3	5.2–7.5	0.16	0.13–0.20	0.14	0.11–0.17	5.0	3.9–6.1	0.98	0.77–1.2
Global	208	177–242	19	14–24	17	12–21	97	72–122	76	56–95

^a Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

FIG. 4.21

Global trends in the estimated number of TB deaths (left) and the mortality rate (right), 2000–2019

Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone for TB deaths of the End TB Strategy.

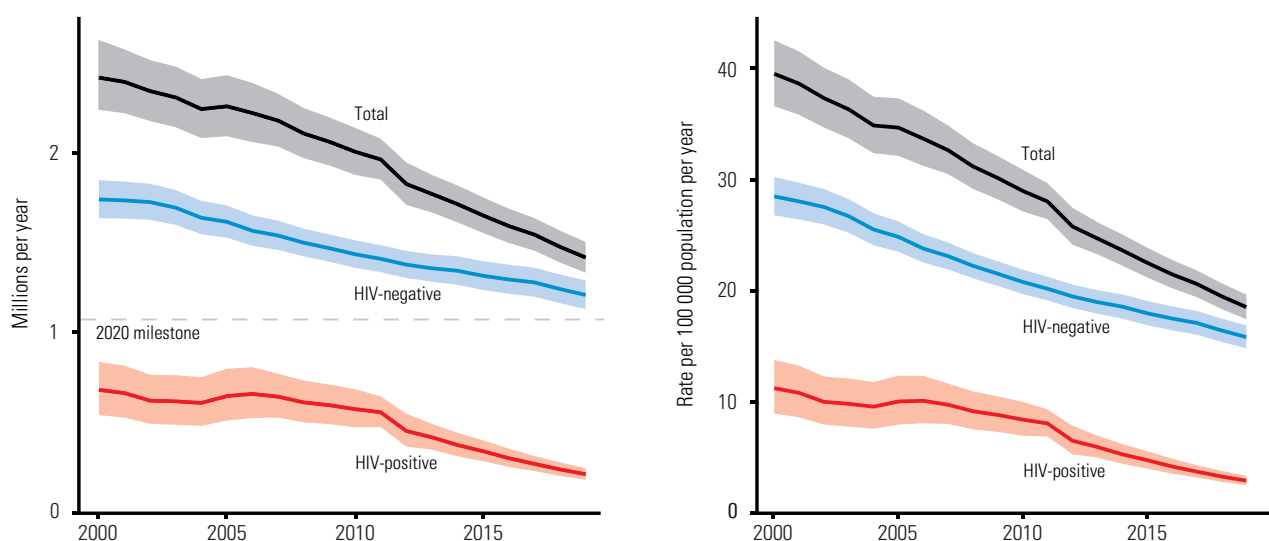
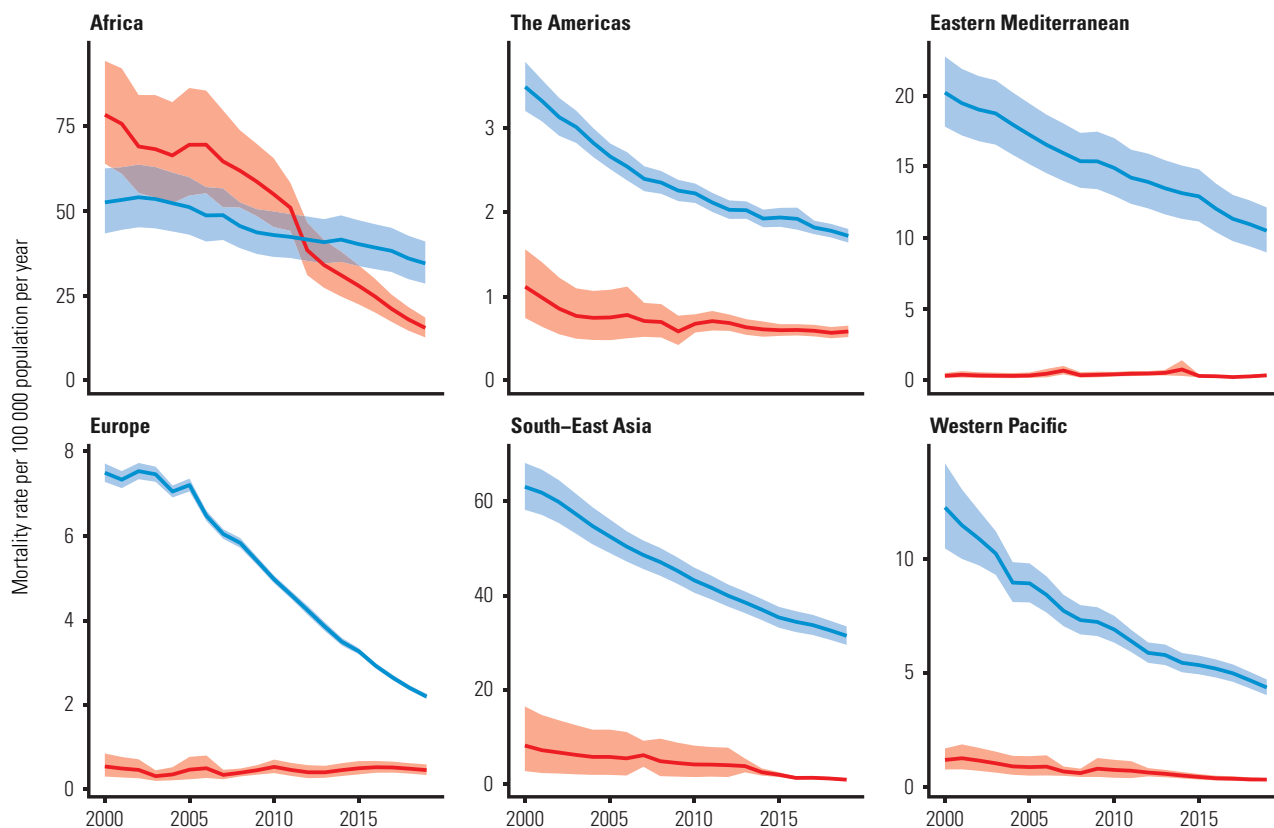


FIG. 4.22**Trends in estimated TB mortality rates by WHO region, 2000–2019**

Estimated TB mortality rates among HIV-negative people are shown in blue and estimated mortality rates among HIV-positive people are shown in red. Shaded areas represent uncertainty intervals.



As noted in [Section 4.1.4](#), this needs to include multisectoral action on the broader determinants of TB incidence (e.g. levels of undernutrition, poverty, smoking and diabetes) and investment in research to develop a new treatment or vaccine to substantially lower the risk of developing TB in people who already have a latent TB infection.

4.2.5 The case fatality ratio

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 the number of new cases in the same year. The CFR allows the 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). Achieving the End TB Strategy 2020 milestone of a 35% reduction in TB deaths for the period 2015–2020 requires a reduction in the global CFR, from 17% in 2015 to 10% in 2020.

In 2019, 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 HIV-negative and HIV-positive peo-

ple)¹ was 14%, down from 23% in 2000 and 16% in 2015. It varied widely among countries ([Fig. 4.26](#)), from less than 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.

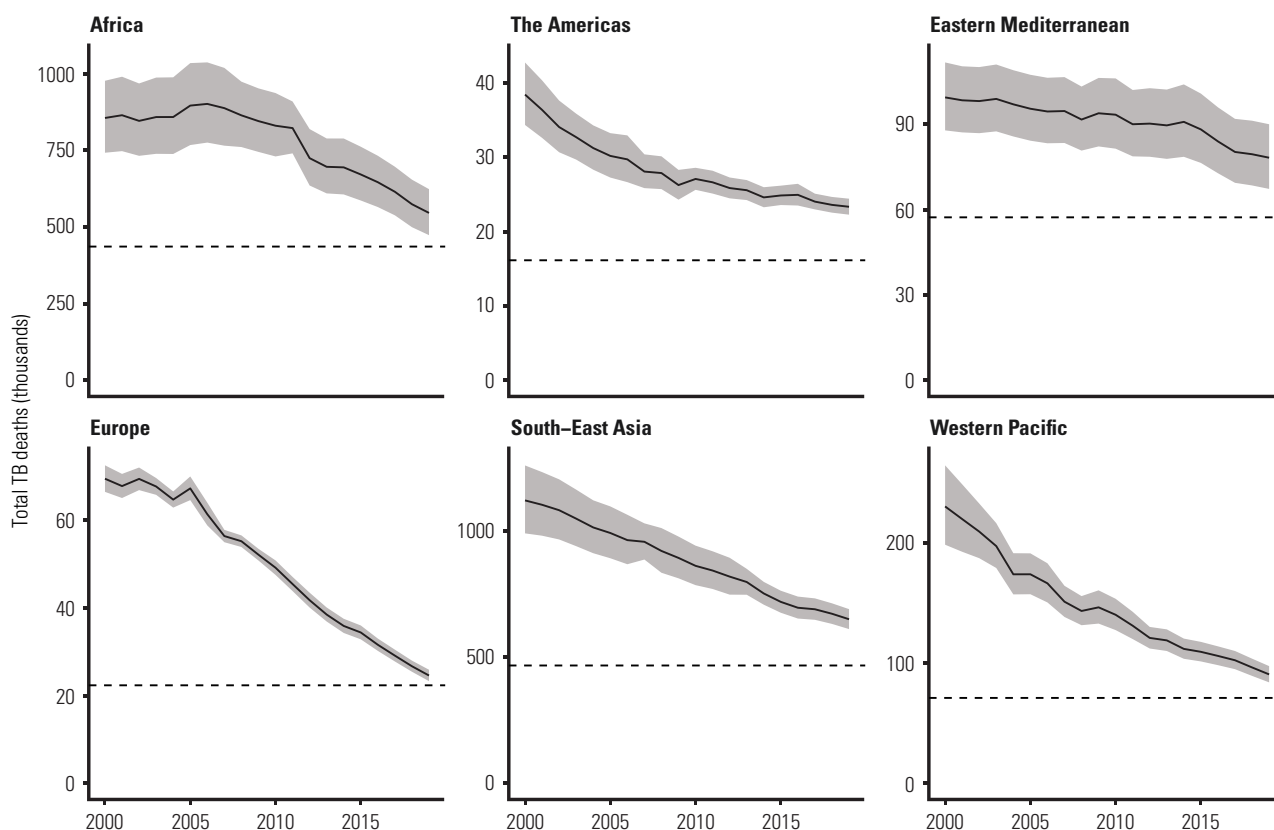
4.2.6 Estimated number of deaths averted by TB treatment, 2000–2019

To estimate the number of deaths averted by TB interventions, the actual numbers of TB deaths (presented in [Section 4.2](#)) can be compared with the number of TB deaths that would have occurred in the absence of TB treatment (and without ART provided alongside TB treatment for HIV-positive cases). The latter number can be estimated conservatively as the number of estimated incident cases ([Section 4.1](#)) multiplied by the relevant estimated CFR for

¹ 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.

FIG. 4.23**Trends in the estimated absolute number of TB deaths (HIV-positive and HIV-negative) by WHO region, 2000–2019**

Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone for TB deaths of the End TB Strategy.



untreated TB.¹ Estimates are conservative because they do not account for the impact of TB services or availability of ART on the level of TB incidence; they also do not account for the indirect, downstream impact of these interventions on future levels of infections, cases and deaths.

Between 2000 and 2019, TB treatment alone averted an estimated 52 million deaths among HIV-negative people (Table 4.8). Among HIV-positive people, TB treatment supported by ART averted an additional 11 million deaths.

4.3 Drug-resistant TB

Drug-resistant TB remains a major public health concern in many countries. Rifampicin-resistant TB (RR-TB) requires treatment with second-line drugs and includes multidrug-resistant TB (MDR-TB) that is resistant to both rifampicin and isoniazid, the two most effective anti-TB drugs. Patients with resistance to isoniazid, but not concurrently to rifampicin, also require a modified treatment regimen. This section focuses on estimates for MDR/RR-TB and isoniazid-resistant TB; it also presents global data on resistance to fluoroquinolones, which are a critical component of treatment regimens for drug-resistant TB.

¹ Further details about methods used to estimate deaths averted, including CFRs for different categories of TB case, are provided in the [online technical appendix](http://www.who.int/tb/data), available at <http://www.who.int/tb/data>.

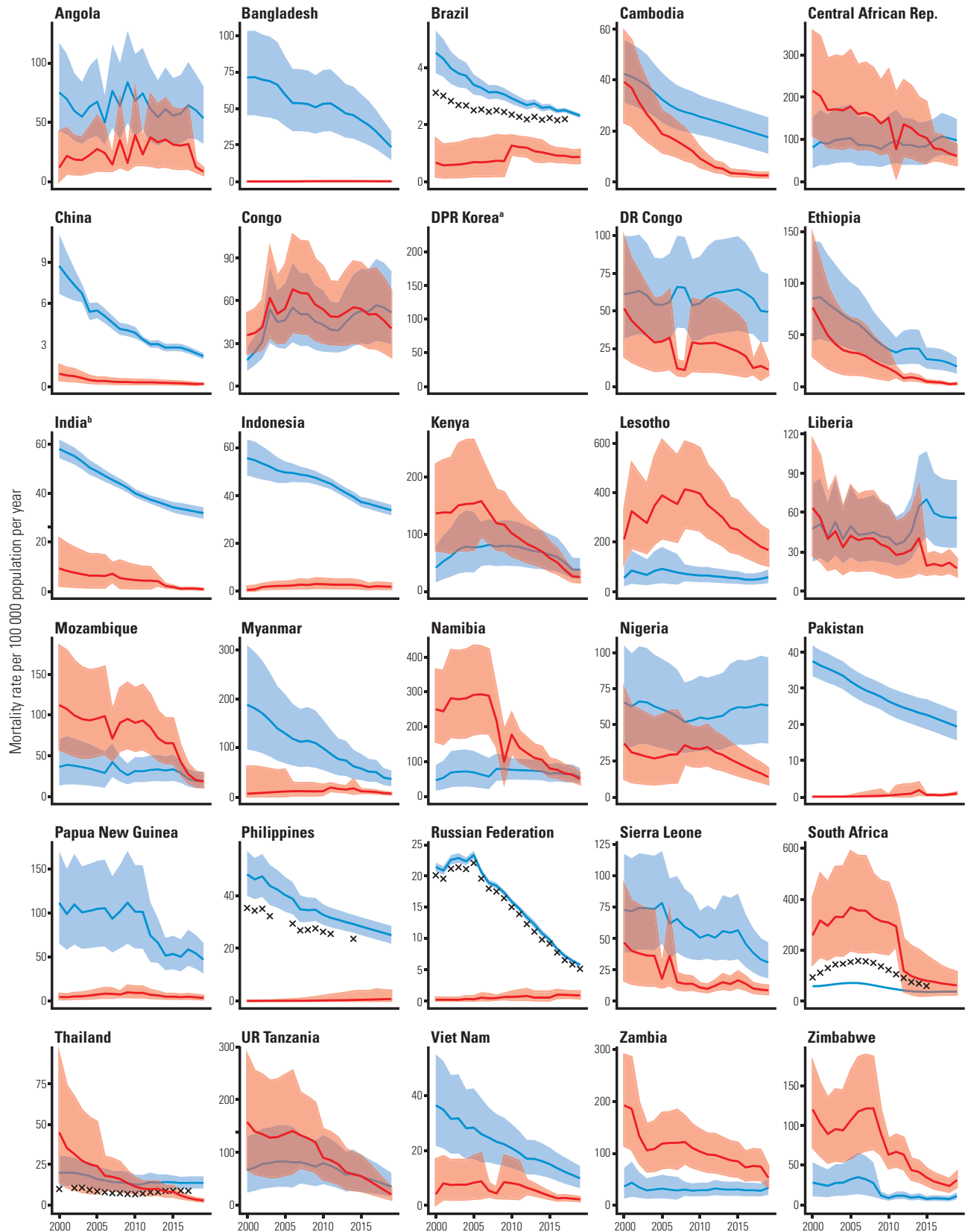
4.3.1 Global surveillance of anti-TB drug resistance

Since the launch of the Global Project on Anti-TB Drug Resistance Surveillance in 1994, data on drug resistance have been systematically collected and analysed from 169 countries worldwide (87% of the 194 WHO Member States), which collectively have more than 99% of the world's population and TB cases. This includes 113 countries that have continuous surveillance systems based on routine diagnostic drug susceptibility testing (DST) of *M. tuberculosis* isolates obtained from TB patients, and 56 countries that rely on epidemiological surveys of bacterial isolates collected from representative samples of patients (Fig. 4.27). National 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. However, with the expansion of rapid molecular tools, an increasing number of countries are transitioning from a reliance on periodic surveys to the establishment of continuous surveillance systems based on routine diagnostic testing (Box 4.3).

FIG. 4.24

Trends in estimated TB mortality rates in the 30 high TB burden countries, 2000–2019

TB mortality rates in HIV-negative people are shown in blue and mortality rates of HIV-positive TB are shown in red. The black crosses show observations from vital registration systems. Shaded areas represent uncertainty intervals.



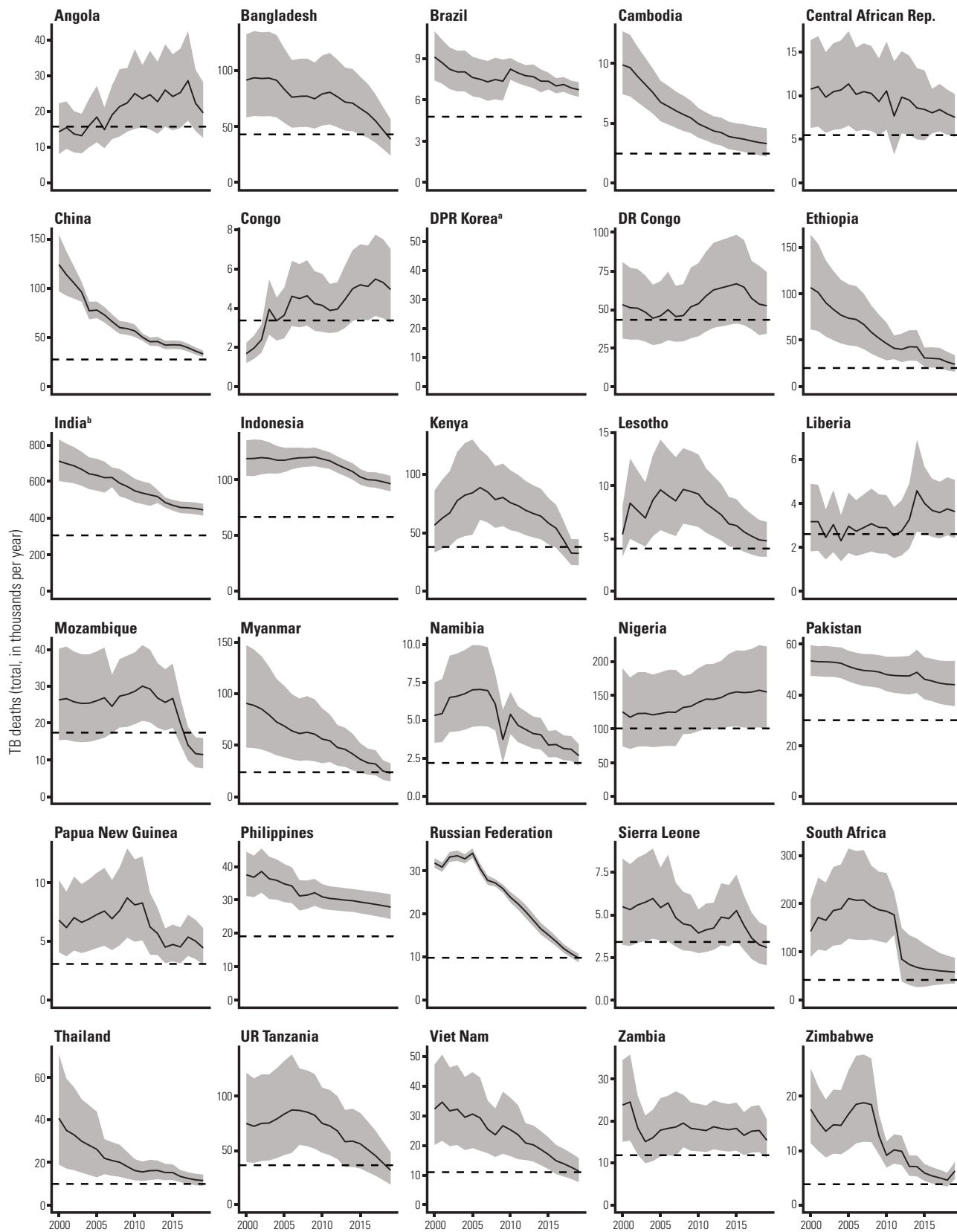
^a WHO estimates are not shown for DPR Korea because they had not been approved by national authorities at the time of report publication.

^b Estimates of TB mortality for India are interim, pending results from the national TB prevalence survey (2020/2021).

FIG. 4.25

Trends in the estimated absolute number of TB deaths (HIV-positive and HIV-negative TB) in the 30 high TB burden countries, 2000–2019

Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone of the End TB Strategy.



^a WHO estimates are not shown for DPR Korea because they had not been approved by national authorities at the time of report publication.

^b Estimates of TB deaths for India are interim, pending results from the national TB prevalence survey (2020/2021).

FIG. 4.26

Estimates of the case fatality ratio (CFR), including HIV-negative and HIV-positive people, 2019

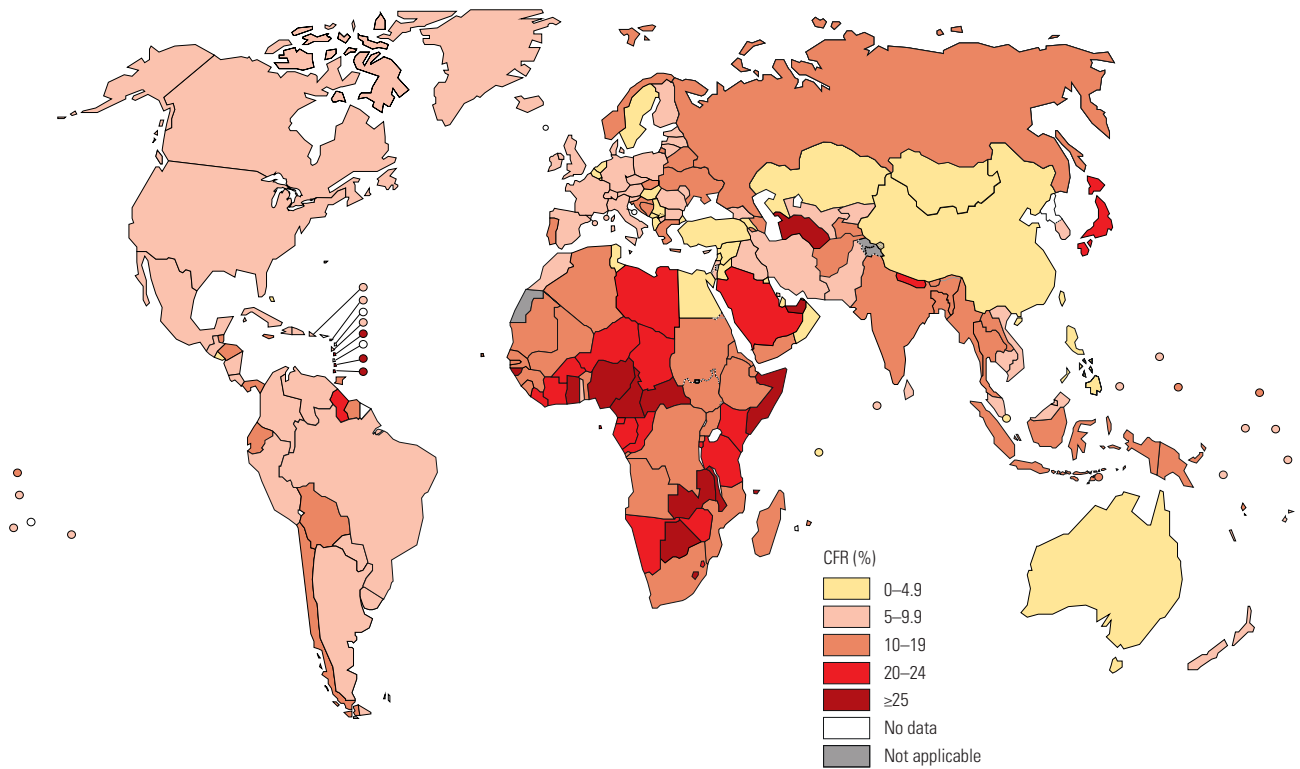


FIG. 4.27

Source of data for rifampicin resistance among new cases, 1995–2020

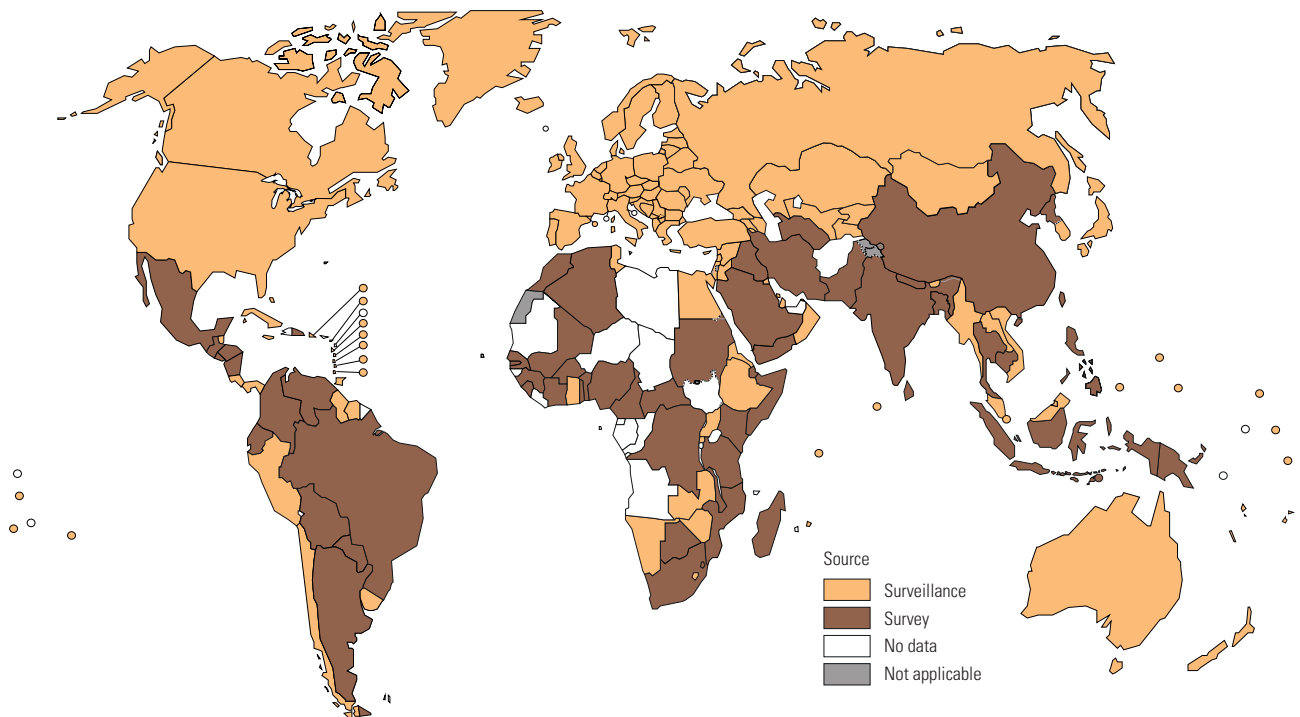


TABLE 4.8

Cumulative number of deaths averted by TB and TB/HIV interventions 2000–2019 (in millions), globally and by WHO region^a

WHO REGION	HIV-NEGATIVE PEOPLE		HIV-POSITIVE PEOPLE		TOTAL	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
Africa	6.4	5.3–7.4	7.4	6.5–8.4	14	12–15
The Americas	1.7	1.6–1.9	0.34	0.31–0.37	2.1	1.9–2.2
Eastern Mediterranean	4.6	4.0–5.1	0.09	0.07–0.11	4.7	4.1–5.2
Europe	2.0	1.8–2.3	0.32	0.28–0.36	2.4	2.1–2.6
South-East Asia	23	19–27	2.0	1.4–2.6	25	21–29
Western Pacific	14	13–16	0.42	0.35–0.48	15	14–16
Global	52	46–58	11	9.3–12	63	56–69

^a Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

BOX 4.3

Transitioning to continuous surveillance systems for drug-resistant TB

Establishment of continuous surveillance systems for drug-resistant TB leads to improved access to timely and appropriate treatment and care, thereby supporting efforts to achieve UHC. It also offers programmatic benefits including rapid detection of outbreaks, real-time monitoring of the effectiveness of interventions and an understanding of trends.

Before 2015, only 80 countries^a had achieved good testing coverage for rifampicin, which is defined by WHO as documentation of a rifampicin test result for at least 80% of people with bacteriologically confirmed pulmonary TB. Significant progress has been made over the past 5 years – by the end of 2019, 113 countries had achieved good testing coverage (Fig. 4.27), including 17 of the 40 countries^b in WHO’s lists of high TB and/or high MDR-TB burden countries^a for the period 2016–2020: Azerbaijan, Belarus, Ethiopia, Kazakhstan, Kyrgyzstan, Lesotho, Myanmar, Namibia, Peru, Republic of Moldova, the Russian Federation, Tajikistan, Ukraine, Uzbekistan, Viet Nam, Zambia and Zimbabwe.

The ongoing shift from reliance on periodic surveys towards continuous surveillance systems is largely due to the increased availability of Xpert MTB/RIF testing at peripheral health facilities. Further gains will require investments in specimen referral and transport systems to ensure that GeneXpert instruments can be used at or close to full capacity, combined with data connectivity solutions to accurately record, report and analyse surveillance data (including to trigger public health responses).

Diagnostic algorithms for drug resistance are often driven by testing for resistance to rifampicin, with further DST conducted only for those with a positive result for rifampicin resistance. Testing coverage for isoniazid resistance remains low, meaning that an important group of TB patients who are susceptible to rifampicin but resistant to isoniazid may not be detected, and consequently not be treated with the WHO-recommended modified regimen, thus risking poorer treatment outcomes and development of further resistance. Testing coverage for resistance to fluoroquinolones, which form a critical component of recommended treatment regimens for both rifampicin- and isoniazid-resistant TB, is also low. In 2019, only 69 countries achieved good testing coverage, which is defined by WHO as documentation of a test result for resistance to fluoroquinolones for at least 80% of people with RR-TB as well as documentation of a rifampicin test result for at least 80% of people with bacteriologically confirmed TB.

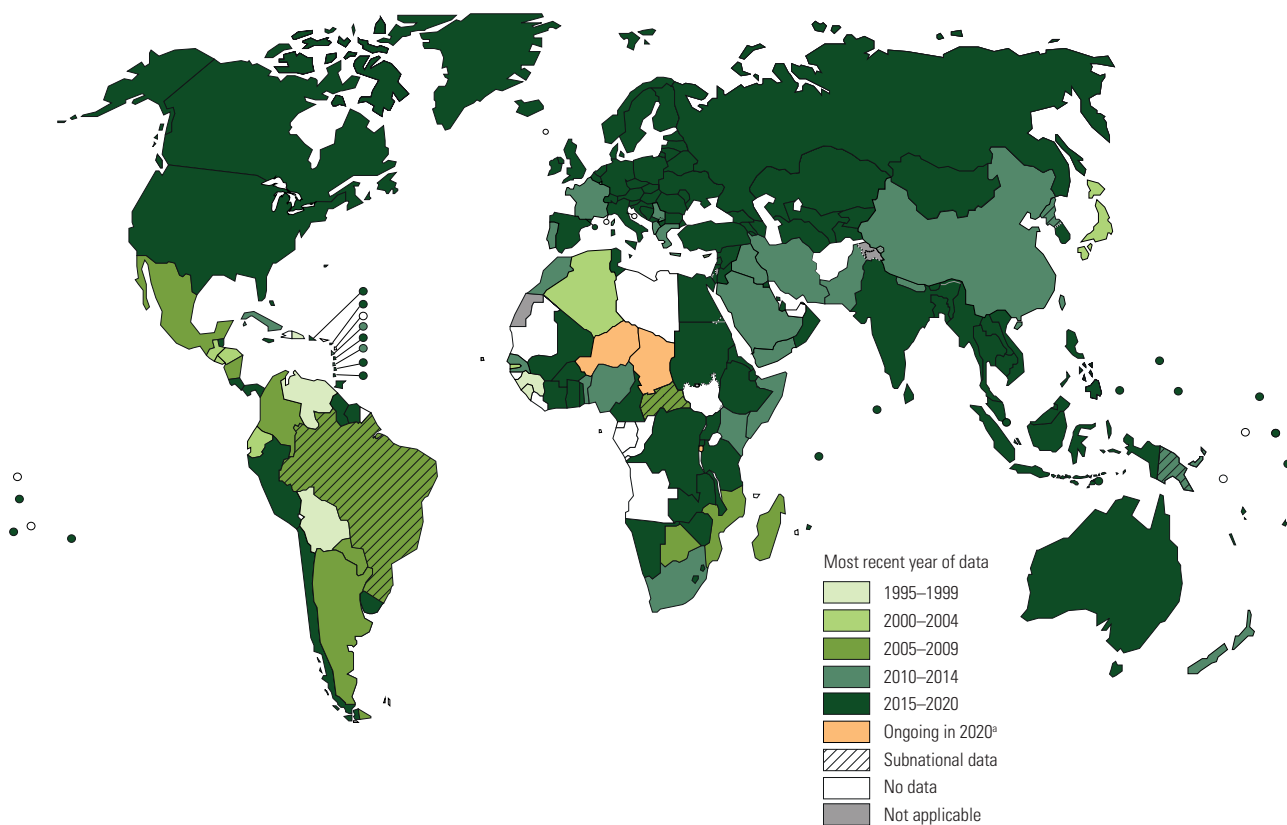
Tests with good accuracy are available for isoniazid and fluoroquinolones (e.g. line probe assays), but they cannot be easily integrated into routine diagnostic algorithms in many countries. This gap may be lessened with the arrival of new molecular tools for the rapid diagnosis of isoniazid and fluoroquinolone resistance at peripheral-level health facilities. Such tools include the Xpert MTB/XDR cartridge, for which WHO will conduct a review of diagnostic accuracy later in 2020 (further information is provided in Chapter 9).

^a Only WHO Member States are considered

^b These lists are defined and explained in Annex 2.

FIG. 4.28

Most recent year of data on rifampicin resistance among new cases, 1995–2020



^a *Ongoing in 2020* refers to first-ever national surveys of anti-TB drug resistance that are being planned or implemented. For countries that are planning or implementing repeat surveys, the most recent year of data is shown (i.e. Guinea, Nepal, Mozambique, Myanmar and Zambia).

The global coverage of drug-resistance surveillance data is shown in **Fig. 4.28**. Among the 30 high TB burden countries and 30 high MDR-TB burden countries (which comprise a total of 40 countries, because of overlap between the two groups¹), 37 have data on levels of drug resistance. The three countries that have never conducted a drug-resistance survey are Angola, Congo and Liberia. Four countries (Brazil, Central African Republic, Democratic People’s Republic of Korea and Papua New Guinea) rely on drug-resistance data gathered from subnational areas only, and the most recent data for Sierra Leone are from 1997. The number of data points on rifampicin resistance is shown for each country in **Fig. 4.29**.

In 2018–2020, first-ever national drug-resistance surveys were completed in Eritrea, Indonesia, Lao People’s Democratic Republic, Mali, Timor-Leste and Togo, and repeat surveys were completed in Bangladesh, Cambodia, Eswatini, Ethiopia, Malawi, the Philippines, Sri Lanka, Thailand, Turkmenistan and the United Republic of Tanzania.² In 2019–2020, drug-resistance surveys were being planned or implemented in eight countries, with the first nationwide surveys in three countries (Burun-

di, Chad and Niger) and repeat surveys in five countries (Guinea, Mozambique, Myanmar, Nepal and Zambia).

4.3.2 Estimates of the disease burden caused by drug-resistant TB

Globally in 2019, an estimated 3.3% (95% confidence interval [CI]: 2.3–4.3%) of new cases and 18% (95% CI: 9.7–27%) of previously treated cases had MDR/RR-TB (**Table 4.9**).³ The proportions of new and previously treated TB cases with MDR/RR-TB at the country level are shown in **Fig. 4.30** and **Fig. 4.31**. The highest proportions are in several countries of the former Soviet Union (above 20% in new cases and above 50% in previously treated cases).

Overall, there were an estimated 465 000 (range, 400 000–535 000) incident cases of MDR/RR-TB in 2019⁴ and the global proportion of RR-TB cases estimated to have MDR-TB was 78% (**Table 4.9**). The geographical distribution of cases of MDR/RR-TB is shown in **Fig. 4.32**; nearly 50% of global cases were in India (27%), China (14%) and the Russian Federation (8%). In

¹ For a full list of the high TB burden and high MDR-TB burden countries, see **Annex 2**.

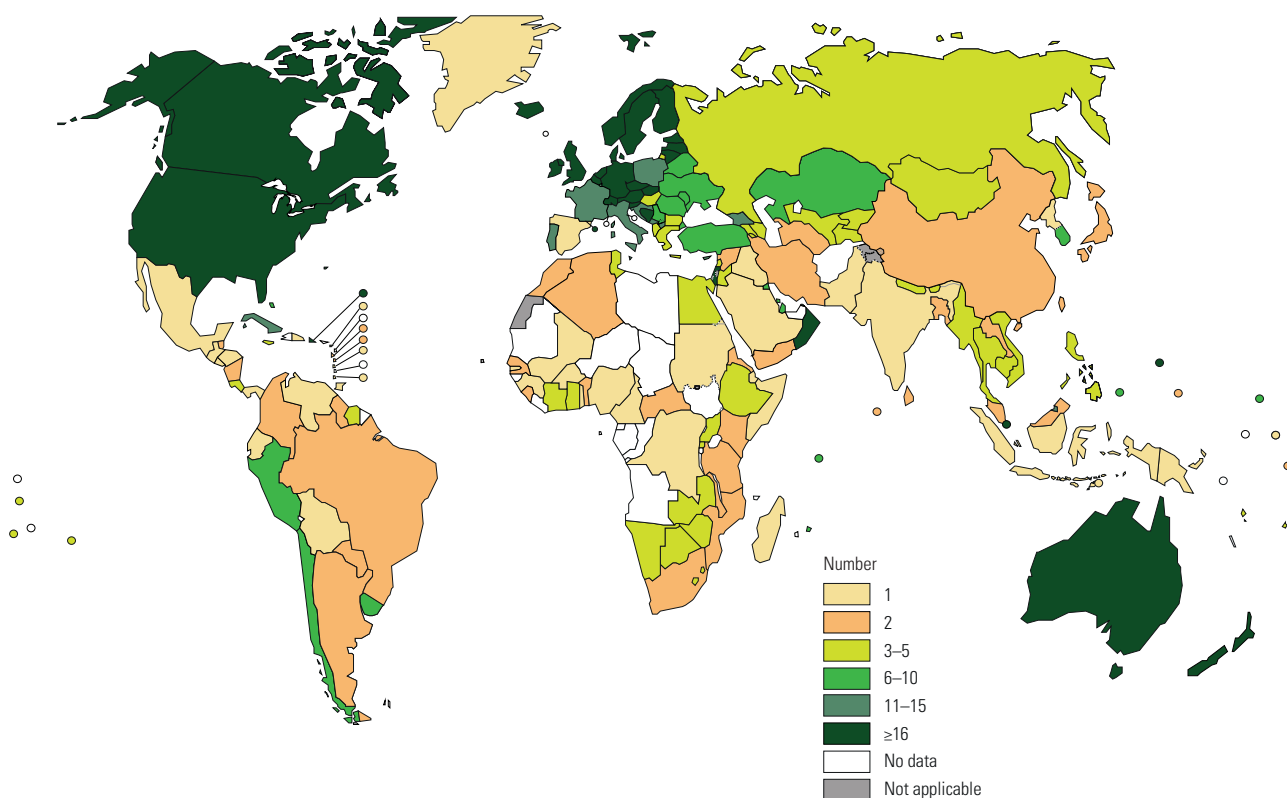
² Estimates are provisional for Malawi, Mali and Timor-Leste.

³ In 2018, these values were 3.4% and 18%, respectively.

⁴ This is slightly lower than the 484 000 (range, 417 000–556 000) estimated for 2018 in the 2019 edition of the WHO global TB report (3). The downward revision is explained in **Box 4.2**.

FIG. 4.29

Number of data points on rifampicin resistance among new cases, 1995–2020



2019, there were an estimated 182 000 (range, 113 000–250 000) deaths from MDR/RR-TB.¹

Globally in 2019, an estimated 13.1% (95% CI: 9.9–16.9%) of new cases and 17.4% (95% CI: 0.5–54%) of previously treated cases had isoniazid resistance. These proportions translate into an estimated 1.4 million (range, 1.0–1.9 million) incident cases of isoniazid-resistant TB in 2019, of which 1.1 million (range, 0.6–1.5 million) were susceptible to rifampicin (Table 4.10). In other words, 11% (range, 6.5–15%) of all incident cases of TB had isoniazid-resistant and rifampicin-susceptible TB. People with isoniazid-resistant TB can be missed in settings where diagnostic algorithms prioritize the detection of rifampicin resistance, meaning that they do not receive the recommended modified treatment regimen (Box 4.3).

4.3.3 Trends in drug resistance

Globally, the burden of MDR/RR-TB relative to the number of new and previously treated cases remains stable. At the national level, the proportion of TB cases with MDR/RR-TB should be interpreted within the overall context of the country’s TB epidemic. Fig. 4.33 shows the annual rate

of change in the percentage of new TB cases with MDR-TB for 23 countries with more than three data points on the level of MDR-TB from 2010–2019 and a population of at least 10 million in 2019.

4.3.4 Resistance to fluoroquinolones

Globally, 105 countries have representative data from the past 15 years on resistance to fluoroquinolones. Among these countries, the proportion of MDR/RR-TB cases with resistance to any fluoroquinolone for which testing was done was 20.1% (95% CI: 15.5–25.0%). Of these countries, 26 were among the 40 with a high TB or MDR-TB burden.

¹ This is lower than the 214 000 (range, 133 000–295 000) estimated for 2018 in the 2019 edition of the WHO global TB report (3). The downward revision reflects a slightly lower estimate of MDR/RR-TB incidence in 2019 compared with 2018.

TABLE 4.9

Estimated incidence of MDR/RR-TB^a in 2019 for 30 high MDR-TB burden countries, WHO regions and globally

COUNTRY	ESTIMATED % OF NEW CASES WITH MDR/RR-TB		ESTIMATED % OF PREVIOUSLY TREATED CASES WITH MDR/RR-TB		INCIDENCE OF MDR/RR-TB				
	BEST ESTIMATE ^b	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	NUMBER (IN 1000s)	UNCERTAINTY INTERVAL	RATE ^c	UNCERTAINTY INTERVAL	% OF RR-TB WITH MDR-TB
Angola	2.5	1.2–4.1	14	10–19	4.1	1.8–7.2	13	5.8–23	95
Azerbaijan	11	10–13	24	23–26	1.2	0.87–1.5	12	8.7–15	58
Bangladesh	0.70	0.40–1.2	11	10–12	3.3	1.6–5.5	2.0	0.98–3.4	99
Belarus	38	35–40	60	56–64	1.2	0.92–1.6	13	9.8–17	91
China	7.1	5.6–8.7	23	23–24	65	49–83	4.5	3.4–5.8	74
DPR Korea	2.2	0.82–4.2	16	9.1–25	5.2	2.5–8.8	20	9.9–34	88
DR Congo	1.8	1.0–3.2	11	9.8–12	6.5	2.7–12	7.5	3.2–14	53
Ethiopia	0.71	0.62–0.80	12	11–13	1.4	0.97–2.0	1.3	0.87–1.8	100
India	2.8	2.3–3.5	14	14–14	124	73–189	9.1	5.3–14	67
Indonesia	2.4	1.8–3.3	13	9.0–18	24	17–32	8.8	6.2–12	99
Kazakhstan	27	26–28	44	43–46	4.1	2.6–5.9	22	14–32	71
Kenya	1.3	0.74–2.0	4.6	4.0–5.4	2.2	0.95–3.9	4.1	1.8–7.4	56
Kyrgyzstan	29	28–31	60	57–63	2.8	2.3–3.3	43	36–51	86
Mozambique	3.7	2.5–5.2	13	11–14	4.9	2.5–8.0	16	8.3–26	95
Myanmar	4.9	4.7–5.1	18	17–19	10	6.0–15	19	11–28	91
Nigeria	4.3	3.2–5.5	14	10–19	21	13–32	11	6.3–16	70
Pakistan	4.2	3.2–5.3	7.3	6.8–7.8	25	16–36	12	7.3–17	89
Papua New Guinea	3.4	1.7–5.0	26	15–36	2.0	1.2–2.9	22	14–33	78
Peru	6.3	5.9–6.7	20	19–22	3.1	2.4–4.0	9.6	7.3–12	86
Philippines	1.8	1.3–2.6	28	27–29	21	10–34	19	9.6–32	75
Republic of Moldova	33	30–35	60	56–64	1.4	1.1–1.6	34	28–40	81
Russian Federation	35	35–36	71	70–71	39	25–56	27	17–38	92
Somalia	8.7	6.1–12	88	73–96	4.1	2.2–6.5	26	14–42	61
South Africa	3.4	2.5–4.3	7.1	4.8–9.5	14	8.5–20	23	15–34	62
Tajikistan	29	27–31	40	36–45	2.4	1.8–3.0	26	20–33	51
Thailand	1.7	1.1–2.7	10	9.4–11	2.5	1.4–3.9	3.6	2.0–5.6	74
Ukraine	27	26–28	43	42–44	11	7.1–16	25	16–36	75
Uzbekistan	12	11–13	22	20–24	3.2	2.2–4.4	9.7	6.7–13	90
Viet Nam	3.6	3.4–3.8	17	17–18	8.4	5.3–12	8.8	5.5–13	78
Zimbabwe	3.1	2.7–3.4	14	8.9–20	1.2	0.85–1.6	8.2	5.8–11	82
MDR-TB HBCs	3.6	2.7–4.6	18	12–26	419	354–489	8.9	7.5–10	77
Africa	2.6	1.6–3.7	11	2.2–27	77	64–90	7.0	5.8–8.3	76
The Americas	2.5	1.5–3.8	12	3.9–23	11	9.2–12	1.0	0.91–1.2	87
Eastern Mediterranean	4.0	2.8–5.4	12	1.5–32	36	26–47	5.0	3.6–6.6	82
Europe	17	16–18	52	45–59	70	55–87	7.5	5.9–9.4	86
South-East Asia	2.5	1.9–3.3	14	7.7–21	171	117–236	8.6	5.9–12	75
Western Pacific	4.6	3.5–5.9	24	16–32	101	81–123	5.2	4.2–6.4	75
Global	3.3	2.4–4.4	18	9.7–27	465	400–535	6.1	5.2–7.0	78

Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

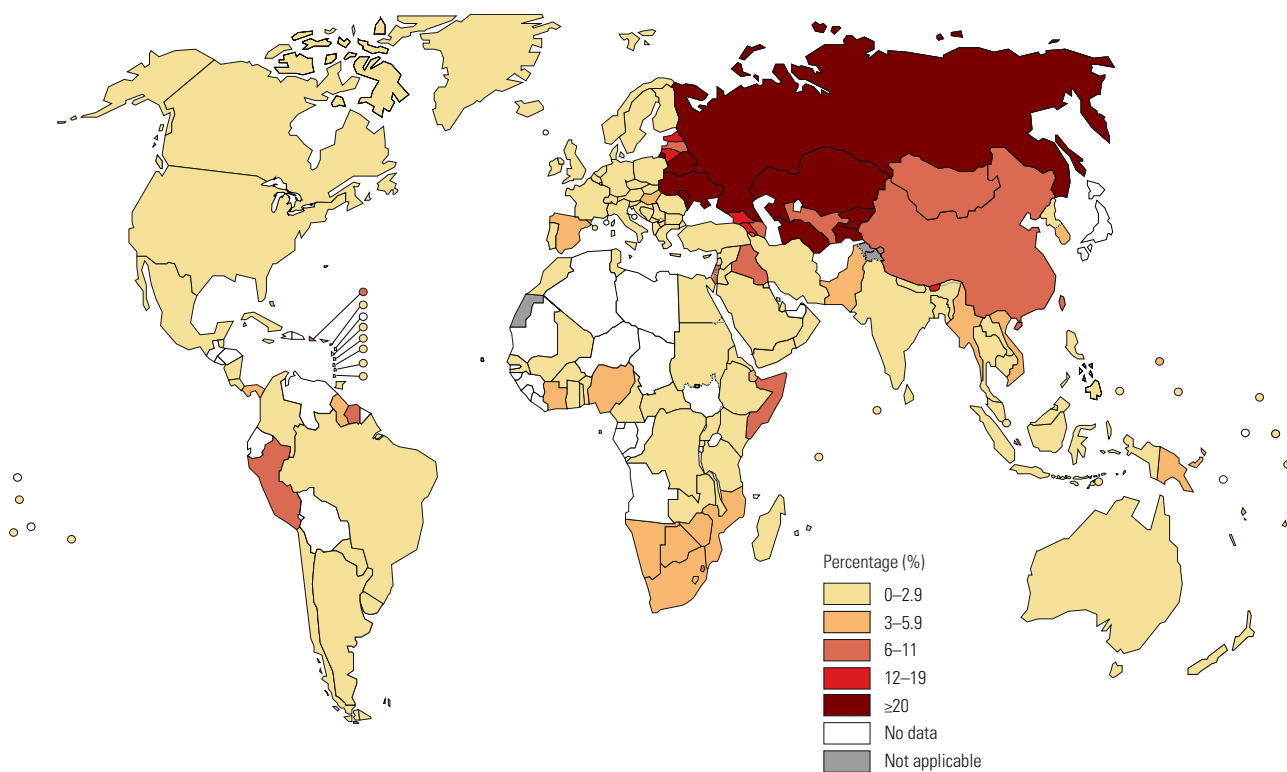
^a MDR-TB is a subset of RR-TB (78% globally).

^b Best estimates are for the latest available year.

^c Rates are per 100 000 population.

FIG. 4.30

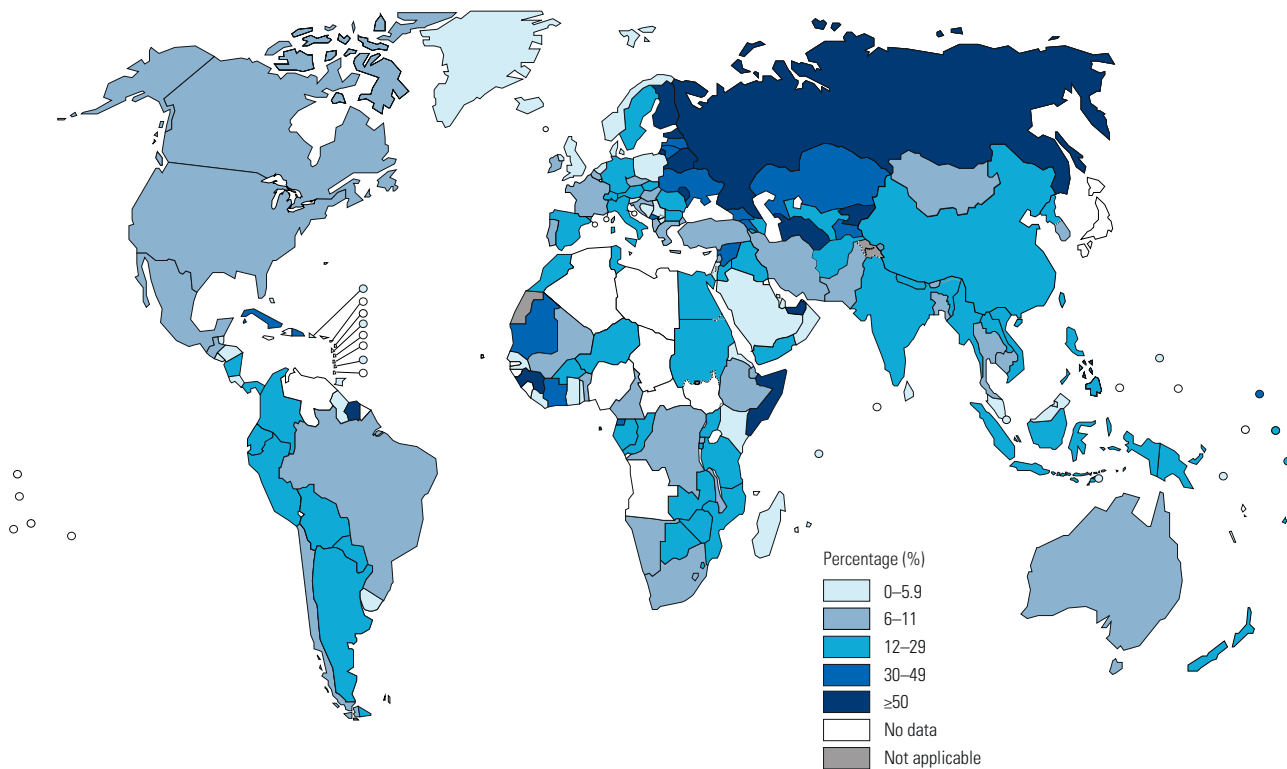
Percentage of new TB cases with MDR/RR-TB^a



^a Percentages are based on the most recent data point for countries with representative data from 2005 to 2020. Model-based estimates for countries without data are not shown. MDR-TB is a subset of RR-TB.

FIG. 4.31

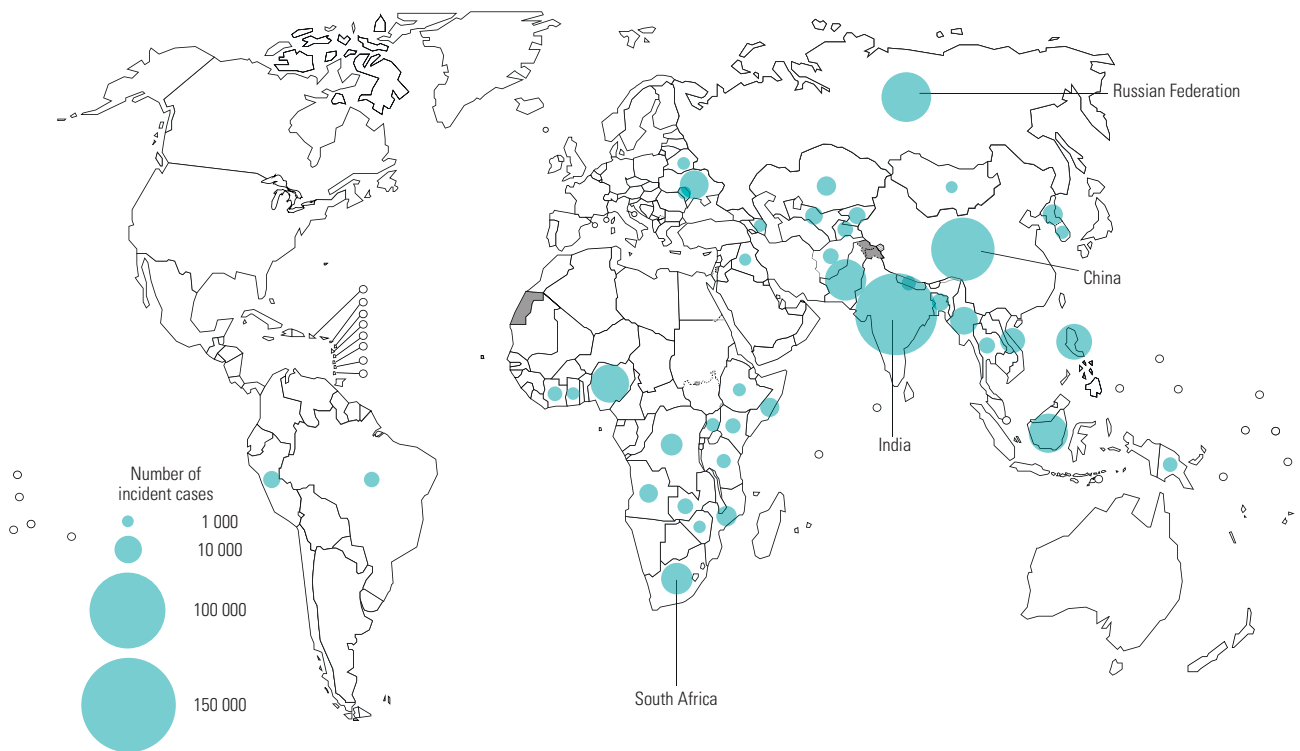
Percentage of previously treated TB cases with MDR/RR-TB^a



^a Percentages are based on the most recent data point for countries with representative data from 2005 to 2020. Model-based estimates for countries without data are not shown. MDR-TB is a subset of RR-TB.

FIG. 4.32

Estimated incidence of MDR/RR-TB^a in 2019, for countries with at least 1000 incident cases



^a MDR-TB is a subset of RR-TB.

TABLE 4.10

Estimated global incidence of rifampicin-resistant and/or isoniazid-resistant TB, 2019

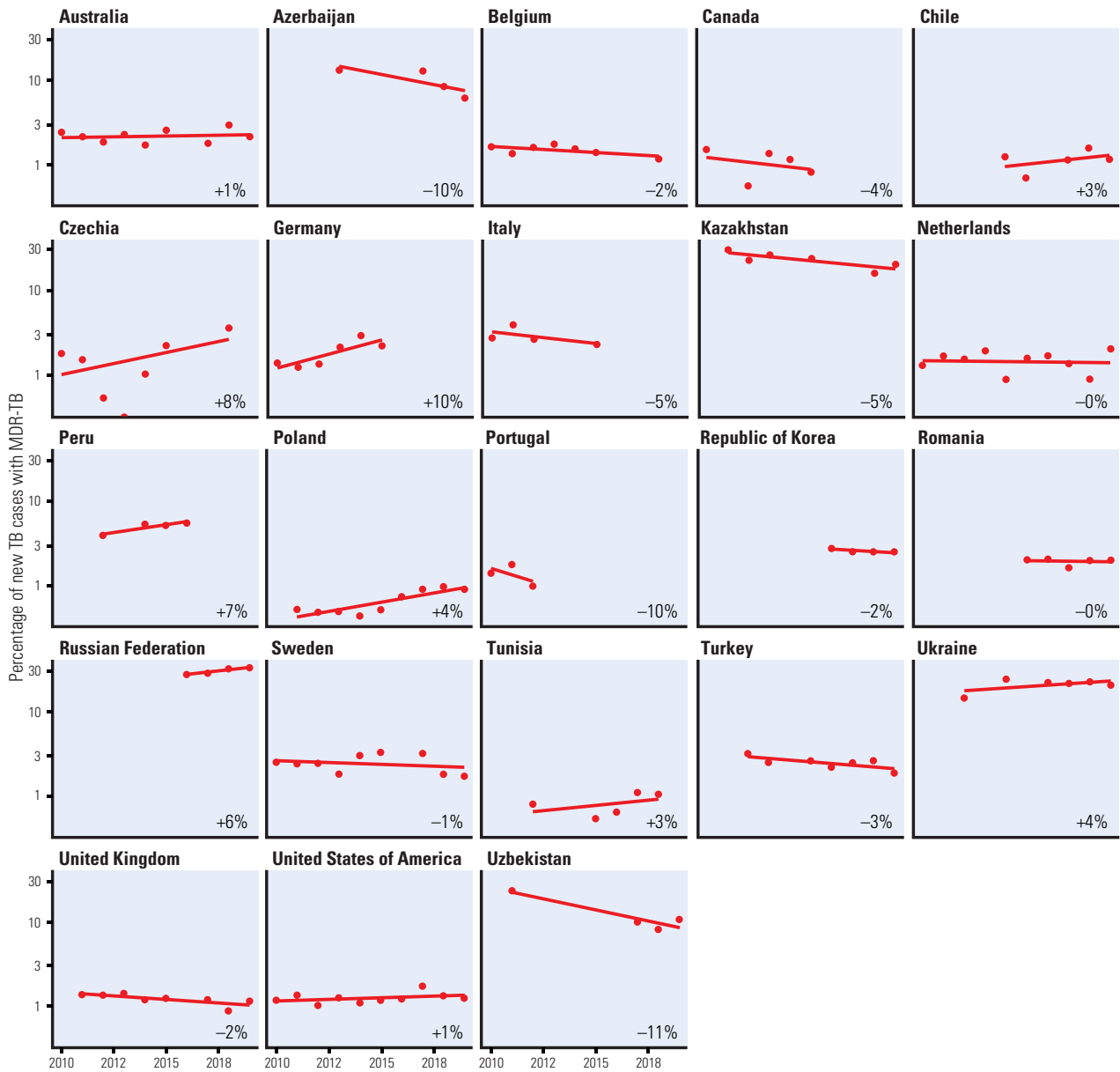
Number in thousands.^a

	RIFAMPICIN-RESISTANT		RIFAMPICIN-SUSCEPTIBLE		GLOBAL	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
ISONIAZID-RESISTANT	361	308–413	1 060	639–1 490	1 420	1 030–1 880
ISONIAZID-SUSCEPTIBLE	105	89–120	8 430	7 480–9 380	8 540	7 590–9 490
GLOBAL	465	400–535	9 490	8 450–10 500	9 960	8 940–11 000

^a Numbers shown to two significant figures if under 100 and to three significant figures otherwise.

FIG. 4.33

Average annual rate of change (represented by the slope of the red line) in the percentage of new TB cases with MDR-TB, 2010–2019^a



^a Countries shown had a population of at least 10 million in 2019 and at least three data points on MDR-TB.

4.4 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 2016–2035.¹ Furthermore, indirect estimates of prevalence suffer from considerable uncertainty, because they are derived from estimates of incidence and assumptions about disease duration. Nonetheless, in an important subset of countries with a large proportion of the world's TB burden (Fig. 4.2), national TB prevalence surveys continue to provide the best method for directly measuring the number of cases and informing estimates of TB incidence (including its distribution by age and sex), and directly measuring trends when repeat surveys are done. Findings from surveys can also inform assessment of actions needed to reduce the burden of TB disease.

The Task Force retained national TB prevalence surveys within its strategic areas of work for 2016–2020 (Box 4.1). The group of countries where these surveys continue to be relevant are defined as those with a relatively high estimated burden of TB (about 150 incident cases per 100 000 population per year) that do not yet have health systems, national notification systems and VR systems of the quality and coverage required to provide reliable and routine direct measurements of the number of TB cases and deaths.²

Countries in which national prevalence surveys were implemented in 2000–2020 or are planned to start in 2021 are shown in Fig. 4.34 and Fig. 4.35. 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 4.1).

Between 2007 and the end of 2019, a total of 33 surveys in 30 countries (with repeat surveys in Myanmar, the Philippines and Viet Nam) were completed that used the screening and diagnostic methods recommended in the second edition of the WHO handbook on prevalence surveys (18). This included 16 surveys in Asian countries and 17 in African countries. In 2018–2019, the first national surveys were completed in Eswatini, Lesotho, Mozambique, Nepal and South Africa. As of August 2020, field operations of the first national survey in India were on hold due to the COVID-19 pandemic. The survey is one of

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

² 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. 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 should be met (18). For further details on the meeting, see WHO (2016) (8).

FIG. 4.34

National surveys of the prevalence of TB disease, actual (2000–2020) and planned (2021)

2000	China				
2001					
2002	Cambodia				
2003	Malaysia				
2004	Indonesia ^a				
2005	Eritrea ^b				
2006	Thailand				
2007	Philippines	Viet Nam			
2008	Bangladesh ^b				
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	DPK Korea	Philippines			
2017	Mozambique	Myanmar	Namibia	South Africa	Viet Nam
2018	Eswatini	Nepal			
2019	Lesotho				
2020	India ^c				
2021	Botswana				

^a The survey in Indonesia (2004) did not use chest X-ray to screen individuals for sputum submission.

^b 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.

^c Field operations are ongoing.

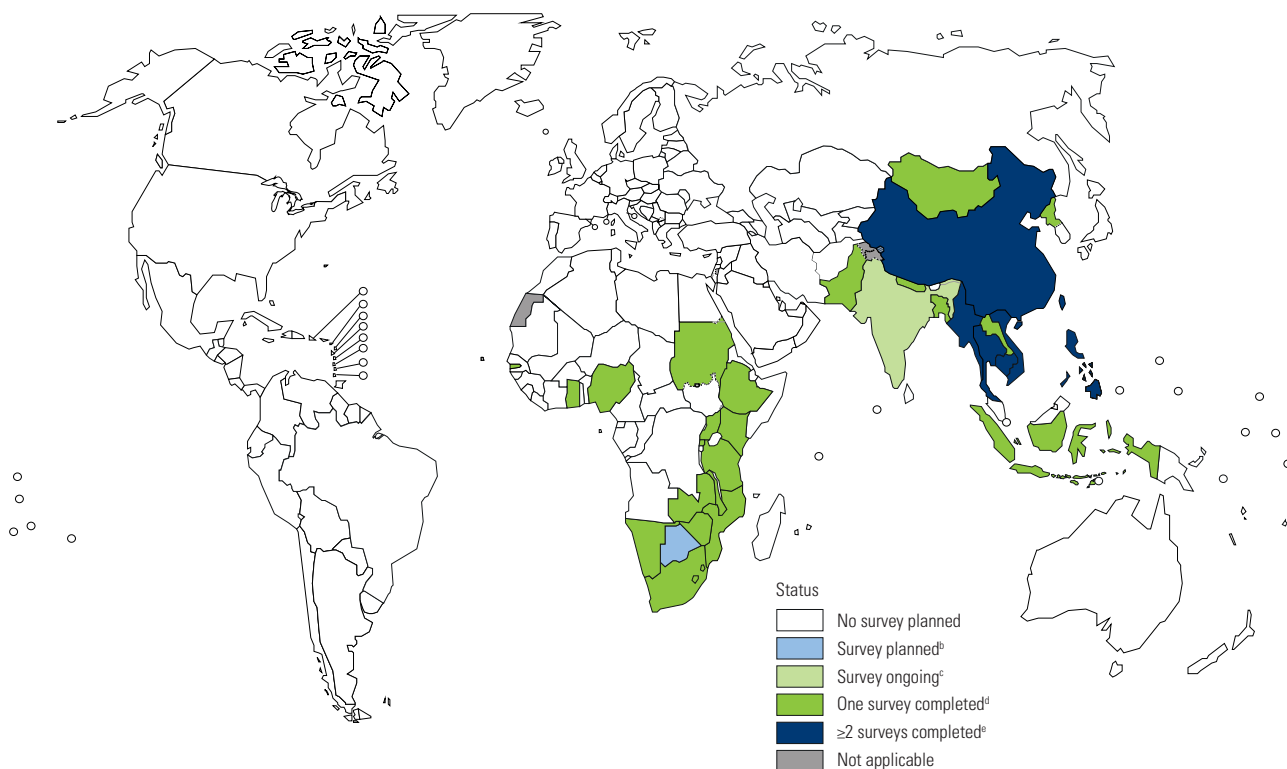
the largest ever undertaken, with a planned sample size of about 500 000 people. Planning is underway for a first-ever national survey in Botswana (currently scheduled to start in 2021),³ and repeat surveys are under discussion in Ethiopia, Ghana, Nigeria, Pakistan and the United Republic of Tanzania.

The distribution of TB disease by age (≥15 years) and sex based on prevalence survey data from the 33 surveys implemented in 2007–2019 is shown in Fig. 4.36a, Fig 4.36b and Fig. 4.37. In most Asian countries and some African countries (e.g. Ghana, Lesotho, Malawi, Mozambique, Rwanda and the United Republic of Tanzania), prevalence increased with age. However, in several African countries (e.g. Ethiopia, Gambia, Namibia, Nigeria, South Africa, Sudan, Uganda and Zambia), prevalence per 100 000 population peaked among those aged 35–54 years. The M:F ratio of cases for the same set of

³ A combined survey of the prevalence of TB and HIV was piloted in Botswana in 2019 but was found to be too logistically difficult to implement. As a result, a decision was made to separate the two surveys.

FIG. 4.35

Countries in which national population-based surveys of the prevalence of TB disease have been implemented using currently recommended screening and diagnostic methods^a since 2000 or are planned (status in August 2020)



^a Screening methods include field chest X-ray; at least culture was used to confirm diagnosis. The most recent surveys in Bangladesh, Eswatini, Kenya, Lesotho, Myanmar, Mozambique, Namibia, Nepal, Philippines, South Africa and Viet Nam 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 2020.

^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.

surveys showed 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 pulmonary TB. In most countries, the ratio was in the range 2–4, with generally higher ratios in Asia than in Africa.

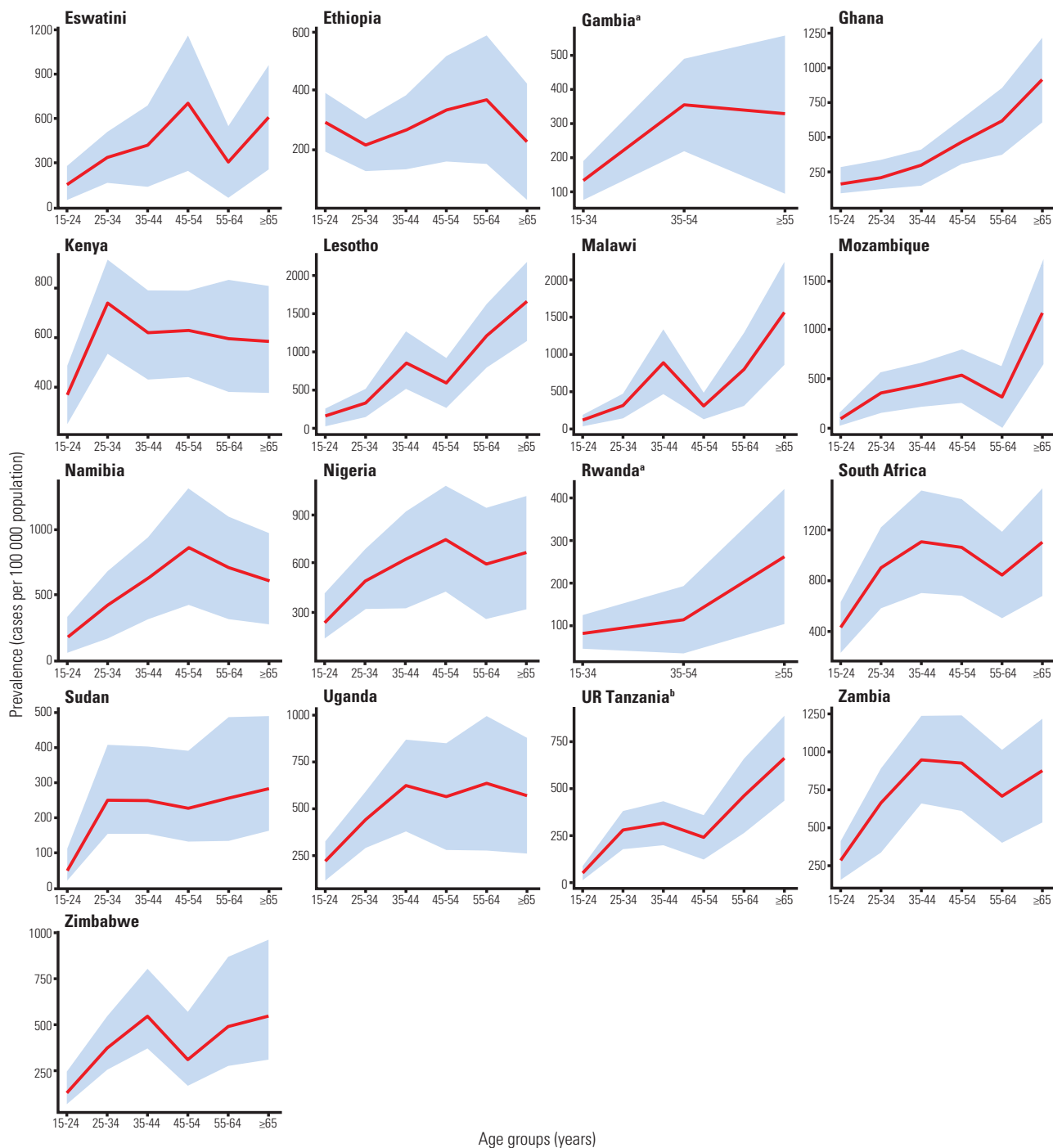
The ratio of prevalence to notifications (P:N)¹ can be used to assess detection and reporting gaps (Fig. 4.38a) and variation in these gaps by sex (Fig. 4.38b). The P:N ratios from the 33 surveys implemented in 2007–2019 suggest that these gaps are marginally higher in Asia than in Africa. The data also 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, indicates a need for strategies to improve access to and use of health services among men (19).

¹ The unit of the P:N ratio is expressed in years.

FIG. 4.36A

Estimated age-specific prevalence of bacteriologically confirmed pulmonary TB for surveys implemented in Africa in 2010–2019

The red line denotes the best estimate and the blue shaded areas are the 95% confidence intervals.



^a Age groups were restricted to only three categories because the number of survey cases was low.

^b Bacteriologically confirmed TB cases could not be verified for United Republic of Tanzania, so smear-positive TB prevalence rates are shown instead.

FIG. 4.36B

Estimated age-specific prevalence of bacteriologically confirmed pulmonary TB for surveys implemented in Asia in 2007–2019

The red line denotes the best estimate and the blue shaded areas are the 95% confidence intervals.

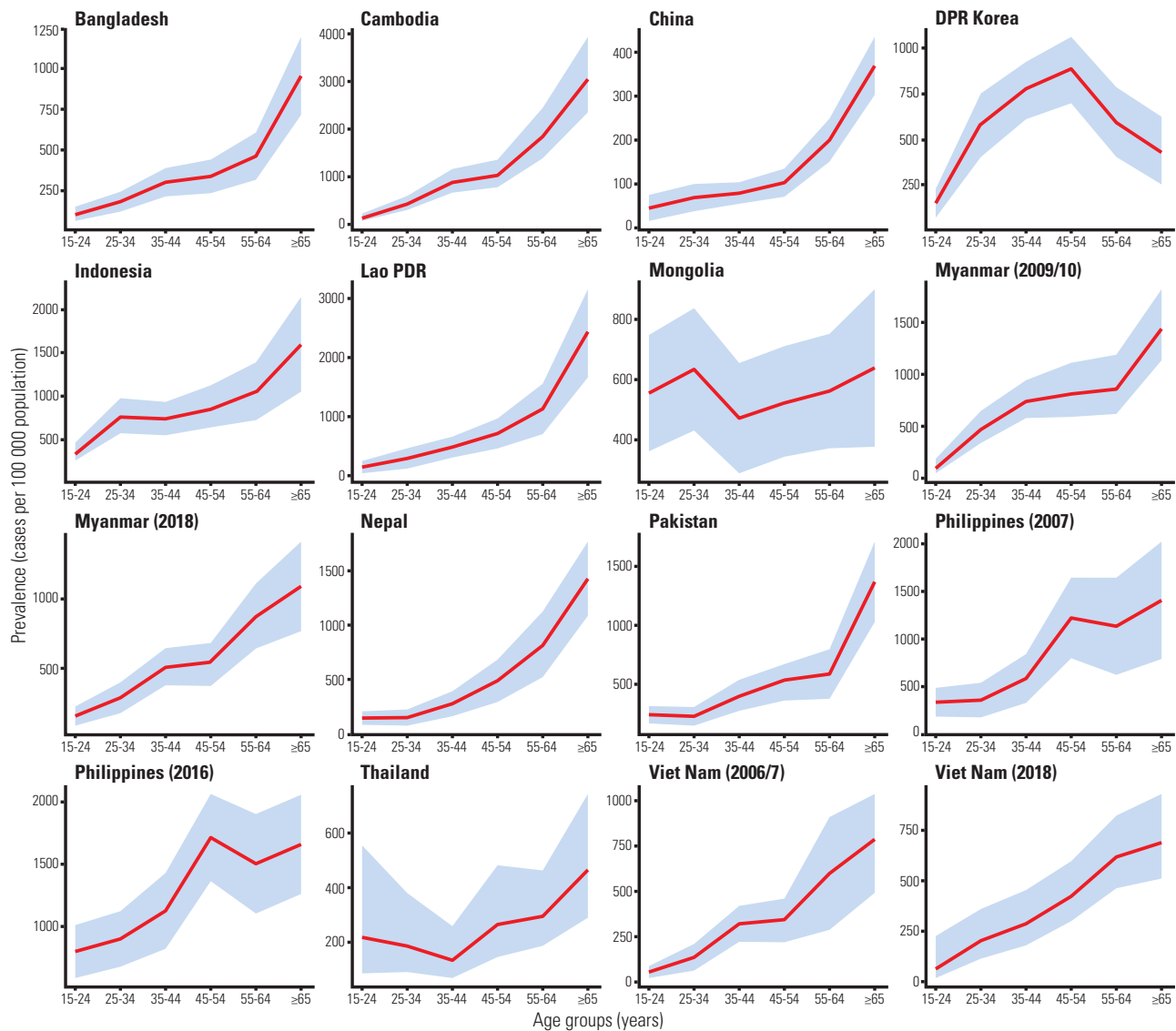
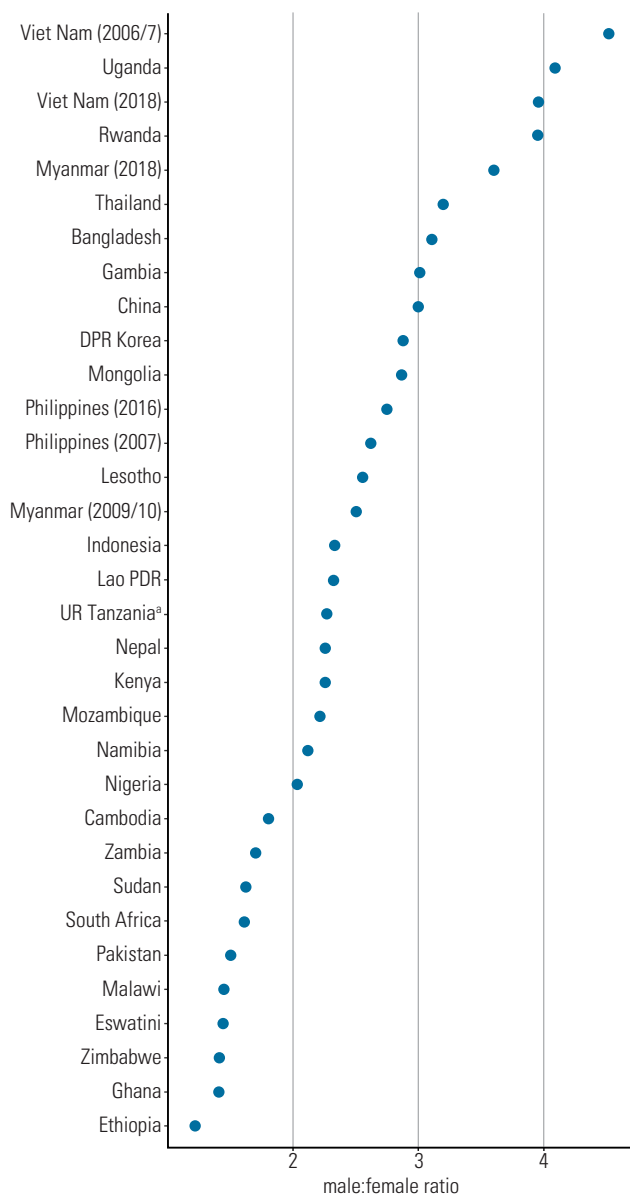


FIG. 4.37

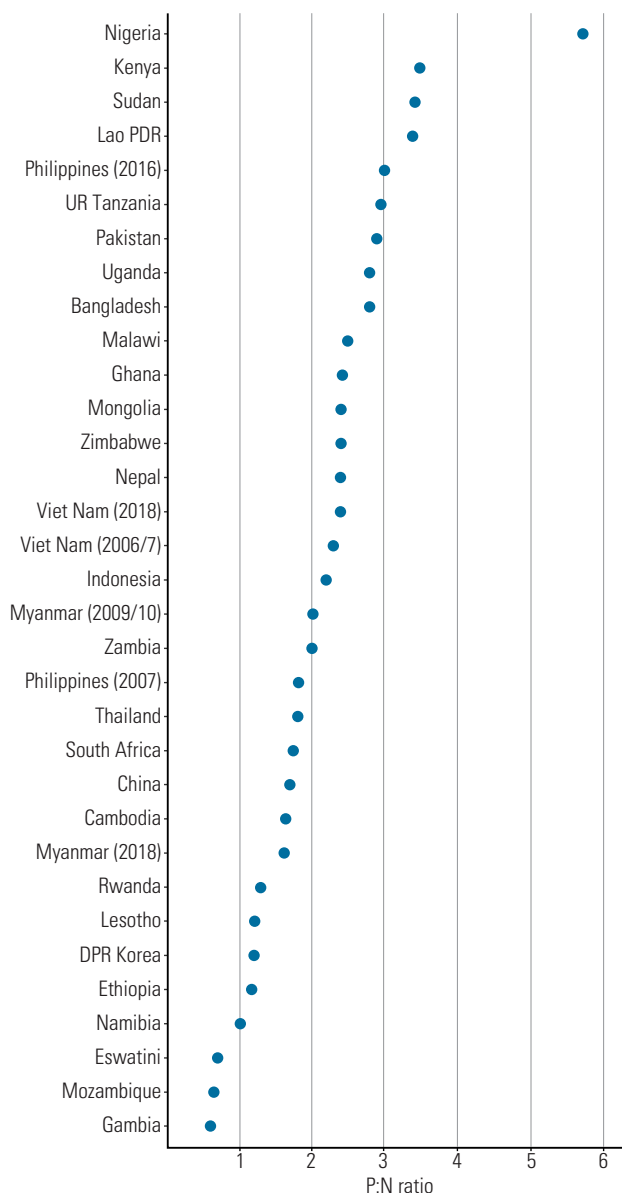
The male to female ratio for bacteriologically confirmed adult TB cases detected in prevalence surveys implemented 2007–2019



^a Due to laboratory challenges during the survey in UR Tanzania, it was only possible to directly estimate the prevalence of smear-positive (as opposed to bacteriologically confirmed TB).

FIG. 4.38A

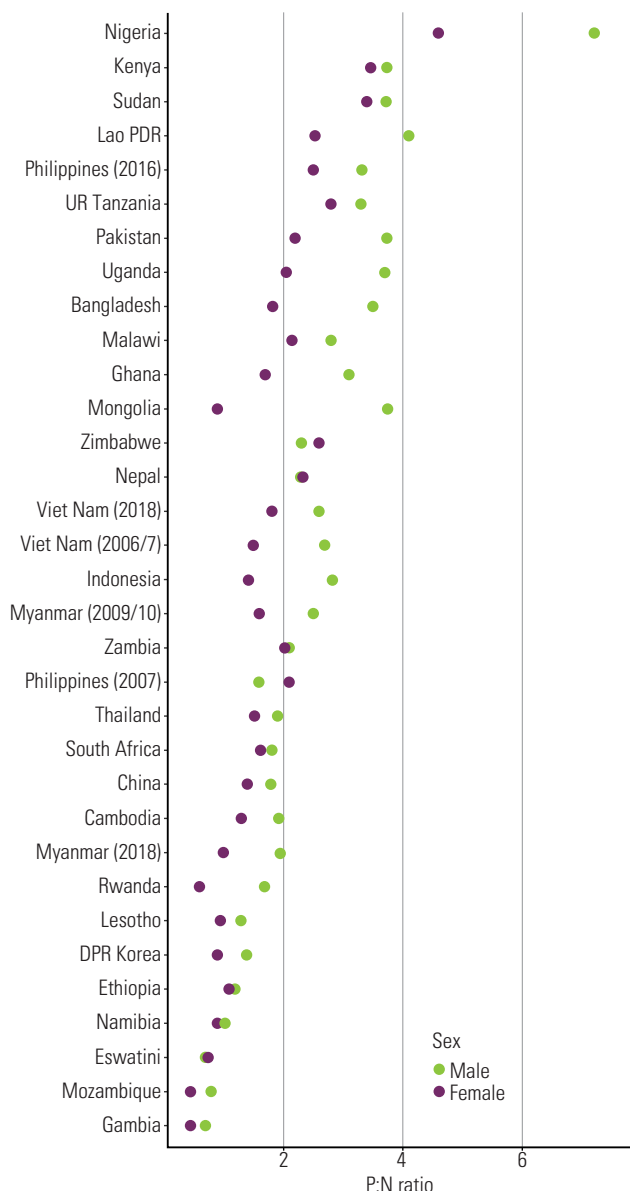
The prevalence to notification (P:N) ratio for adult TB cases detected in prevalence surveys implemented 2007–2019^a



^a The P:N ratio is for smear-positive TB, except for Bangladesh, DPR Korea, Kenya, Myanmar (2018), Namibia (2018), Uganda, Viet Nam (2017) and Zimbabwe where it was 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.

FIG. 4.38B

The prevalence to notification (P:N) ratio by sex for adult TB cases detected in prevalence surveys implemented 2007–2019^a



^a The P:N ratio is for smear-positive TB, except for Bangladesh, DPR Korea, Kenya, Myanmar (2018), Namibia (2018), Uganda, Viet Nam (2017) and Zimbabwe where it was 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.

4.5 Strengthening TB surveillance

National surveillance systems that produce timely data of high quality and coverage are the best way to reliably track TB epidemics, assess progress towards national and global targets for TB, and guide programmatic decisions and policies related to TB. Since 2007, the WHO Global Task Force on TB Impact Measurement has included strengthening of national notification and VR systems as one of its strategic areas of work (Box 4.1). The ultimate goal is for all countries to reliably track their TB epidemics, in terms of TB incidence and TB mortality, using data from national notification and VR systems, respectively.

In 2011–2012, the Task Force developed the WHO checklist of standards and benchmarks for TB surveillance (4). This can be used to assess the extent to which a national surveillance system meets the standards required for notification and VR data to provide a direct measurement of TB incidence and mortality, and to identify gaps that need to be addressed. It then provides the basis for recommendations about the investments and actions needed to close any gaps that are identified. The checklist includes 10 core and three supplementary standards (Table 4.11). The standards are general statements about the criteria that a high-performing TB surveillance system needs to meet; the benchmarks define in quantitative terms the level of performance considered sufficient to meet each standard. A standard is then defined as met, partially met or not met.

There has been substantial progress in the assessment of TB surveillance systems using the checklist. In the period January 2013–August 2020, 82 countries completed at least one assessment (Fig. 4.1), including 29 of the 30 high TB burden countries (Table 4.2). Of these assessments, 51 were implemented since January 2018. Repeat assessments that allow evaluation of whether progress is being made in strengthening surveillance have been completed in 41 countries, including 19 high TB burden countries. Eight countries (Eswatini, Indonesia, Nigeria, Pakistan, Philippines, Rwanda, Zambia and Zimbabwe) have completed three assessments.

An overview of the main results from the most recent assessment in the 29 high TB burden countries¹ (Fig. 4.39) shows the following:

- ▶ there was impressive standardization and consistency in the case definitions used, and the type of data collected, according to the WHO recording and reporting framework (27 countries met the first two standards).
- ▶ the completeness of reporting of data from lower administrative levels (e.g. districts, provinces) to the national level requires improvement in many countries. Reporting was complete (100% of expected reports received at the national level) in only 10 of the 29 countries.

¹ The exception is China, where a partial assessment has been completed (Table 4.2).

- ▶ the transition from a paper (standard B1.4) to a digital case-based surveillance system (standard B1.5) remains a key priority.
- ▶ in both paper-based and digital surveillance systems, there are challenges with the quality, accuracy and completeness of data.
- ▶ the standard for external consistency of data (standard B1.6) was met more often (17 countries) than that of internal consistency (standard B1.7) (8 countries). When the external consistency standard was not met, it was mostly due to underreporting of childhood TB, which poses well-recognized challenges (Box 4.2). This situation suggests that systematic issues exist in terms of the diagnosis and reporting of TB in children (standard B2.3).
- ▶ significant gaps remain with the coverage of the TB surveillance system (only the Russian Federation met standard B1.8) and overall access to health care (standard B1.9).
- ▶ only Brazil and the Russian Federation have national VR systems with standard coding of causes of death, good coverage and high-quality data (standard B1.10).¹
- ▶ surveillance of drug-resistant TB is of high quality in 13 countries and of medium quality in six (standard B2.1).
- ▶ surveillance of HIV infection among TB patients is of high-quality in 17 countries and of medium quality in an additional five (standard B2.2).

Results from repeat assessments of the performance of TB surveillance generally show that progress is being made (Fig. 4.40). Of the 41 countries where a repeat assessment has been completed, 30 made a net improvement (in terms of their overall score); among the remaining 11 countries, there was no change in five and a deterioration in six. Reasons for the latter included a worsening in internal consistency, the coverage of testing for drug-resistant TB and the coverage of the TB surveillance system.

Of the 19 high TB burden countries that completed a repeat assessment, 17 made a net improvement; there was no change in Zimbabwe and a deterioration in Lesotho (the internal and external consistency of data worsened and there was evidence of increasing financial barriers to accessing health care).

Other findings from repeat assessments in high TB burden countries were that:

- ▶ standardization of case definitions and the type of data collected based on the WHO definitions and reporting framework for TB was maintained or improved;
- ▶ strong improvements were made in the completeness of data reporting from lower to higher administrative levels, and in the internal consistency of surveillance data;

¹ Mortality data from VR systems or mortality surveys are available for a further seven countries (Table 4.2), and were used for the country-specific estimates of TB mortality included in this report. Standards for VR quality and coverage in the TB standards and benchmarks differ from standards in Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. WHO 2018, and the forthcoming Global Health Estimates 2019.

FIG. 4.39

Summary of results from the latest national assessment of TB surveillance using the WHO checklist of standards and benchmarks, 29 out of 30 high TB burden countries^a



VR, vital registration; DR, drug-resistant TB

^a The number of countries is shown within the bars; Standard B1.4 was not applicable in 9 countries; standard B1.5 was not applicable in 14 countries; the high TB burden country for which full results are not available is China.

- ▶ there were only limited improvements in the transition from paper to digital case-based surveillance, with large gaps still evident;
- ▶ there were improvements or consistently good levels of performance in the surveillance of drug-resistant TB and TB/HIV; and
- ▶ there were minimal improvements or persistent gaps in the coverage of the TB surveillance system, access to health care and VR data.

The top-five priority recommendations from TB surveillance assessments (and the national TB epidemiological reviews of which they are almost always a part) are shown in Table 4.12.

As part of the work of the WHO Global Task Force on TB Impact Measurement (Box 4.1), a comprehensive background document about the key findings and recommendations from the 82 countries where an assessment has been carried out is in preparation, and will provide the basis for a second edition of the TB surveillance checklist (in 2021). A new product – standardized country profiles to highlight key results and recommendations from each assessment – is also in development. The aim is that NTPs and their partners can use these profiles to help inform investments and actions to strengthen TB surveillance.

FIG. 4.40

Net change in summary score in the latest assessment of the performance of TB surveillance using the WHO checklist of standards and benchmarks, for 41 countries where a repeat assessment had been completed by August 2020

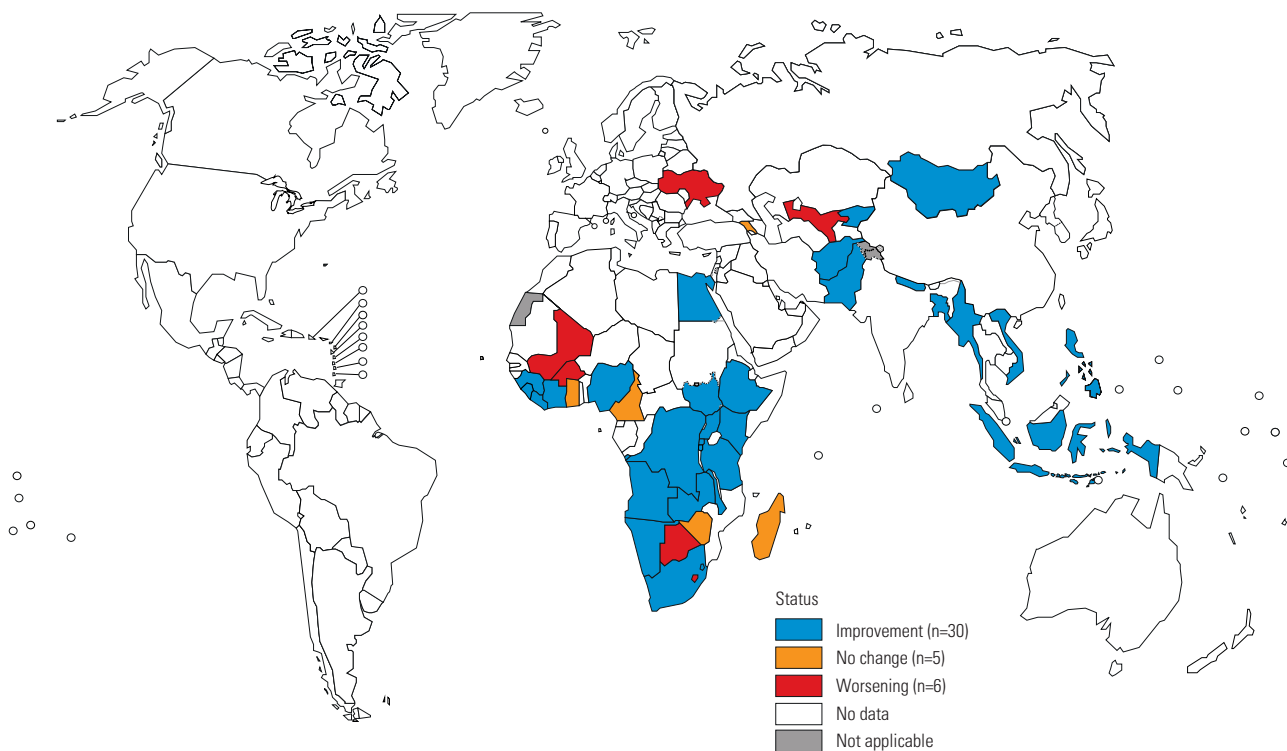


TABLE 4.11
Standards included in the WHO TB surveillance checklist

Grouping		Standards
Core	Data quality	B1.1 Case definitions are consistent with WHO guidelines
		B1.2 TB surveillance system is designed to capture a minimum set of variables for all reported TB cases
		B1.3 All scheduled periodic data submissions, e.g. digital data files or quarterly paper reports, have been received and processed at the national level
		B1.4 Data in quarterly reports (or equivalent) are accurate, complete and internally consistent (For paper-based systems only)
		B1.5 Data in national database are accurate, complete, internally consistent and free of duplicates (For digital case-based or patient-based systems only)
		B1.6 TB surveillance data are externally consistent
		B1.7 Number of reported TB cases is internally consistent (within country)
	System coverage	B1.8 All diagnosed cases of TB are reported
		B1.9 Population has good access to health care
	Vital registration	B1.10 Vital registration system has high national coverage and quality
Supplementary	Subpopulations	B2.1 Surveillance data provide a direct measure of drug-resistant TB in new cases
		B2.2 Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases
		B2.3 Surveillance data for children reported with TB (defined as ages 0-14 years) are reliable and accurate or all diagnosed childhood TB cases are reported

TABLE 4.12

The top-five priority recommendations from assessments of TB surveillance using the WHO checklist of standards and benchmarks^a

High TB burden countries (n=29)	Other countries (n=52)
Transition towards or strengthen case-based digital platform (n=29)	Transition towards or strengthen case-based digital platform (n=48)
Develop or review SOPs or tool for data quality and validity (n=21)	Improve diagnostic capacity (e.g. by including TB in UHC package, improving the coverage of the health facility network) (n=41)
Improve diagnostic capacity (e.g. by including TB in UHC package, improving the coverage of the health facility network) (n=17)	Develop or review SOPs or tool for data quality and validity (n=34)
Improve reporting from the public and private sectors (n=16)	Strengthen routine supervision for data quality checks or hold a data validation workshop (n=28)
Improve the availability and quality of TB mortality data (e.g. CRVS and use of specific ICD codes) (n=16)	Measure the level of underreporting by implementing an inventory study (n=27)
	Provide staff training on recording and reporting to improve data quality (n=27)
	Improve the availability and quality of TB mortality data (e.g. CRVS and use of specific ICD codes) (n=27)

CRVS, Civil registration and vital statistics; ICD, International Classification of Diseases; SOPs, Standard operating procedures; UHC, Universal health coverage.

^a Of the 82 countries that had completed an assessment by August 2020 (Fig. 4.1), recommendations were not available for one country.

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**A doctor examining a TB patient
in a government TB hospital, India.**
Prabhat Kumar Verma/Pacific Press/Alamy

Chapter 5

TB diagnosis and treatment

Key facts and messages

The political declaration at the United Nations high-level meeting on tuberculosis (TB) in 2018 included targets to diagnose and treat 40 million people with TB (including 3.5 million children) and 1.5 million people with drug-resistant TB (including 115 000 children) in the 5-year period 2018–2022.

Globally, 7.1 million people with TB were reported to have been newly diagnosed in 2019 – a small increase from 7.0 million in 2018 but a large increase from 6.4 million in 2017 and 5.7–5.8 million annually in the period 2009–2012. The combined total for 2018–2019 (14.1 million) was 35% of the way towards the 5-year target.

Most of the increase since 2013 is explained by trends in India and Indonesia, the two countries that rank first and second worldwide in terms of estimated incident cases per year. In India, notifications of people newly diagnosed with TB rose from 1.2 million in 2013 to 2.2 million in 2019 (+74%). In Indonesia, notifications rose from 331 703 in 2015 to 562 049 in 2019 (+69%).

In 2020, the COVID-19 pandemic has had a negative impact on access to TB diagnosis and treatment; provisional data are discussed in Chapter 3.

Of the 7.1 million people with a new episode of TB who were diagnosed and notified in 2019, 58% were men, 34% were women and 8% were children. About half a million children were diagnosed and notified in both 2018 and 2019; the combined total of 1.04 million was 30% of the 5-year target of 3.5 million.

There is still a large global gap between the estimated number of incident cases (10.0 million, range 8.9–11.0 million, in 2019) and the number of people newly diagnosed (7.1 million in 2019), due to underreporting of detected cases and

underdiagnosis (if people with TB cannot access health care or are not diagnosed when they do). Five countries accounted for more than half of the global gap: India (17%), Nigeria (11%), Indonesia (10%), Pakistan (8%) and the Philippines (7%). In these countries especially, intensified efforts are required to reduce underreporting and improve access to diagnosis and treatment.

Globally, TB treatment coverage (the number of people notified and treated divided by the estimated incidence) was 71% (range, 64–79%) in 2019, up from 69% (range, 62–77%) in 2018 and 59% (range, 52–67%) in 2015. Four World Health Organization (WHO) regions achieved levels above 75%: the Americas, Europe, South-East Asia and the Western Pacific.

Of the 30 high TB burden countries, those with high levels of treatment coverage in 2019 (>80%) included Brazil, China, the Russian Federation and Thailand. The lowest levels, with best estimates of 50% or less, were in Central African Republic and Nigeria.

Globally in 2019, 57% of pulmonary TB cases were bacteriologically confirmed (others were clinically diagnosed). This was a slight increase from 55% in 2018, but the proportion has remained almost unchanged since 2005. In high-income countries, 84% of pulmonary cases were bacteriologically confirmed.

As countries intensify efforts to close gaps between incidence and notifications, bacteriological confirmation of TB needs to be monitored to ensure that people are correctly diagnosed and started on the most effective treatment. The aim should be to increase the percentage of notified cases confirmed bacteriologically by scaling up the use of WHO-recommended diagnostics that are more sensitive than smear microscopy.

Bacteriological confirmation of TB is necessary to test for drug resistance. Globally in 2019, 61% of people with bacteriologically confirmed pulmonary TB were tested for rifampicin resistance, up from 51% in 2018.

A global total of 206 030 people with multidrug- or rifampicin-resistant TB (MDR/RR-TB) were detected and notified in 2019, a 10% increase from 186 883 in 2018. The number enrolled on treatment was 177 099, up from 156 205 in 2018. Despite these improvements, the total number of people treated in 2018–2019, at 333 304, was only 22% of the way towards the 5-year global target of 1.5 million. For children, the total was 8986, less than 10% of the 5-year target of 115 000.

Closing the incidence-treatment enrolment gap for MDR/RR-TB requires increasing one or more of the following: the proportion of people with TB who are detected and, of these, the proportion for whom TB is bacteriologically confirmed; the proportion of people with bacteriologically confirmed TB who are tested for drug resistance; and the proportion of people with MDR/RR-TB who are enrolled on treatment.

Globally in 2019, 69% of notified TB patients had a documented HIV test result, up from 64% in 2018. In the WHO African Region, where the burden of HIV-associated TB is highest, 86% of TB patients had a documented HIV test result. A total of 456 426 TB cases among people living with HIV were reported (56% of the estimated incidence of 815 000 cases). Of these, 88% were on antiretroviral therapy.

The latest data show treatment success rates of 85% for TB, 57% for MDR/RR-TB and 76% for TB patients living with HIV.

Prompt and accurate diagnosis followed by provision of treatment in line with international standards prevents deaths and limits ill health among people who develop tuberculosis (TB). It also prevents further transmission of the 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 (i.e. the proportion of people with TB who die from the disease) to fall to 10% by 2020 and 6.5% by 2025. The latter is only feasible if all people with TB are diagnosed promptly and treated effectively. 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 5.1](#)).

BOX 5.1

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, 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 6](#).

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 8](#).

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

The political declaration at the first United Nations (UN) high-level meeting on TB, held in 2018, included commitments by Member States to global targets for TB treatment ([Chapter 2](#)) (1). The targets are to diagnose and treat 40 million people with TB in the 5-year period 2018–2022 (including 3.5 million children) and 1.5 million people with drug-resistant TB (including 115 000 children). The annual breakdown of the 40 million target is about 7 million in 2018 and about 8 million in subsequent years.

This chapter provides the latest national data reported to the World Health Organization (WHO) on the diagnosis and treatment of TB in 2019, as well as data for previous years. [Section 5.1](#) presents and discusses data on notifications of TB cases (overall, and disaggregated by age and sex, and by type and site of disease) and the coverage of diagnostic testing. It includes data on the contribution to case-finding efforts of public–public and public–private mix (PPM) and community engagement initiatives. [Section 5.2](#) focuses on treatment coverage (and on detection and treatment gaps) for people with TB, HIV-associated TB and drug-resistant TB, comparing numbers detected and treated with underlying estimates of disease burden. [Section 5.3](#) contains the most recent data on treatment outcomes and time trends for three groups: new and relapse TB patients, TB patients living with HIV, and patients with multidrug- or rifampicin-resistant TB (MDR/RR-TB).

Throughout the chapter, data are presented at global, regional and country levels, giving particular attention to high burden countries.¹ Further country-specific details for all of the indicators covered in this chapter are available online and in the global TB report mobile app ([Annex 1](#)).

In 2020, the COVID-19 pandemic has had a negative impact on access to TB diagnosis and treatment. Provisional data on trends in monthly TB notifications in 2020 in selected high TB burden countries are discussed in [Chapter 3](#). Impacts on approaches to service delivery and mitigation strategies reported by 184 countries in WHO’s 2020 round of global TB data collection are also summarized.

5.1 Case notifications and testing coverage

5.1.1 TB case notifications in 2019 and trends since 2000

Globally in 2019, 7.1 million people with a new episode of TB (new and relapse cases) were diagnosed and notified to national TB programmes (NTPs) and reported to WHO ([Table 5.1](#)). This was an increase from 7.0 million in 2018 and 6.4 million in 2017. The first milestone required to reach the UN high-level meeting target of 40 million between 2018 and 2022 was reached in 2018, but the number in 2019 fell short of the approximately 8 million needed to be on track to reach the target. The combined total for 2018–2019 (14.1 million) was 35% of the way towards the 5-year target.

¹ The three WHO lists of high burden countries (for TB, HIV-associated TB and multidrug-resistant TB [MDR-TB]) are explained in [Annex 2](#).

TABLE 5.1

Notifications of TB, HIV-positive TB, MDR/RR-TB and XDR-TB cases, globally and for WHO regions, 2019

WHO REGION	TOTAL NOTIFIED	NEW AND RELAPSE ^a	PULMONARY NEW AND RELAPSE		EXTRA-PULMONARY NEW AND RELAPSE (%)	HIV-POSITIVE NEW AND RELAPSE	MDR/RR-TB	XDR-TB ^b
			NUMBER	OF WHICH BACTERIOLOGICALLY CONFIRMED (%)				
Africa	1 436 330	1 400 293	1 191 433	66%	15%	318 238	29 155	618
The Americas	250 341	235 600	199 417	78%	15%	20 122	4 979	138
Eastern Mediterranean	506 641	497 998	377 324	55%	24%	1 705	6 328	73
Europe	243 789	200 322	168 574	66%	16%	25 100	47 936	8 560
South-East Asia	3 641 245	3 378 887	2 728 541	57%	19%	75 366	86 623	2 444
Western Pacific	1 416 592	1 389 744	1 281 527	46%	8%	15 895	31 009	517
Global	7 494 938	7 102 844	5 946 816	57%	16%	456 426	206 030	12 350

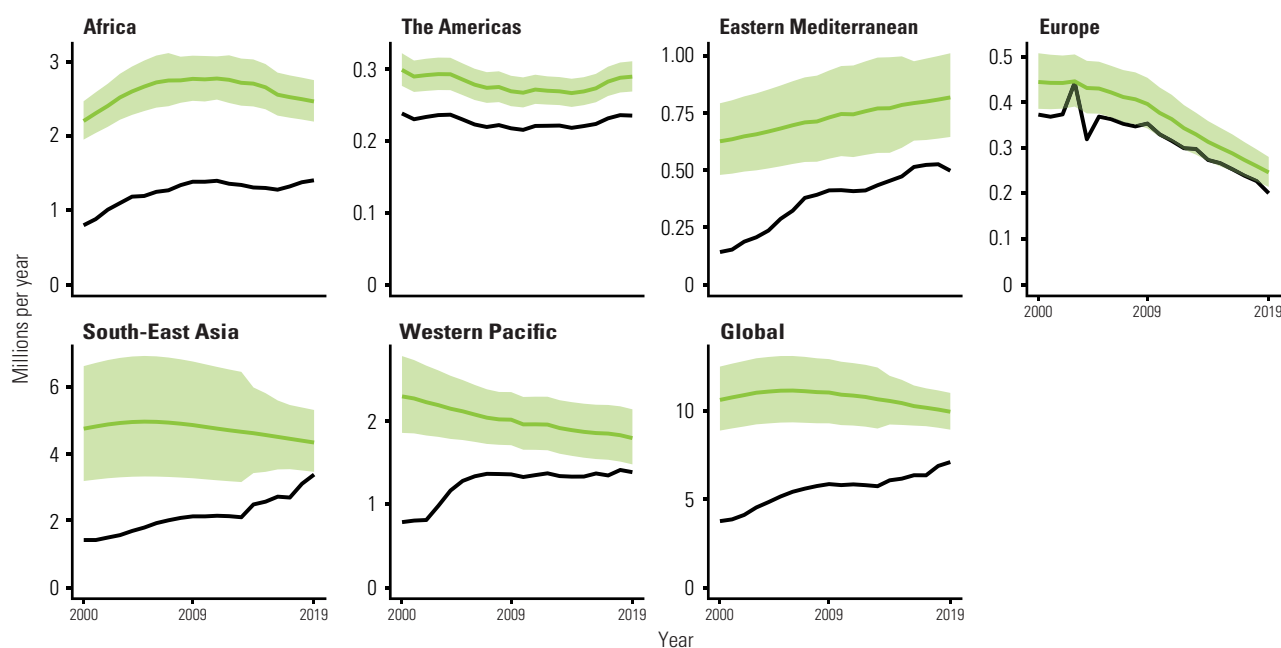
^a *New and relapse* includes cases for which the treatment history is unknown. It excludes cases that have been re-registered as *treatment after failure*, as *treatment after loss to follow-up* or as *other previously treated* (whose outcome after the most recent course of treatment is unknown or undocumented).

^b XDR-TB is MDR-TB plus resistance to a fluoroquinolone and an injectable agent.

FIG. 5.1

Notifications of TB cases (new and relapse cases, all forms) (black) compared with estimated TB incident cases (green), globally and for WHO regions, 2000–2019

Shaded areas represent uncertainty intervals.



An additional 0.4 million people who had been previously diagnosed with TB and whose treatment was changed to a retreatment regimen were also notified.

Trends in notifications of new and relapse cases since 2000 are shown in Fig. 5.1. Numbers increased between 2000 and 2009, stabilized at about 5.7–5.8 million annually during 2009–2012, and then started to increase again. Many countries have increased the number of people newly diagnosed with TB since 2012 (Fig. 5.2), but most of the worldwide increase is accounted for by the two countries that rank first and second globally in terms of their estimated number of incident TB cases: India and Indonesia.¹

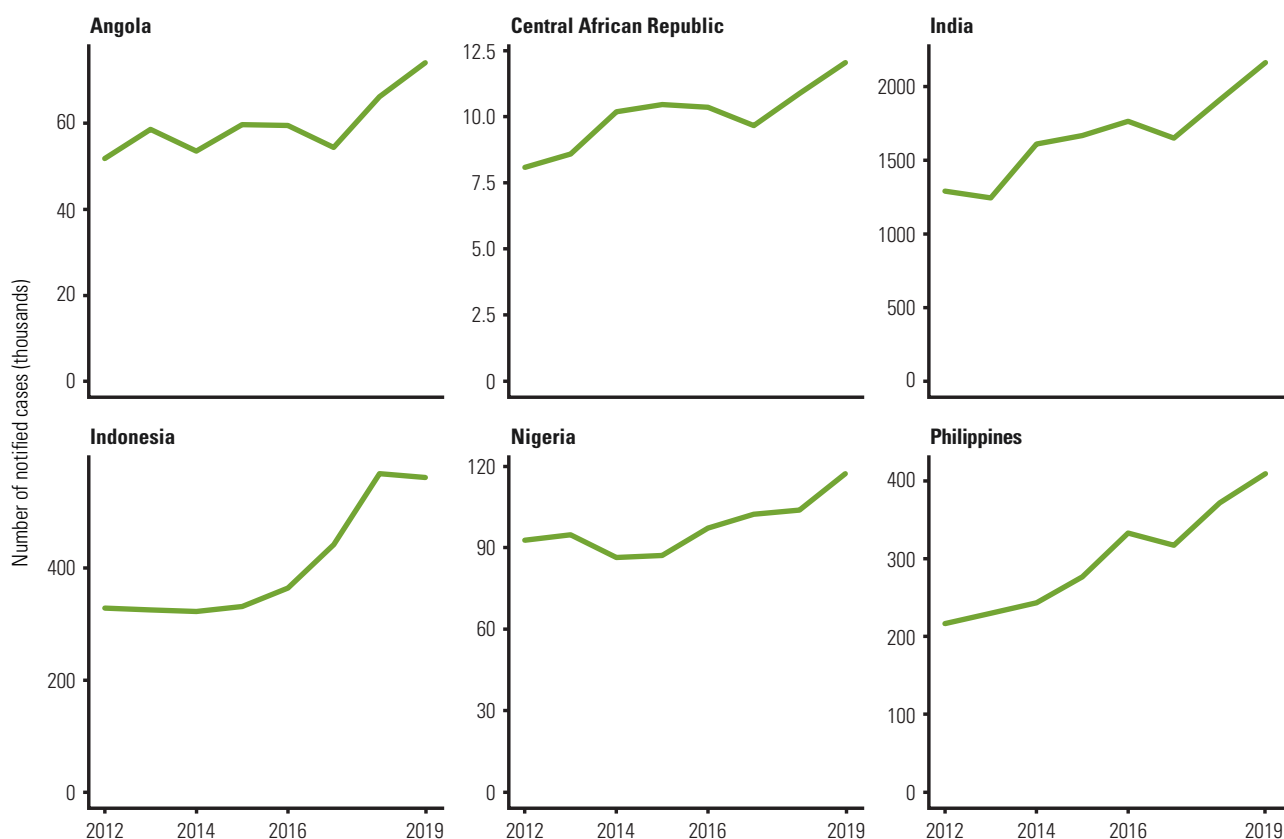
¹ Estimates of TB incidence are provided in Chapter 4. See, for example, Table 4.3.

In India, notifications of new and relapse cases increased from 1.2 million in 2013 to 2.2 million in 2019 (+74%), including an increase of 250 000 (+13%) between 2018 and 2019. This followed the introduction of a national policy of mandatory notification in 2012, and the roll-out (also since 2012) of a nationwide web- and case-based reporting system (called “Nikshay”), which facilitates reporting of detected cases by care providers in the public and private sectors.

In Indonesia, notifications of new and relapse cases increased from 331 703 in 2015 to 562 049 in 2019 (+69%), following the introduction of a national policy of mandatory notification and increased public–private partnership engagement for case reporting and patient treatment.

FIG. 5.2**Trends in TB case notifications in selected high TB burden countries, 2012–2019**

The countries shown are those in which case notifications increased by at least 10% per year between 2017 and 2019.



This progress was driven by evidence from a national TB prevalence survey in 2013–2014 and a national inventory study of underreporting of detected TB cases in 2017, which indicated that most of the gap between the estimated number of incident cases and official notifications of TB cases was attributable to underreporting of cases in both the public and private sectors.

The worldwide increase in notifications has also occurred in the context of two global initiatives. The first is a joint initiative, “Find. Treat. All. #EndTB” (2), which aims to reach 40 million people with quality TB care between 2018 and 2022, in line with the target set at the UN high-level meeting on TB. This initiative is jointly implemented by WHO, the Stop TB Partnership and the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund). The second is a strategic initiative on finding an additional 1.5 million people with TB between 2017 and the end of 2019, compared with a baseline year of 2016, with a focus on 13 priority countries. This initiative is funded by the Global Fund, and supported by WHO and the Stop TB Partnership (3).

Engagement of all care providers in the public and private sectors should be an integral component of national TB strategies, to ensure that everyone with TB is detected and appropriately treated. PPM initiatives have particu-

lar relevance to high burden countries in Africa and Asia. The contribution of PPM to total notifications in countries that have reported PPM data for several years is summarized in **Box 5.2**.

5.1.2 Notifications disaggregated by age and sex

The distribution of notified cases in 2019 by age and sex is shown globally and for the six WHO regions in **Fig. 5.3**. Of the global total, 58% were men, 34% were women and 8% were children (aged <15 years). About half a million children were diagnosed and notified in both 2018 and 2019; the combined total of 1.04 million was 30% of the 5-year global target (for 2018–2022) of 3.5 million.

The global male:female (M:F) ratio for notifications in 2019 was 1.6, but ranged across regions from 1.1 (WHO Eastern Mediterranean Region) to 2.0 (Western Pacific Region), and among the 30 high TB burden countries from 1.1 (Mozambique and Papua New Guinea) to 2.5 (Viet Nam). In contrast, the overall M:F ratio in 33 national TB disease prevalence surveys of adults in African and Asian countries implemented in 2007–2019 was about 2.4, ranging from 1.2 in Ethiopia to 4.5 in Viet Nam; in most countries, the ratio was in the range 2–4, with generally higher ratios in Asia than in Africa (see **Chapter 4** for further details).

Trends in the contribution of PPM approaches to TB case notifications

Engaging with all health providers through PPM^a approaches is essential to reach the approximately 3 million people with TB who miss out on access to quality care each year, due to either underreporting or underdiagnosis. These gaps are more pronounced in high TB burden countries where the private sector dominates the provision of health care or where a large proportion of health care providers in the public sector are not linked with NTPs.

Seven countries (Bangladesh, India, Indonesia, Myanmar, Nigeria, Pakistan and the Philippines) account for more than 60% of the global gap between estimated incidence and the number of people diagnosed with TB and reported to national authorities. They have been designated as the “Big Seven” PPM priority countries.^b The annual number of notifications associated with PPM in these seven countries increased from 225 000 cases in 2010 to more than 1.8 million cases in 2019. The proportion of total notifications contributed by public–private mix in these countries increased from 10% to nearly 30% in the same period; for public–public mix, the increase was from 6% to 12% (Fig. B5.2.1). Trends in other countries that have prioritized either public–public or public–private mix engagement are shown in Fig. B5.2.2 and Fig. B5.2.3.

Recent PPM-associated contributions to notifications have been boosted by the targets set at the UN high-level meeting on TB in 2018, by global initiatives such as the WHO Director-General’s flagship initiative Find. Treat. All. #EndTB^c (a collaboration with the Global Fund and Stop TB Partnership) and the Global Fund’s

Strategic Initiative to find an additional 1.5 million people with TB by the end of 2019,^d and by continued support from the US Agency for International Development (USAID) at global and national levels.

Global attention to PPM has also been bolstered by the rollout in 20 countries of a PPM roadmap released in 2018 by WHO, the Public–Private Mix Working Group of the Stop TB Partnership, USAID, the Global Fund and other international partners.^b The roadmap sets out 10 priority actions needed to accelerate and expand the engagement of all care providers in global efforts to end TB.

Alongside the increased contribution of PPM to notifications, there is also evidence that, in many places, the quality of TB care in the private sector falls short of international standards. For example, PPM-associated

^a “Public–public” mix refers to engagement by a country’s NTP with public health sector providers of TB care that are not under the direct purview of the NTP. Examples include public hospitals, public medical colleges, prisons and detention centres, military facilities, and public health insurance organizations. “Public–private” mix refers to engagement by the NTP with private sector providers of TB care. Examples include private individual and institutional providers, the corporate or business sector, mission hospitals, nongovernmental organizations, and faith-based organizations.

^b Public–private mix (PPM) for TB prevention and care: a roadmap. Geneva: World Health Organization; 2018 (<https://www.who.int/tb/publications/2018/PPMRoadmap/en/>) (4).

^c Joint Initiative “FIND. TREAT. ALL. #ENDTB” [website]. Geneva: World Health Organization; 2019 (<https://www.who.int/tb/joint-initiative/en/>, accessed 18 August 2020) (2).

^d WHO and Global Fund sign cooperation agreement. Strategic Initiative to reach missed TB cases a critical component of grant [website]. Geneva: World Health Organization; 2019 (https://www.who.int/tb/features_archive/WHO_Global_Fund_agreement/en/, accessed 18 August 2020) (3).

FIG. B5.2.1

Contribution of public-private mix to TB case notifications in the “Big Seven” PPM priority countries, 2010–2019

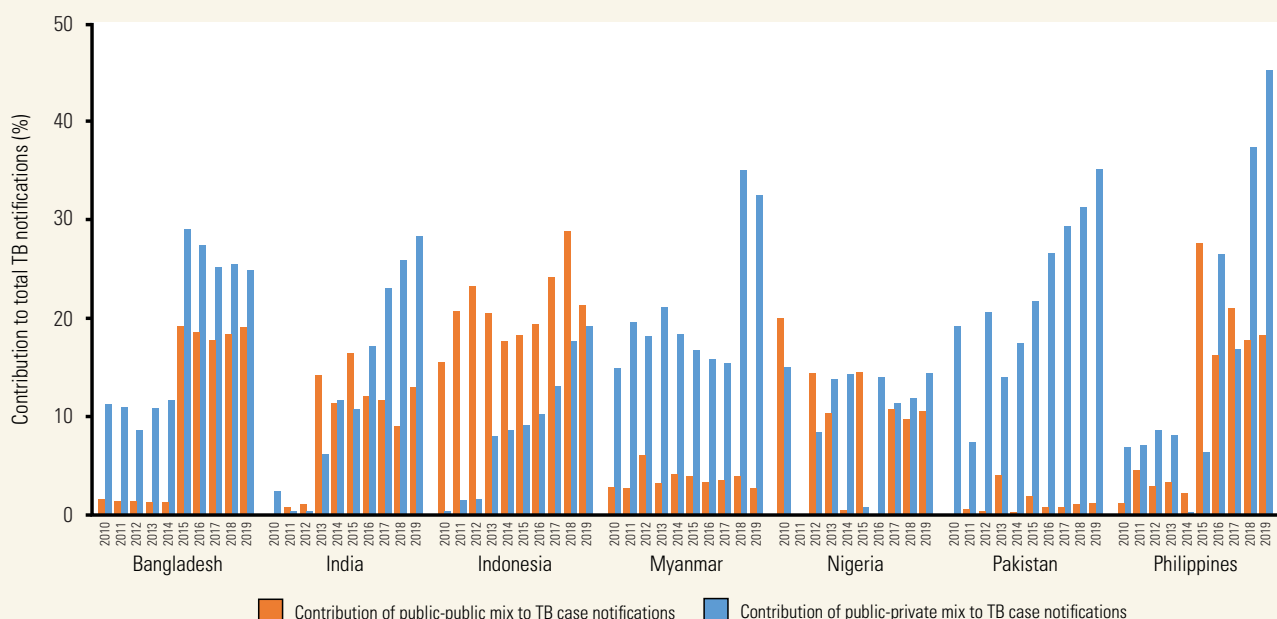
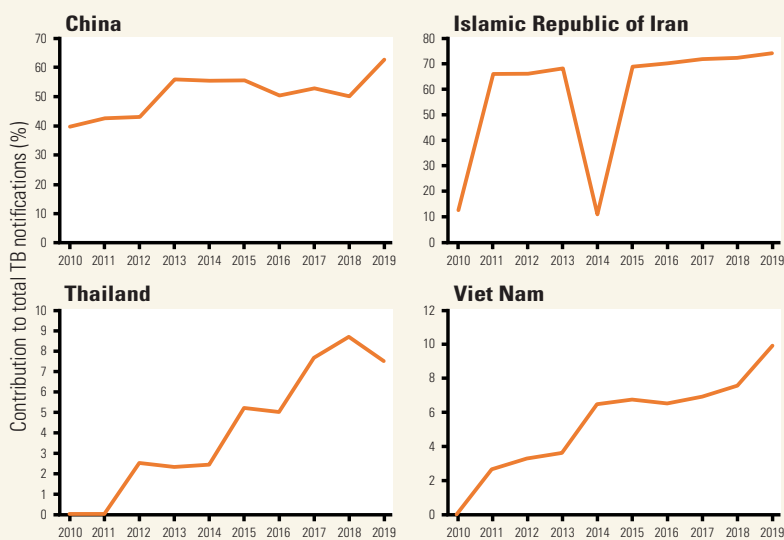


FIG. B5.2.2
Contribution of public-public mix to TB case notifications in four countries, 2010–2019



notifications are often of people with clinically diagnosed TB (without any bacteriological evidence of disease), treatment regimens may be suboptimal and treatment outcomes are not always reported. These issues need to be addressed as part of overall efforts to progress towards UHC. The expanded use of digital surveillance and solutions for the provision of health care can also help to address these challenges (Box 5.4), as in India and Indonesia. National TB inventory studies that quantify the level of underreporting of detected TB cases in all health sectors and for all types of health facilities can also be useful for better understanding the quality of care provided in different sectors and by different types of provider; this improved understanding can, in turn, inform the development of approaches to address shortcomings.

FIG. B5.2.3
Contribution of public-private mix to TB case notifications in eight countries, 2010–2019

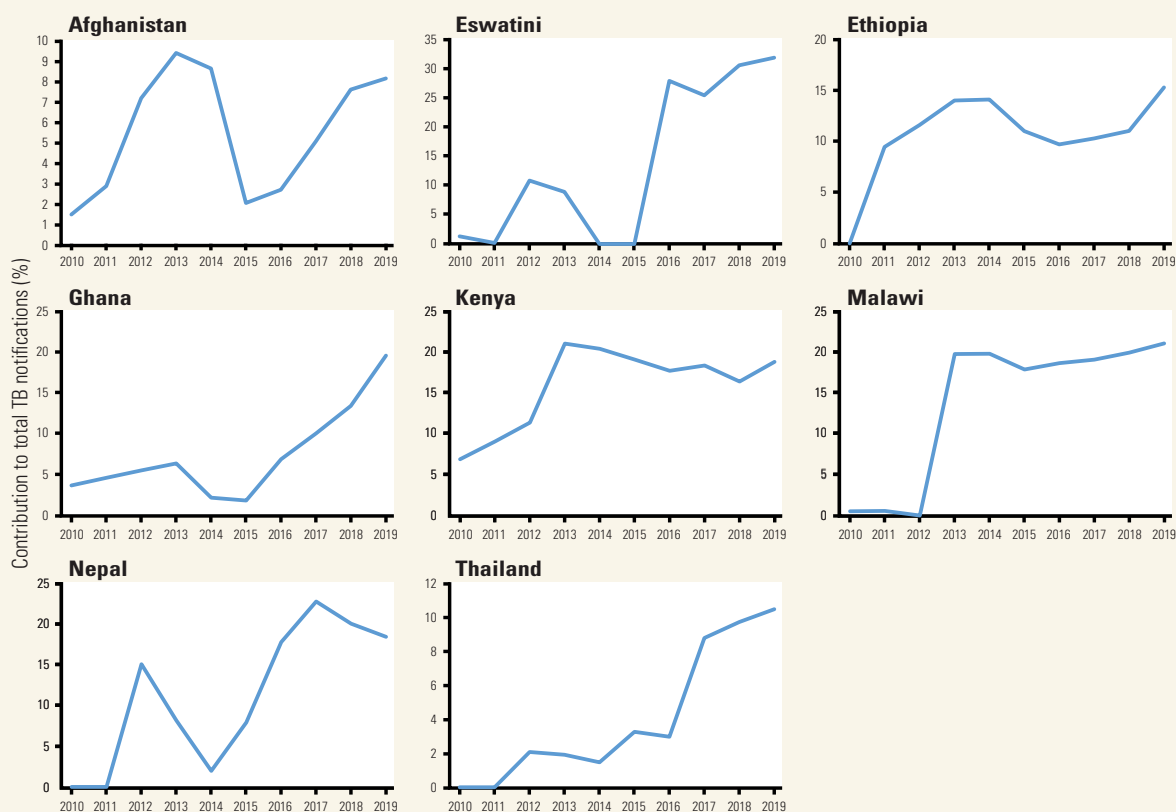
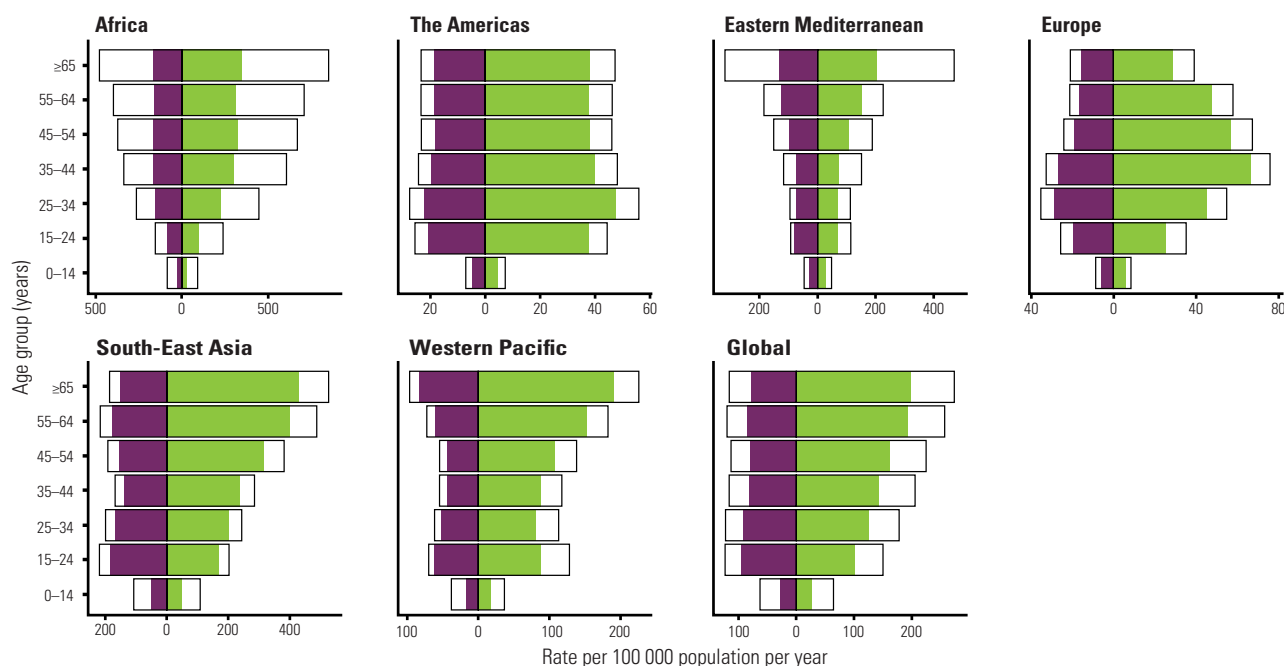


FIG. 5.3

Estimated TB incidence (black outline) and new and relapse TB case notification rates by age and sex^a (female in purple; male in green), globally and for WHO regions, 2019



^a Countries not reporting cases in these categories are excluded. Cases included accounted for 89% of reported cases.

In the WHO regions of the Eastern Mediterranean, South-East Asia and Western Pacific, 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, notification rates were highest among adults aged 45–54 years in the WHO African Region, 25–34 years in the Region of the Americas and 35–44 years in the European Region (Fig. 5.3). In eight high TB burden countries (Bangladesh, Brazil, China, the Democratic People’s Republic of Korea, Lesotho, the Russian Federation, Thailand and Viet Nam) less than 5% of notified cases were children (Fig. 5.4).

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 diagnostic and reporting practices. In general, notification data appear to understate the share of the TB burden accounted for by men and children (see Chapter 4 for further details). Particular issues with diagnosis and reporting of TB in children include variable case definitions and underreporting of cases diagnosed by paediatricians in the public and private sectors. Greater attention to the quality of TB notification data for children is warranted in many countries; recent efforts to strengthen data collection for children and adolescents are highlighted in Box 5.3.

5.1.3 Notifications disaggregated by type and site of TB disease

As countries seek to improve TB diagnosis and treatment, and to close gaps between estimated incidence and notifications of TB cases – especially in the context of recent global initiatives to “find the missing people with TB” and the global target set at the UN high-level meeting on TB in 2018 (Section 5.1.1) – the proportion of notified cases that are bacteriologically confirmed needs to be monitored. The microbiological detection of TB is critical because it allows people to be correctly diagnosed and started on the most effective treatment regimen as early as possible. 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. The aims should be to increase the percentage of cases confirmed bacteriologically (based on scaling up the use of recommended diagnostics that are more sensitive than smear microscopy), and to ensure that people with a negative bacteriological test result are not started on TB treatment unless they meet the relevant clinical criteria.

Of the 7.1 million new and relapse cases notified in 2019, 5.9 million (84%) had pulmonary TB (Table 5.1). Of these, 57% were bacteriologically confirmed. This was a slight increase from 55% in 2018, but the percentage has remained virtually unchanged since 2005 (Fig. 5.5).¹ The

¹ A bacteriologically confirmed case is one from whom a biological specimen is positive by smear microscopy, culture or WHO-recommended rapid diagnostic test, such as the Xpert MTB/RIF[®] assay.

FIG. 5.4

Percentage of new and relapse TB cases that were children (aged <15 years), 2019

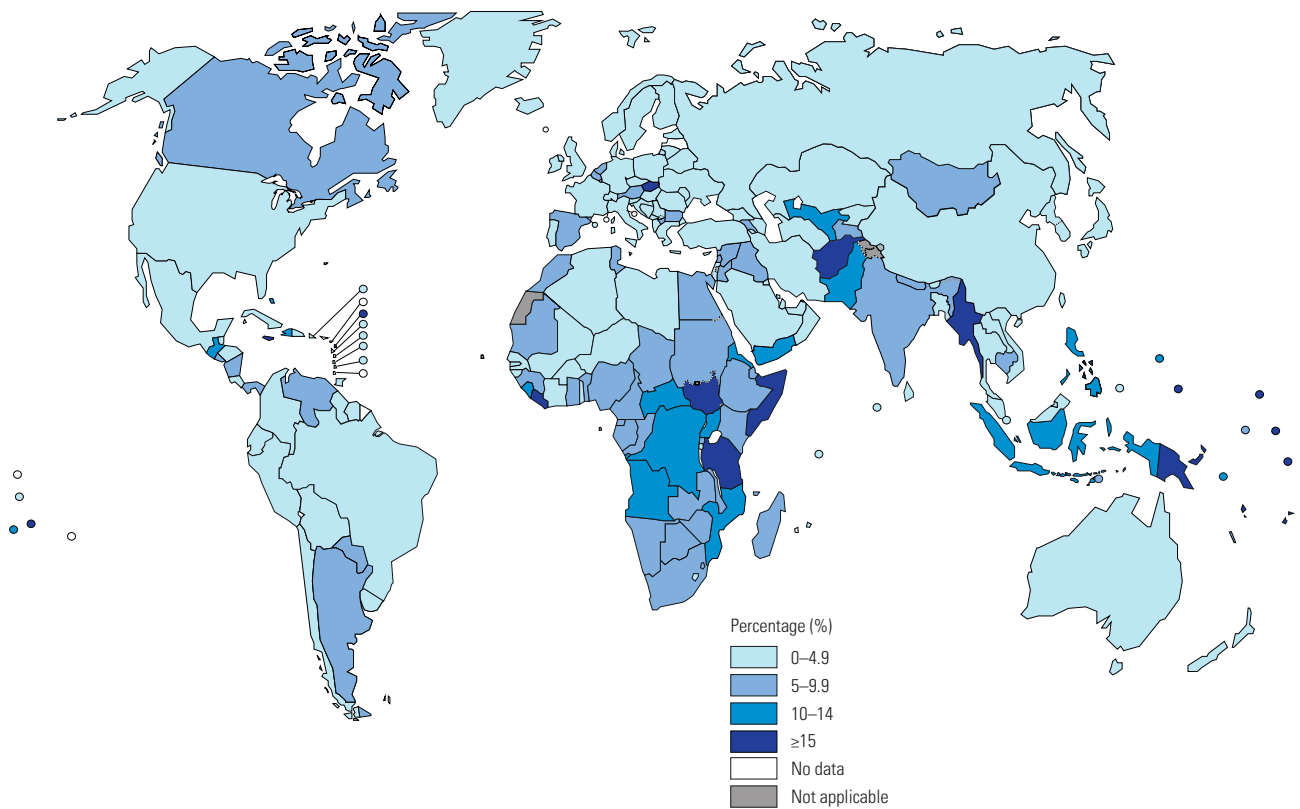
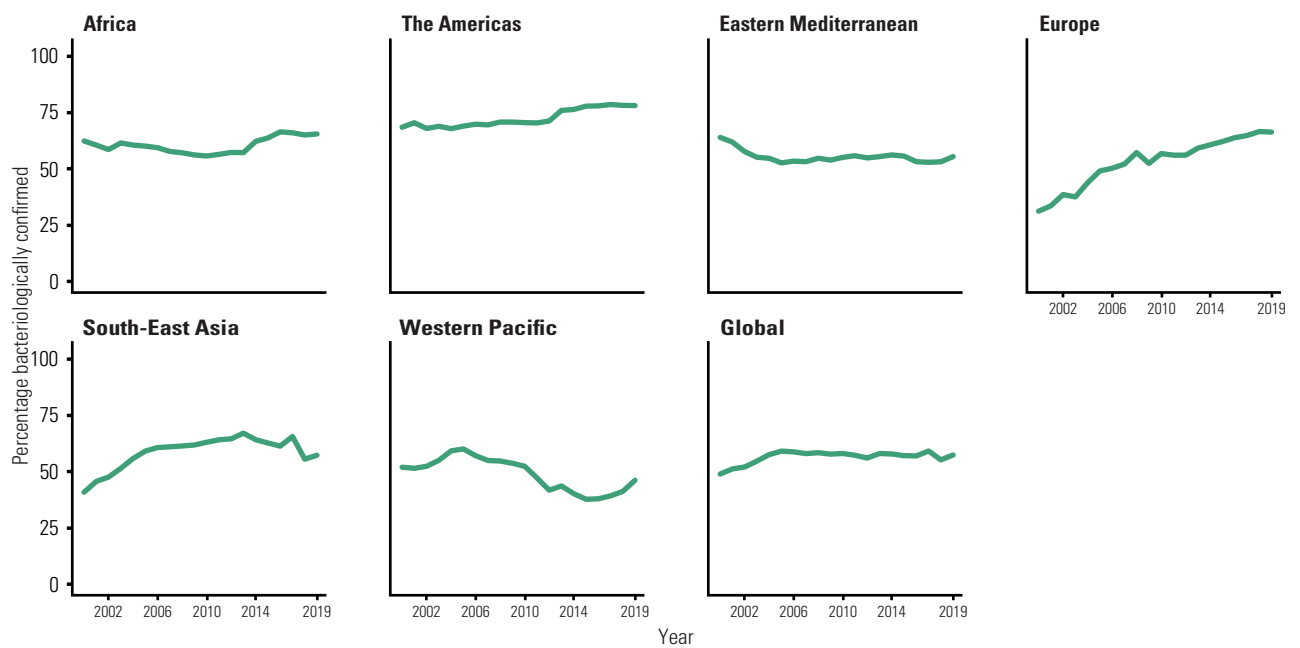


FIG. 5.5

Percentage of new and relapse^a pulmonary TB cases with bacteriological confirmation, globally and for WHO regions, 2000–2019



^a The calculation for new and relapse pulmonary cases in years prior to 2013 is based on smear results, except for the European Region where data on confirmation by culture was also available for the period 2002–2012.

BOX 5.3

Strengthening data collection for children and adolescents with TB

Following a *Call to action for childhood TB in 2011*,^a the availability of surveillance and national level study data have improved and expanded, as have estimates of disease burden (**Fig B5.3.1**).

The *Roadmap towards ending TB in children and adolescents*,^b launched alongside the UN high-level meeting on TB in 2018, provides an agenda for scaling up interventions for children (<10 years) and adolescents (10–19 years); it also highlights the main remaining gaps related to data collection, reporting and analysis. In 2020, to address some of these gaps, WHO asked countries to report data on national notifications for more disaggregated age groups (0–4, 5–9, 10–14 and 15–19 years, compared with the previous groupings of 0–4 and 5–14 years), the number of children and young adolescents enrolled in treatment for MDR/RR-TB, and treatment outcomes for children and young adolescents specifically (as opposed to all age groups only).

Notifications of children and adolescents diagnosed with TB

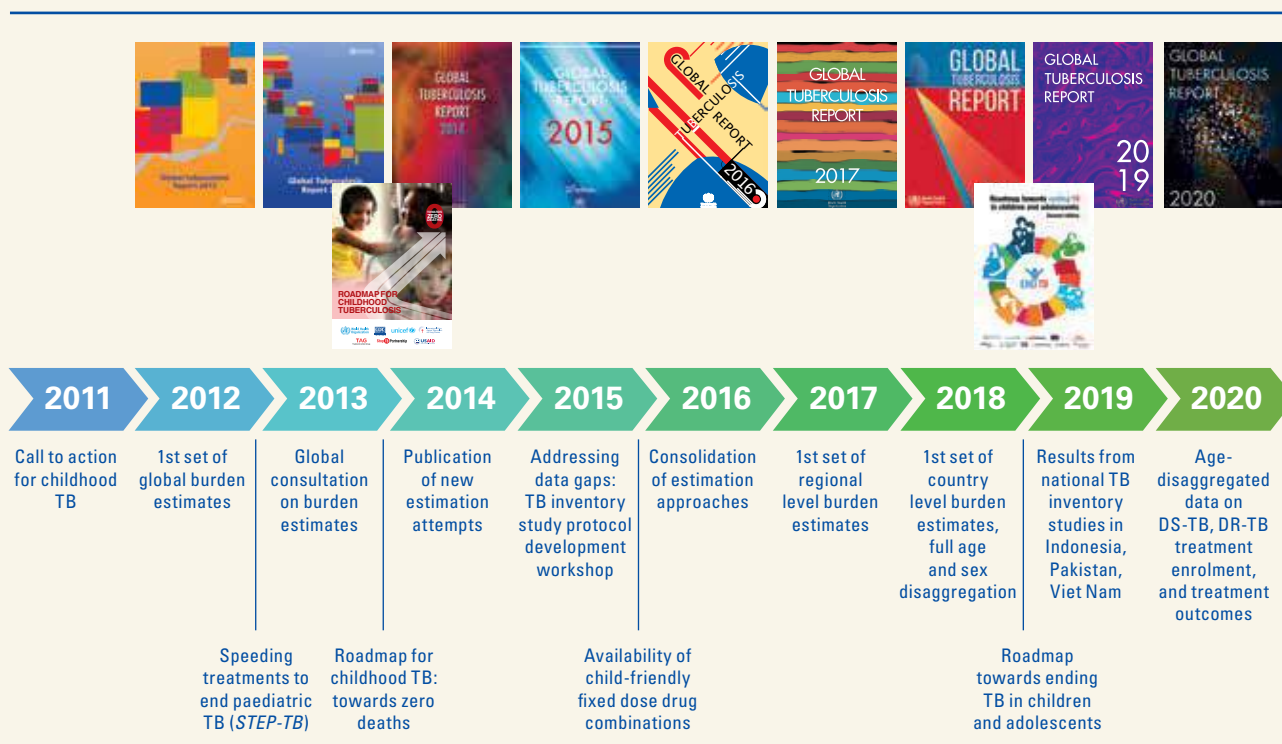
Globally, the number of TB notifications among children and young adolescents aged 0–14 years increased from less than 400 000 in 2015 to 523 000 in 2019 (**Fig B5.3.2**). The 2018–2019 total of 1.04 million represents 30% of the 5-year (2018–2022) target of 3.5 million set at the UN high-level meeting. Of total global notifications in 2019, 97% were reported with age disaggregations at national level that included the category 0–14 years (**Fig B5.3.3**). WHO recommendations have evolved from a focus on age disaggregation for new smear-positive TB cases until 2006, followed by the addition of disaggregated data for new smear-negative and new extrapulmonary TB cases between 2007–2012, and finally to age disaggregation for all new and relapse cases since 2013.

^a Call to action for childhood TB [website]. Stop TB Partnership: 2011 (http://www.stoptb.org/getinvolved/ctb_cta.asp, accessed 18 August 2020) (5).

^b Roadmap towards ending TB in children and adolescents. Geneva: World Health Organization; 2018 (<https://www.who.int/tb/publications/2018/tb-childhoodroadmap/en/>, accessed 18 August 2020) (6).

FIG. B5.3.1

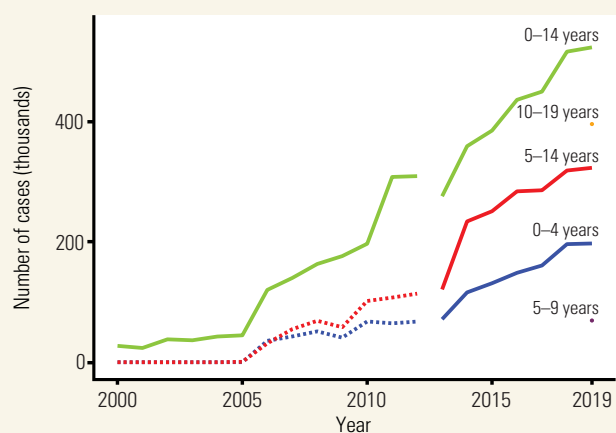
Global milestones related to TB in children and adolescents, 2011–2020



BOX B5.3

FIG. B5.3.2

Global notifications of TB in children and adolescents, 2000–2019^{a,b}



- ^a The gaps in the line graphs mark the new WHO TB recording and reporting framework and respective TB case definitions that were introduced in 2013.
- ^b Case notification data for more disaggregated age groups (0–4, 5–9, 10–14 and 15–19 years, compared with the previous groupings of 0–4 and 5–14 years) were collected by WHO for the first time in 2020.

A total of 95 countries were able to report data disaggregated into the four age categories for children and adolescents, including 10 high TB burden countries. In 2019, 396 000 cases among children and adolescents aged 10–19 years were reported – equivalent to 10% of total notifications in these countries. Age-specific notification rates for the four age groups in the 10 high TB burden countries that reported data are shown in **Fig B5.3.4**.

Treatment of MDR/RR-TB in children

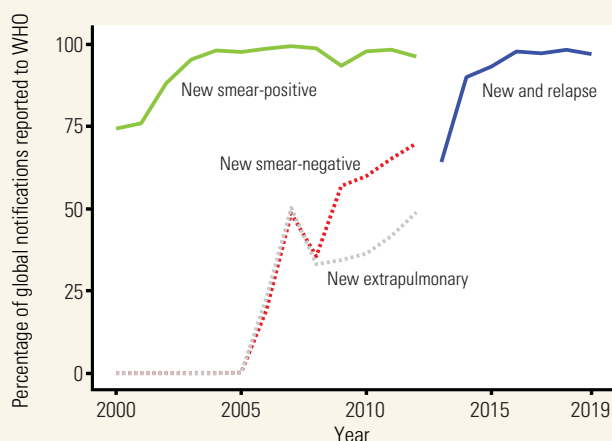
There was a small increase in the number and proportion of children and young adolescents treated for MDR/RR-TB between 2018 and 2019 (**Table B5.3.1**). However, the 8986 children treated for MDR/RR-TB in 2018–2019 represented only 7.8% of the 5-year (2018–2022) target of 115 000.

TB treatment outcomes in children

Data for all five categories of treatment outcome were available for 13 185 children and young adolescents in 99 countries in the 2018 patient cohort, all of which were in the WHO Region of the Americas and the European Region. This included two high TB burden countries (Brazil and the Russian Federation). The treatment success rate was 84% (**Table B5.3.2**), similar to that of adults. Further review of the data is required to understand the reasons for the relatively high proportion of children for whom the treatment outcome was not evaluated (9.5% compared with 6% for adults).

FIG. B5.3.3

Availability of national TB notification data disaggregated by age group, including the category 0–14 years, 2000–2019^a



- ^a The gaps in the line graphs mark the new WHO TB recording and reporting framework and respective TB case definitions that were introduced in 2013.

FIG. B5.3.4

New and relapse TB case notification rates by age group for children and adolescents in 10 high TB burden countries, 2019

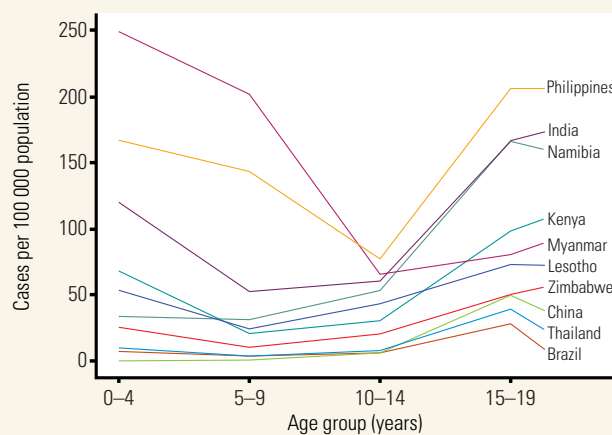


TABLE B5.3.1

Numbers of people enrolled in treatment for MDR/RR-TB, for all ages and for children, 2018–2019

	ALL AGES	CHILDREN AGED 0–14 YEARS	SHARE OF CHILDREN IN TOTAL (%)
2018	156 205	3 398	2.2%
2019	177 099	5 586	3.2%

BOX B5.3

TABLE B5.3.2

Treatment outcomes in children (0–14 years), 2018 cohort (n=13 185 children from 99 countries)

Treatment outcome	Percentage
Treatment success	84
Failure	0.5
Death	1.9
Lost to follow-up	3.9
Not evaluated	9.5

A total of 123 countries reported the treatment success rate among children and young adolescents, including 19 high TB burden countries. The overall figure was 85%, ranging from 73% in Papua New Guinea to 97% in Bangladesh.

Conclusions and next steps

The availability of data on TB in children and adolescents is important to inform policy, planning and programmatic action, including targeted interventions, for these subpopulations. For example, it can help with the development and uptake of child-friendly formulations, and guide decisions on procurement and supply chain management.

Faster progress towards the targets set at the UN high-level meeting will require action on various fronts. Examples include better case detection through active contact investigation, increased use of WHO-recommended diagnostics on easier-to-collect specimens from children (for example, stool specimens), expansion of access to chest radiography, and building capacity in the clinical diagnosis of TB in children with probable or possible TB who have negative bacteriological results or do not have access to bacteriological testing. For children with a clinical diagnosis of drug-resistant TB, treatment regimens are based on the drug susceptibility pattern of the most likely source case. Special attention needs to be paid to vulnerable children (e.g. those with pneumonia, malnutrition or HIV). Coordination and integration with primary health care, and with maternal and child, nutrition, and HIV programmes are crucial.

Adolescents are an important subpopulation with relatively high notification rates, necessitating specific adolescent-friendly interventions to reduce stigma, discrimination and risky behaviour, to diagnose and manage HIV coinfection, and to address educational needs.

All countries are encouraged to transition to case-based digital systems (Box 5.4) for the collection of more detailed data, including on children, adolescents and young adults.

remaining patients were diagnosed clinically (i.e. based on symptoms, abnormalities on chest radiography or suggestive histology).

During the period of increasing global notifications between 2013 and 2019, the percentage of notified TB cases that were bacteriologically confirmed has varied at regional level (Fig. 5.5). In the WHO South-East Asia Region – which includes the two countries (India and Indonesia) that accounted for most of the rise in notifications worldwide – the percentage rose from 61% in 2016 to 66% in 2017, then declined to 55% in 2018 and was 57% in 2019. In three other WHO regions, steady improvements were observed: the African Region (57% to 66%), European Region (59% to 66%) and Region of the Americas (76% to 78%).

Trends in the proportion of cases bacteriologically confirmed from 2000 to 2019 in the 30 high TB burden countries are shown in Fig. 5.6 and levels in all countries in 2019 are shown in Fig. 5.7. There is considerable variation, even among countries with a similar epidemiological profile. In general, levels of confirmation are lower in low-income countries and highest in high-income countries (median, 84%), where there is wide access to the most sensitive diagnostic tests (Fig. 5.8).

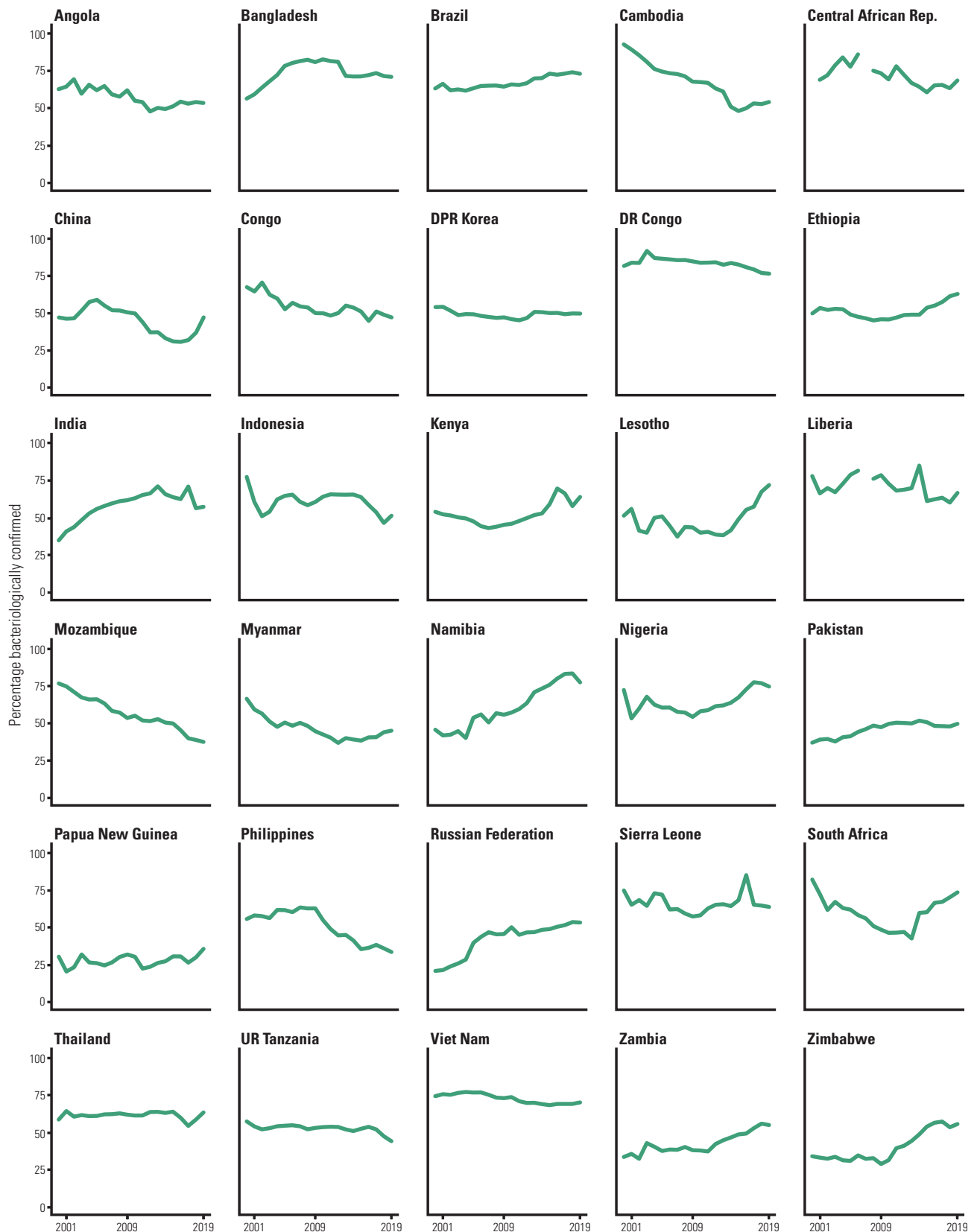
Reliance on direct smear microscopy alone is inherently associated with a relatively high proportion of unconfirmed pulmonary TB cases. However, in high TB burden countries, differences in diagnostic and reporting practices are the most likely cause of variation in the proportion of pulmonary cases that are bacteriologically confirmed: the percentage ranges from 30% in the Philippines to 78% in Namibia.

Increases in notifications in high TB burden countries in 2018–2019 were associated with a decrease in the proportion of cases that were bacteriologically confirmed (Fig. 5.9). If the proportion falls below 50% in a given setting, a review of the diagnostic tests being used and the validity of clinical diagnoses would be warranted (e.g. via a clinical audit). In general, greater efforts are needed to improve the availability and use of the most sensitive diagnostic tests for TB, and to ensure that international standards for TB care are met, to avoid both missed diagnoses of people who have TB and overtreatment of people who do not have TB. The aim should be to increase the percentage of cases confirmed bacteriologically.

Extrapulmonary TB represented 16% of the 7.1 million incident cases that were notified in 2019, ranging from 8% in the WHO Western Pacific Region to 24% in the Eastern Mediterranean Region (Fig. 5.10 and Table 5.1).

FIG. 5.6

Percentage of new and relapse^a pulmonary TB cases with bacteriological confirmation in the 30 high TB burden countries, 2000–2019



^a The calculation for new and relapse pulmonary cases in years prior to 2013 is based on smear results, except for the Russian Federation where data on confirmation by culture was also available for the period 2002–2012.

FIG. 5.7

Percentage of new and relapse pulmonary TB cases with bacteriological confirmation, 2019

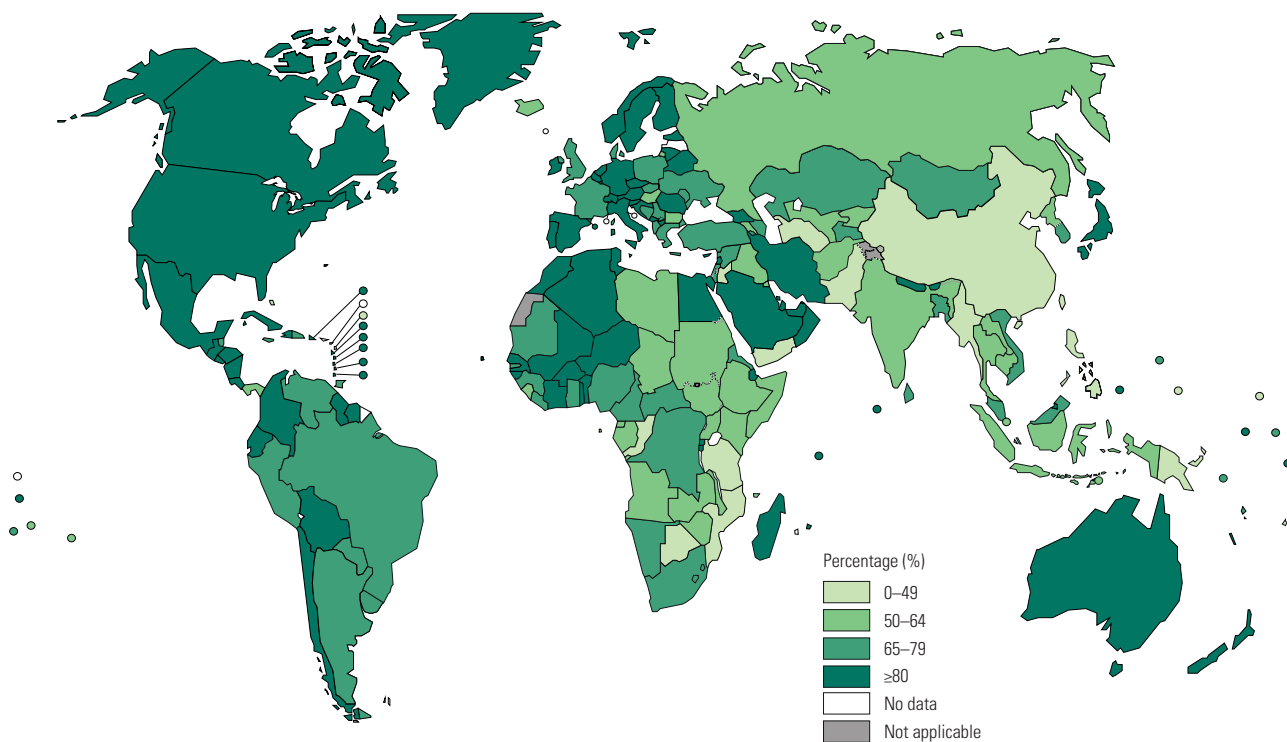


FIG. 5.8

Distribution of the proportion of notified pulmonary cases that were bacteriologically confirmed in 2019, by country income group

Boxes indicate the first, second (median) and third quartiles weighted by a country's number of pulmonary cases; vertical lines extend to the minimum and maximum values, excluding countries with <10 cases.

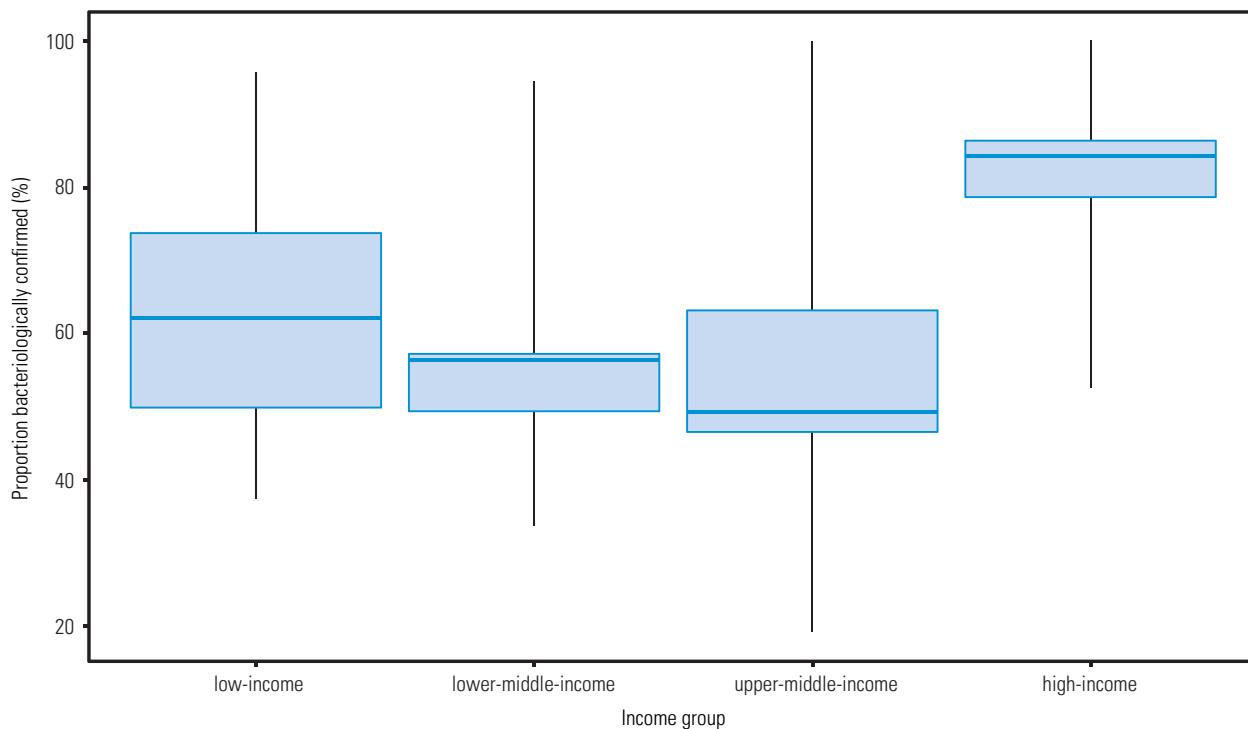


FIG. 5.9

Changes in the proportion of bacteriologically confirmed pulmonary cases in relation to changes in case notification rates, 30 high TB burden countries, 2018–2019

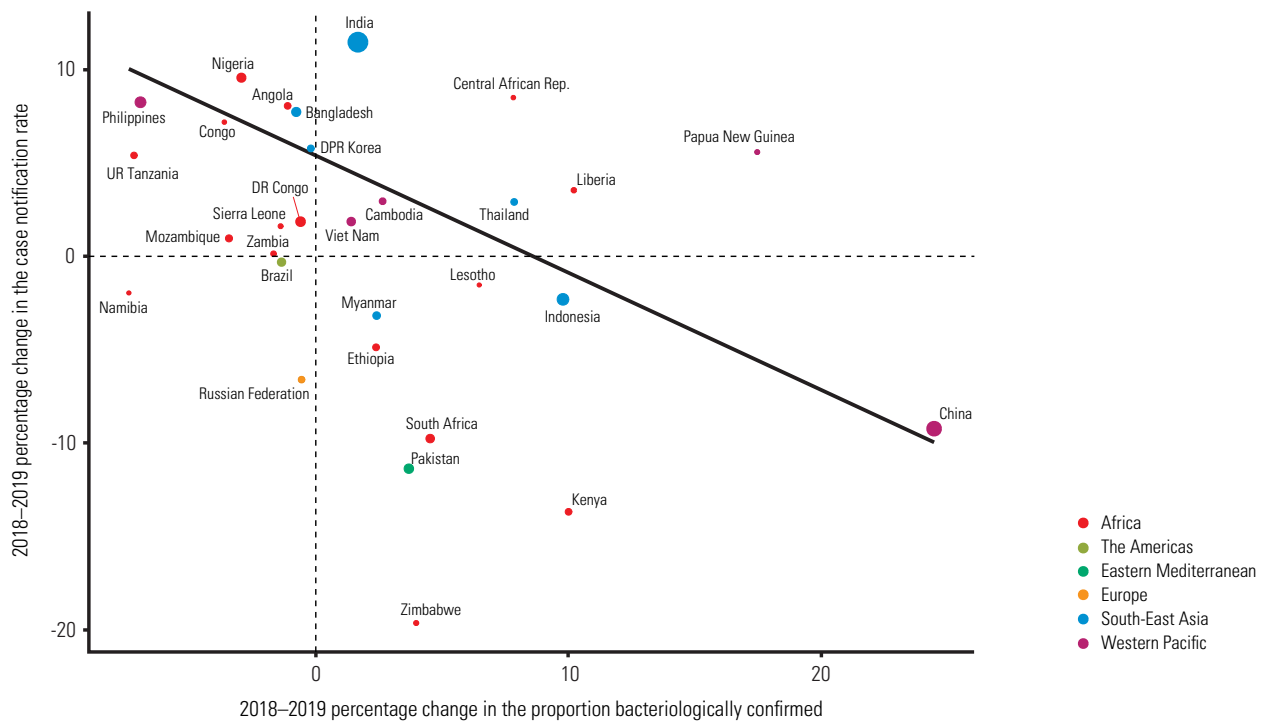
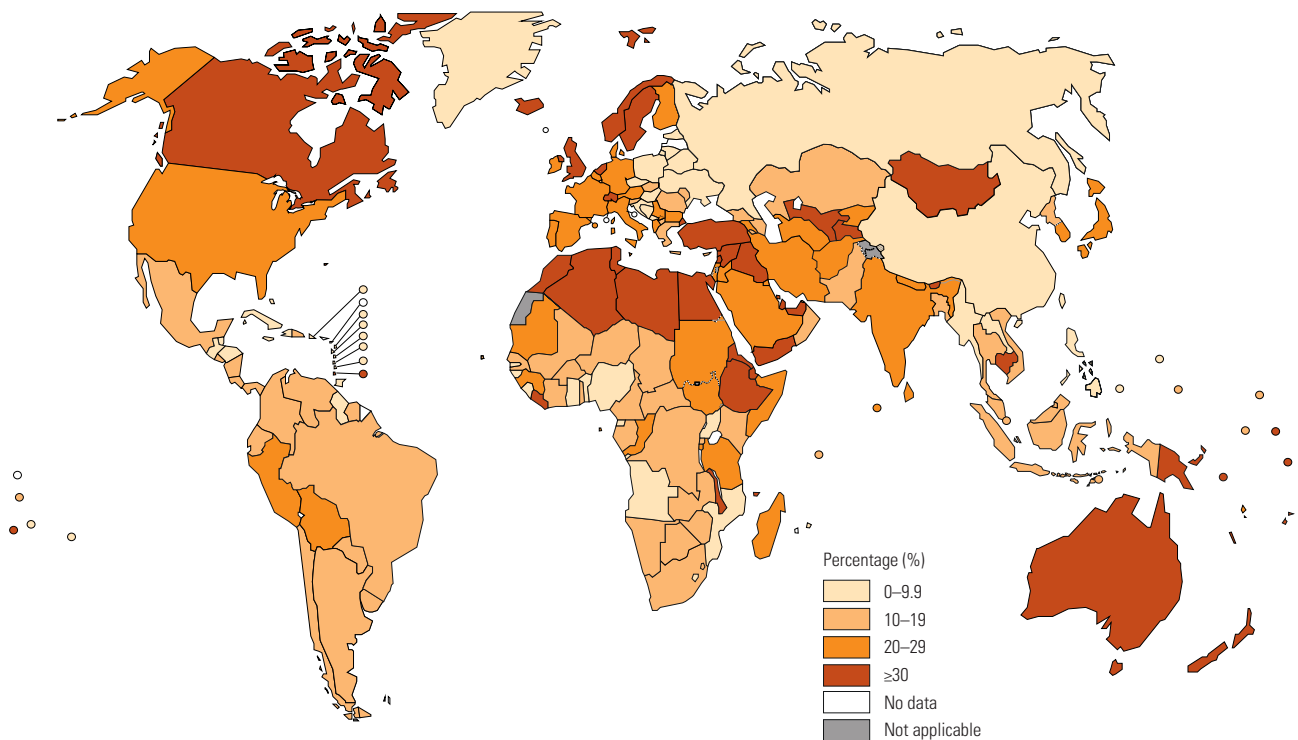


FIG. 5.10

Percentage of extrapulmonary cases among new and relapse TB cases, 2019



5.1.4 HIV testing for TB patients and TB detection among people living with HIV

WHO recommends systematic screening for TB symptoms among people living with HIV as an essential component of the HIV care package, together with linkage to diagnostic services, as necessary. In 2019, 86 countries reported annual data on the number of TB cases notified among those newly enrolled in HIV treatment. In total, 110 102 (7%) of the 1.5 million people who were reported to be newly enrolled in HIV treatment in 2019 were diagnosed with TB during the same year; data for the 15 high TB/HIV burden countries that reported data are shown in **Table 5.2**.

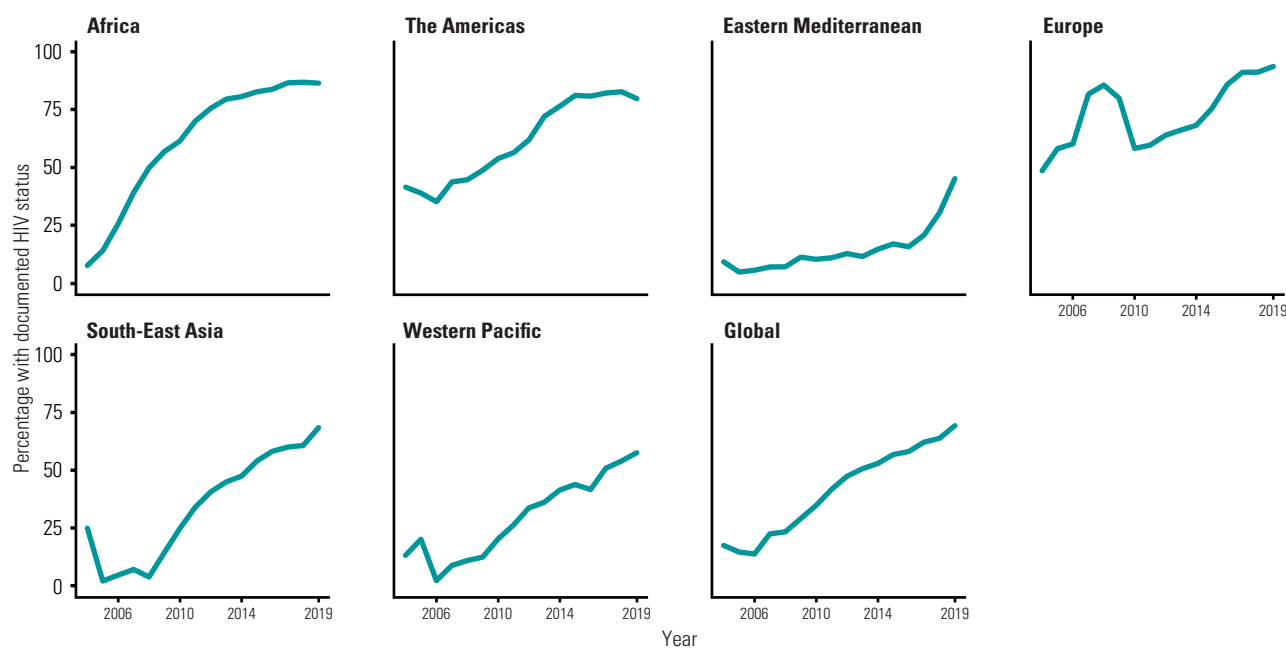
In 2019, 172 countries reported 4.8 million notified new and relapse TB patients with a documented HIV test result; this was a 12% increase from 4.3 million in 2018 and was equivalent to 69% of notified TB cases (**Fig. 5.11**). In 80 countries and territories, at least 90% of TB cases knew their HIV status (**Fig. 5.12**). Documentation of HIV status averaged 76% of TB patients in high TB burden countries, but varied considerably, from 11% in Congo to above 80% in 19 countries. In the WHO African Region, which accounted for 73% of the global burden of HIV-associated TB in 2019 (**Chapter 4**), 86% of TB patients knew their HIV status.

Globally, 456 426 cases of TB among people living with HIV were notified in 2019 (**Table 5.1**), equivalent to 9.5% of the 4.8 million TB patients with an HIV test result.

TABLE 5.2
Number of people newly enrolled in HIV care in 2019 who were also notified as a TB case in 2019, 15 high TB/HIV burden countries that reported annual data

COUNTRY	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	36 443	2 666	7.3
Botswana	14 713	1 399	9.5
DR Congo	74 450	6 797	9.1
Eswatini	16 723	383	2.3
Ethiopia	36 434	1 914	5.3
Ghana	35 424	2 620	7.4
India	174 261	26 354	15
Indonesia	53 690	10 730	20
Kenya	149 524	6 722	4.5
Malawi	127 830	1 089	0.85
Myanmar	35 572	3 915	11
Papua New Guinea	4 037	733	18
Uganda	93 597	6 235	6.7
UR Tanzania	316 702	19 146	6.0
Zimbabwe	118 800	2 178	1.8
Total	1 288 200	92 881	7.2

FIG. 5.11
Percentage of new and relapse^a TB cases with documented HIV status, globally and for WHO regions,^b 2004–2019

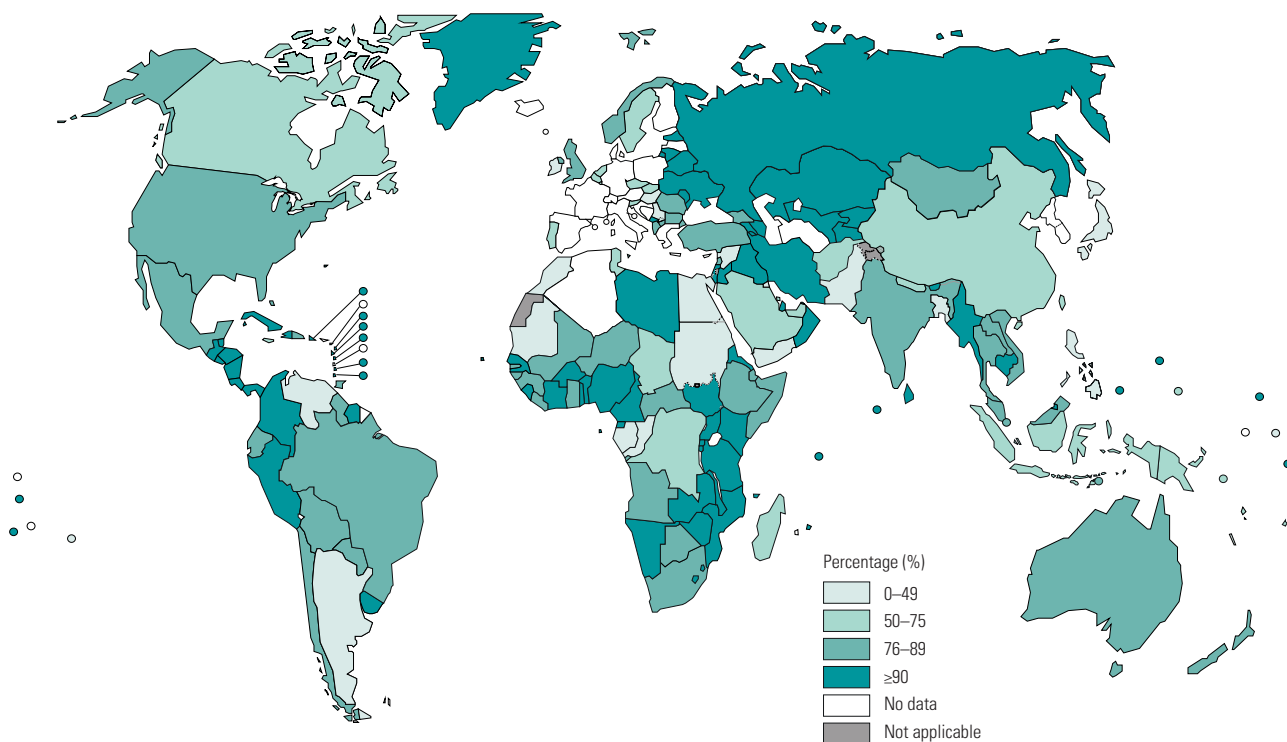


^a The calculation is for all cases in years prior to 2015.

^b Countries were excluded if the number with documented HIV status was not reported to WHO.

FIG. 5.12

Percentage of new and relapse TB cases with documented HIV status, 2019



Overall, the percentage of TB patients testing HIV-positive has fallen globally over the past 10 years. This decline is evident in all WHO regions except the European Region, where the rate is now triple what it was in 2009, in part due to the overall upward trajectory of the HIV epidemic in this region.

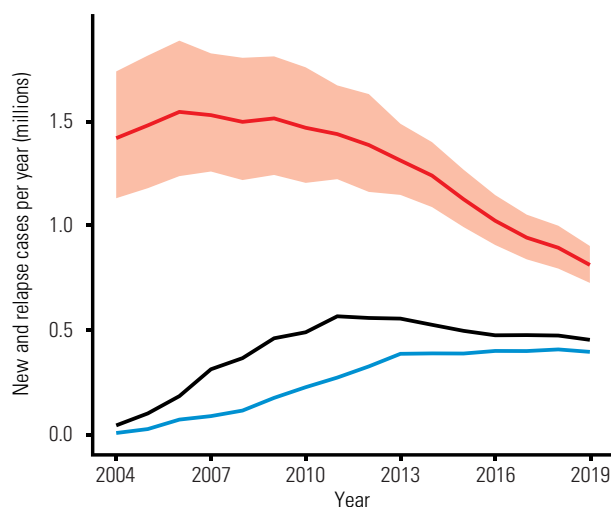
The number of people reported to have TB and HIV globally was only 56% of the total estimated number of HIV-positive incident TB cases (Fig. 5.13), exposing a considerable detection gap. The biggest gaps – where more than half of the people with HIV-associated TB were not reported – were in the WHO Eastern Mediterranean (75% gap), Western Pacific (57% gap) and African regions (51% gap). Globally, the estimated percentage of people living with HIV who knew their HIV status reached 81% in 2019. To enhance patient follow-up and reduce the higher mortality rates in this population, there is a need for more intensified TB case-finding among people attending HIV care services, and for strengthened linkages between TB and HIV recording and reporting systems.

In 2020, WHO released new guidelines on strategic information related to HIV (7). The guidelines include five indicators for identifying and addressing gaps in the TB screening and diagnostic cascade; these indicators are applicable in all countries but are considered a particular priority in high TB/HIV burden countries. Adoption and use of these indicators should help to improve TB case detection among people living with HIV.

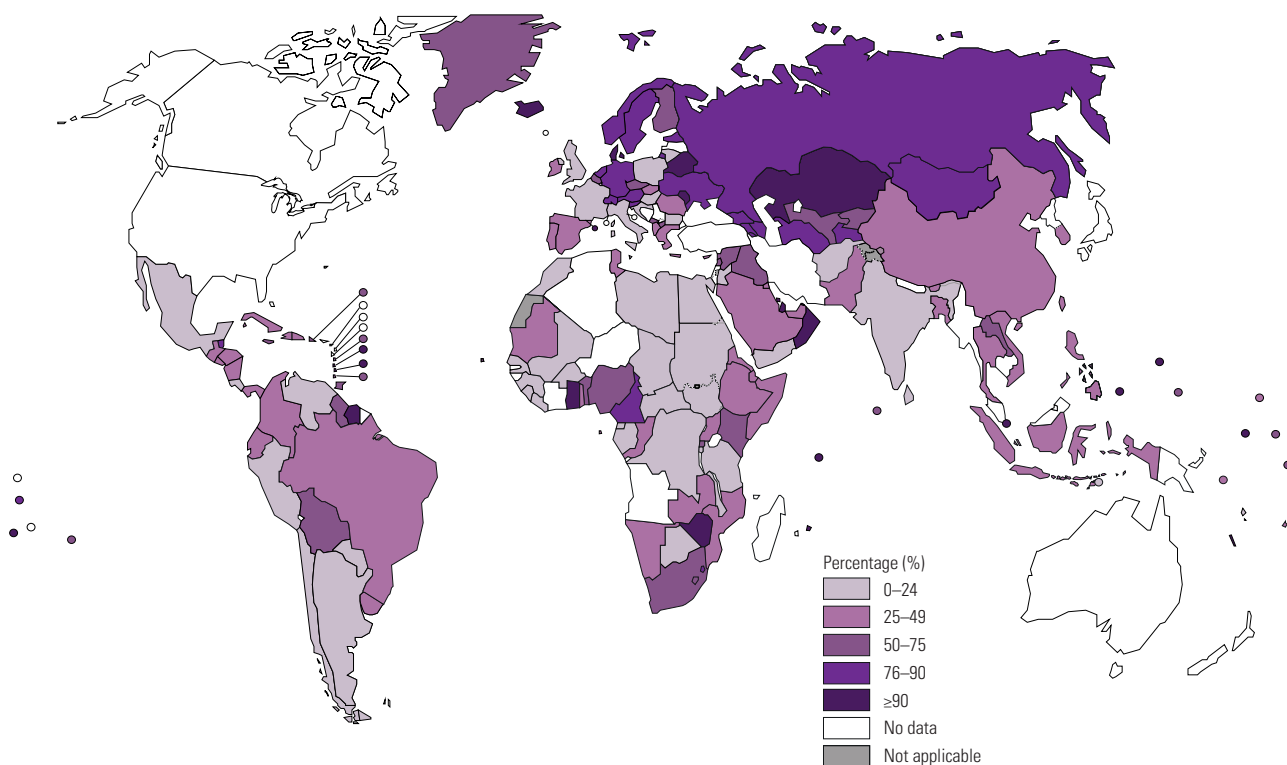
FIG. 5.13

Estimated global number of incident HIV-positive TB cases (red) compared with the global number of notified new and relapse TB cases known to be HIV-positive (black) and the global number of TB patients started on antiretroviral therapy (blue), 2004–2019

Shaded area represents uncertainty intervals.



* The calculation is for all cases in years prior to 2015.

FIG. 5.14**Percentage of new and relapse TB cases initially tested with a WHO-recommended rapid diagnostic test, 2019****5.1.5 Rapid testing for TB**

Increasing access to early and accurate diagnosis using a molecular WHO-recommended rapid diagnostic test¹ is one of the main components of TB laboratory-strengthening efforts under the End TB Strategy.

As a first step, countries should adopt policies that include diagnostic algorithms in which a WHO-recommended rapid diagnostic test is the initial test for all people with signs or symptoms of TB (8). Such policies are particularly important for the 48 countries included in one or more of the lists of high TB, TB/HIV and MDR-TB burden countries; of these 48 countries, 41 reported having policies that included such an algorithm by the end of 2019 (Table 5.3).

Policy adoption can be assessed using a second indicator recommended by WHO (8), which is the percentage of new and relapse TB cases initially tested with a WHO-recommended rapid diagnostic test. Globally, 2.0 million new and relapse TB cases were identified by a WHO-recommended rapid diagnostic test in 2019, equivalent to

58% of all bacteriologically confirmed pulmonary cases. Among the 48 high burden countries, 18 reported that a WHO-recommended rapid diagnostic test had been used as the initial test for more than half of their notified TB cases (Fig. 5.14).

Data on the quality of laboratory services in the 48 countries are shown in Table 5.4. One third (33%) of the national reference laboratories in these countries have attained the standard² for medical laboratory quality and competence defined by the International Organization for Standardization (ISO) (9). Among countries reporting data, an average of 63% of testing sites were covered by a comprehensive external quality assessment system for the Xpert MTB/RIF assay, the most commonly used WHO-recommended rapid diagnostic test worldwide.

The lateral flow urine lipoarabinomannan assay (LF-LAM) can provide a timely diagnosis of TB and help to reduce TB mortality among people living with HIV. WHO has recommended use of the test since 2015, and a policy update was issued in 2019 (10). Among the 30 high burden TB/HIV countries, only 13 had a national policy and algorithm that includes the use of LF-LAM to assist in the diagnosis of TB in people living with HIV (Table 5.3), showing a slow adoption of this life-saving, easy-to-use diagnostic tool.

¹ WHO-recommended rapid diagnostic tests use molecular techniques to detect TB among people with signs or symptoms of TB. They include the Xpert MTB/RIF and Xpert MTB/RIF Ultra (Cepheid, Sunnyvale, United States of America [USA]) assays; the loop-mediated isothermal amplification test (TB-LAMP; Eiken Chemical, Tokyo, Japan); the Truenat™ MTB, MTB Plus and MTBRIF Dx tests (Molbio Diagnostics, Goa, India), and lateral flow urine lipoarabinomannan assay (LF-LAM; Alere Determine™ TB LAM Ag, USA).

² ISO 15189, which defines the components necessary for quality management systems to be effective in medical laboratories.

TABLE 5.3

National policies to increase access to rapid TB testing and universal DST, and their implementation,^a 2019

<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	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 ^b	PERCENTAGE OF NOTIFIED RR-TB CASES WITH DST RESULTS FOR FLUOROQUINOLONES	NATIONAL POLICY AND ALGORITHM INDICATE THE USE OF LATERAL FLOW URINE LIPOARABINOMANNAN ASSAY (LF-LAM) TO ASSIST IN THE DETECTION OF TB IN PEOPLE LIVING WITH HIV
Angola	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	-	<input checked="" type="checkbox"/>	87	0	<input type="checkbox"/>
Azerbaijan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	85	<input checked="" type="checkbox"/>	99	94	<input type="checkbox"/>
Bangladesh	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	26	<input checked="" type="checkbox"/>	29	91	<input type="checkbox"/>
Belarus	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	92	<input checked="" type="checkbox"/>	100	100	<input type="checkbox"/>
Botswana	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	17	<input checked="" type="checkbox"/>	42		<input checked="" type="checkbox"/>
Brazil	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	34	<input checked="" type="checkbox"/>	45		<input type="checkbox"/>
Cambodia	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	-	<input checked="" type="checkbox"/>			<input type="checkbox"/>
Cameroon	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	83	<input type="checkbox"/>	24	50	<input type="checkbox"/>
Central African Rep.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	2.4	<input checked="" type="checkbox"/>	5.7	0	<input checked="" type="checkbox"/>
Chad	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	3.8	<input checked="" type="checkbox"/>	33	0	<input checked="" type="checkbox"/>
China	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	31	<input checked="" type="checkbox"/>	81	32	<input type="checkbox"/>
Congo	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	30	<input checked="" type="checkbox"/>	27	0	<input type="checkbox"/>
DPR Korea	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	-	<input checked="" type="checkbox"/>	7.2		<input type="checkbox"/>
DR Congo	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	2.0	<input checked="" type="checkbox"/>	10	36	<input type="checkbox"/>
Eswatini	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	87	<input checked="" type="checkbox"/>	100	100	<input checked="" type="checkbox"/>
Ethiopia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	36	<input checked="" type="checkbox"/>	39	64	<input type="checkbox"/>
Ghana	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	100	<input checked="" type="checkbox"/>	100	44	<input type="checkbox"/>
Guinea-Bissau	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	-	<input checked="" type="checkbox"/>	1.7	52	<input checked="" type="checkbox"/>
India	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	17	<input checked="" type="checkbox"/>	78	99	<input type="checkbox"/>
Indonesia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	27	<input checked="" type="checkbox"/>	57	29	<input type="checkbox"/>
Kazakhstan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	92	<input checked="" type="checkbox"/>	96	83	<input type="checkbox"/>
Kenya	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	63	<input checked="" type="checkbox"/>	77	40	<input checked="" type="checkbox"/>
Kyrgyzstan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	75	<input checked="" type="checkbox"/>	94	70	<input type="checkbox"/>
Lesotho	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	67	<input checked="" type="checkbox"/>	86	9.6	<input type="checkbox"/>
Liberia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	18	<input checked="" type="checkbox"/>	43	100	<input type="checkbox"/>
Malawi	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	22	<input type="checkbox"/>	44		<input checked="" type="checkbox"/>
Mozambique	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	46	<input checked="" type="checkbox"/>	56	29	<input type="checkbox"/>
Myanmar	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	53	<input checked="" type="checkbox"/>	77	60	<input type="checkbox"/>
Namibia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	47	<input checked="" type="checkbox"/>	64	30	<input checked="" type="checkbox"/>
Nigeria	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	57	<input checked="" type="checkbox"/>	80	100	<input checked="" type="checkbox"/>
Pakistan	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	42	<input checked="" type="checkbox"/>	62	66	<input type="checkbox"/>
Papua New Guinea	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	-	<input checked="" type="checkbox"/>			<input type="checkbox"/>
Peru	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	15	<input checked="" type="checkbox"/>	75	69	<input type="checkbox"/>
Philippines	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	37	<input checked="" type="checkbox"/>	61	21	<input type="checkbox"/>
Republic of Moldova	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	100	<input checked="" type="checkbox"/>	77	100	<input type="checkbox"/>
Russian Federation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	80	<input checked="" type="checkbox"/>	92	96	<input type="checkbox"/>
Sierra Leone	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	9.1	<input checked="" type="checkbox"/>			<input type="checkbox"/>
Somalia	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	27	<input checked="" type="checkbox"/>	57	52	<input type="checkbox"/>
South Africa	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	70	<input checked="" type="checkbox"/>			<input checked="" type="checkbox"/>
Tajikistan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	85	<input checked="" type="checkbox"/>	100	41	<input type="checkbox"/>
Thailand	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	38	<input checked="" type="checkbox"/>	58	76	<input type="checkbox"/>
Uganda	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	49	<input checked="" type="checkbox"/>	94	96	<input checked="" type="checkbox"/>
Ukraine	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	89	<input checked="" type="checkbox"/>	96	100	<input checked="" type="checkbox"/>
UR Tanzania	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	23	<input checked="" type="checkbox"/>	79	84	<input type="checkbox"/>
Uzbekistan	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	74	<input checked="" type="checkbox"/>	100	43	<input type="checkbox"/>
Viet Nam	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	32	<input checked="" type="checkbox"/>	81	78	<input type="checkbox"/>
Zambia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	45	<input checked="" type="checkbox"/>	91	30	<input checked="" type="checkbox"/>
Zimbabwe	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	95	<input checked="" type="checkbox"/>	91	43	<input checked="" type="checkbox"/>

Blank cells indicate data not reported. “-” indicates value that cannot be calculated. WRD, WHO-recommended rapid diagnostic. DST, drug susceptibility testing.

^a The 48 countries shown in the table are the countries that are in one or more of the three WHO lists of high TB, TB/HIV and MDR-TB burden countries (see [Annex 2](#)).

^b 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.

TABLE 5.4

Quality of laboratory services^a, 2019

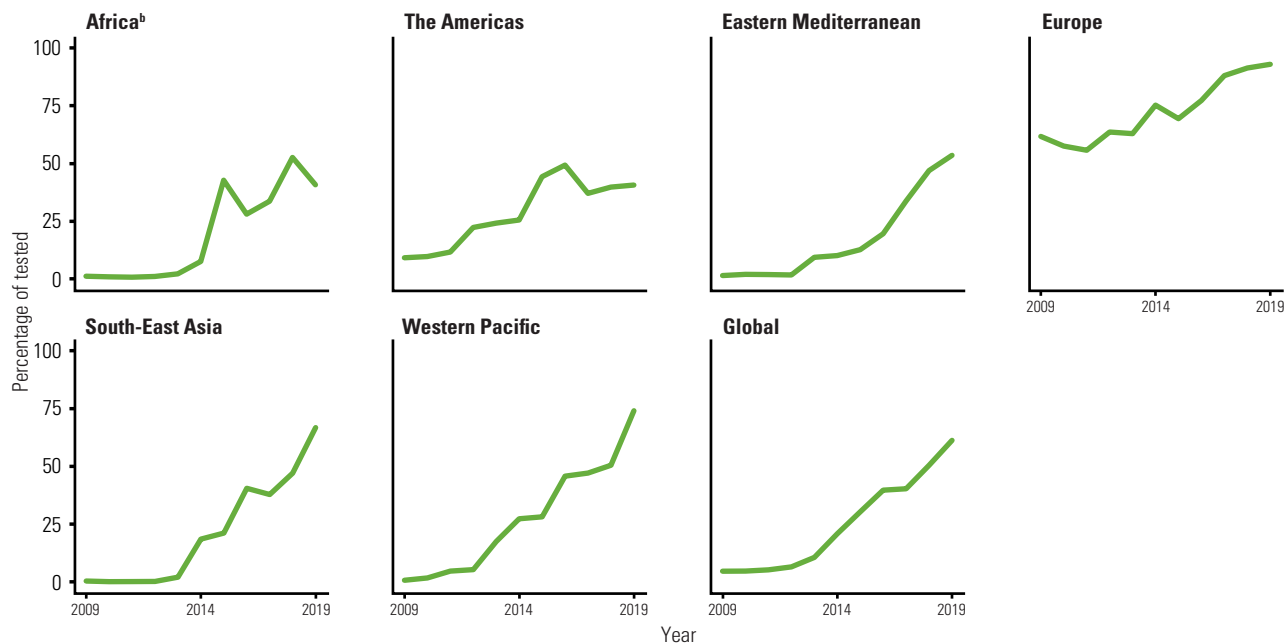
■ YES □ NO	NATIONAL REFERENCE LABORATORY ACCREDITED ACCORDING TO THE ISO 15189 STANDARD	PERCENTAGE OF TESTING SITES COVERED BY A COMPREHENSIVE EQA SYSTEM		PERCENTAGE OF TESTING SITES THAT DEMONSTRATED PROFICIENCY BY PANEL TESTING			
		SMEAR MICROSCOPY	XPRT MTB/RIF	PHENOTYPIC DST FOR FIRST-LINE DRUGS ONLY	PHENOTYPIC DST FOR FIRST-LINE AND SECOND-LINE DRUGS	LPA FOR RIFAMPICIN AND ISONIAZID ONLY	LPA FOR RIFAMPICIN, ISONIAZID, FLUOROQUINOLONES AND SECOND-LINE INJECTABLES
Angola	□	0	0	-	-	-	-
Azerbaijan	□	64	100	100	100	100	100
Bangladesh	□	100	0	0	-	-	100
Belarus	□	91	31	100	100	100	100
Botswana	■	100	100	100	100	100	100
Brazil	■	25	100	69	100	-	100
Cambodia	□	100	9.4	100	100	-	100
Cameroon	■	64	100	-	100	100	100
Central African Rep.	□	52	25	-	100	-	100
Chad	□	100	100	-	-	-	-
China	□	100	73	100	98	86	-
Congo	□	6.5	100	-	-	-	-
DPR Korea	□	100	0	0	0	-	-
DR Congo	□	100	11	-	100	-	100
Eswatini	■	100	100	-	100	-	100
Ethiopia	■	64	95	100	100	-	100
Ghana	□	41	100	20	-	-	0
Guinea-Bissau	□	100	0	0	-	-	0
India	■	100	100	100	100	100	100
Indonesia	■	34	76	-	100	-	0
Kazakhstan	□	99	15	-	100	100	100
Kenya	■	90	100	-	100	-	100
Kyrgyzstan	□	100	0	100	100	100	100
Lesotho	□	100	100	-	100	-	100
Liberia	□	70	100	0	-	-	-
Malawi	□	57	90	50	100	-	-
Mozambique	■	30	41	100	100	-	67
Myanmar	□	91	89	100	100	100	100
Namibia	□	100	94	-	100	-	100
Nigeria	□	72	99	0	33	90	90
Pakistan	□	74	79	67	80	-	80
Papua New Guinea	□	84	-	-	-	-	-
Peru	■	75	0	100	100	100	100
Philippines	■	59	100	-	40	-	0
Republic of Moldova	□	100	100	-	100	-	100
Russian Federation	□	9.6	5.7	-	31	-	-
Sierra Leone	□	20	100	100	-	100	100
Somalia	□	100	82	100	100	-	100
South Africa	■	97	100	100	100	100	100
Tajikistan	□	93	0	100	100	17	17
Thailand	■	90	77	70	100	0	100
Uganda	■	66	95	100	67	-	100
Ukraine	□	96	37	100	100	100	100
UR Tanzania	■	81	7.1	100	100	67	67
Uzbekistan	□	91	94	-	25	-	67
Viet Nam	■	89	100	100	100	-	100
Zambia	□	38	24	-	100	100	100
Zimbabwe	□	89	62	-	50	67	0

Blank cells indicate data not reported. “-” indicates value that cannot be calculated. DST, drug susceptibility testing. EQA, external quality assurance. ISO, International Organization for Standardization; LPA, line probe assay.

^a The 48 countries shown in the table are the countries that are in one or more of the three WHO lists of high TB, TB/HIV and MDR-TB burden countries (see [Annex 2](#)).

FIG. 5.15

Percentage of bacteriologically confirmed TB cases tested for RR-TB,^a globally and for WHO regions, 2009–2019

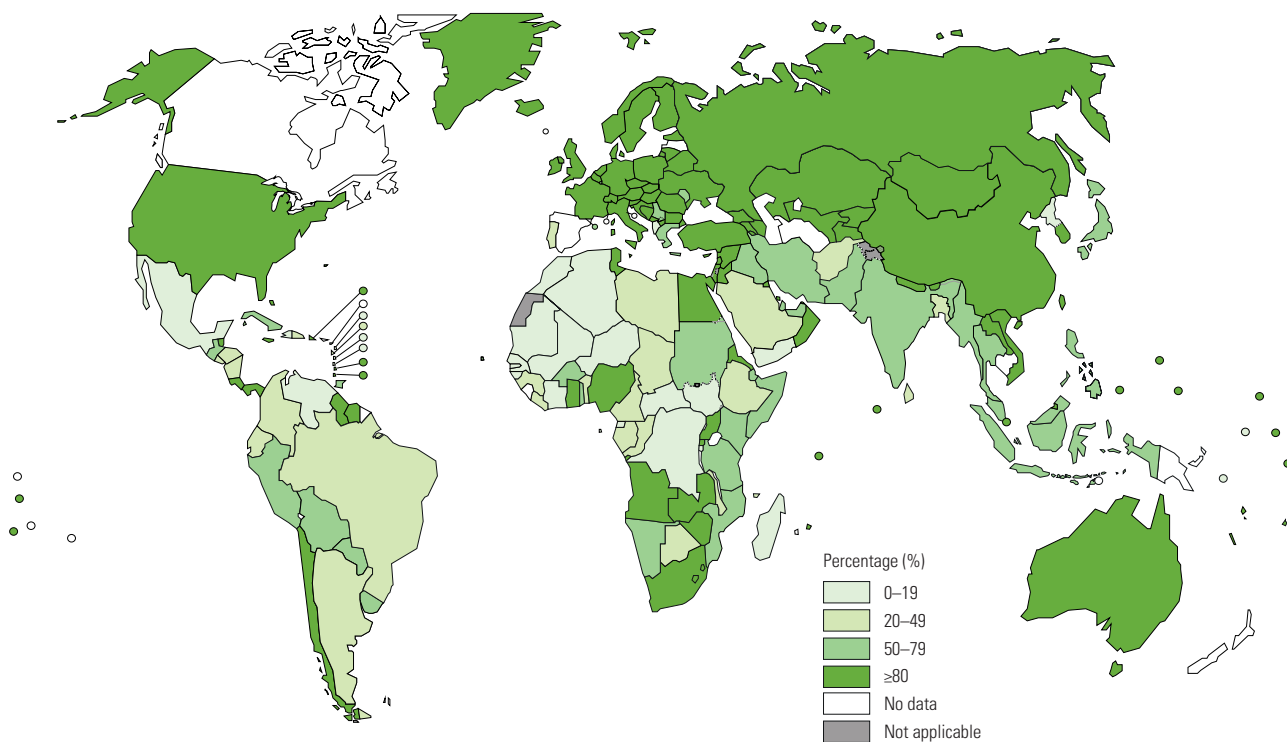


^a Includes both new and previously treated TB cases; data for 2017 onwards are for pulmonary TB cases only.

^b The increase in the African Region from 2014 to 2015 was due to a large increase in reporting of laboratory results for cases in South Africa in 2015.

FIG. 5.16

Percentage of bacteriologically confirmed TB cases tested for RR-TB, 2019^a



^a Includes both new and previously treated cases; data are for pulmonary cases only.

5.1.6 Drug susceptibility testing and detection of drug-resistant TB

Drug-resistant TB threatens global TB care and prevention, and remains a major public health concern in many countries. The three major categories used for global surveillance and treatment of drug-resistant TB are rifampicin-resistant TB (RR-TB), MDR-TB and MDR-TB with additional resistance to fluoroquinolones (Chapter 4). MDR-TB is TB that is resistant to both rifampicin and isoniazid, the two most effective anti-TB drugs.¹ All forms of drug-resistant TB require treatment with a second-line regimen (11). With increasing use of Xpert MTB/RIF for simultaneous detection of TB and resistance to rifampicin, a growing number of RR-TB cases are being detected and notified.

The End TB Strategy calls for universal access to drug susceptibility testing (DST). The focus in this section is on DST for notified TB patients with bacteriologically confirmed TB, who can then be tested for MDR/RR-TB, using diagnostic tests recommended by WHO.

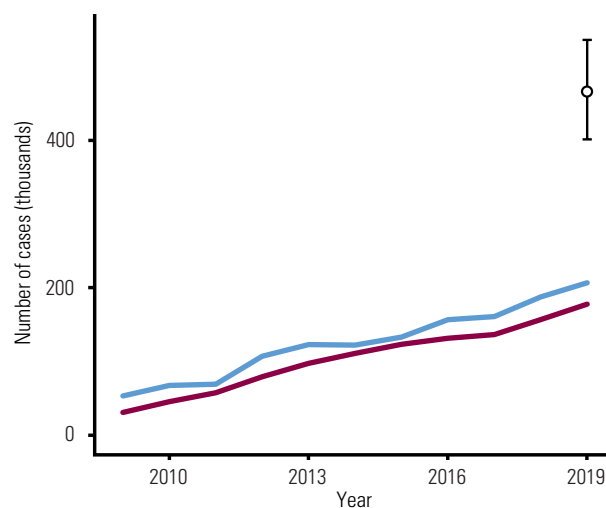
DST for first-line drugs and detection of MDR/RR-TB

There has been considerable progress in increasing the coverage of DST, especially since 2012 (Fig. 5.15).² Globally in 2019, 2.2 million (61%) of the 3.6 million bacteriologically confirmed pulmonary TB cases notified globally were tested for rifampicin resistance, up from 1.7 million (51%) in 2018 and 0.2 million (7%) in 2012. In 2019, coverage was 59% for new and 80% for previously treated TB patients. DST coverage increased in five of the six WHO regions between 2018 and 2019 (the exception was the African Region). The biggest increase was in the WHO Western Pacific Region (50% to 75%). Coverage ranged from 41% in the WHO Region of the Americas and the African Region, to 93% in the European Region. DST coverage varied substantially among countries (even within the same region) (Fig. 5.16).

Globally, 206 030 cases of MDR/RR-TB were detected and notified in 2019, representing a 10% increase from 186 883 in 2018 (Table 5.1, Fig. 5.17). High MDR-TB burden countries that made particularly good progress in increasing detection and enrolment of MDR/RR-TB cases on treatment included Angola, China, India, Indonesia, Mozambique, Nigeria, Papua New Guinea and the Philippines (Fig. 5.18).

FIG. 5.17

Global number of MDR/RR-TB cases detected (blue) and number enrolled on MDR-TB treatment (maroon), 2009–2019, compared with the estimate for 2019 of the number of incident cases of MDR/RR-TB (uncertainty interval shown in black)



The global number of MDR/RR-TB cases notified in 2019 was 44% of the estimated 465 000 MDR/RR-TB incident cases in 2019 (Fig. 5.17; incidence estimates are discussed in more detail in Chapter 4). Closing this large detection gap will require improvements in overall TB detection (Section 5.2.1), the percentage of TB cases with bacteriological confirmation (Section 5.1.3) and coverage of diagnostic DST (Box 4.3). Alongside other factors (discussed in Section 5.2), these require further strengthening of laboratory capacity and wider uptake of WHO-recommended rapid diagnostic tests.

DST for second-line drugs

Globally, among MDR/RR-TB patients notified in 2019, 71% were tested for resistance to fluoroquinolones, a considerable increase from 65% in 2018 (Fig. 5.19). Coverage varied widely among regions (Fig. 5.20).

¹ Surveillance and survey data show that about 78% of RR-TB cases have MDR-TB (Chapter 4).

² The time-series starts in 2009 because this was the year in which WHO intensified efforts to track progress in the programmatic response to drug-resistant TB. This followed a ministerial conference for high MDR-TB burden countries, held in Beijing, China, in April 2009; a World Health Assembly resolution was adopted the following month (12).

FIG. 5.18

Number of MDR/RR-TB cases detected (blue) and enrolled on MDR-TB treatment (maroon) in the 30 high MDR/RR-TB burden countries, 2009–2019

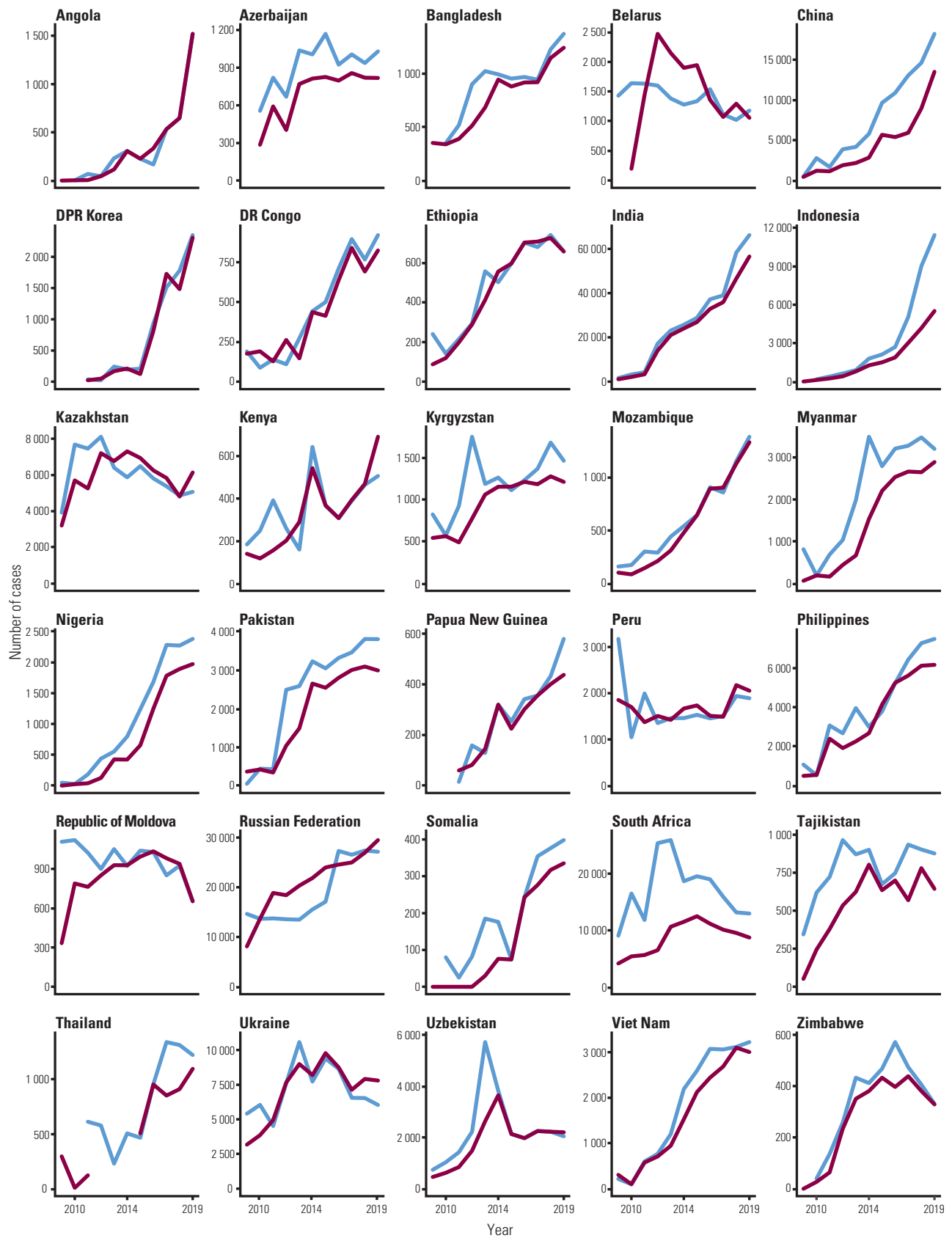


FIG. 5.19

Percentage of MDR/RR-TB cases tested for susceptibility to fluoroquinolones, 2019

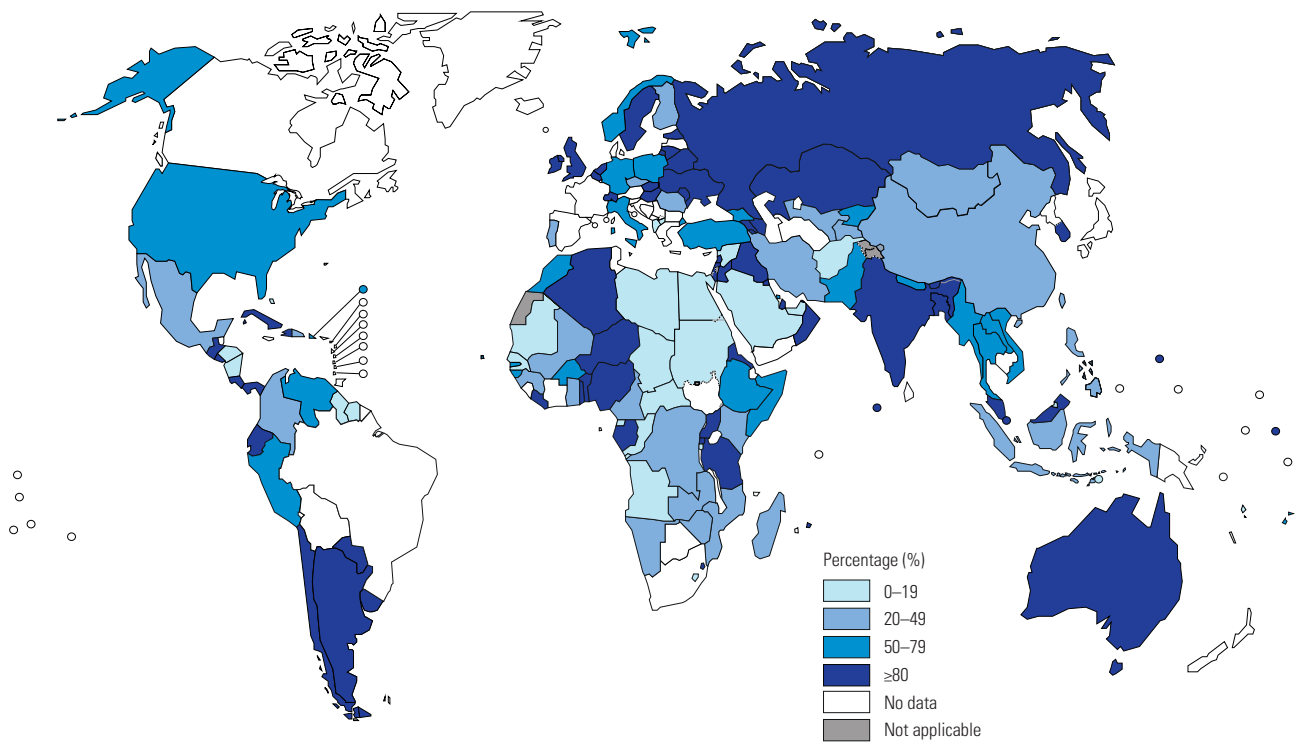
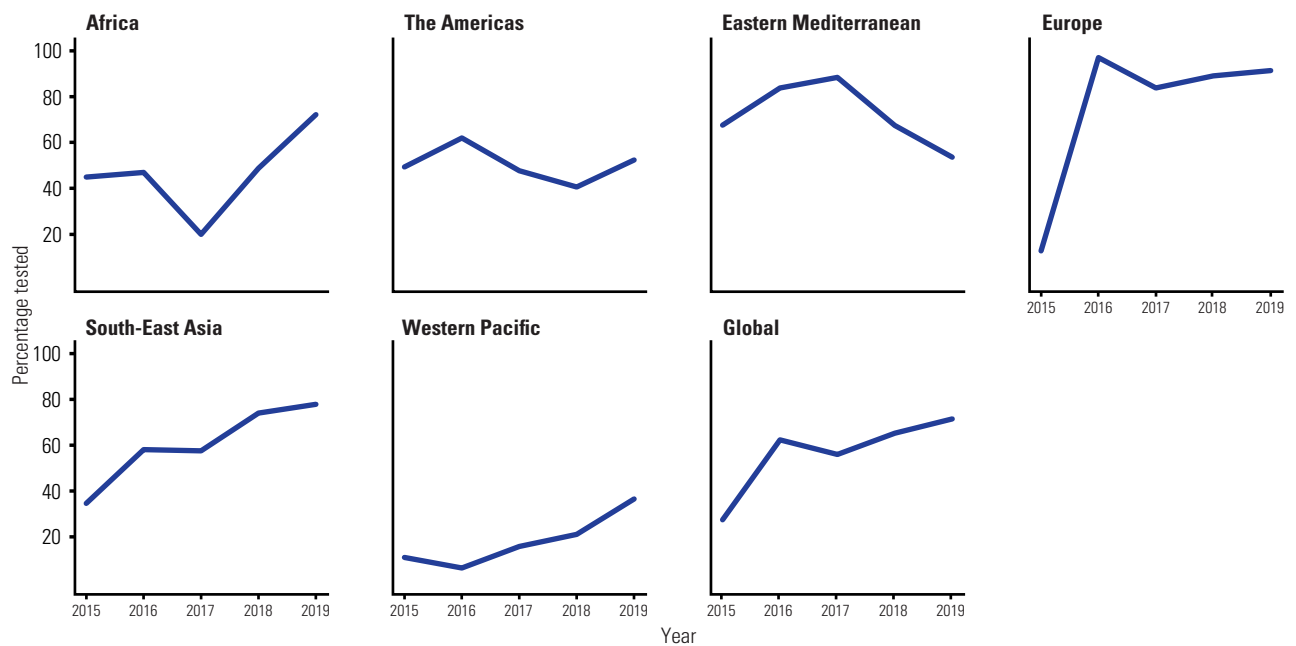


FIG. 5.20

Percentage of MDR/RR-TB cases tested for susceptibility to fluoroquinolones,^a globally and for WHO regions, 2015–2019



^a Testing in years prior to 2019 also included susceptibility to second-line injectables.

5.1.7 Digital, case-based surveillance for TB

Globally, a growing number of countries are capturing data for notified TB cases in digital case-based surveillance systems. These systems have several advantages compared with more traditional paper-based reporting of aggregated data, including more timely access to data (up to “real time”) and the availability of data for individual patients at the level of health facilities up to national level. They also greatly facilitate data analysis (including by age, sex and location) to inform adaptation and targeting of response efforts, both geographically and for specific population groups. WHO has promoted case-based digital surveillance for TB for several years, following guidance issued in 2012 (13).

As of August 2020, data on the type of TB surveillance system in place at national level were available for 211 countries (Fig. 5.21). Of these, 136 had a case-based digital surveillance system that covered all TB cases (both drug-susceptible and drug-resistant TB). These countries accounted for 72% of global TB notifications in 2019.

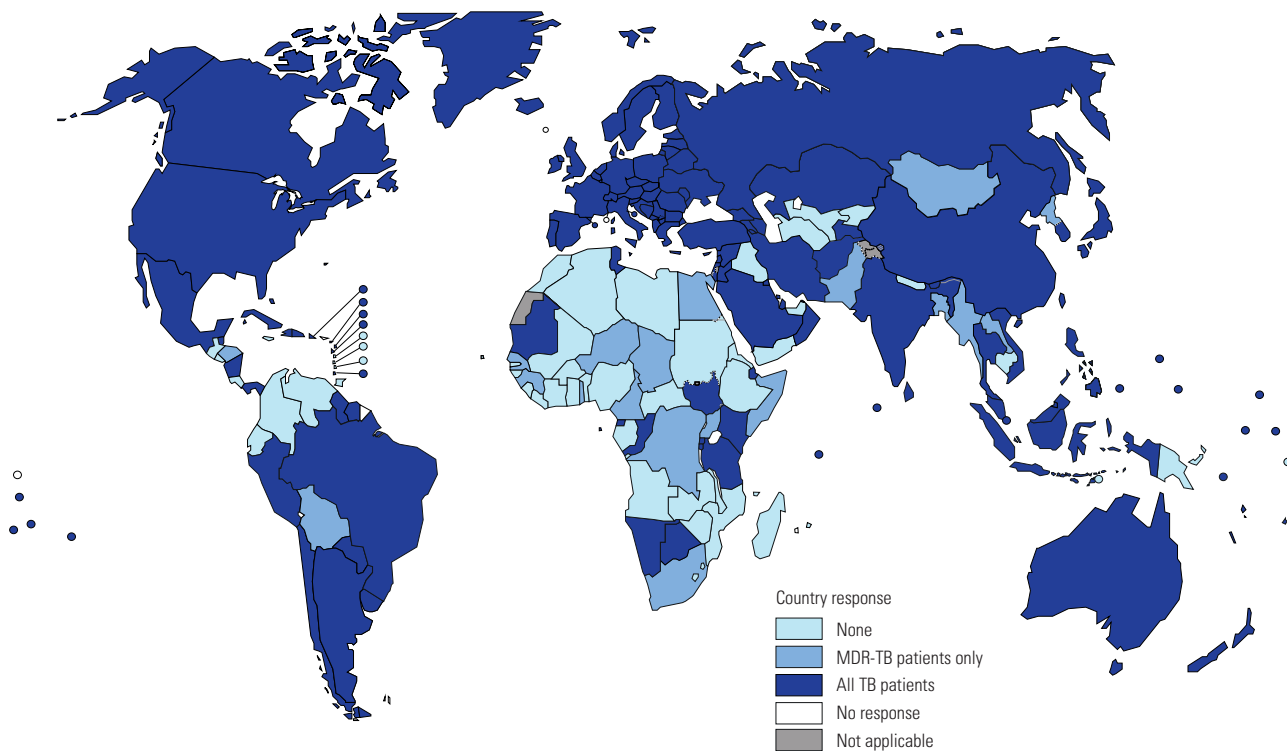
A further 18 countries, mainly in the WHO African and South-East Asia regions, had a case-based surveillance system for all cases of drug-resistant TB. These countries are in a transition phase between aggregate paper-based reporting and case-based digital surveillance. The initial prioritization of MDR-TB is explained by the additional complexity of monitoring treatment and treatment outcomes compared with drug-susceptible TB, which is much easier to manage with case-based surveillance; and by the fact that often the numbers of treatment centres and laboratories that need to be involved are smaller, making introduction more feasible from a logistics perspective.

About half of the countries in the WHO African Region still have paper-based systems for recording and reporting of data.

Global guidance and tools to support the adoption of case-based surveillance for TB are profiled in Box 5.4.

FIG. 5.21

Countries with national case-based digital surveillance systems for TB, 2019



Global guidance and tools for strengthening routine country health information systems and the analysis and use of data they produce

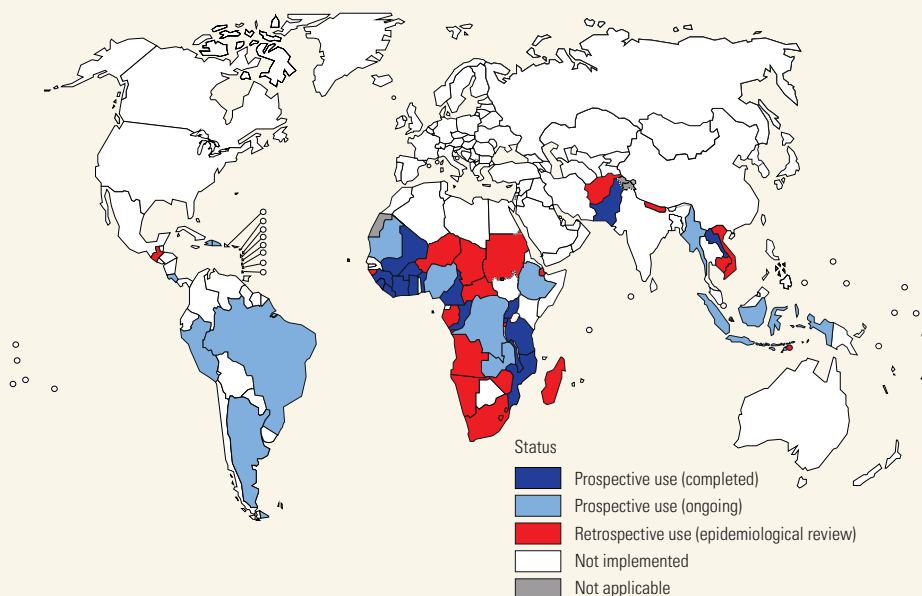
WHO's Global TB Programme has been working with other WHO departments, the University of Oslo and the Global Fund to develop and implement packages for analysis and use of data collected through routine health facility information systems.^a In doing so, it has built on the WHO guidance for the establishment of case-based digital TB surveillance issued in 2012,^b as well as guidance on the routine analysis and use of TB data^c and the WHO TB surveillance checklist of standards and benchmarks.^d

The packages are based on WHO data standards and have been developed in the DHIS2 software,^e but can easily be adapted for use with different software. Each package contains a facility analysis guide with a core set of indicators and dashboards, an accompanying exercise book and machine-readable DHIS2 configuration.

A TB-specific package for the digital management of data in aggregated format^f has been available since early 2019, for use by countries that are not yet ready to transition to case-based digital surveillance. The TB package for case-based data, which enables digital management of data for both drug-susceptible and drug-resistant TB in one system, is now available for download as a digital data configuration package in both English and French.^g Both TB packages are based on the WHO recording and reporting framework,^h and both allow extensive data analysis at different levels of the health system (e.g. health facility and subnational administrative area). The standard dashboards include graphs, tables and maps for core surveillance indicators (e.g. notifications, coverage of testing for drug resistance and HIV, and treatment outcomes) and data quality indicators (e.g. completeness and internal consistency).

FIG. B5.4.1

DHIS2 TB package for aggregated data (status of implementation as of August 2020)



The TB-specific package for aggregated data has been implemented in countries for prospective use, either to compile quarterly reports at the health facility or subnational level, or to analyse data from these reports through standardized dashboards (depending on country needs). It has also been implemented for retrospective use, by uploading historical data (e.g. as part of a national TB epidemiological review). As of August 2020, 52 countries have used the TB package for aggregate data: a total of 18 countries had implemented the package for prospective use; an additional 12 countries were in the process of doing so; and, during the period 2018–2020, an additional 22 countries had used it to facilitate analysis and use of data in the context of a national TB epidemiological review (Fig. B5.4.1).

^a Analysis and use of health facility data [website]. Geneva: World Health Organization; 2019 (https://www.who.int/healthinfo/tools_data_analysis_routine_facility/en/, accessed 18 August 2020). (14)

^b Electronic recording and reporting for tuberculosis care and control. Geneva: World Health Organization; 2012 (https://www.who.int/tb/publications/electronic_recording_reporting/en/, accessed 18 August 2020). (13)

^c Understanding and using tuberculosis data. Geneva: World Health Organization Global Task Force on TB Impact Measurement; 2014 (https://www.who.int/tb/publications/understanding_and_using_tb_data/en/, accessed 20 July 2020). (15)

^d Standards and benchmarks for tuberculosis surveillance and vital registration systems: checklist and user guide. Geneva: World Health Organization; 2014 (<https://www.who.int/tb/publications/standardsandbenchmarks/en/>, accessed 18 August 2020). (16)

^e DHIS2 was chosen because many countries already use this software within their health information systems. It is an open-source software with no licence fees, supported by a wide range of international technical and funding partners.

^f A full demonstration is available at <https://tbhistoric.org/>.

^g WHO cross-cutting and disease-specific digital data configuration packages in DHIS2 are available at <https://www.dhis2.org/who-package-downloads>.

^h Definitions and reporting framework for tuberculosis – 2013 revision (updated December 2014) (WHO/HTM/TB/2013.2). Geneva: World Health Organization; 2013 (https://apps.who.int/iris/bitstream/handle/10665/79199/9789241505345_eng.pdf;jsessionid=FD522CF3B90C25716F96288BFDEA6C75?sequence=1, accessed 18 August 2020). (17)

5.2 Treatment coverage

The Sustainable Development Goals (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”. 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, priority indicators for monitoring progress in implementing the End TB Strategy include both TB treatment coverage and the percentage of TB patients and their households that face catastrophic costs as a result of TB disease.¹

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 2019 are used as the numerator for the indicator, because these are the data 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 be started on treatment.

Antiretroviral therapy (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.

5.2.1 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. 5.22](#). Estimates of TB treatment coverage in 2019 are shown globally, for WHO regions and the 30 high TB burden countries, in [Fig. 5.23](#).

Globally, TB treatment coverage was 71% (range, 64–79%)² in 2019, up from 59% (range, 52–67%) in 2015, 53% (range, 46–64%) in 2010 and 35% (range, 30–43%) in 2000. Four WHO regions achieved levels above 75%: the Americas, Europe, South-East Asia and Western Pacific. High TB burden countries with the highest levels of treatment coverage in 2019 (>80%) included Brazil, China, the Russian Federation and Thailand.³ The lowest levels, with best estimates of 50% or less, were in the Central African Republic and Nigeria.

¹ The latter is discussed in detail in [Chapter 8](#).

² Range refers to the 95% uncertainty interval.

³ The estimated level of treatment coverage in Mozambique is higher than that published in previous years. This follows a substantial downward revision in the estimated level of TB incidence, following results from the 2018–2019 national TB prevalence survey ([Chapter 4](#)). It is possible that there is some overdiagnosis of cases that is inflating the numerator used in the estimation of treatment coverage. The percentage of pulmonary cases with bacteriological confirmation has fallen from 77% in 2000 to 37% in 2019.

Globally in 2019, there was a gap of about 2.9 million cases between the 7.1 million new and relapse cases that were notified, and the estimated 10.0 million (range, 8.9–11.0 million) incident TB cases in that year ([Fig. 5.1](#)). The global gap has been narrowing since 2013, especially in the WHO South-East Asia and Western Pacific regions, and to a lesser extent in the Eastern Mediterranean Region ([Fig. 5.1](#)). Ten countries account for almost 70% of the total estimated global gap between incidence and notifications ([Fig. 5.24](#)), with India (17%), Nigeria (11%), Indonesia (10%), Pakistan (8%) and the Philippines (7%) accounting for more than half the global total. Despite India accounting for the single largest gap, the country has made substantial progress, as evidenced by a considerable closing of the gap between notifications and incidence since 2013 ([Fig. 5.22](#)).

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

- ▶ **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.
- ▶ **underdiagnosis of people with TB** – underdiagnosis can occur for reasons such as poor geographical and financial access to health care; delays in seeking health care because of lack of symptoms or symptoms not being perceived as TB-specific; failure to test for TB when people do present to health facilities; and diagnostic tests that are not sufficiently sensitive or specific to ensure accurate identification of all people with TB.

It is also possible that the gap could be underestimated due to overdiagnosis, especially in settings where a relatively low proportion of TB cases are bacteriologically confirmed.

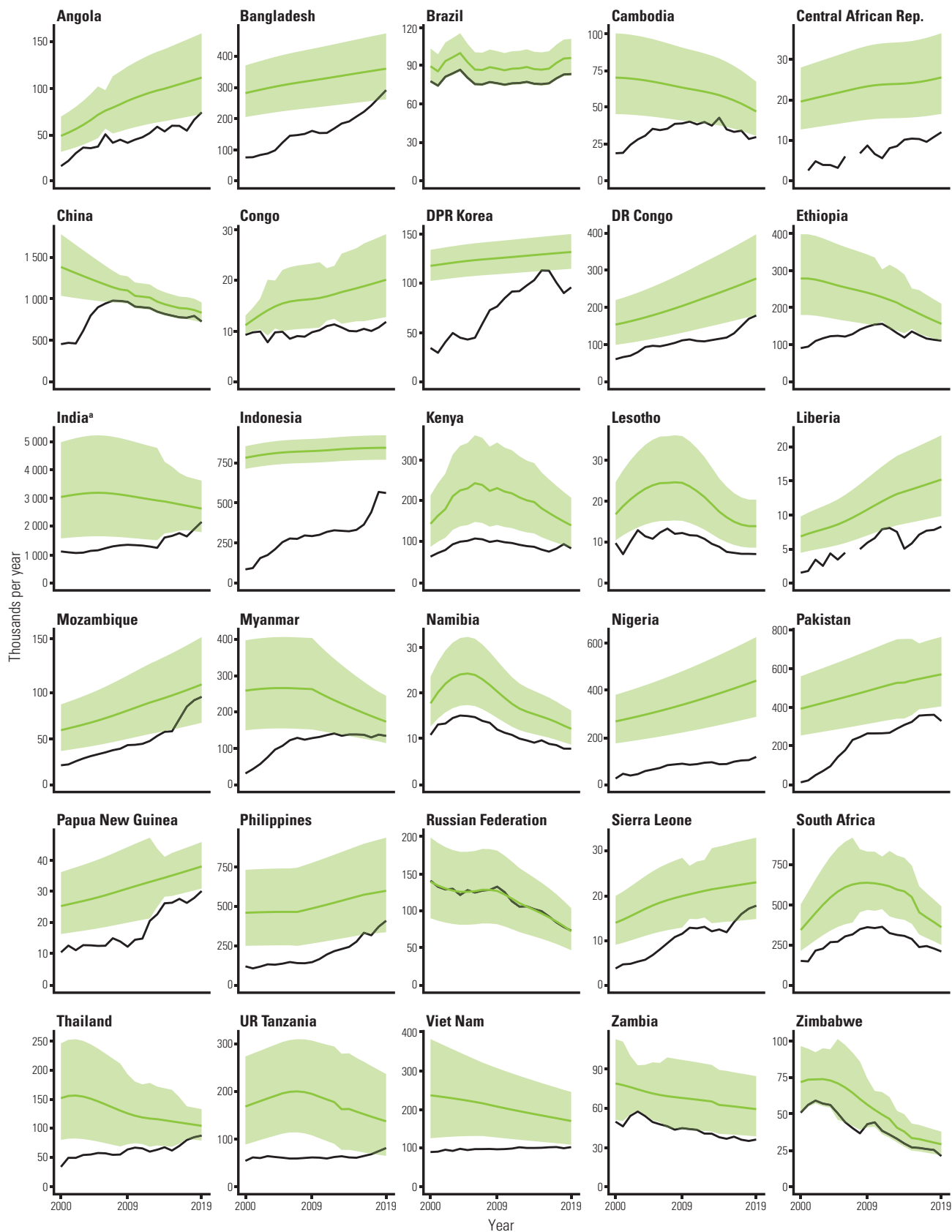
Some of the countries with the largest estimated gaps between notifications and TB incidence already possess good evidence about the reasons for such gaps, and are either taking or planning action to address them. As highlighted in [Section 5.1.1](#), two excellent examples are India and Indonesia, where studies that showed high levels of underreporting of detected TB cases have been followed by actions such as the introduction of policies on mandatory notification, intensified engagement with care providers not yet reporting to national authorities, establishment of data linkages between existing national databases of TB cases, and the development and implementation of digital systems to facilitate and simplify the reporting of cases. These actions have been followed by marked increases in notifications ([Fig. 5.2](#)).

One source of evidence about underreporting in India and Indonesia was a national inventory study, in which digital lists of notified cases are compared with digital lists of TB cases detected by all care providers

FIG. 5.22

Case notification numbers (new and relapse cases, all forms) (black) compared with estimated TB incidence numbers (green) in the 30 high TB burden countries, 2000–2019

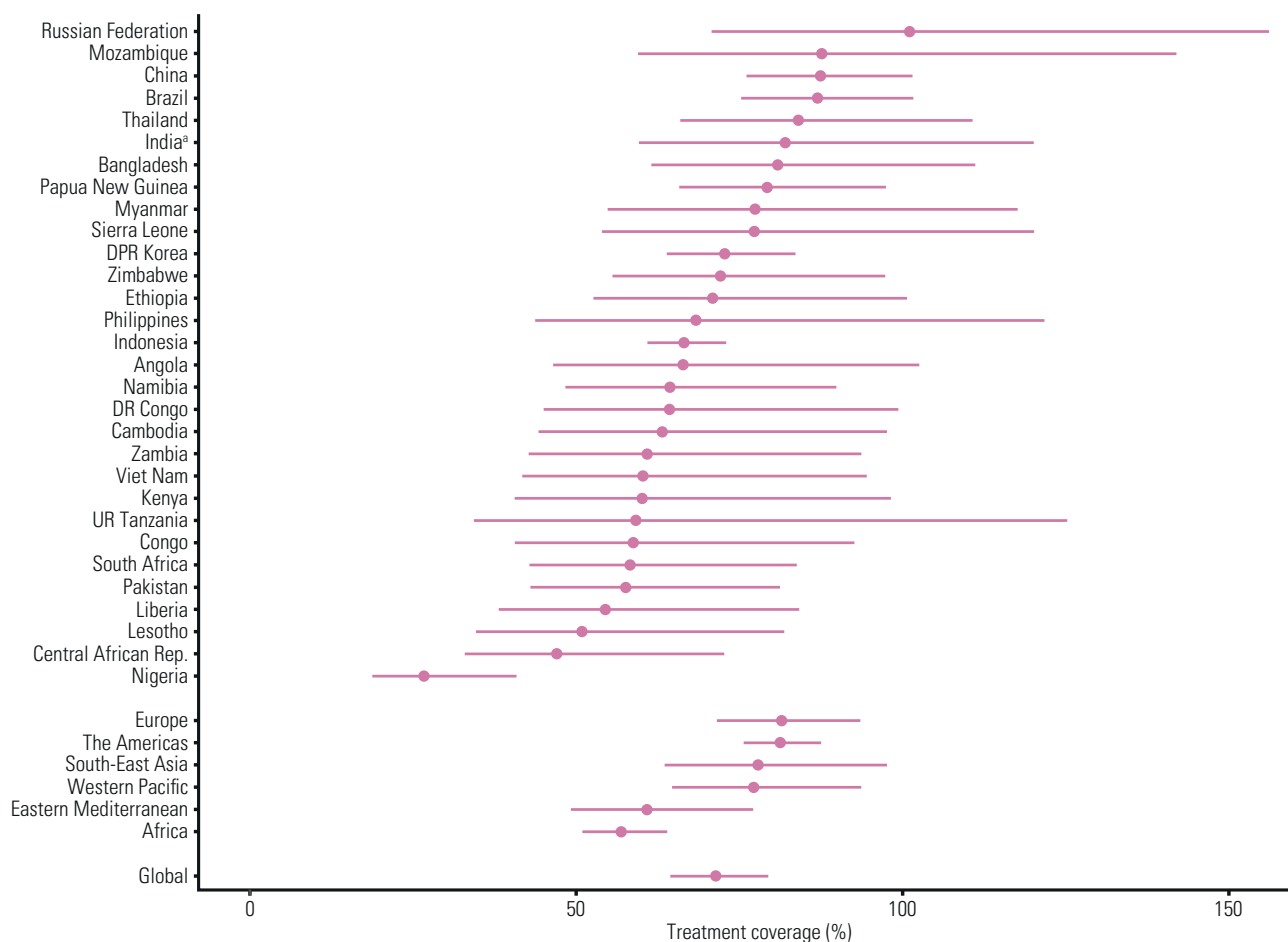
Shaded areas represent uncertainty intervals.



* Estimates of TB incidence for India are interim, pending results from the national TB prevalence survey (2020/2021).

FIG. 5.23

Estimated TB treatment coverage (new and relapse patients as a percentage of estimated TB incidence) in the 30 high TB burden countries, WHO regions and globally, 2019



^a Estimates of TB incidence for India are interim, pending results from the national TB prevalence survey (2020/2021).

(ideally employing unique identifiers).¹ Other high TB burden countries that have implemented an inventory study are China, Kenya, Pakistan and Viet Nam.² In 2020, studies were started in South Africa and the United Republic of Tanzania, and designed in the Philippines (where implementation is scheduled for 2021; the study was postponed from 2020 to 2021 owing to the COVID-19 pandemic).

A clear example of a country where underdiagnosis is a major challenge is Nigeria. The 2012 national TB prevalence survey found that 75% of the people with smear-positive pulmonary TB who were detected had symptoms that met national screening criteria but had not been previously diagnosed. This demonstrated a need to strengthen access to high-quality screening, diagnostic and treatment services. National TB prevalence surveys in many countries in Africa and Asia have also shown that detection and reporting gaps are systematically higher for men than for women (19), suggesting that specific efforts

are needed to improve access to TB diagnosis and treatment for men.³

Systematic screening for active TB among specific populations can help to ensure early diagnosis and reduce levels of underdiagnosis. WHO recommends such screening for contacts of bacteriologically confirmed cases, people living with HIV, people with diabetes and people exposed to silica dust (20).⁴ Other individuals at risk should be considered for systematic screening based on an assessment of TB epidemiology in each setting. To date, in countries that are introducing or scaling up systematic screening, there have been few assessments of its implementation or outcomes. However, this is expected to become a more prominent part of national programme monitoring and evaluation efforts in future. Engaging communities can also help to improve case detection and patient support (Box 5.5).

¹ For a guide to inventory studies, see WHO (2012) (18). When this type of study is done prospectively (as opposed to retrospectively, using 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.

² Results from these studies have been used to inform estimates of TB incidence.

³ Results from 33 national surveys in 30 countries completed in 2007–2019 are featured in Chapter 4.

⁴ The data requested as part of WHO’s global monitoring focus on screening among people living with HIV and close contacts. Hence, the data requested in WHO’s annual round of global TB data collection also focus on screening among people living with HIV and close contacts. These data are presented in Chapter 6. Updated WHO guidance on systematic screening for active TB will be available in 2021.

FIG. 5.24

The ten countries with the largest gaps between notifications of new and relapse (incident) TB cases and the best estimates of TB incidence, 2019^a



^a The ten countries ranked in order of the size of the gap between notified cases and best estimates of TB incidence in 2019 are India, Nigeria, Indonesia, Pakistan, Philippines, South Africa, China, DR Congo, Bangladesh and Viet Nam. Estimates of TB incidence for India are interim, pending results from the national TB prevalence survey (2020/2021).

BOX 5.5

Community contributions to TB notifications and treatment support

WHO's End TB Strategy calls for close collaboration between NTPs, communities or people affected by TB and civil society organizations in the planning and implementation of programmatic activities, and of monitoring and evaluation.

Community-based TB activities can contribute to prevention, diagnosis, treatment and care, and can positively influence the quality and outcome of health services. They are delivered primarily by community health workers (CHWs) and community volunteers (CVs)^a who are drawn from within the community, and thus are both accessible and acceptable to community members.

In the context of the SDGs and UHC, primary health care is receiving greater attention. A growing number of countries are taking steps to absorb cadres of CHWs into the workforce of national health systems. WHO guidelines promote the establishment of CHW programmes as an integral part of primary health care.^b Harnessing the full potential of CHWs can remove barriers to care and promote equitable access to health services at the community level.

In the context of the COVID-19 pandemic, country health systems are facing additional strains that affect the delivery of essential TB services. This has contributed to a sharpened focus on the engagement of civil society and communities affected by TB, to mitigate the effects of the pandemic on the TB response.^c

^a CHWs and CVs are defined in WHO guidance. See: 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: World Health Organization; 2012 (https://www.who.int/tb/publications/2012/engage_tb_policy/en/, accessed 18 August 2020). (21)

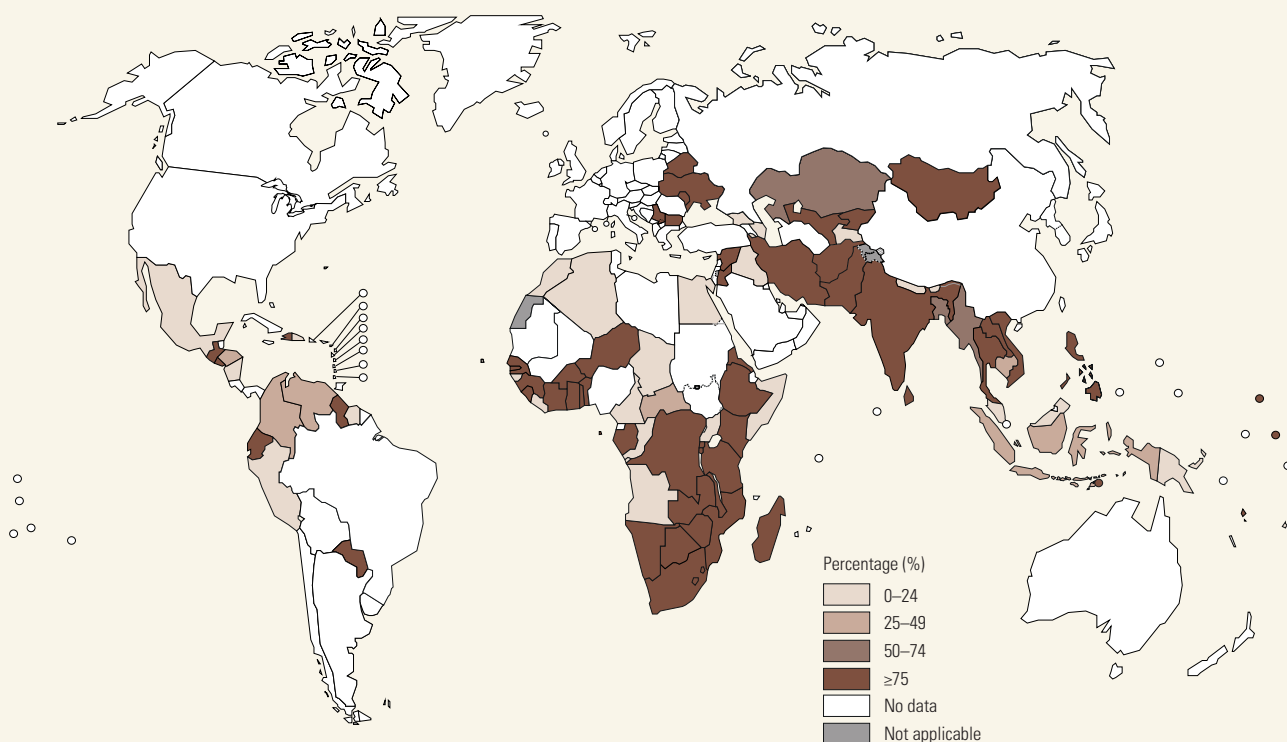
^b WHO guideline on health policy and system support to optimize community health worker programmes. Geneva: World Health Organization; 2018 (<https://www.who.int/hrh/resources/health-policy-system-support-hw-programmes/en/>, accessed 18 August 2020). (22)

^c Community-based health care, including outreach and campaigns, in the context of the COVID-19 pandemic: interim guidance. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/community-based-health-care-including-outreach-and-campaigns-in-the-context-of-the-covid-19-pandemic>, accessed 27 July 2020). (23)

BOX 5.5

FIG. B5.5.1

Percentage of basic management units in which there was community contribution to new case finding and/or to treatment adherence support, 2019^a



^a Data only requested from 101 countries.

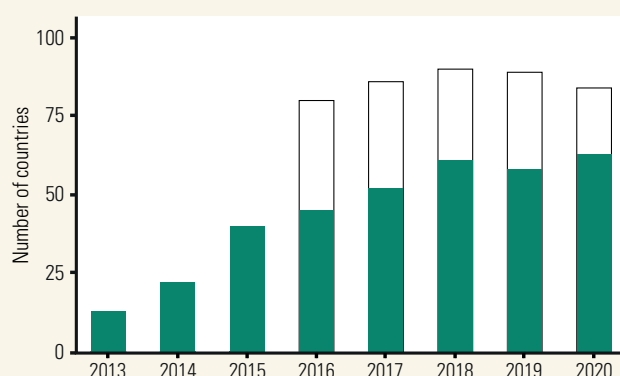
Out of the 101 countries that were asked to report 2019 data on community contributions to TB care, 84 (83%) countries reported implementing community-based TB activities (down from 89 in 2018), on average, in 78% of their TB basic management units (Fig. B5.5.1, Fig. B5.5.2). Reasons for the reduction in the number of countries reporting implementation have not yet been systematically analysed, but one explanation may be reduced national capacity to analyse and report data in settings where TB staff have been deployed to assist with the response to the COVID-19 pandemic.

Of the 84 countries, 62 (up from 58 in 2019) reported detailed data on the contribution of communities, through CHWs or CVs, to TB case notifications or TB treatment outcomes. This represents an almost fivefold increase in reporting since 2013, when data were first collected on these two core indicators for monitoring community contributions to TB detection and treatment.

The contribution of community referrals to TB case notifications in 2019 was reported by 61 countries and averaged 27%. Treatment success rates for people who benefited from any form of community treatment support were reported by 43 countries (up from 36 the previous year) and averaged 81%.

FIG. B5.5.2

Number of countries reporting implementing any community-based activity in line with WHO community indicators^a (black line) and countries reporting on these indicators (green), 2013–2020



^a Data have been collected since 2016.

5.2.2 Treatment coverage of ART for HIV-positive TB cases

WHO recommends ART for all HIV-positive TB patients as soon as possible, but within the first 8 weeks of starting TB treatment, and within 2 weeks of starting treatment in profoundly immunosuppressed HIV-positive TB patients with CD4 counts of less than 50. The number of notified HIV-positive TB patients on ART reached 398 719 in 2019, equivalent to 88% of the notified TB patients known to be HIV-positive (Fig. 5.13).¹ In the 30 high TB/HIV burden countries, overall, 89% of the TB patients known to be HIV-positive were on ART; 12 countries (Botswana, Cameroon, Eswatini, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Uganda, the United Republic of Tanzania and Zambia) maintained coverage of at least 90% in the three years 2017–2019. Coverage in India was 95% in 2019, demonstrating what can be achieved in the context of a concentrated HIV epidemic; contributory factors include the strategic decentralization of services, and provision of HIV and TB services in the same health facilities. In contrast, coverage was less than 50% in two other high TB/HIV burden countries with concentrated epidemics: Brazil and Indonesia.

Coverage of ART for all HIV-positive people with TB is shown in Fig. 5.25 and Fig. 5.26. Globally in 2019, the number of HIV-positive TB patients on ART was 49% of the estimated global number of incident TB cases among people living with HIV; this is considerably lower than the global ART coverage of 67% among all people living with HIV in 2019 (24). Among the high TB/HIV burden countries, best estimates of coverage varied widely, from 7% in Congo to 83% in Mozambique. Only 14 of the 30 countries achieved ART coverage among TB patients of more than 50% (Eswatini, Ethiopia, India, Kenya, Malawi, Mozambique, Myanmar, Namibia, Papua New Guinea, Thailand, Uganda, the United Republic of Tanzania, Zambia and Zimbabwe).

Improvements are still needed in the detection of active TB disease among people living with HIV, coverage of HIV testing among TB patients and 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 6.

5.2.3 Treatment coverage for MDR/RR-TB

Trends in the number of patients enrolled on MDR-TB treatment globally and in the 30 high MDR-TB countries since 2009 are shown in Fig. 5.17 and Fig. 5.18, respectively. The number of people enrolled on treatment globally was 177 099 in 2019, up from 156 205 in 2018 and almost a sixfold increase from 30 500 in 2009 (when WHO first asked countries to report data). Despite these improvements, the total number of people treated in 2018–2019,

at 333 304, was only 22% of the way towards the 5-year (2018–2022) global target of 1.5 million that was set at the UN high-level meeting on TB. For children, the total was 8986, less than 10% of the 5-year target of 115 000 (Table 5.3.1). The number of enrolments also fell in 11 high MDR-TB burden countries (Fig. 5.18).

The number of people starting MDR-TB treatment in 2019 was equivalent to 86% of the 206 030 people reported to have been diagnosed with MDR/RR-TB in 2019 (Fig. 5.17). The figure exceeded 90% in 14 high MDR-TB burden countries (Fig. 5.18), including several in the WHO European Region; however, it was lower in many countries of the African and Western Pacific regions.² These percentages show that progress in detection is outstripping the capacity to provide treatment; they may also reflect weaknesses in data collection systems. In many countries, one of the barriers to adequate access to treatment of drug-resistant TB may be that the network for the programmatic management of drug-resistant TB is too centralized and too reliant on hospital-based models of care. Greater decentralization of services and expansion of ambulatory models of care are needed.

Globally, the 177 099 patients starting second-line MDR-TB treatment in 2019 represented 38% of the estimated 465 000 (range, 400 000–535 000)³ incident cases of MDR/RR-TB in 2019 (Fig. 5.17). Estimates of treatment coverage in the 30 high TB burden countries and WHO regions varied widely (Fig. 5.27).

Ten countries accounted for 77% of the global gap between the estimated global incidence of MDR/RR-TB and the number of people enrolled on treatment in 2019 (Fig. 5.28). Substantial improvements in treatment coverage at the global level require an intensification of efforts to diagnose and treat MDR/RR-TB in these countries, particularly in China and India.⁴ Closing the gap between incidence and treatment enrolment requires one or more of the following to be increased: the proportion of people with TB who are detected and, of these, the proportion for whom TB is bacteriologically confirmed; the proportion of people with bacteriologically confirmed TB who are tested for drug resistance; and the proportion of people diagnosed with MDR/RR-TB who are enrolled in treatment.

Globally, 12 960 patients with MDR-TB and resistance to fluoroquinolones were enrolled on treatment in 80 countries and territories – a 13% increase compared with 2018. In 25 of these countries, the number of people with such resistance patterns enrolled on treatment was less than the number notified.

¹ There may be discrepancies in data on provision of ART to HIV-positive TB patients as reported by NTPs and national HIV programmes. These discrepancies have reduced in recent years and have mostly been resolved through follow-up and validation efforts.

² Data for WHO regions are available online and in the Global TB Report mobile app (Annex 1, Annex 3).

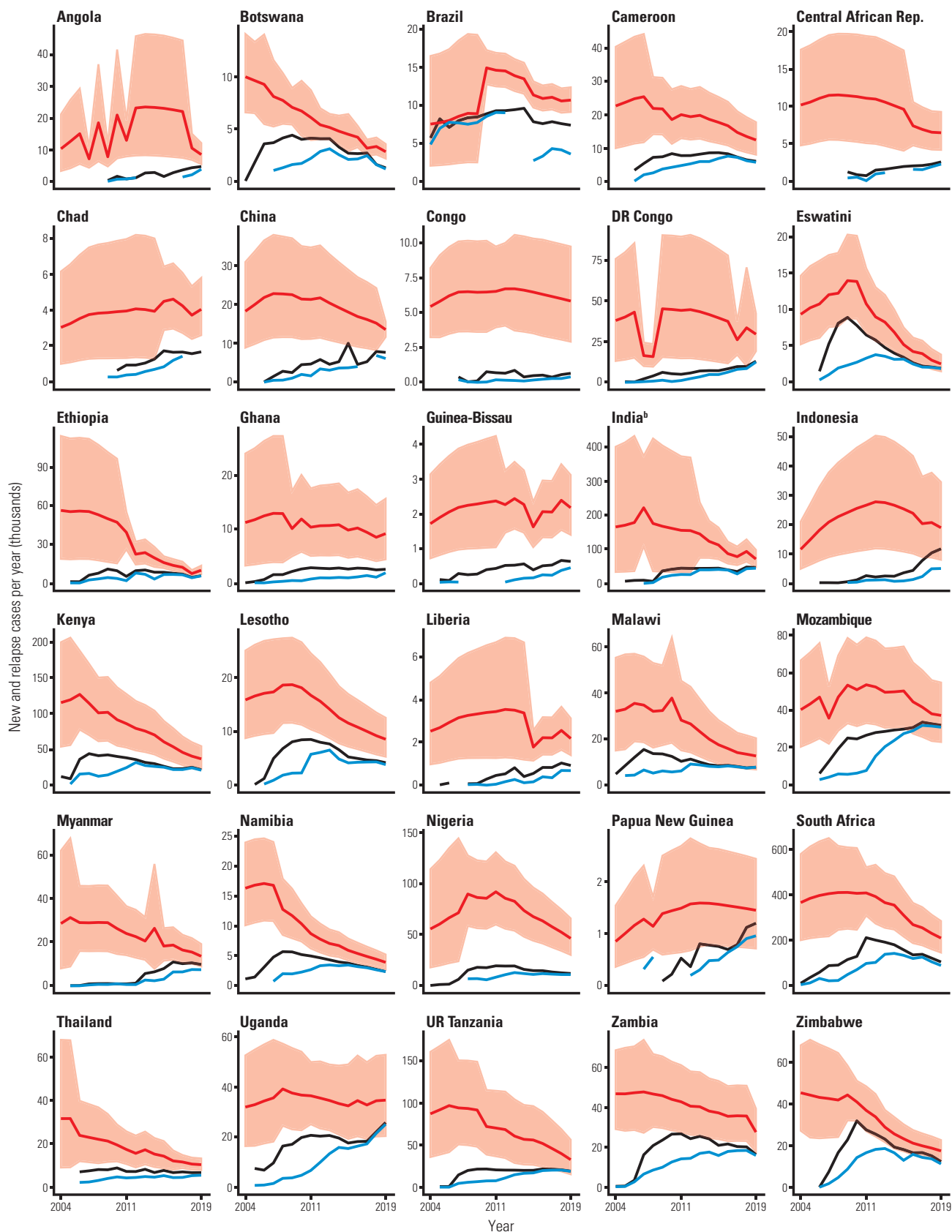
³ Range refers to the 95% uncertainty interval.

⁴ In combination, China and India accounted for 41% of the global gap in 2019.

FIG. 5.25

Number of new and relapse cases^a known to be HIV-positive (black) and number started on ART (blue) compared with the estimated number of incident HIV-positive TB cases (red) in the 30 high TB/HIV burden countries, 2004–2019

Shaded areas represent uncertainty intervals.

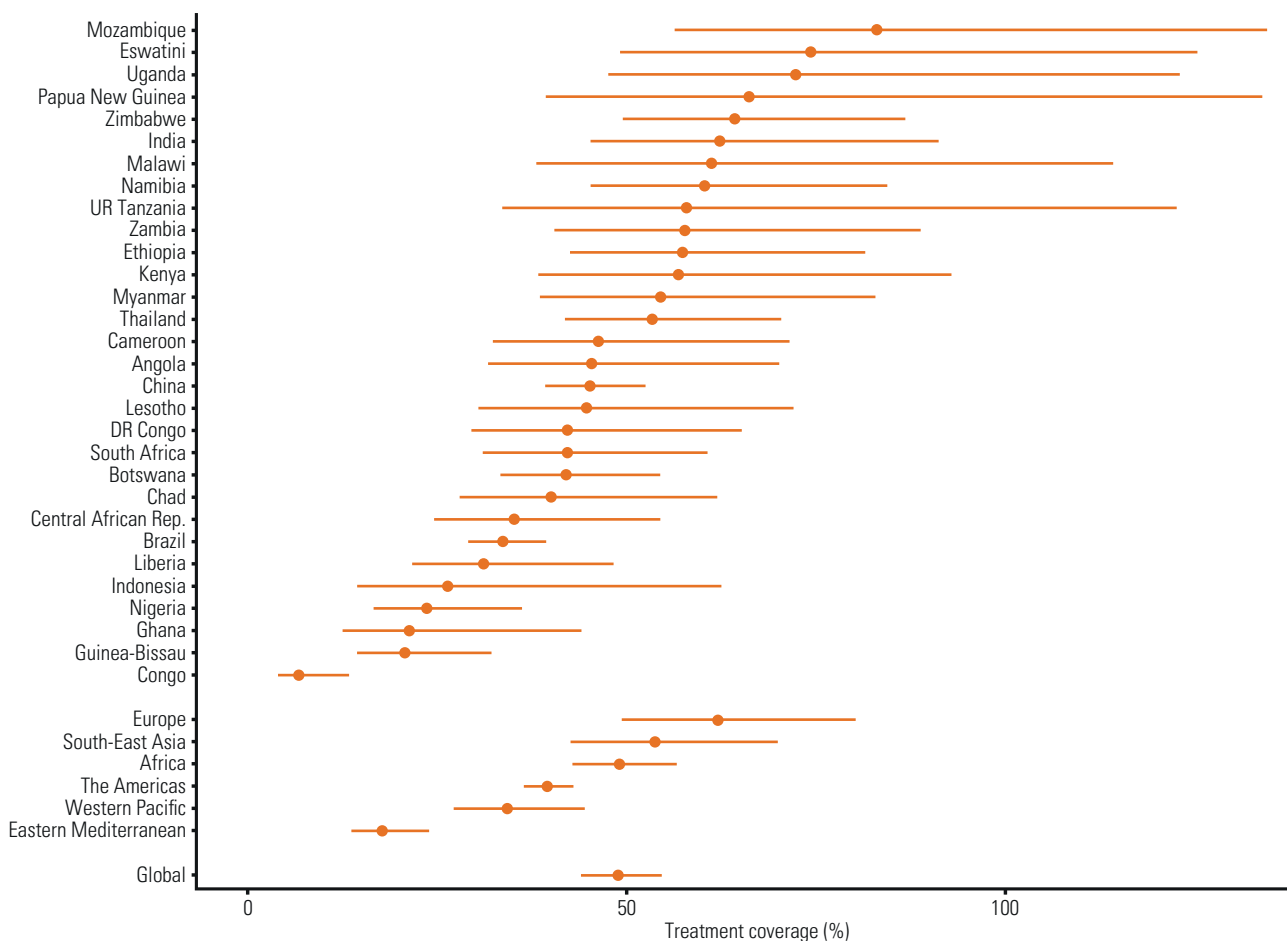


^a The calculation is for all cases in years prior to 2015.

^b Estimates of TB incidence for India are interim, pending results from the national TB prevalence survey (2020/2021).

FIG. 5.26

Estimated coverage of ART for HIV-positive TB cases (HIV-positive TB patients on ART as a percentage of the estimated incidence of HIV-positive TB) in the 30 high TB/HIV burden countries, WHO regions and globally, 2019



5.3 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 2018 (including people with HIV-associated TB), and people with MDR/RR-TB who started a second-line MDR-TB regimen in 2017.¹

5.3.1 Treatment outcomes for new and relapse TB patients

Data on treatment outcomes for new and relapse cases of TB in 2018 are shown for the world and the six WHO regions in **Fig. 5.29**, and the 48 high TB, TB/HIV and MDR-TB burden countries in **Table 5.5**. Nine 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. In other countries, treatment success rates still need to be improved, especially in Angola and Congo (50% and 62%, respectively, with a large percentage of TB patients in the categories of “not evaluated” or “lost to follow-up”).

Reasons for country variation in treatment success rates (for all TB cases, but also for drug-resistant -TB and HIV-associated TB) include programmatic capacity to correctly treat and support patients, the size of the patient case-load (cohort), the prevalence and severity of drug resistance among new and previously treated cases, access to health care, the availability of treatment support and associated adherence to treatment, the coverage of ART for TB patients living with HIV, other health-related risk factors and the completeness of reporting about treatment outcomes.

The global trend for 2012–2018 is shown in **Fig. 5.30**. The treatment success rate for new and relapse cases in the 2018 cohort was 85% (the same level as in 2017).

The absolute number of TB patients reported to have been successfully treated rose substantially over the period 2000–2018, both globally and in all WHO regions (**Fig. 5.31**). Among the six WHO regions, the highest treatment success rates in 2018, of 91% and 89%, respectively, were in the Eastern Mediterranean and Western Pacific regions. The lowest rates were 76% in both the

¹ For definitions of treatment outcomes, see WHO (2013) (17).

TABLE 5.5

Treatment outcomes^a by TB case type, 2018 and treatment outcomes for MDR/RR-TB cases, 2017 for 48 high TB, TB/HIV and MDR-TB burden countries

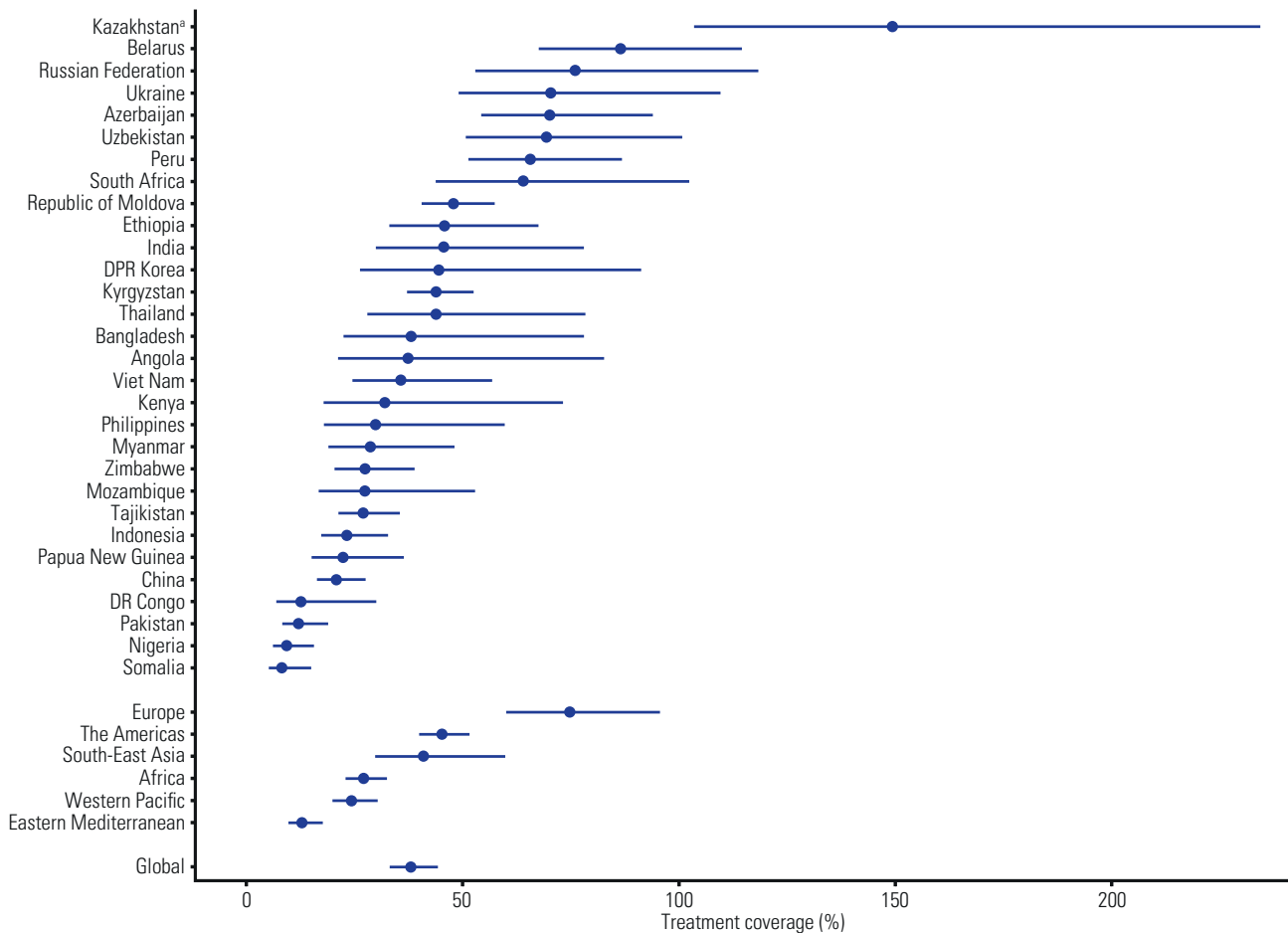
COUNTRY	NEW AND RELAPSE, 2018 COHORT		PREVIOUSLY TREATED, EXCLUDING RELAPSE, 2018 COHORT		NEW AND RELAPSE IN CHILDREN AGED 0–14 YEARS, 2018 COHORT		HIV-POSITIVE TB, 2018 COHORT		MDR/RR-TB, 2017 COHORT	
	COHORT (NUMBER)	SUCCESS (%)	COHORT (NUMBER)	SUCCESS (%)	COHORT (NUMBER)	SUCCESS (%)	COHORT (NUMBER)	SUCCESS (%)	COHORT (NUMBER)	SUCCESS (%)
Angola	66 189	50	4 173	21			4 327		534	0
Azerbaijan ^b	1 751	84	2 433	74					858	59
Bangladesh	267 143	94	1 453	85	11 299	97	67	64	919	73
Belarus	1 418	88	98	69	12	83	89	85	1 067	70
Botswana	4 844	82	79	38	312	82	2 043	79	87	69
Brazil	81 951	71	8 266	38	2 510	77	7 399	51	721	57
Cambodia	28 611	94	137	88					135	70
Cameroon	23 165	84	361	70			6 554	77	137	79
Central African Rep.	10 390	79	123	64			2 247	77	81	80
Chad	13 078	78	228	65	950	76	1 593	79	48	56
China	776 514	94	5 700	81	6 421	93	7 935	80	5 943	54
Congo	10 791	62	238	43	0		597	30	25	88
DPR Korea	89 939	83	5 306	75					1 732	78
DR Congo	169 748	93	1 834	85	18 453	83	9 758	79	838	82
Eswatini	2 771	90	135	86	161	94	2 069	90	226	73
Ethiopia ^b	110 189	88							708	75
Ghana	13 801	84	413	87	747	81	2 504	77	112	63
Guinea-Bissau	1 994	71	37	76			660	63	25	44
India	1 908 683	82	140 834	74	124 797	85	32 493	74	36 043	49
Indonesia	565 980	83	4 993	74	68 529	83	10 328	72	2 997	45
Kazakhstan	7 859	90	165	75	274	97	303	67	5 338	81
Kenya	94 534	84	1 935	72	9 818	89	24 521	79	390	70
Kyrgyzstan	5 333	81	792	51	260	92	145	61	1 166	55
Lesotho	7 059	77	99	75	232	83	4 609	75	147	74
Liberia	7 703	75	16	75			984	66	55	78
Malawi	15 435	88	321	81	1 183	93	7 268	86	58	55
Mozambique	90 947	93	1 165	89			32 621	89	825	61
Myanmar	133 109	88	1 509	80	26 118	96	10 339	75	2 647	79
Namibia	7 777	86	291	73	713	91	2 768	81	380	67
Nigeria	103 921	87	2 612	89	8 293	89	12 700	76	1 786	77
Pakistan	357 893	93	9 263	82			307	51	2 813	64
Papua New Guinea	28 784	73	1 018	61	6 705	73	1 026	61	208	75
Peru	28 585	83	1 097	48	1 263	90	1 601	63	1 289	62
Philippines	369 442	83	8 809	84	45 380	78	1 447	81	5 421	58
Republic of Moldova	2 312	85	131	47	96	91	154	69	962	56
Russian Federation	59 850	69	8 876	48	1 905	95	12 013	44	22 901	55
Sierra Leone	17 144	89	25	44			2 168	70	104	75
Somalia	16 614	87	59	66			181	33	276	75
South Africa	227 999	71	12 905	61			80 444	79	10 094	60
Tajikistan	4 995	89	155	82	302	92	156	74	546	64
Thailand	85 029	85	1 920	65	840	92	6 780	75	851	54
Uganda	54 359	74	2 346	65	7 890	63	21 513	72	384	74
Ukraine	20 221	77	2 972	62	458	95	4 381	68	6 685	51
UR Tanzania	74 067	92	1 107	89	10 487	94	20 595	89	173	83
Uzbekistan	14 423	92	1 225	78					2 265	61
Viet Nam	99 558	91	2 513	85	1 656	82	2 930	75	2 675	69
Zambia	35 071	90	851	88	2 206	88	20 202	89	270	76
Zimbabwe	25 204	84	571	95	1 547	81	15 062	82	439	54

^a Reasons for country variation in treatment success rates include the prevalence and severity of drug resistance among new and previously treated cases, access to health care, the availability of treatment support and associated adherence to treatment, the coverage of ART for TB patients living with HIV, other health-related risk factors and the completeness of reporting about treatment outcomes.

^b Relapses included in the previously treated cohort.

FIG. 5.27

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 the 30 high MDR-TB burden countries, WHO regions and globally, 2019



* Possible reasons for the coverage exceeding 100% include that the numerator included empirical treatment of TB patients considered at risk of having MDR/RR-TB but for whom a laboratory-confirmed diagnosis was missing, duplicated case reporting, or enrolment of 'waiting lists' of people with MDR/RR-TB who were detected before 2019.

WHO Region of the Americas (due to high levels of loss to follow-up and missing data) and the European Region (due to high rates of treatment failure and death, influenced by the high frequency of MDR/RR-TB).

Among the 30 high TB burden countries, 19 provided data on the overall treatment success rate for children aged 0–14 years in 2018, showing an identical level (85%) to the overall average (Fig. 5.32). Among WHO regions, it ranged from 80% in the Western Pacific Region to 95% in the Eastern Mediterranean Region. Seven of the 19 countries reported a treatment success rate of above 90%, whereas eight countries reported a success rate of below 85%.

5.3.2 Treatment outcomes for new and relapse TB patients living with HIV

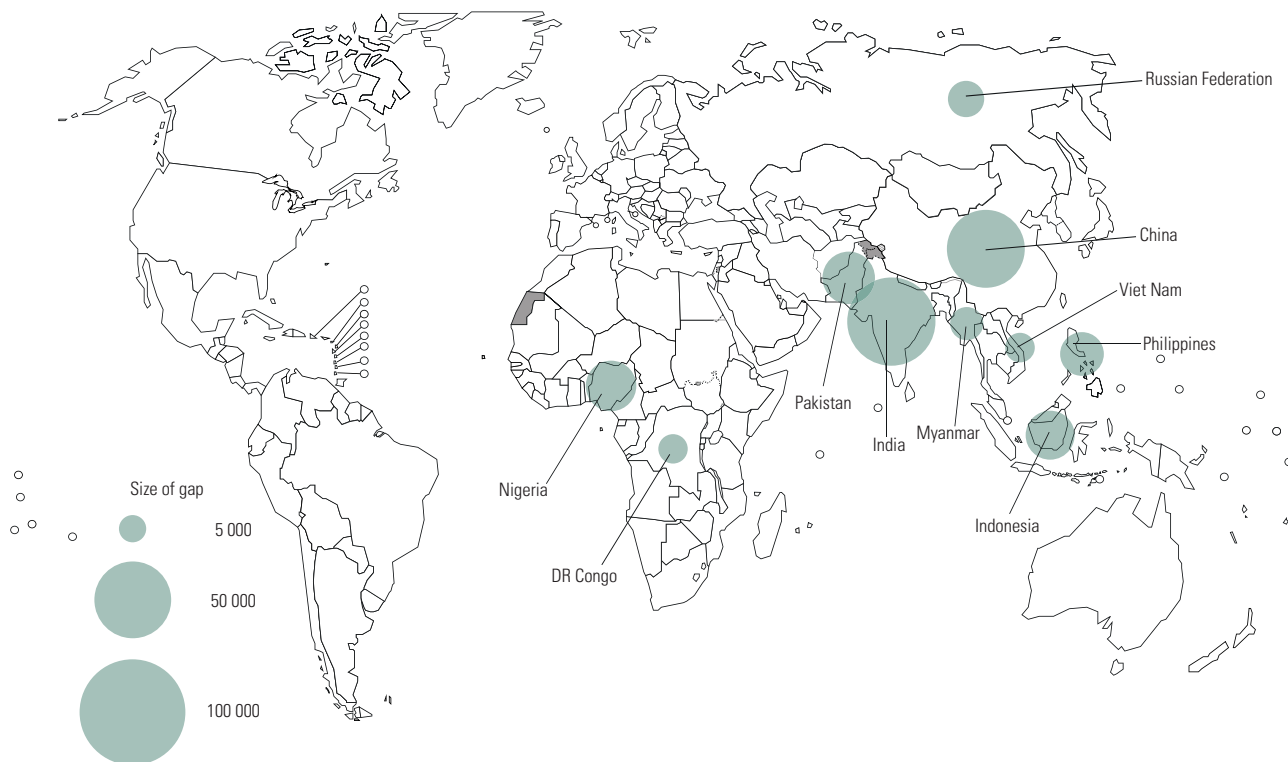
A total of 126 countries reported treatment outcomes for the 2018 patient cohort disaggregated by HIV status, an increase from 103 countries reporting in 2012. These

126 countries included 28 of the 30 high TB/HIV burden countries; no data on treatment outcomes were reported by Angola and Ethiopia (Table 5.5). Overall, the treatment success rate for TB patients coinfecting with HIV was 76% (Fig. 5.32), compared with 85% for all new and relapse TB patients reported in the same countries.

Globally, the proportion of HIV-positive TB patients who died during TB treatment was 11%, which was similar to previous years and three times the level among all new and relapse cases (4%) in the same countries (Fig. 5.33). In the WHO regions, the relative difference was smallest in the WHO African Region (10% versus 5%) and highest in the Eastern Mediterranean Region (10% versus 2%). In the WHO Region of the Americas and the European Region, the proportion of HIV-positive TB patients who died remained relatively high in 2018 (20% and 21%, respectively, the same as in 2017).

FIG. 5.28

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, 2019^a



^a The ten countries ranked in order of the size of the gap between the number of patients started on MDR-TB treatment and the best estimate of MDR/RR-TB incidence in 2019 are India, China, Pakistan, Nigeria, Indonesia, Philippines, Russian Federation, Myanmar, DR Congo and Viet Nam.

Reasons for comparatively poor outcomes for HIV-positive TB patients include late detection of HIV-associated TB and delays in starting ART. To reduce excessive TB mortality in people living with HIV, WHO recommends the following: enhanced joint efforts to find and diagnose people with TB and HIV, including through joint household contact screening; early initiation of ART; improved infection control; and provision of TB preventive treatment. Actions that could help to ensure earlier diagnosis and reduce mortality include strategic placement of WHO-approved rapid molecular TB diagnostics within HIV care settings, expanded use of LF-LAM,¹ and removal of structural and legislative barriers to accessing services for key populations most at risk of both HIV and TB (e.g. those with drug use disorders and people in prisons or other places of detention).

5.3.3 Treatment outcomes for TB patients with drug-resistant TB

A total of 146 countries and territories reported treatment outcomes for people started on MDR-TB treatment in 2017.² The number of cases reported in annual cohorts has increased steadily over time, reaching 131 113 globally in the 2017 cohort. Overall, the proportion of people with MDR/RR-TB in the 2017 cohort who successfully completed treatment (i.e. cured or treatment completed) was 57%; for the rest of the cohort, treatment failed for 7%, 15% died and 16% were lost to follow-up (there was no outcome information for the remaining 5%) (Table 5.5, Fig. 5.34).

¹ Further information about this assay is provided in Chapter 9.

² This is the latest year for which data on treatment outcomes for drug-resistant TB have been reported to WHO. The longer duration of treatment for drug-resistant TB means that there is a longer lag time for reporting of data.

FIG. 5.29

Treatment outcomes for new and relapse TB cases, WHO regions and globally, 2018

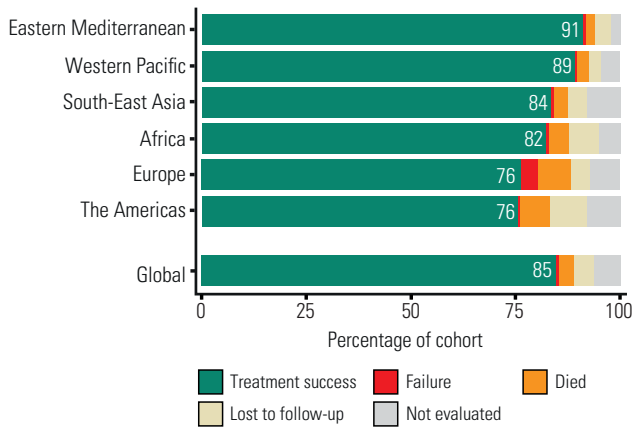


FIG. 5.31

Treatment outcomes for new and relapse TB cases^a (absolute numbers), globally and for WHO regions, 2000–2018

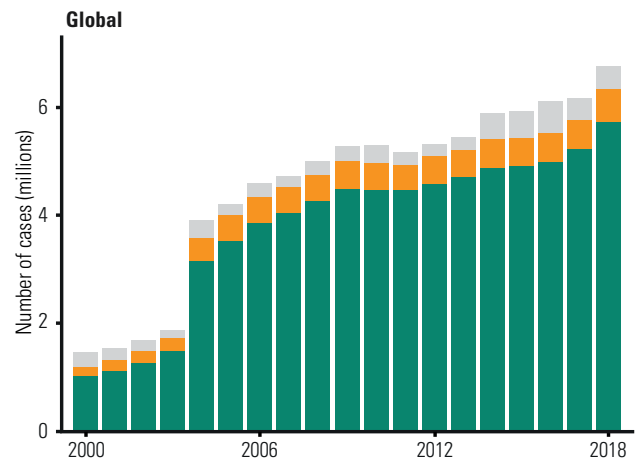
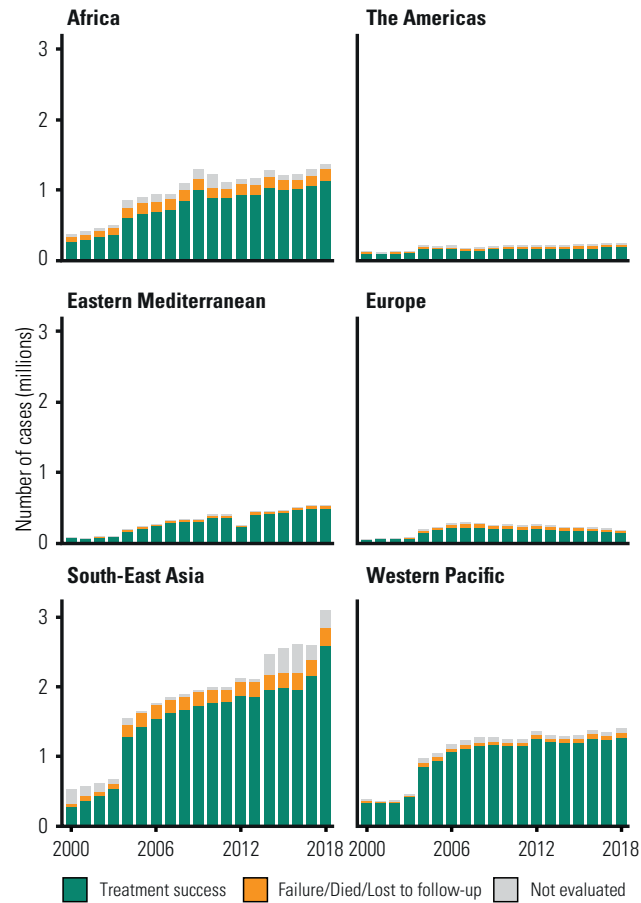
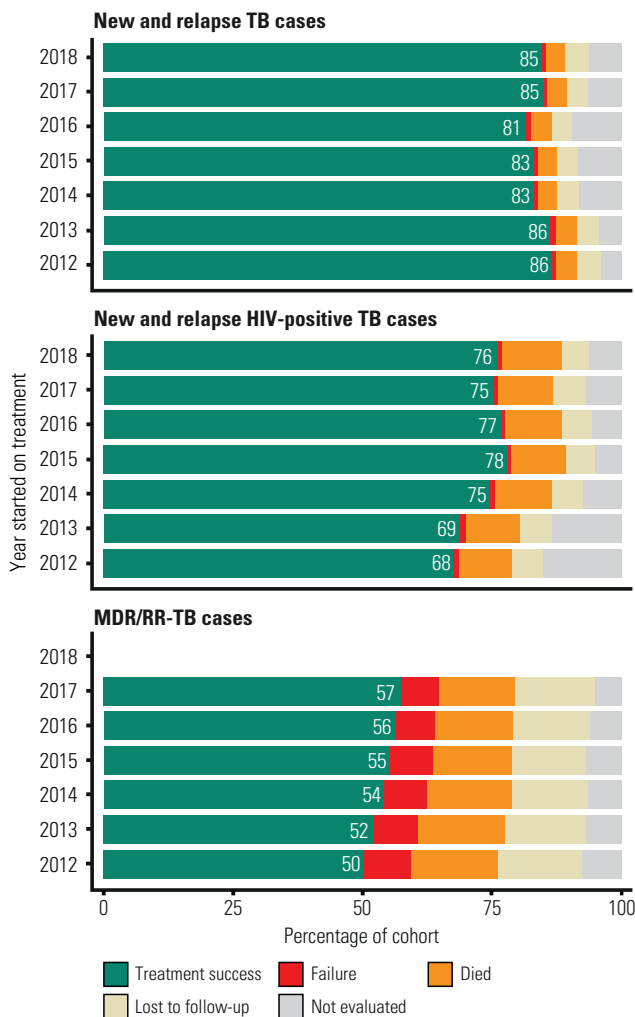


FIG. 5.30

Treatment outcomes for new and relapse TB cases, new and relapse HIV-positive TB cases, and MDR/RR-TB cases, globally^a, 2012–2018



^a Cohorts before 2012 included new cases only.

^a Outcomes for MDR/RR-TB annual treatment cohorts are reported one year later than other TB cohorts.

FIG. 5.32

Treatment success rate for new and relapse TB cases in children aged 0–14 years, WHO regions and globally, 2018

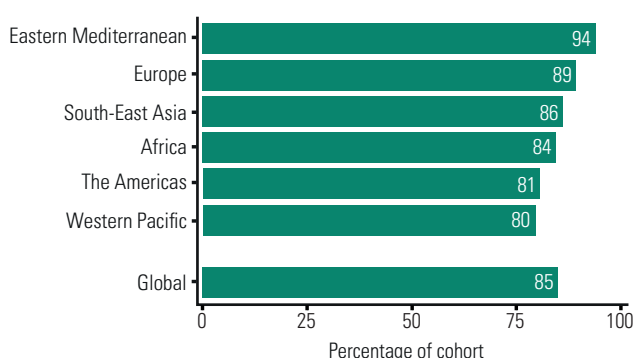


FIG. 5.33

Treatment outcomes for new and relapse HIV-positive TB cases, WHO regions and globally, 2018

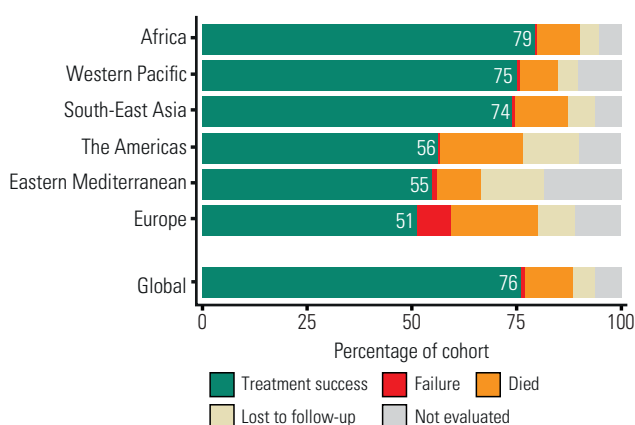
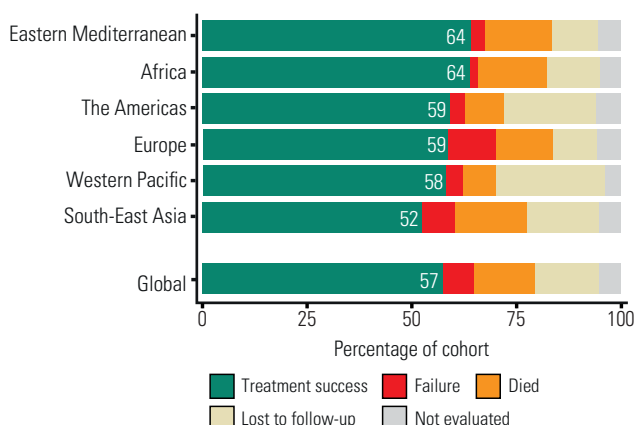


FIG. 5.34

Treatment outcomes for MDR/RR-TB cases started on treatment, WHO regions and globally, 2017



Globally, treatment success has increased in recent years (Fig. 5.30). For the 2017 patient cohort, the treatment success rate was highest in the WHO Eastern Mediterranean and African regions (both 64%) and lowest in the South-East Asia Region (52%). Treatment failure was highest in the WHO European Region (11%), and the death rate was highest in the South-East Asia Region (17%). Loss to follow-up was highest in the WHO Western Pacific Region (26%), whereas all WHO regions had a similar percentage of cases without outcome information (4–6%).

Among the 30 high MDR-TB burden countries, eight had treatment success rates of at least 75% in their 2017 patient cohorts. However, the treatment success rate was below 50% in India and Indonesia, in part owing to high rates of death and loss to follow-up (18% and 26% in Indonesia; 18% and 19% in India, respectively). Loss to follow-up was highest in the Philippines and China (33% and 29%, respectively), and outcome data were missing for a high proportion of patients in Somalia and Zimbabwe (15% and 17%, respectively).

Among 11 210 patients who started treatment for MDR/RR-TB and were also resistant to fluoroquinolones, and for whom outcomes were reported, 47% completed treatment successfully, 24% died, treatment failed for 11%, and 18% were lost to follow-up or their treatment outcome was not evaluated. India, the Russian Federation and Ukraine accounted for 73% of this cohort of patients. Among all countries with a cohort of at least 100 patients, the death rate was highest in India and South Africa (37% and 26%, respectively).

Although improving in some countries, the treatment success rates for drug-resistant TB globally remain unacceptably low. The wider use of more effective MDR-TB treatment regimens designed on the basis of the latest available evidence, and the use of patient-centred models of care, are expected to help improve this situation.

By the end of 2019, 89 countries, mostly in Africa and Asia, reported having used shorter MDR-TB regimens (Fig. 5.35), and 86 countries had used all-oral longer MDR-TB regimens (Fig. 5.36). By the end of 2019, 109 countries reported having imported or started using bedaquiline (Fig. 5.37). Four countries (India, South Africa, the Russian Federation and Ukraine) accounted for 68% of the patients treated with bedaquiline globally in 2019.

Global surveillance of active TB drug-safety monitoring and management¹ shows that, by the end of 2019, 128 countries (including 24 high MDR-TB burden countries) were systematically collecting data on adverse events in their TB information systems (Fig. 5.38).

¹ WHO global database for TB active drug safety monitoring home page [website]. Geneva: World Health Organization; 2019 (https://www.who.int/tdr/research/tb_hiv/adsm/en/, accessed 18 August 2020).

FIG. 5.35

Countries that used shorter MDR-TB treatment regimens by the end of 2019

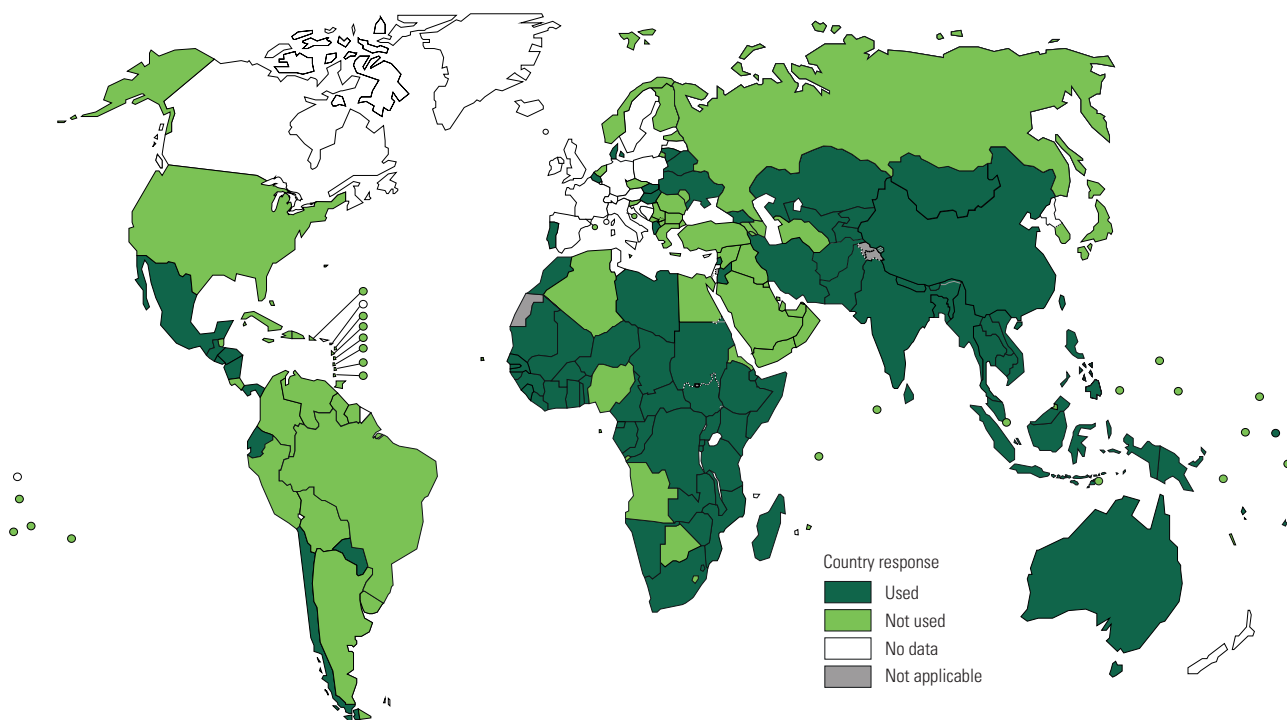


FIG. 5.36

Countries that used all-oral longer MDR-TB treatment regimens by the end of 2019

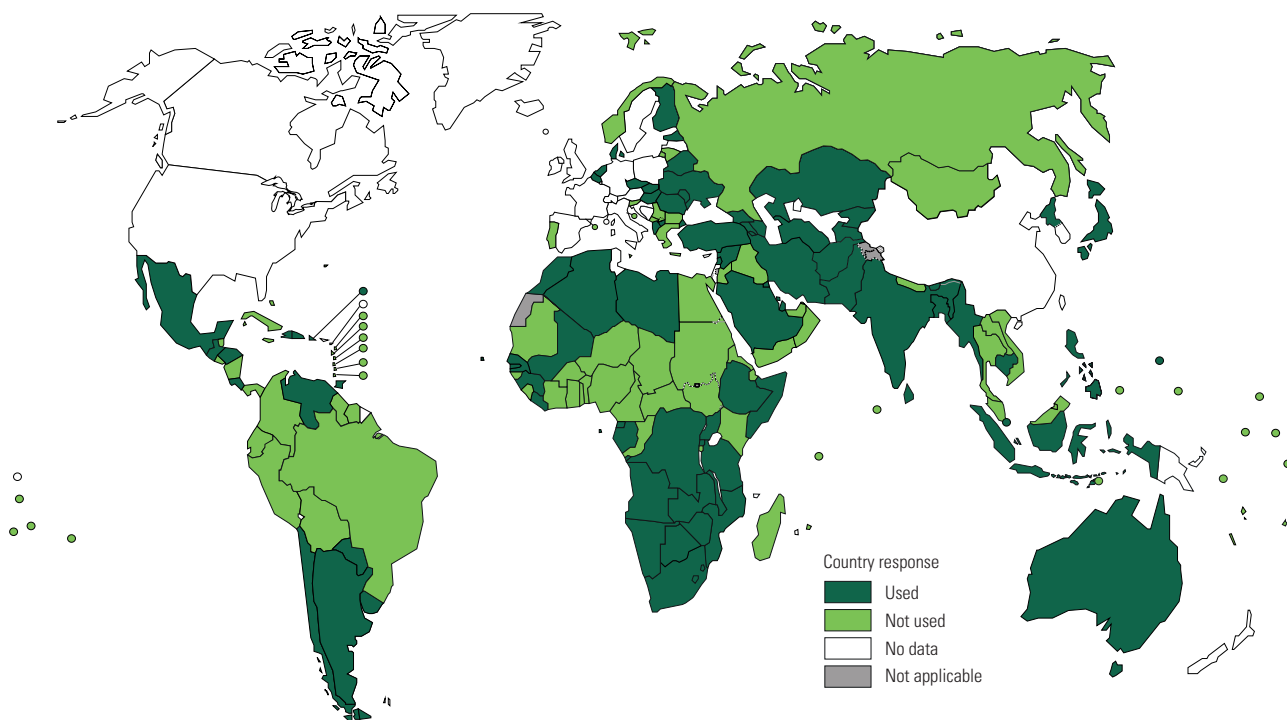


FIG. 5.37

Countries that used bedaquiline for the treatment of MDR/XDR-TB as part of expanded access, compassionate use or under normal programmatic conditions by the end of 2019

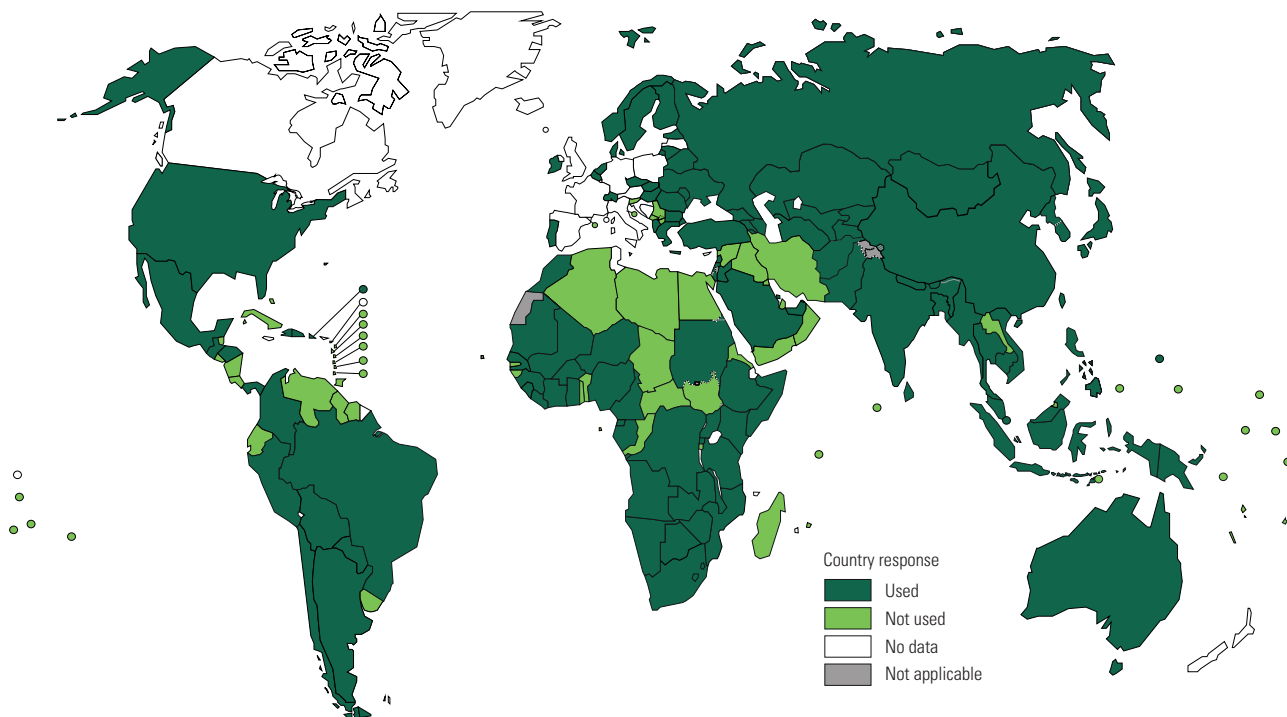
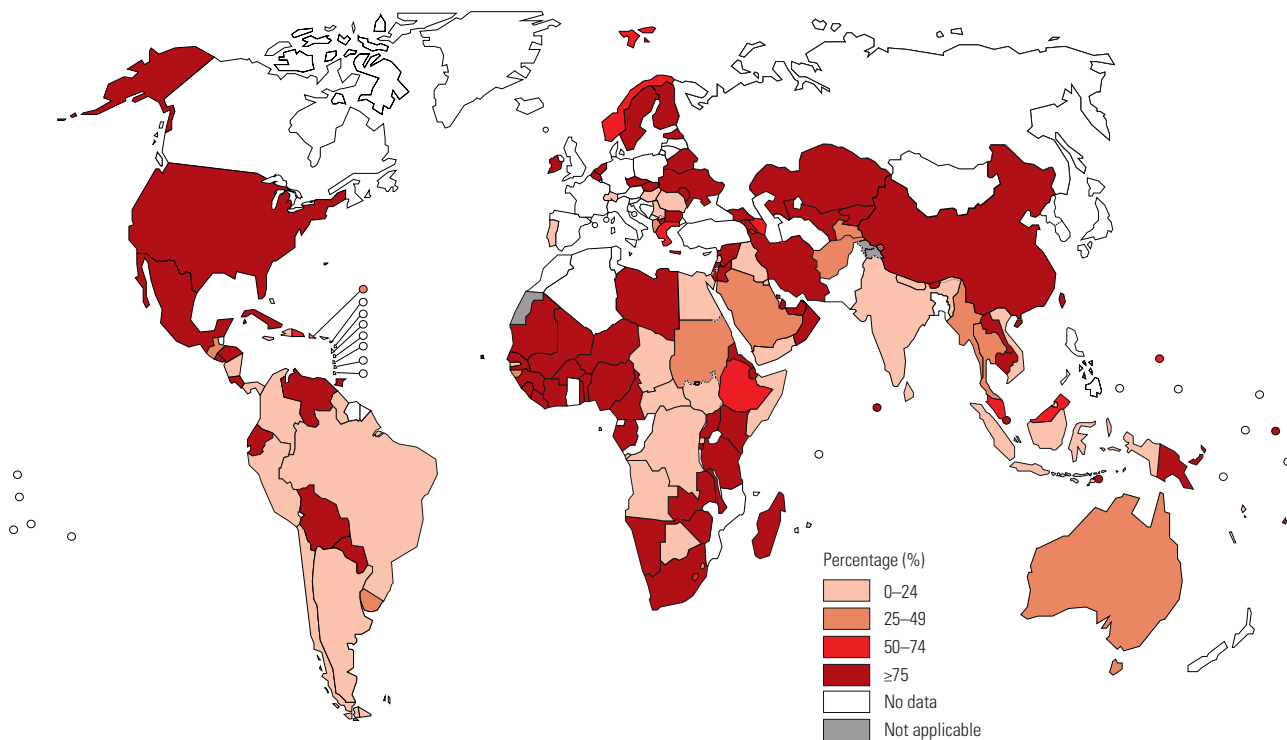


FIG. 5.38

Number of patients with active follow-up of adverse events as a proportion of patients enrolled on treatment for drug-resistant TB, 2019



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**A family affected by TB
outside their home in Haiti.**

Jake Lyell/Alamy

Chapter 6

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 ill health and death caused by TB, and to achieve the End TB Strategy targets set for 2030 and 2035. Current health interventions for TB prevention are treatment of people with TB infection (TB preventive treatment), prevention of transmission of *M. tuberculosis* through infection prevention and control, and vaccination of children with the bacille Calmette-Guérin (BCG) vaccine.

At the first United Nations (UN) high-level meeting on TB in 2018, Member States committed to providing TB preventive treatment to at least 30 million people in the 5-year period 2018–2022: 6 million people living with HIV, 4 million children aged under 5 years who are household contacts of people with bacteriologically confirmed TB, and 20 million household contacts in older age groups. They also committed to greater investment in research to accelerate the development of new treatments and vaccines.

The number of people provided with TB preventive treatment has increased in recent years, from 1.0 million in 2015 to 2.2 million in 2018 and 4.1 million in 2019. The combined total of 6.3 million in 2018–2019 is 21% of the 5-year (2018–2022) target of 30 million.

Most of those provided with TB preventive treatment were people living with HIV: 1.8 million in 2018 and 3.5 million in 2019. The combined total of 5.3 million suggests that the subtarget of providing treatment to 6 million people living with HIV in the period 2018–2022 will be achieved in 2020.

Of the 38 high TB or TB/HIV burden countries, 23 reported providing TB preventive treatment to people living with HIV who were started on antiretroviral treatment (ART) in 2019. Coverage ranged from less than 1% in Thailand to 89% in Zimbabwe; the overall figure for 62 countries that reported data was 50%. Three countries – India, the United Republic of Tanzania and South Africa – accounted for 25%, 17% and 14%, respectively, of the total number of people treated.

Numbers of household contacts provided with TB preventive treatment have been much smaller: 423 607 in 2018 and 538 396 in 2019. Of these, 81% were children under 5 years (349 796 in 2018 and 433 156 in 2019, equivalent to 27% and 33% of the 1.3 million estimated to be eligible) and 19% were people in older age groups (73 811 in 2018 and 105 240 in 2019).

The numbers of household contacts provided with TB preventive treatment in 2018 and 2019 fall far short of those required to achieve the targets for 2018–2022 set at the UN high-level meeting on TB. The combined 2018–2019 totals for children under 5 years and people in older age groups represent 20% and 0.9% of the 5-year targets (4 million and 20 million), respectively.

Access to and provision of TB preventive treatment needs to be substantially expanded, including by scaling up household contact investigation, updating national policies and strategies for TB preventive treatment in line with World Health Organization (WHO) recommendations, increasing investments and building synergies

with contact tracing efforts implemented in response to the COVID-19 pandemic.

In 2019, countries identified 9.8 million contacts of bacteriologically confirmed pulmonary TB cases, of whom 5.6 million (57%) were screened for TB disease and infection.

The ratio of the TB notification rate among health care workers to the TB notification rate in the general adult population reflects the level of TB infection control in health facilities, and should be about 1. In 2019, a total of 22 314 cases of TB among health care workers from 76 countries were reported; India accounted for 47% and China for 18%. Among countries reporting more than five health care workers with TB in 2019, the ratio was at least 2 in Botswana, Dominican Republic, Honduras, India, Lesotho, Uganda, the United Republic of Tanzania and Zimbabwe.

BCG vaccination is recommended as part of national childhood immunization programmes, in line with a country's TB epidemiology. The most recent data indicate that 153 countries have a policy of BCG vaccination for the whole population: 87 of these countries reported coverage of at least 90%. In a further 25 countries, BCG vaccination is reserved for specific population groups only.

Prevention of new infections of *Mycobacterium tuberculosis* and action to reduce progression to tuberculosis (TB) disease are critical to reduce the burden of ill health and death caused by TB, and to achieve the End TB Strategy targets set for 2030 and 2035. The targets of an 80% reduction in TB incidence from the 2015 level by 2030, and a 90% reduction by 2035, require a historically unprecedented acceleration in the rate at which TB incidence falls after 2025 (**Chapter 2**).

Achieving this accelerated rate (which averages 17% per year between 2025 and 2035) will require substantial reductions in the probability of progression from TB infection to TB disease among the approximately 2 billion people already infected worldwide (1).¹ Health care interventions that could help to cut the risk of progression from infection to TB disease include new diagnostic tests that are better at predicting who is at risk of developing TB disease, more effective treatments for people infected with *M. tuberculosis*, and development of a vaccine to prevent reactivation of TB in adults. Action on the broader determinants of TB could also cut the risk, as discussed in **Chapter 8**.

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

- ▶ TB preventive treatment;
- ▶ prevention of transmission of *M. tuberculosis* through infection prevention and control; and
- ▶ vaccination of children with the bacille Calmette-Guérin (BCG) vaccine.

At the first United Nations (UN) high-level meeting on TB, held in 2018, Member States made a range of commitments to accelerate progress towards ending the TB epidemic (3). This included setting a new global target of providing TB preventive treatment to at least 30 million people in the 5-year period 2018–2022: 6 million people living with HIV, 4 million children aged under 5 years who are household contacts of people diagnosed with TB and 20 million household contacts in older age groups. Member States also committed to greater investment in research to accelerate the development of new treatments and vaccines.

The recent availability of shorter drug regimens for TB preventive treatment, combined with the global targets, provide an opportunity to galvanize national and global efforts to scale up effective preventive interventions. There are also now possibilities to build synergies with contact tracing efforts implemented in response to the COVID-19 pandemic.

This chapter presents and discusses the latest data about progress in TB preventive treatment (**Section 6.1**), infection prevention and control (**Section 6.2**), and provision of BCG vaccination (**Section 6.3**). Particular attention is given to the 30 high TB burden countries and the 30 high TB/HIV burden countries.²

¹ The lifetime risk is about 5–10% (2).

² The lists of high TB burden countries defined by WHO for the period 2016–2020 are explained in **Annex 2**.

6.1 TB preventive treatment

The World Health Organization (WHO) guidance for TB preventive treatment recommends systematic treatment for three high-risk population groups: household contacts of people diagnosed with bacteriologically confirmed pulmonary TB, people living with HIV and clinical risk groups. Updated recommendations were published in March 2020, alongside operational guidance and other implementation aids to support the rapid uptake of recommendations at country level (**Box 6.1**).

Recommended options for TB preventive treatment include a weekly dose of rifapentine and isoniazid for 3 months (3HP), a daily dose of rifampicin plus isoniazid for 3 months (3HR), a daily dose of rifapentine plus isoniazid for 1 month (1HP), a daily dose of rifampicin for 4 months (4R) and a daily dose of isoniazid for 6 months (6H) or longer.

This section presents the latest data (for 2019) reported to WHO on provision of TB preventive treatment, and data available for previous years. Data are presented overall and also for the priority groups for which targets were set at the UN high-level meeting on TB: people living with HIV, household contacts aged under 5 years and household contacts in older age groups.

The period for which WHO has gathered data for these groups reflects the evolution of WHO guidance. Initially, attention was given to monitoring the provision of TB preventive treatment to people living with HIV, and data are available for 2005–2019. In 2016, this was expanded to household contacts aged under 5 years and, in 2019, it was expanded to all age groups; for these two groups, data are available for 2015–2019 and 2018–2019, respectively.

6.1.1 Number of people provided with TB preventive treatment, 2015–2019

The number of people provided with TB preventive treatment has increased considerably in recent years, from 1.0 million in 2015, to 2.2 million in 2018 and 4.1 million in 2019 (**Fig. 6.1**). The combined total of 6.3 million in 2018–2019 is 21% of the 5-year (2018–2022) target of 30 million (**Fig. 6.2**).

Most of those provided with TB preventive treatment were people living with HIV: 1.8 million in 2018 and 3.5 million in 2019. The combined total for 2018–2019 of 5.3 million suggests that the subtarget of providing treatment to 6 million people living with HIV in the period 2018–2022 could be achieved in 2020 (**Fig. 6.2**).

Numbers of household contacts provided with TB preventive treatment have been much smaller (**Fig. 6.1**), although they are growing (423 607 in 2018 and 538 396 in 2019). In 2019, 433 196 children aged under 5 years were provided with TB preventive treatment, up from 349 796 in 2018 and a large increase from 87 242 in 2015. For other age groups, the number was 105 240 in 2019, up from 73 811 in 2018 (the first year for which global data are available).

Updated WHO recommendations on TB preventive treatment

In March 2020, WHO issued updated recommendations for the programmatic management of TB preventive treatment.^a These recommendations are intended primarily for staff in national TB and HIV programmes (or their equivalents in ministries of health), as well as policy-makers working on TB and HIV in the public and private sectors, and in the community.

There are 18 recommendations, which cover critical steps in programmatic management according to the cascade of preventive TB care (identifying individuals at risk, ruling out TB disease, testing for TB infection and options for TB prevention treatment).

The main changes introduced since the previous guidance issued in 2018 are:

- ▶ a new recommendation for a 1-month regimen of daily rifampentine and isoniazid (1HP);
- ▶ a revised recommendation for a 4-month regimen of daily rifampicin (4R);
- ▶ updated advice on isoniazid preventive treatment in pregnancy; and
- ▶ updated advice on the concomitant use of rifampentine and dolutegravir for people living with HIV who are on antiretroviral treatment.

The guidance highlights the programmatic challenges that countries need to overcome to achieve global targets. These challenges are discussed in greater detail in an accompanying operational handbook released in association with the updated guidance.^b

Three core indicators – contact investigation coverage, treatment initiation and treatment completion – are recommended for monitoring the provision of TB preventive treatment in all countries.

The 2020 guidelines on TB preventive treatment were the first to be released as part of WHO consolidated TB guidelines, which will eventually cover (in modular format) all WHO recommendations on TB prevention and care.^c

WHO is developing new tools to improve access to the consolidated TB guidelines, capture data critical to the monitoring of TB preventive treatment and TB screening, and support the adoption of guidance at country level.^d WHO is also developing a repository of current TB recommendations linked to the evidence and expert considerations underpinning them.^e

^a WHO consolidated guidelines on tuberculosis: Module 1: Prevention – tuberculosis preventive treatment. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/who-consolidated-guidelines-on-tuberculosis-module-1-prevention-tuberculosis-preventive-treatment>, accessed 21 July 2020). (4)

^b WHO operational handbook on tuberculosis: Module 1: Prevention – tuberculosis preventive treatment. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/who-operational-handbook-on-tuberculosis-module-1-prevention-tuberculosis-preventive-treatment>, accessed 21 July 2020). (5)

^c In 2020, updated guidelines on the treatment of drug-resistant TB and TB diagnostics were also published and updated guidelines on systematic screening of active TB disease are in preparation.

^d Prevent TB Digital Platform [website]. 2020 (<https://www.who.int/activities/preventing-tb/>, accessed 21 July 2020). (6)

^e eTB guidelines. Database of recommendations for TB prevention and care [website]. 2020 (<https://tuberculosis.evidenceprime.com/>, accessed 21 July 2020). (7)

FIG. 6.1

The global number of people reported to have been provided with TB preventive treatment, 2015–2019

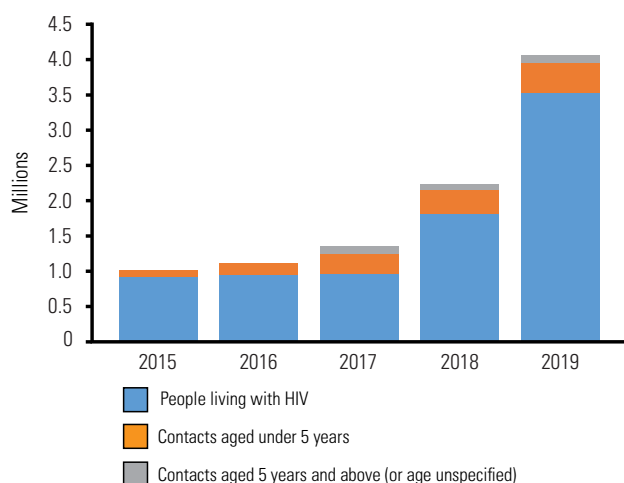


FIG. 6.2

Global progress in provision of TB preventive treatment in 2018 and 2019 compared with cumulative targets set for 2018–2022 at the UN high-level meeting on TB

The centre of each circle shows the target, the colour coding shows progress made by the end of 2019 and the text to the right of each circle quantifies the status of progress at the end of 2019.

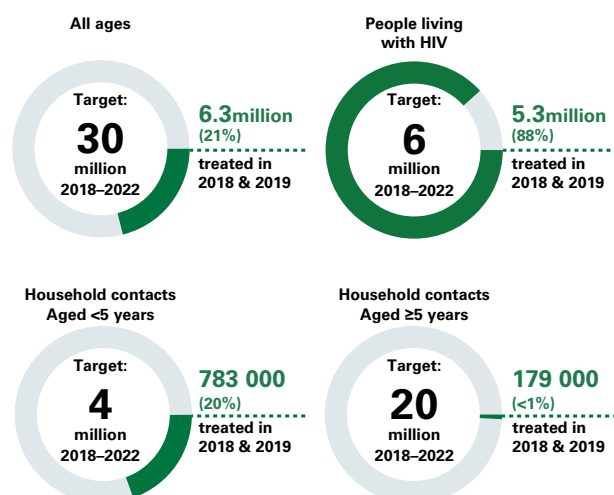
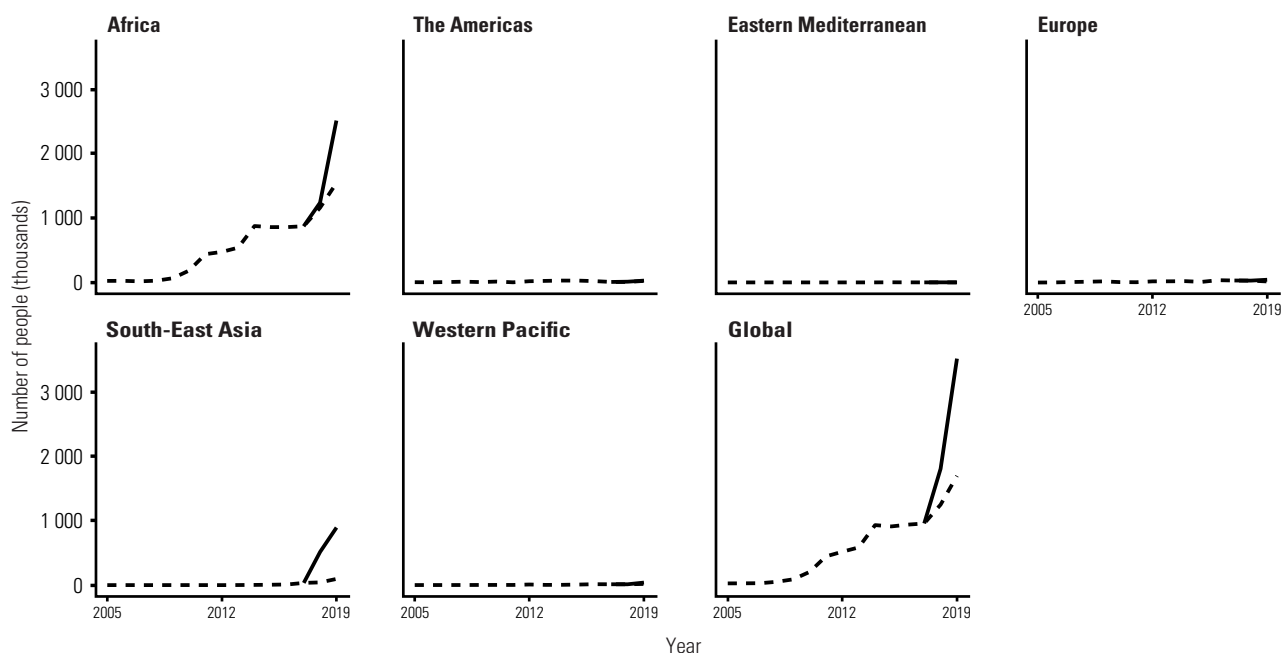


FIG. 6.3

Provision of TB preventive treatment to people living with HIV,^a 2005–2019



^a For the period 2005–2016, countries were requested to report data for people newly enrolled in HIV care (dotted lines). Subsequently, countries have been encouraged to report data for people currently on antiretroviral treatment (ART) (solid lines).

The number of household contacts provided with TB preventive treatment in 2018 and 2019 falls far short of what is required to achieve the targets for 2018–2022 set at the UN high-level meeting on TB (Fig. 6.2). The combined 2018–2019 totals for children aged under 5 years and people in older age groups represent 20% and 0.9% of the 5-year targets (4 million and 20 million), respectively.

Access to and provision of TB preventive treatment needs to be substantially expanded; for example, by scaling up household contact investigation, updating national policies and strategies for TB preventive treatment in line with WHO recommendations, increasing investments and building synergies with contact tracing efforts implemented in response to the COVID-19 pandemic.¹

6.1.2 People living with HIV, 2005–2019

Data on provision of TB preventive treatment to people living with HIV are collected annually by the Joint United Nations Programme on HIV/AIDS (UNAIDS) (8), and are jointly reviewed and validated with WHO. For the period 2005–2016, countries were requested to report data for people newly enrolled in HIV care. Subsequently, countries have been encouraged to report data for all people currently on antiretroviral treatment (ART) (9),² and a growing number of countries are doing so.

¹ The links between the COVID-19 pandemic and TB are discussed in more detail in Chapter 3.

² For reporting of data for 2019, the terminology of people “enrolled in HIV care” was replaced with “on antiretroviral treatment”, to reflect the increased emphasis on and scaling up of HIV test-and-treat policies.

Globally, substantial progress has been made. Based on reporting by 75 countries, the number of people on ART who were provided with TB preventive treatment by national HIV programmes and other providers reached 3.5 million in 2019 (including 1.5 million people in 64 countries who were started on ART). This was an increase from 1.8 million in 2018 and a particularly large increase from fewer than 30 000 in 2005 (Fig. 6.3).

In 2019, India accounted for 25% (863 355) of the global total, followed by the United Republic of Tanzania (17%, 586 111) and South Africa (14%, 509 762) (Fig. 6.4). Among countries that reported data on TB preventive treatment in 2018, increases exceeding 100 000 between 2018 and 2019 were reported by India (+368 057), the United Republic of Tanzania (+294 298) and Malawi (+159 169). Four countries did not report data for 2018 but reported more than 100 000 people started on TB preventive treatment in 2019: Zambia (188 594), Namibia (134 305), Kenya (124 469) and Eswatini (122 414). For the high TB/HIV burden countries of Cameroon, Central African Republic, Ghana, Thailand and Uganda, data were reported for the first time in at least 4 years.

In 2019, 23 of the 38 high TB and TB/HIV burden countries reported provision of TB preventive treatment to the subpopulation of people started on ART, up from 16 countries in 2018. Coverage could be calculated for 21 of the 23 countries; it ranged from less than 1% in Thailand to 89% in Zimbabwe (Table 6.1). In the 62 countries for which data were available globally, coverage was 50%, similar to the 49% reported in 2018.

TABLE 6.1

TB preventive treatment for people living with HIV and children under 5 years of age who were household contacts of a person with bacteriologically confirmed pulmonary TB, high TB or TB/HIV burden countries, 2019

COUNTRY	PEOPLE LIVING WITH HIV STARTED ON ANTIRETROVIRAL TREATMENT (ART)			PEOPLE LIVING WITH HIV ON ART	ESTIMATED NUMBER OF CHILD CONTACTS UNDER 5 YEARS OF AGE ELIGIBLE FOR TB PREVENTIVE TREATMENT ^a		CHILDREN UNDER 5 YEARS OF AGE STARTED ON TB PREVENTIVE TREATMENT		
	NUMBER	NUMBER OF PEOPLE STARTED ON TB PREVENTIVE TREATMENT	COVERAGE %		NUMBER OF PEOPLE STARTED ON TB PREVENTIVE TREATMENT	BEST ESTIMATE	UNCERTAINTY INTERVAL	NUMBER	COVERAGE ^b %
				BEST ESTIMATE					UNCERTAINTY INTERVAL
Angola	36 443	983	2.7	932	28 300	25 700–30 800			
Bangladesh					58 900	53 700–64 200	29 880	51	47–56
Botswana					215	195–234	294	>100	
Brazil					2 980	1 930–4 030	1 658	56	41–86
Cambodia					4 600	4 190–5 010	2 088	45	42–50
Cameroon				6 359	10 800	9 830–11 800	2 933	27	25–30
Central African Rep.		56		56	4 470	4 070–4 870			
Chad					6 090	5 550–6 640	308	5.1	4.6–5.6
China					16 000	10 300–21 600			
Congo					2 490	2 270–2 710			
DPR Korea					9 140	8 330–9 960	14 090	>100	
DR Congo	74 450	29 988	40		95 900	87 400–104 000	34 763	36	33–40
Eswatini	16 723	10 881	65	122 414	961	875–1 050	307	32	29–35
Ethiopia		16 071			29 400	26 800–32 000	9 732	33	30–36
Ghana	35 424	1 460	4.1		3 930	3 570–4 280	18	0.46	0.42–0.50
Guinea-Bissau					2 300	2 090–2 500	364	16	15–17
India	174 261	77 952	45	863 355	335 000	305 000–365 000	109 816	33	30–36
Indonesia	53 690	6 529	12	20 318	81 300	74 100–88 600	7 641	9.4	8.6–10
Kenya	151 815	124 469	82		20 000	18 200–21 800	7 713	39	35–42
Lesotho				39 717	1 630	1 490–1 780	1 193	73	67–80
Liberia				1 115	2 290	2 080–2 490			
Malawi	127 830	32 618	26	199 219	4 200	3 820–4 570	2 551	61	56–67
Mozambique				187 306	21 800	19 800–23 700	30 766	>100	
Myanmar	35 572	9 365	26		17 400	15 800–18 900	1 226	7.1	6.5–7.8
Namibia	13 744	8 440	61	134 305	2 450	2 230–2 670	1 547	63	58–69
Nigeria	231 440	168 355	73		61 000	55 600–66 500	9 772	16	15–18
Pakistan					102 000	92 500–111 000	5 689	5.6	5.1–6.2
Papua New Guinea	4 037	1 016	25		3 620	3 290–3 940	1 249	35	32–38
Philippines	11 654	6 281	54	17 911	56 800	51 800–61 900	1 915	3.4	3.1–3.7
Russian Federation					1 480	957–2 000	8 192	>100	
Sierra Leone	8 745	5 658	65		8 090	7 370–8 810			
South Africa	736 078	509 762	69	509 762	40 600	37 000–44 200	22 689	56	51–61
Thailand	34 425	140	0.41		8 110	7 390–8 830	4 512	56	51–61
Uganda	182 154	83 546	46		22 800	20 800–24 800	6 500	29	26–31
UR Tanzania	316 702	18 939	6.0	586 111	20 100	18 300–21 900	7 917	39	36–43
Viet Nam	19 948	8 771	44	18 801	15 900	14 500–17 300	3 239	20	19–22
Zambia	384 062	188 594	49		13 100	12 000–14 300	1 760	13	12–15
Zimbabwe	118 800	105 443	89		5 560	5 070–6 060	2 612	47	43–52

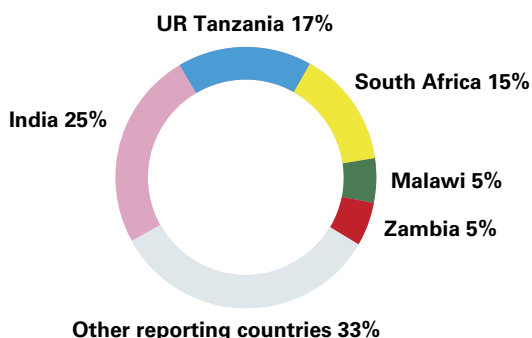
Blank cells indicate data not reported.

^a Estimates are shown to three significant figures.

^b Reasons for a higher than expected coverage might be that the numerator reported did not fully meet WHO's definition, e.g. it included non-household contacts, household contacts of clinically diagnosed TB cases or children five years or older. Uncertainty intervals could not be calculated when coverage was >100%.

FIG. 6.4

The top 5 countries providing TB preventive treatment to people living with HIV who were on antiretroviral treatment (ART), 2019



Despite progress, there are still considerable gaps in screening for TB, detection of TB and provision of TB preventive treatment among people living with HIV, even in high TB and TB/HIV burden countries (Fig. 6.5, Fig. 6.6). In some instances, it is possible that coverage was underestimated because country reports may not have included all people living with HIV who were started on TB preventive treatment in sites supported by the initiatives of the United States President’s Emergency Plan for AIDS Relief (PEPFAR) in 2019.

Data collected in 2020 using the UNAIDS National Commitments and Policy Instrument provide some insights about barriers to and enablers of the scale-up of TB preventive treatment, such as the availability of diagnostic tests (10). Making chest radiography and testing for TB infection with tuberculin skin tests (TSTs) or interferon gamma release assays (IGRAs) obligatory before initiation of TB preventive treatment can be limiting factors.

Conversely, shortening the treatment regimen is a critical enabler that increases adherence and facilitates multi-month prescriptions (see also Section 6.1.6). In terms of investigations before initiation of TB preventive treatment, of 21 high TB and TB/HIV countries that reported information, tests for TB infection were a prerequisite in only four countries, and chest radiography in nine. Only six countries (Botswana, Eswatini, Ghana, Lesotho, Malawi and Zambia) had transitioned to using the 3HP regimen; 14 recommended at least 6 months of isoniazid monotherapy as the only treatment option.

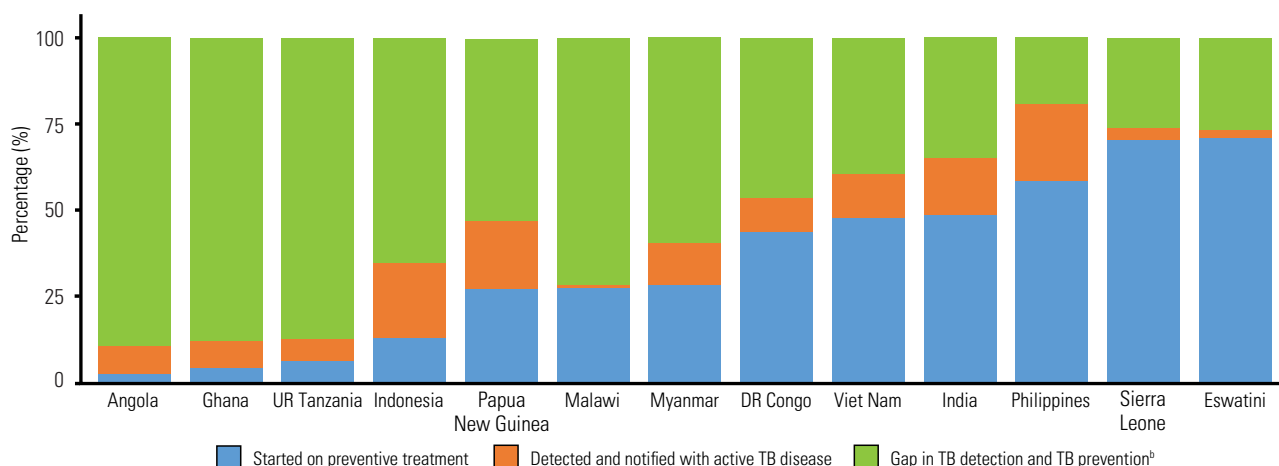
In 2020, WHO released updated consolidated guidance on HIV strategic information (the previous guidelines were published in 2015) (9). These guidelines aim to strengthen the ability of national programmes to identify and close gaps in service access, coverage and quality across the HIV services cascade. There are 15 core national HIV indicators, two of which are “initiation of TB preventive treatment” and “completion of TB preventive treatment among people living with HIV”. Monitoring these indicators may require countries to update their recording and reporting systems.

6.1.3 Household contacts of TB patients identified and screened in 2019

In 2019, 188 countries reported at least one patient with bacteriologically confirmed pulmonary TB, of which 114 countries (61%) also reported data about household contacts identified as eligible for TB preventive treatment. The ratio of the number of contacts identified to the number of people with bacteriologically confirmed TB ranged from 0.2 to 10 in the 16 high TB burden countries that reported data and up to 33 elsewhere. There was no clear association between the number of contacts identified per person with TB and country estimates of average household size (data not shown).

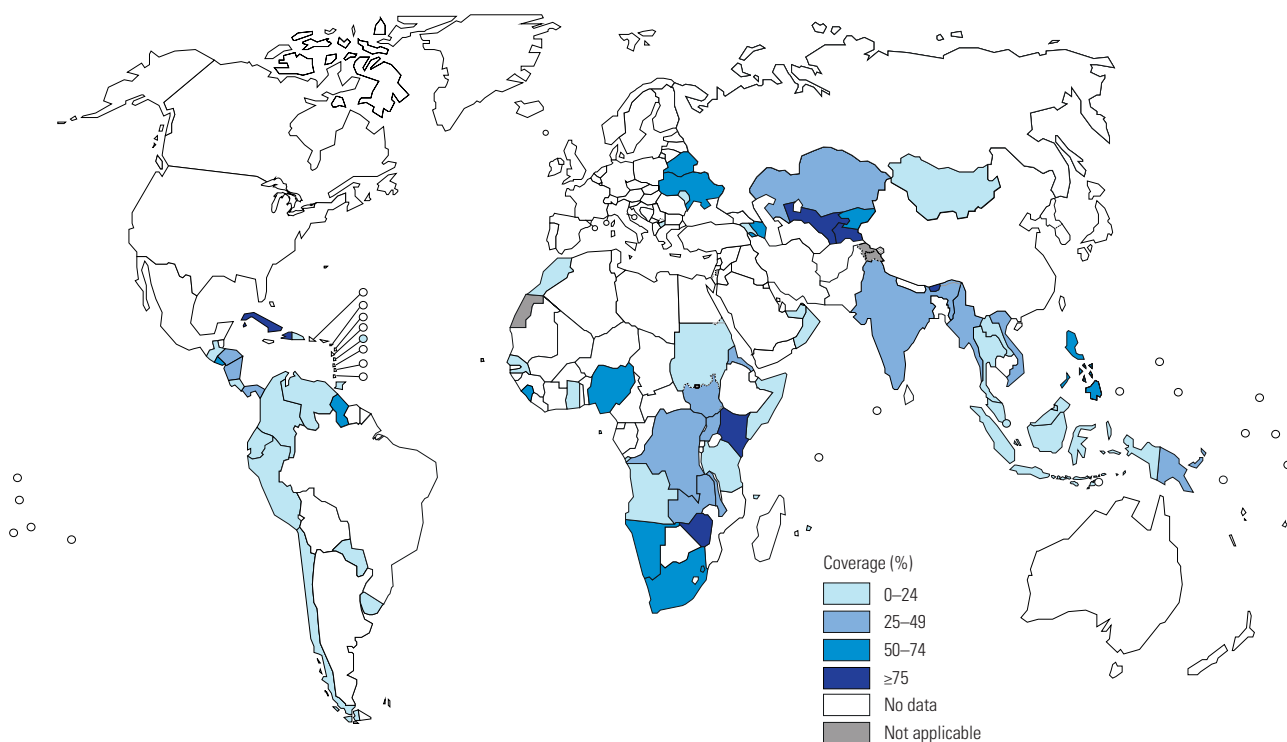
FIG. 6.5

Gaps in TB prevention and TB detection for people living with HIV who were started on antiretroviral treatment (ART) in selected high TB or TB/HIV burden countries^a, 2019



^a The selected countries are high TB or TB/HIV burden countries that reported on all three of the following: the number of people started on ART; the number of TB cases detected among people started on ART; and the number of people started on ART who were also started on TB preventive treatment. In high TB burden countries, testing for TB infection is not a requirement for initiation of TB preventive treatment, such that all those without active TB disease are eligible for TB preventive treatment.

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

FIG. 6.6**Coverage of TB preventive treatment among people living with HIV who started antiretroviral treatment (ART), 2019**

Of the 114 countries that reported data about household contacts, 109 (96%) provided data about the number of household contacts who were evaluated for TB disease and TB infection. Overall, among the 2.4 million people with bacteriologically confirmed pulmonary TB, 9.8 million contacts were identified, of whom 5.6 million (57%) were screened (Fig. 6.7).

In several countries, reporting remains unreliable, and interruptions in data availability make it difficult to draw conclusions about trends. In some countries, the reporting of data on contacts identified and screened is limited to individuals who start TB preventive treatment; thus, available data underestimate the actual numbers eligible and overestimate treatment coverage. Overestimation of coverage (including numerators that exceed denominators) also occurs when the number of children aged under 5 years who are eligible for treatment based on WHO guidelines is underestimated (11), or when the numerator includes children who are not household contacts or are aged 5 years or more.

6.1.4 Household contacts aged under 5 years starting TB preventive treatment, 2015–2019

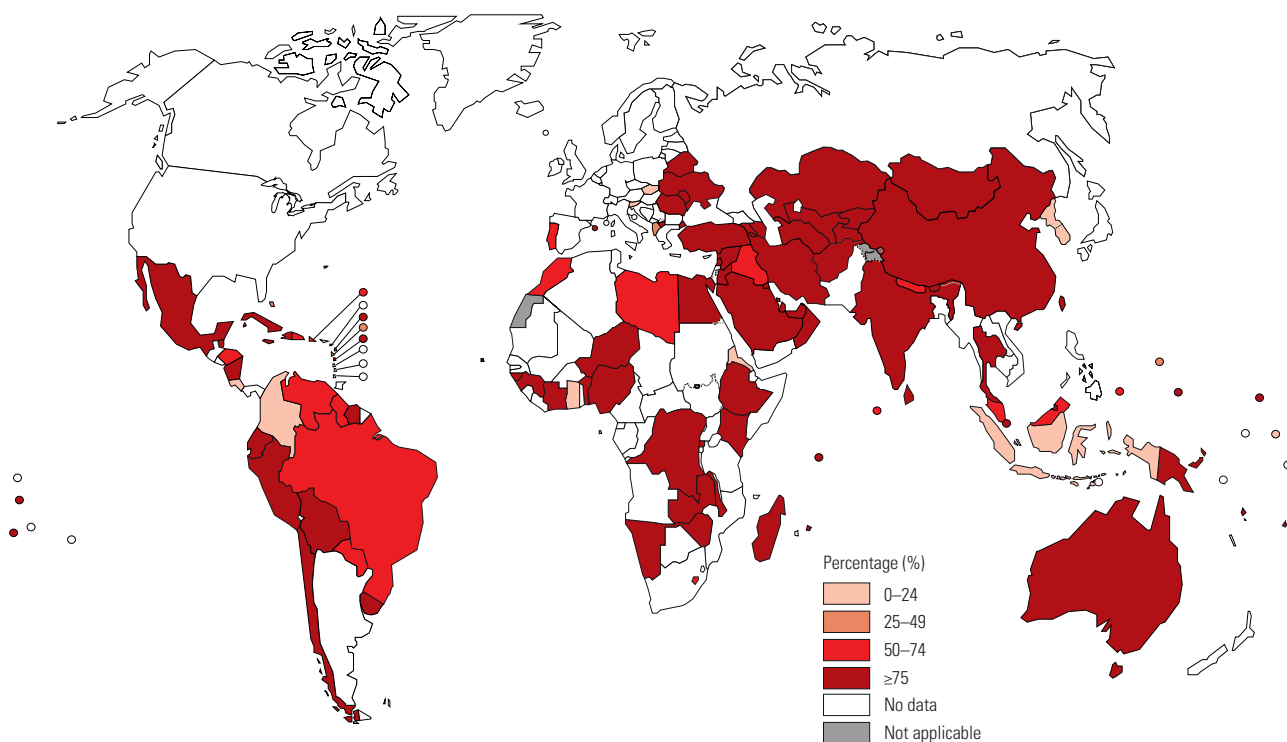
In 2019, of the 188 countries with at least one case of bacteriologically confirmed pulmonary TB, 121 reported that children aged under 5 years were started on TB preventive

treatment (up from 118 countries in 2018). This included 32 of the 38 high TB or high TB/HIV burden countries (Table 6.1), of which three reported data to WHO for the first time (Brazil, Chad and Ghana).

A total of 433 156 child contacts aged under 5 years were initiated on TB preventive treatment in 2019. This was an increase of 24% from 349 796 in 2018, and close to a five-fold increase from 87 242 in 2015. However, this number falls far short of what is needed to achieve the global target of 4 million during the years 2018–2022 (Fig. 6.2).

The largest numbers of child contacts aged under 5 years starting TB preventive treatment were reported by the WHO African Region (40% of the global total; 30 countries reported data) and the South-East Asia Region (40% of the global total; 11 countries reported data). In the 32 high TB and TB/HIV burden countries that reported data, 334 934 children started TB preventive treatment (77% of the global total). At country level, India reported the highest number (109 816), followed by the Democratic Republic of the Congo (34 763), Mozambique (30 766) and Bangladesh (29 880) (Table 6.1).

Globally, the 433 156 child contacts aged under 5 years who were started on TB preventive treatment in 2019 represented 33% of the approximately 1.3 million children estimated to be eligible for treatment (up from 27% in 2018). The highest levels of coverage were estimated for 18 countries in the WHO European Region (of which 16

FIG. 6.7**Percentage of household contacts of bacteriologically confirmed pulmonary new and relapse TB cases evaluated for TB disease and TB infection, 2019**

reached coverage of $\geq 75\%$), followed by 17 countries in the Region of the Americas (of which 11 reached coverage of $\geq 75\%$) and 13 countries in the Eastern Mediterranean Region (of which 9 reached coverage of $\geq 75\%$) (Fig. 6.8).

6.1.5 Household contacts aged 5 years and older starting TB preventive treatment, 2018–2019

In 89 countries, at least one contact aged 5 years and older was reported to have been started on TB preventive treatment in 2019. In 34 countries reporting at least one contact started on treatment, the total number of household contacts reported was identical to the number of contacts aged under 5 years, and in another six countries, only contacts aged under 5 years were reported: this implies that many national systems are primarily focused on contacts or data collection for this age group.

A total of 105 240 household contacts aged 5 years and older were reported to have been initiated on TB preventive treatment in 2019. Although this is an increase of 43% from 73 811 in 2018, it is far short of the number needed to achieve the global target set at the UN high-level meeting on TB (Fig. 6.2).

In 2019, the largest numbers were reported by the WHO European Region (59 694, 57% of the global total) and the Region of the Americas (22 052, 21% of the global total). Six countries reported that more than 5000 contacts aged 5 years or older started TB preventive treatment in 2019: Azerbaijan, Brazil, Thailand, Turkey, Ukraine and Uzbekistan.

6.1.6 Uptake of shorter rifamycin-containing regimens

The inclusion of rifamycins (rifampicin or rifapentine) in regimens for TB preventive treatment makes it possible to shorten the regimens, increasing the likelihood that they will be completed as prescribed. WHO recommends two rifapentine-containing treatment regimens for programmatic use: 3HP and, since 2020, 1HP.

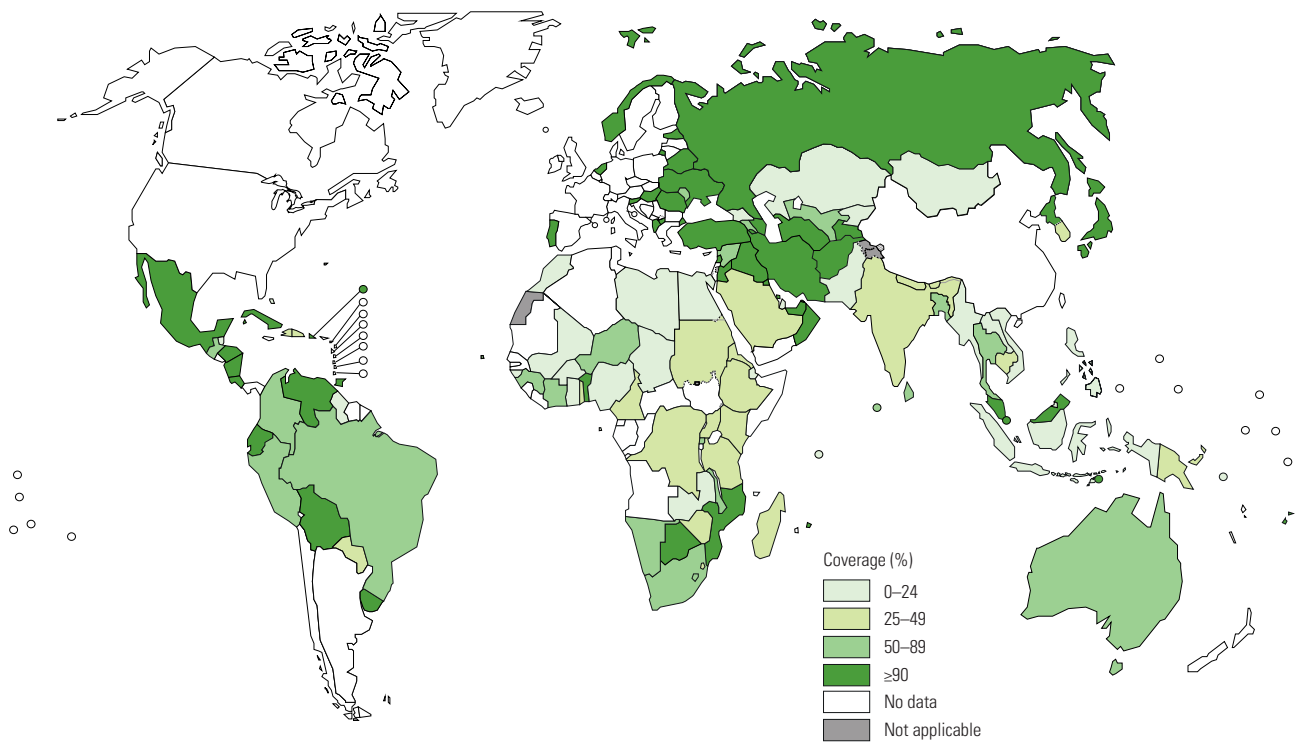
In 2019, 27 countries including four high TB burden countries (Bangladesh, Brazil, Lesotho and Thailand) reported using shorter rifamycin-containing regimens, up from 22 in 2018. The extent of use in these countries varied. Between 2018 and 2019, the reported number of people treated increased from 7018 to 8005.

By the end of June 2020, rifapentine had been supplied to at least 30 low-, middle- and high-income countries located in all WHO regions for use in shorter treatment regimens (Fig. 6.9). It has been used in trials in a further seven countries, and registered for TB preventive treatment by regulatory authorities in 14 countries. Several countries in which rifapentine is not yet registered have accessed it using local waiver mechanisms.

In recent years, global initiatives have been launched to increase the uptake of shorter regimens in eligible patients, including projects in high TB burden countries (Box 6.2). Since October 2019, public sector providers from 100 low- and middle-income countries have been eligible to procure rifapentine at a discounted price through an agreement reached between Unitaid, the Global Fund to Fight AIDS, Tuberculosis and Malaria and the manufacturer Sanofi (12).

FIG. 6.8

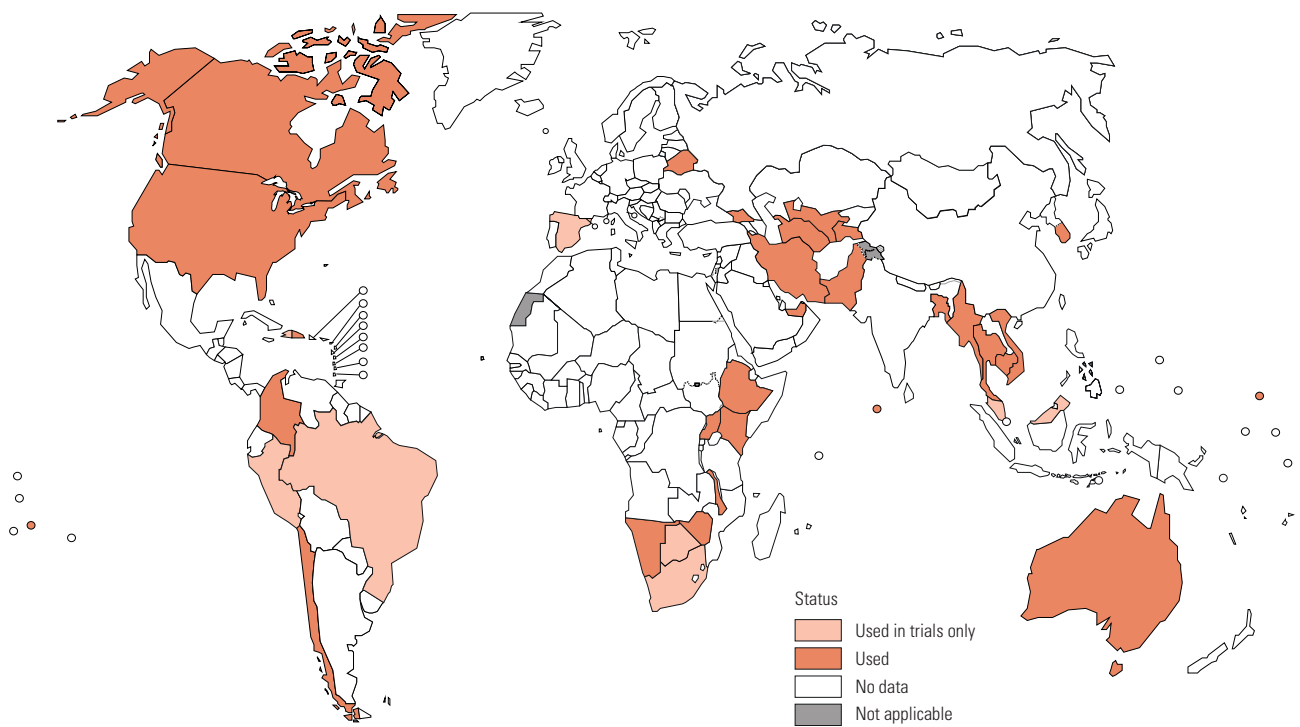
Coverage of TB preventive treatment among eligible children aged under 5 years,^a 2019



^a Children aged <5 years who were household contacts of bacteriologically confirmed pulmonary TB patients.

FIG. 6.9

Use of rifapentine in TB preventive treatment regimens,^a by June 2020



^a Currently registered for use in China, Hong Kong SAR, DR Congo, Ghana, India, Indonesia, Mongolia, Myanmar, Philippines, Singapore, South Africa, Thailand, Turkmenistan, Uganda, USA (Source: Sanofi, 2020) - data as of 15 June 2020. Several countries in which rifapentine is not yet registered have accessed it using local waiver mechanisms.

New initiatives to improve uptake and scale-up of TB preventive treatment

For several years, Unitaid has supported expanded access to two novel short-course regimens for TB preventive treatment: 3HP and 3HR. This has been done through improved access to medicines, the development of models for early detection of TB infection and the delivery of preventive services in high TB burden countries. Two major projects are being implemented between 2017 and 2021 with funding from Unitaid: IMPAACT4TB and CaP TB.

IMPAACT4TB

IMPAACT4TB (Increasing market and public health outcomes through scaling up affordable access models of short-course preventive therapy for TB) aims to identify and promote the use of affordable, quality-assured 3HP among people living with HIV and household contacts aged under 5 years. It is being implemented in 12 countries that account for about half of global TB incidence (Brazil, Cambodia, Ethiopia, Ghana, India, Indonesia, Kenya, Malawi, Mozambique, South Africa, the United Republic of Tanzania and Zimbabwe). The project provides support to new manufacturers of rifapentine-based regimens; assists countries with the procurement, registration and importation of rifapentine; and assists with the development of tools to identify eligible individuals, improve medication adherence and manage adverse events. Training material and job aids have also been developed.

The project has invested in three safety, tolerability and drug–drug interaction studies among adults and children living with HIV who are on dolutegravir-based antiretroviral treatment. Two implementation research studies are being supported, one focusing

on “Opt-out 3HP prescribing” and the other examining community-based contact investigation. The safety and treatment completion of 1HP compared with 3HP in household contacts and people living with HIV is being investigated.

CaP TB

CaP TB (Catalyzing Paediatric Tuberculosis Innovations) is being implemented in India and nine sub-Saharan African countries (Cameroon, Côte d’Ivoire, Democratic Republic of Congo, Kenya, Lesotho, Malawi, the United Republic of Tanzania, Uganda and Zimbabwe). The aim is to increase the uptake of innovative approaches to TB diagnosis, treatment, and care in children and adolescents aged 14 years or under. The project component on TB preventive treatment focuses on household contacts aged under 5 years and people living with HIV. In collaboration with WHO, CaP TB teams are supporting the updating of national guidelines to include recommendations on the use of shorter regimens. By July 2020, the project had supported the rollout of child-friendly formulations of 3HR in Cameroon, Kenya and Zimbabwe.

The project includes an evaluation of intervention impact. In addition, a cluster randomized study in Cameroon and Uganda (the CONTACT Study) will compare community-based child contact screening and 3HR with the current standard of care. The study will also include a cost–effectiveness analysis and a qualitative component, to assess user acceptability and social determinants of TB disease, treatment and prevention.

6.2 TB infection prevention and control

Strengthening TB infection prevention and control is part of Pillar 2 of the End TB Strategy; it is also one of the collaborative TB/HIV activities that fall under Pillar 1 (Chapter 2). Transmission of *M. tuberculosis* can occur in a variety of congregate and other settings, including health care facilities and households. Health care workers may be at increased risk of TB infection, and nosocomial transmission of drug-resistant TB in hospitalized patients has been documented (13–15).

The risk of TB among health care workers relative to the risk in the general adult population is one of the indicators recommended by WHO for measuring the impact of interventions for TB infection prevention and control in health care facilities. If effective prevention and control measures are in place, the risk ratio for TB in health care workers compared with the general adult population should be close to 1.

In 2019, 22 314 TB cases among health care workers were reported from 76 countries; India accounted for 47% of these cases and China accounted for 18%. The notification rate among health care workers could be calculated for 63 of the 76 countries. In 42 countries reporting at least five TB cases among health care workers in 2019, the rate ranged from 9.5 to 1972 cases per 100 000 health care workers, with the highest rate observed in Lesotho.

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 latest estimated size of the adult population from the UN population division (16), with the population restricted to those aged 15–64 years for comparability with the health workforce. The ratios of the TB notification rate among health care workers to the rate in the general adult population are shown in Fig. 6.10. In 2019, the rate of TB cases among health care workers was more than double the TB notification rate

in the general adult population in eight of the 42 countries reporting more than five health care workers with TB (Botswana, Dominican Republic, Honduras, India, Lesotho, Uganda, the United Republic of Tanzania and Zimbabwe). The ratio was below 1 in 22 of these countries.

In 2019, WHO released new guidance on TB infection prevention and control based on the most recent evidence (17). The recommended approaches include administrative, environmental and personal protection measures. To ensure that appropriate measures are in place, it is essential to have regular monitoring and audits, and timely feedback of health care practices (18), including TB infection prevention and control services. Common approaches to mitigate the dual risks of TB and COVID-19 infection are discussed in [Chapter 3](#).

6.3 TB vaccination

The BCG vaccine remains the only licensed vaccine against TB; it provides moderate protection against severe forms of TB (TB meningitis and miliary TB) in infants and young children. 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.

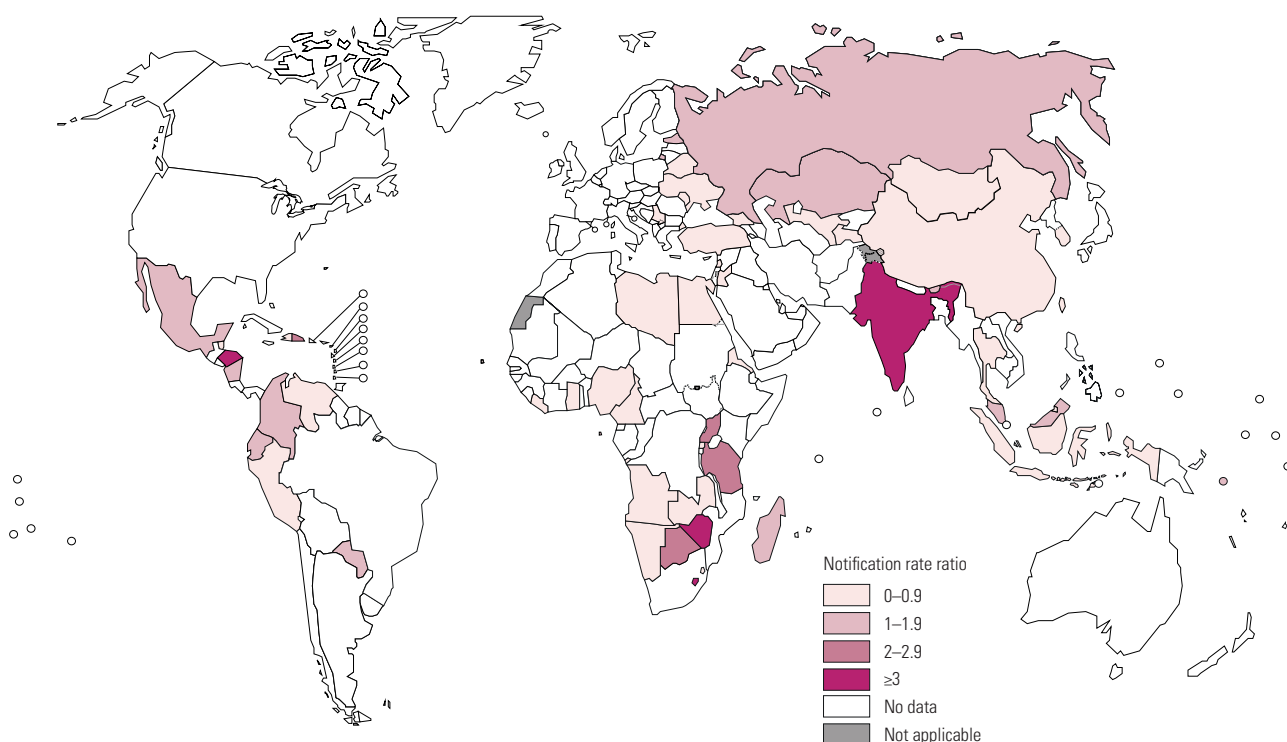
Fig. 6.11 summarizes national policies on BCG vaccination (19). Among 178 countries for which data were collected, 153 recommended universal BCG vaccination and 25 reported a national BCG policy for at-risk individuals in high-risk groups.

In 2019, 213 countries reported vaccination coverage to WHO, of which 147 provided data for BCG coverage (20). Among the countries that recommend universal BCG vaccination, 115 reported BCG coverage greater than 80% and 87 reported coverage greater than 90%. Among the 30 high TB burden countries, coverage ranged from 45% in Papua New Guinea to 99% in Bangladesh, China, Thailand and the United Republic of Tanzania.

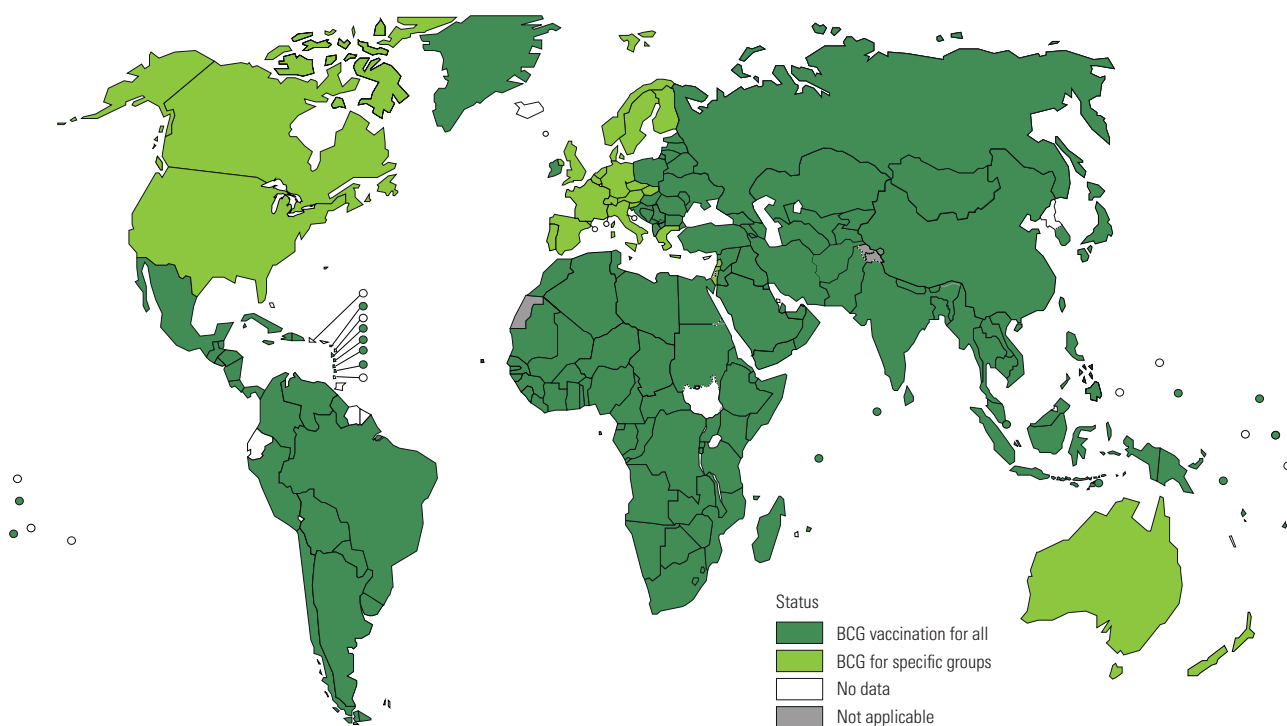
In 2018, the experimental TB vaccine candidate M72/AS01E, developed by GlaxoSmithKline and the International AIDS Vaccine Initiative, was found to be significantly protective against TB disease in individuals with evidence of TB infection in a Phase IIb trial conducted in Kenya, South Africa and Zambia. The best estimate of vaccine efficacy was 50% (90% confidence interval [CI], 12–71%) after about 3 years of follow-up (21, 22). Further details are provided in [Chapter 9](#).

Meanwhile, sustaining and improving BCG vaccination coverage continues to be important. This requires sufficient production capacity, effective demand forecasting and procurement strategies at national level, and effective engagement with all segments of society to ensure high vaccination coverage.

FIG. 6.10
Notification rate ratio of TB among healthcare workers compared with the adult population,^a 2019



^a Data from 7 countries were excluded where the number of health care workers reported was less than 1000.

FIG. 6.11**BCG vaccination practices by country**

Source: The BCG World Atlas 2nd Edition, <http://www.bcgatlas.org/>, accessed August 2020

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TB patients outside a hospital where they are being treated, Angola

Stephen Eisenhammer/Reuters

Chapter 7

Financing for TB prevention, diagnosis and treatment

Key facts and messages

The political declaration at the first United Nations (UN) high-level meeting on tuberculosis (TB), held in September 2018, includes a target to mobilize at least US\$ 13 billion^{a,b} annually by 2022 for TB prevention, diagnosis and treatment. The Stop TB Partnership's *Global Plan to End TB, 2018–2022* (the Global Plan), released in December 2019, estimates that US\$ 13 billion is required in low- and middle-income countries in 2020, rising to US\$ 15 billion in 2022.

Based on data reported to the World Health Organization (WHO) by 121 low- and middle-income countries that account for 98% of the world's notified TB cases, US\$ 6.5 billion is available in 2020, up from US\$ 6.0 billion in 2019 and US\$ 5.0 billion in 2010.^a However, funding needs to double to reach the funding target set at the UN high-level meeting. There is an urgent need to step up efforts to mobilize additional funding from domestic sources and international donors.

Of the total of US\$ 6.5 billion available in 2020, US\$ 4.2 billion is for diagnosis and treatment of drug-susceptible TB, and US\$ 2.26 billion is for diagnosis and treatment of multidrug-resistant TB (MDR-TB); both these amounts are only slightly more than half of what the Global Plan estimates is required. The remaining amount (<US\$ 0.1 billion) includes funding for TB preventive treatment (covering drugs only), interventions specifically related to HIV-associated TB and miscellaneous items.

Overall, of the US\$ 6.5 billion available in 2020, US\$ 5.5 billion (85% of the total) 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). The BRICS group accounts for 57% (US\$ 3.7 billion) of available funding in 2020 and 47% of the world's TB cases; 97% of their funding is from domestic sources (81% in South Africa, 92% in India, and 100% in Brazil, China and the Russian Federation).

In other low- and middle-income countries, international donor funding remains crucial. In 2020, such funding accounts for 44% of total funding in the 25 high TB burden countries outside BRICS (which have 40% of the world's notified TB cases) and for 57% of total funding in low-income countries.

International donor funding, as reported by national TB programmes (NTPs), increased from US\$ 0.9 billion in 2019 to US\$ 1.0 billion in 2020. The single largest source (77% of the total in 2020) is the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund).

International donor funding documented in the Organisation for Economic Co-operation and Development (OECD) creditor reporting system includes funding for TB that flows through NTPs, as well as funding provided to other recipients. The total amount recorded in 2018 (the latest year for which data

are available) was US\$ 0.9 billion, of which 58% was from the Global Fund (from 2006 to 2018, the Global Fund's contribution averaged 63%).

The OECD documented that funding for TB (US\$ 0.9 billion) in 2018 was much lower than for HIV (US\$ 6.9 billion) and malaria (US\$ 1.8 billion). To provide some context for these amounts, the latest estimates (for 2018) of the burden of disease in terms of disability-adjusted life-years (DALYs) lost owing to illness and death are 49 million for HIV/AIDS, 46 million for malaria and 48 million for TB.

The median cost per person treated for TB in 2019 was US\$ 860 for drug-susceptible TB and US\$ 5659 for MDR-TB.

Health financing data from national health accounts provide important insights into the status of progress towards universal health coverage. This is discussed in [Chapter 8](#).

^a All values are in constant 2020 US\$.

^b The declaration also includes a funding target for TB research and development of US\$ 2 billion per year, 2018–2022 ([Chapter 2](#)).

Progress in reducing the burden of tuberculosis (TB) disease requires adequate funding sustained over many years. The World Health Organization (WHO) began annual monitoring of funding for TB prevention, diagnosis and treatment in 2002, and publishes its findings in global TB reports and peer-reviewed publications (1-3). The Treatment Action Group has monitored funding for TB research since 2005, and publishes its findings in an annual report (4).

In 2018, global funding targets for TB were set for the first time, as part of the political declaration at the United Nations (UN) high-level meeting on TB held in September 2018 (Chapter 2) (5). The targets are to mobilize at least US\$ 13 billion annually by 2022 for TB prevention, diagnosis and treatment, and an additional US\$ 2 billion annually for TB research in the 5-year period 2018–2022.

The first part of this chapter provides an up-to-date summary of the financial resources estimated to be needed to achieve the End TB Strategy's 2020 milestones, as well as two new global targets for TB treatment and prevention that were set in the UN high-level meeting political declaration (Section 7.1). It focuses on resources needed for TB prevention, diagnosis and treatment, as opposed to TB research.¹ The next two sections present and discuss trends in funding for TB prevention, diagnosis and treatment by category of expenditure and funding source for the period 2006–2020 (Section 7.2), and funding gaps reported to WHO by national TB programmes (NTPs) for the same period (Section 7.3). Data are shown overall for 121 low- and middle-income countries that account for 98% of reported TB cases, and for major country groupings. More detailed country-specific data for 2020 are shown for 30 high TB burden countries.² Section 7.4 provides the latest estimates (i.e. for 2019) of the unit costs of treatment for drug-susceptible TB and multidrug-resistant TB (MDR-TB).

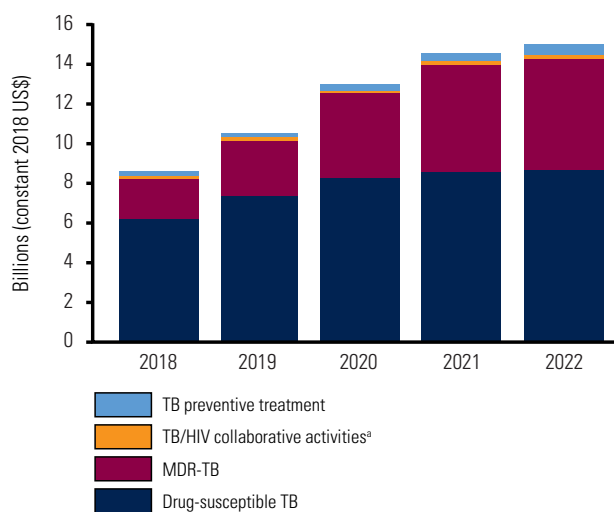
As highlighted in previous editions of the global TB report, analysis of health financing data (overall data, not specific to TB) can provide important insights into progress towards universal health coverage (UHC), which is necessary to achieve the End TB Strategy milestones set for 2020 and 2025 (Chapter 2). Measurement of the costs faced by people with TB 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 facing catastrophic costs due to TB disease. The 2020 milestone of zero set for this indicator requires progress towards UHC and social protection (included under Pillar 2 of the End TB Strategy). Analysis of health financing data, measurement of costs faced by TB patients and their households, UHC and social protection are discussed in Chapter 8.

¹ Chapter 2 provides an overview of progress towards global TB targets, including the two funding targets set at the UN high-level meeting on TB. Chapter 9 also provides a summary of funding for TB research in 2015–2018.

² The WHO list of 30 high TB burden countries defined for the period 2016–2020 is described and explained in Annex 2.

FIG. 7.1

Estimates of funding required for TB prevention, diagnosis and treatment in low- and middle-income countries in the Global Plan to End TB 2018–2022



^a Funding estimates for TB/HIV collaborative activities 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: Stop TB Partnership Global Plan to End TB 2018–2022 (7). This plan is an update of the original Global Plan to End TB, which was for the period 2016–2020.

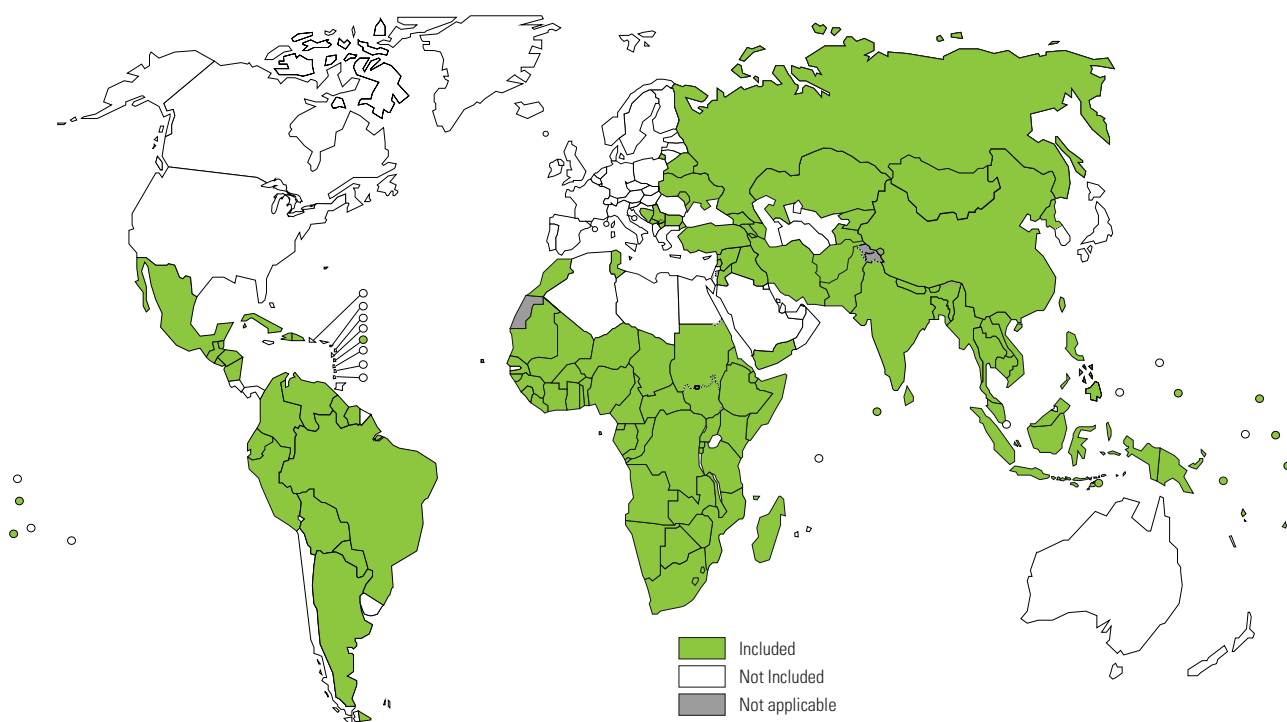
Further country-specific data on TB financing can be found in finance profiles online (6). The methods used to compile, validate and analyse TB financing data reported to WHO and those used to estimate funding for inpatient and outpatient care are described in an online appendix.³

7.1 Estimates of funding required for TB prevention, diagnosis and treatment, 2018–2022

In December 2019, the Stop TB Partnership published the *Global Plan to End TB, 2018–2022* (the Global Plan) (7). The Global Plan includes estimates of the funding required for TB prevention, diagnosis and treatment to reach global TB targets and milestones set in the End TB Strategy as well as the targets (derived from End TB Strategy milestones) for the numbers of people to be provided with TB treatment (40 million, 2018–2022) and TB preventive treatment (30 million, 2018–2022) set at the UN high-level meeting on TB (Chapter 2).

The Global Plan's estimates for 129 low- and middle-income countries are shown in Fig. 7.1. The total for 2018–2022 is US\$ 62 billion (an average of US\$ 12.4 billion per

³ The online appendix is available here: http://www.who.int/tb/publications/global_report/

FIG. 7.2**The 121 low- and middle-income countries included in analyses of TB financing, 2006–2020^a**

^a Countries were included in trend analyses if complete and quality TB finance data were available for at least four years in the period 2006–2020. Of 134 low- and middle-income countries (World Bank classification on 1 July 2020), 121 were included in the analyses: 28/29 low-income, 46/50 lower-middle-income, and 47/55 upper-middle-income countries representing 12%, 59% and 27% of 2019 notified cases, respectively. The following 13 low- and middle-income countries were excluded: Albania, Algeria, Costa Rica, Dominica, Egypt, Gambia, Grenada, Jamaica, Libya, St Vincent and the Grenadines, Turkmenistan, Uzbekistan and the occupied Palestinian territory, including East Jerusalem.

year).¹ The amount estimated to be required in 2020 is US\$ 13 billion (the minimum amount required to reach the 2022 global target set at the UN high-level meeting), increasing to US\$ 15 billion in 2022.

Of the estimated total in 2020, US\$ 8.3 billion (64%) is for diagnosis and treatment of drug-susceptible TB, US\$ 4.3 billion is for diagnosis and treatment of MDR-TB,² US\$ 0.3 billion is for TB prevention services and US\$ 0.2 billion is for interventions specifically related to HIV-associated TB.³ The latter amount is comparatively small because it does not include the funding needed for antiretroviral therapy (ART) for people living with HIV.⁴

¹ The plan estimates that an additional US\$ 3 billion is needed in high-income countries, bringing the global total to US\$ 65 billion. The annual total for all countries increases from US\$ 9.2 billion in 2018 to US\$ 13.6 billion in 2020 and US\$ 15.6 billion in 2022.

² The burden of drug-resistant TB (in terms of new cases per year) is not projected to increase between 2018 and 2022; however, increased amounts of funding are required between 2018 and 2022 to close gaps in detection and treatment (see [Chapter 2](#) and [Chapter 5](#)).

³ The plan includes a more detailed breakdown of resource needs for 10 categories. The 129 low- and middle-income countries included in the Global Plan's analysis of funding requirements are those in the 2018 World Bank classification, plus the Russian Federation.

⁴ Instead, this is included in estimates of funding required for HIV, published by the Joint United Nations Programme on HIV/AIDS (UNAIDS).

The previous Global Plan, for 2016–2020, included estimates of the funding that could be mobilized from domestic sources and the balance needed from international donor sources, for low- and middle-income countries eligible to apply to the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) (8).⁵ In an optimistic scenario for domestic funding, it was estimated that US\$ 2.7 billion per year would be required from international donors. The Global Plan 2018–2022 does not include updated projections of funding needed from domestic and external sources (7).

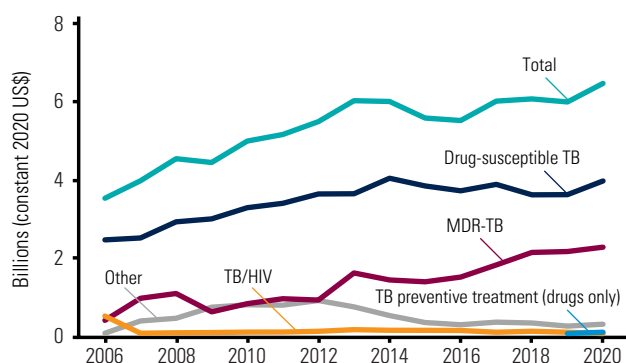
7.2 TB funding, overall and by category of expenditure and source of funding, 2006–2020

Data reported by NTPs to WHO since 2006 were used to analyse funding trends for 2006–2020 in 121 low- and middle-income countries ([Fig. 7.2](#)). These countries accounted for 98% of the global number of TB cases-notified in 2019. In these 121 countries, funding for TB prevention, diagnosis and treatment has reached US\$ 6.5 billion in 2020, an increase from US\$ 6.0 billion in 2019 and US\$ 5.0 billion in 2010 ([Fig. 7.3](#); all figures are in con-

⁵ Countries not eligible to apply to the Global Fund include Brazil, China, the Russian Federation and 46 other countries classified as upper-middle-income.

FIG. 7.3

Funding for TB prevention, diagnosis and treatment in total and by category of expenditure^a, 121 countries with 98% of reported cases, 2006–2020



^a Data for TB preventive treatment (drugs) specifically are only available for 2019 and 2020.

stant 2020 US dollars). Despite this growth in funding, the amount in 2020 is only half of what the Global Plan estimates is needed (Fig. 7.1) and only half of the 2022 target set at the UN high-level meeting on TB (Fig. 7.4).

Of the total of US\$ 6.5 billion available in 2020, US\$ 4.2 billion (65%) is for diagnosis and treatment of drug-susceptible TB.¹ This is just over half of what the Global Plan estimates is needed for 2020 (US\$ 8.3 billion).

Funding for MDR-TB reached US\$ 2.26 billion in 2020, a large increase from the US\$ 1.4 billion available in 2015 (Fig. 7.3). This growth is largely explained by trends in the BRICS group of countries (Brazil, Russian Federation, India, China and South Africa) (Fig. 7.5), which account for 77% of total funding for MDR-TB in the period 2015–2020, and 58% of the total number of people with MDR-TB who were diagnosed and reported in 2019. Nonetheless, the US\$ 2.26 billion available for MDR-TB in 2020 overall is only just over half of the US\$ 4.3 billion that the Global Plan estimates is required in that year.

In 2020, 66 countries reported funding gaps for MDR-TB, with the largest gaps reported by China (US\$ 109 million), Indonesia (US\$ 70 million) and Pakistan (US\$ 55 million) (Fig. 7.10). In addition, the funding required for MDR-TB will continue to increase (Fig. 7.1), reaching an estimated US\$ 5.7 billion in 2022 – nearly triple the amount available in 2020. The need for more funding is evident in the persistently large gaps in detecting and treating people with MDR-TB.²

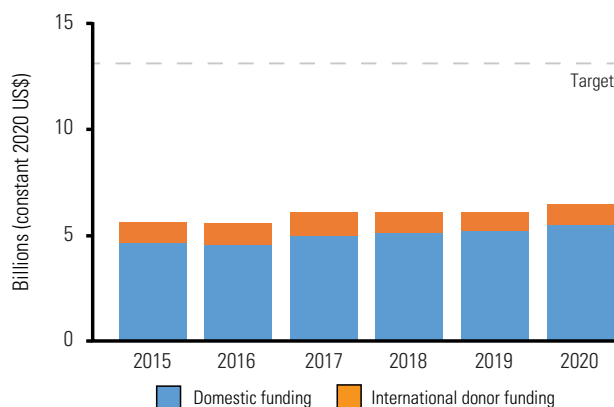
¹ This includes funding for diagnostic testing using the Xpert MTB/RIF[®] or Xpert Ultra assays, which simultaneously test for TB and rifampicin resistance.

² Further details are provided in Chapter 2 and Chapter 5.

FIG. 7.4

Funding for TB prevention, diagnosis and treatment in 121 low- and middle-income countries compared with the global target set at the UN high-level meeting on TB of at least US\$ 13 billion per year by 2022

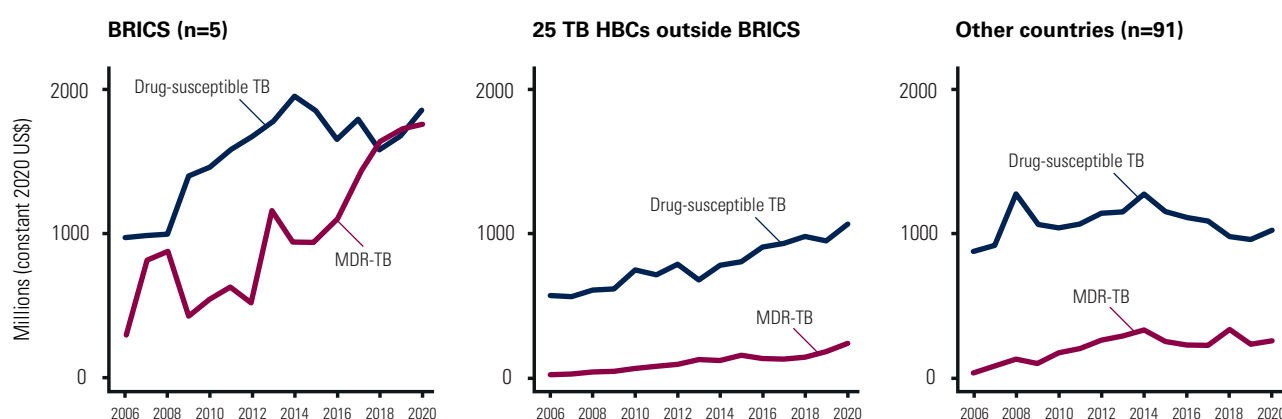
The 121 countries accounted for 98% of the world's officially reported TB cases in 2019.



Overall, most funding during the period 2006–2019 was provided from domestic sources, and this remains the case in 2020 (Fig. 7.6).³ In 2020, US\$ 5.5 billion (85%) of the total funding of US\$ 6.5 billion for TB is from domestic sources. However, aggregated figures for the 121 low- and middle-income countries are strongly influenced by the BRICS group of countries, and they conceal substantial variation among countries in the share of funding from domestic and international sources (Fig. 7.7).

The BRICS group of countries account for US\$ 3.7 billion (57%) of the total of US\$ 6.5 billion available in 2020 (and 47% of the world's TB cases) and overall, 97% of funding is from domestic sources (81% in South Africa, 92% in India, and 100% in Brazil, China and the Russian Federation). In India, there was an impressive increase in the TB-specific budget, and in domestic funding for this budget, from 2016 to 2019, although both amounts are expected to fall from 2019 to 2020 (Fig. 7.8). India's national TB budget in 2020 is almost double what it was in 2016, and domestic funding for this budget in 2020 is 3.7 times the level it was in 2016 (and 13 times the level of 2006).

³ Domestic funding includes both funding for TB-specific budgets, and funding for inpatient and outpatient care (usually funded through more general budget lines), as explained in the online technical appendix. In Fig. 7.6 and Fig. 7.7, it is assumed that funding for inpatient and outpatient care is provided domestically rather than by international donors. This is justified on the basis that middle-income countries account for most (92%) of the funding estimated to be used for inpatient and outpatient care for TB patients (estimated at US\$1.6 billion in 2020), 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).

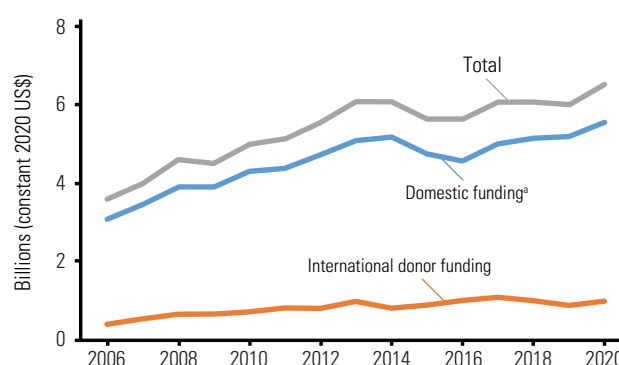
FIG. 7.5**Funding for drug-susceptible TB and MDR-TB by country group^a, 2006–2020**

^a BRICS (Brazil, Russian Federation, India, China and South Africa) accounted for 47% of the total number of TB cases notified globally in 2019. The 25 high TB burden countries outside BRICS accounted for 40%. The remaining countries (n=91) included in financing analyses accounted for 11% of the TB cases notified globally in 2019.

In other low- and middle-income countries, international donor funding remains crucial (Fig. 7.7). For example, in 2020 such funding accounts for 44% of the total funding available in the 25 high TB burden countries outside the BRICS countries¹ (which have 40% of the world's notified TB cases) and 57% of the total funding available in low-income countries. In the 25 high TB burden countries outside BRICS, the share of total funding from domestic sources has ranged from 53% in 2016 to 57% in 2019, and it is 56% in 2020. In this group of high TB burden countries outside BRICS, countries that have substantially increased domestic funding since 2015 (either through dedicated TB allocations or through health care provision) include Bangladesh, Lesotho, Philippines, Thailand, Viet Nam and Indonesia.²

International donor funding committed for 2020 and reported by NTPs³ to WHO amounts to US\$ 1.0 billion, a slight increase from US\$ 0.9 billion in 2019. Of this amount, 77% is from the Global Fund.

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. 7.9, Table 7.1 and Table 7.2).

FIG. 7.6**Funding for TB prevention, diagnosis and treatment by funding source, 121 countries with 98% of reported TB cases, 2006–2020**

^a Domestic funding includes TB-specific budgets and the estimated resources used for inpatient and outpatient care. 92% of the funding of US\$ 1.6 billion for inpatient and outpatient care in 2020 is accounted for by middle-income countries; such countries do not typically receive international donor funding for inpatient and outpatient care services.

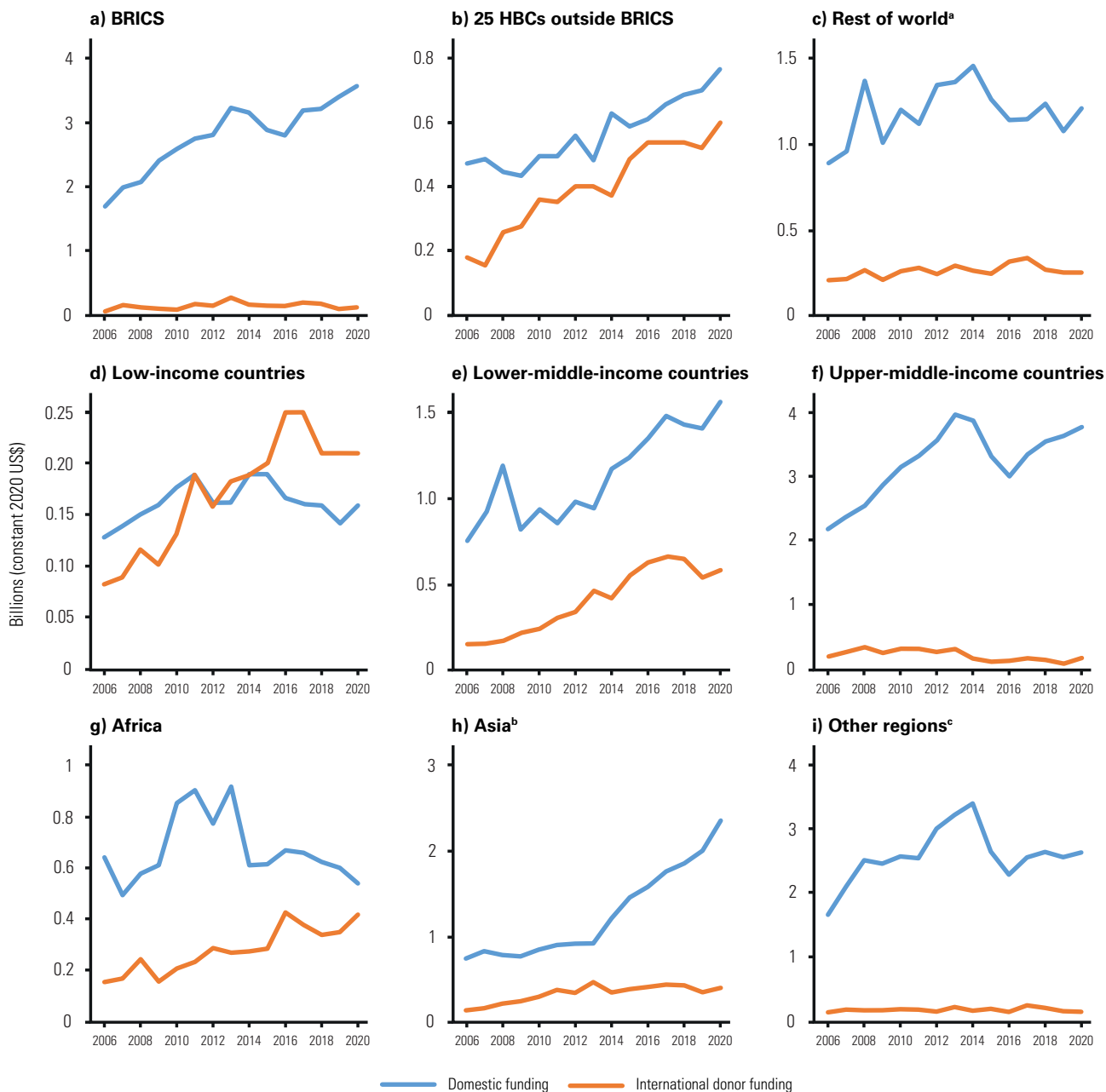
¹ The list of 30 high TB burden countries used by WHO during the period 2016–2020 is explained in Annex 2. The countries are listed in Fig. 7.9, Table 7.1 and Table 7.2.

² For further details, see the online country profiles and the Global TB Report 2020 app (Annex 3).

³ The reported international donor funding is based on reported received amounts, except for a handful of countries (e.g. Liberia, Nigeria and South Africa) that did not report expenditure data in 2020 or previous years. For these countries, imputed amounts that account for committed international funding were used instead.

FIG. 7.7

Funding for TB prevention, diagnosis and treatment from domestic sources and international donors, 9 country groups, 2006–2020



BRICS, Brazil, Russian Federation, India, China and South Africa.

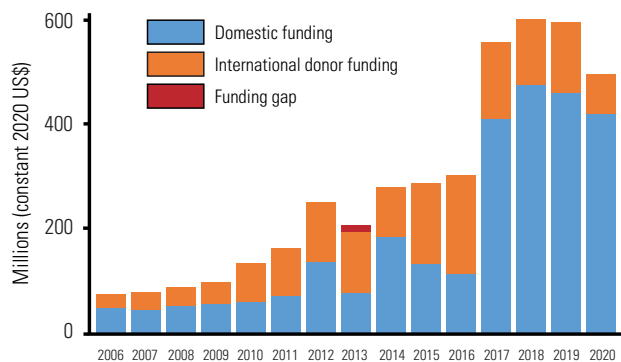
^a Rest of world includes 91 countries that are not in the list of 30 high TB burden countries.

^b Asia includes the WHO regions of South-East Asia and the Western Pacific.

^c Other regions consist of three WHO regions: the Eastern Mediterranean Region, the European Region, and the Region of the Americas.

FIG. 7.8

National budget for TB and sources of funding in India, 2006–2020

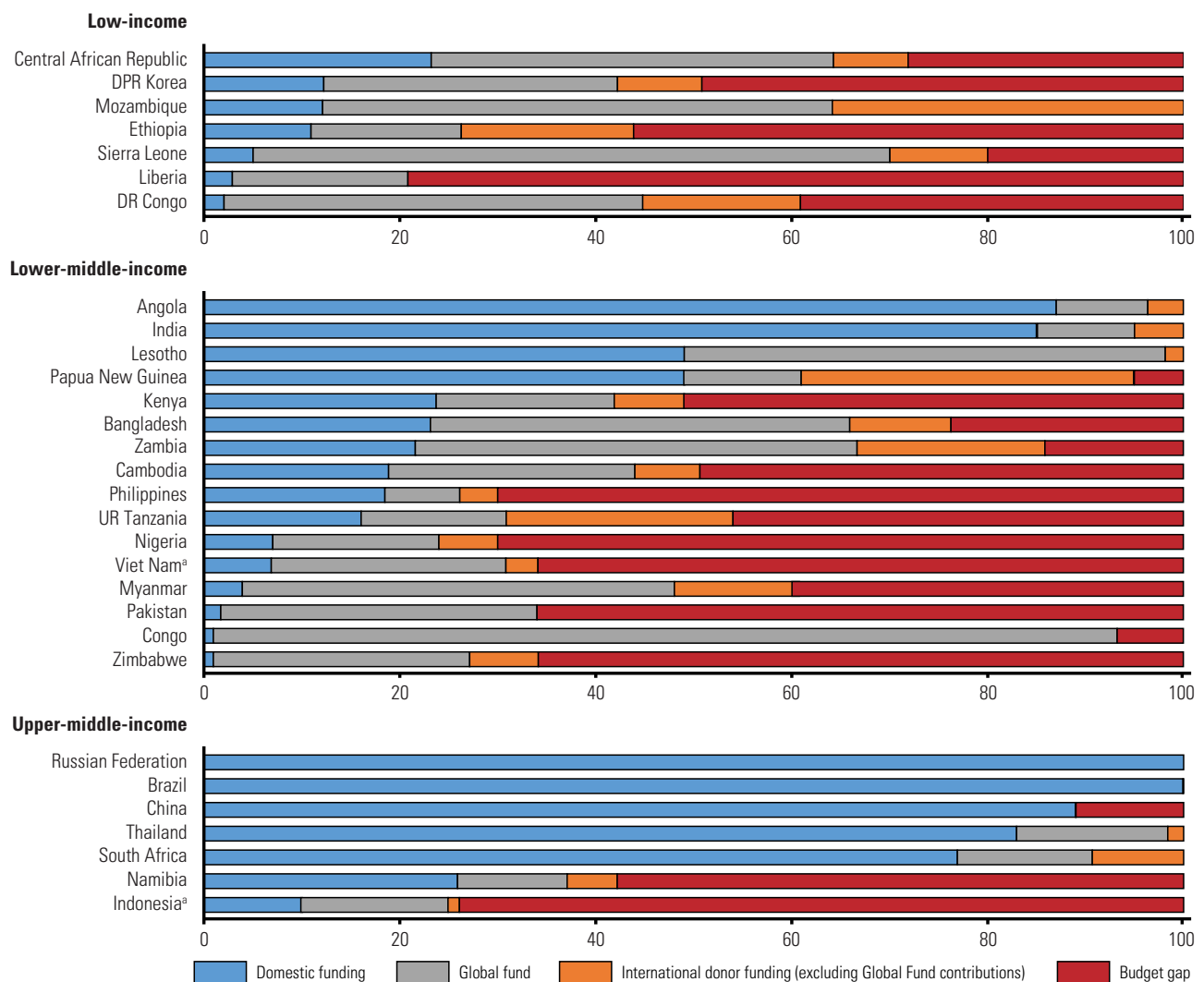


Among one third of 30 high TB burden countries,¹ more than 50% of funding for the TB-specific budgets included in national strategic plans for TB in 2020 is from international donors.

Both Fig. 7.8 and Fig. 7.9 illustrate the potential to increase domestic funding in some high TB burden countries. In 2020, among the group of seven low-income countries, the proportion of the TB budget reported by NTPs as being funded from domestic sources ranges from 2% in the Democratic Republic of the Congo to 23% in the Central African Republic. In the group of 16 lower-middle-income countries, the proportion ranges from 0.8% in Zimbabwe to 87% in Angola. In the group of seven upper-middle-income countries, the proportion

FIG. 7.9

Sources of funding and funding gaps for the TB-specific budgets included in national strategic plans for TB in the 30 high TB burden countries, 2020



^a The funding gap for Indonesia and Viet Nam reflects the fact that amounts of funding from provincial and district budgets are unknown at the national level.

¹ Bangladesh, Central African Republic, Congo, Democratic Republic of the Congo, Lesotho, Mozambique, Myanmar, Papua New Guinea, Sierra Leone and Zambia.

TABLE 7.1

Reported budget in national strategic plans 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, 2020 (current US\$ millions)

COUNTRY	TOTAL BUDGET IN NATIONAL STRATEGIC PLAN FOR TB	DS-TB	MDR-TB	TB/HIV	TB PREVENTION (DRUGS ONLY)	INPATIENT AND OUTPATIENT CARE (DS-TB)	INPATIENT AND OUTPATIENT CARE (MDR-TB)	ESTIMATED TOTAL RESOURCES REQUIRED FOR TB CARE
Angola	20	8.5	11	<0.1	0.75	16	7.7	44
Bangladesh	135	128	5.6	<0.1	1.2	13	1.8	150
Brazil ^a	34	31	3.4	0.14	0	23	1.1	58
Cambodia	33	29	2.5	0.95	0.45	21	0.58	54
Central African Republic	3.3	2.4	0.66	0.11	0.16	1.0	<0.1	4.4
China ^b	994	592	401	0.50	0	—	—	994
Congo	6.5	5.8	0.66	<0.1	0	2.7	<0.1	9.3
DPR Korea	49	31	12	0	5.9	24	7.4	81
DR Congo	41	34	5.0	2.5	0.13	3.3	1.3	46
Ethiopia	85	68	11	6.4	0.42	28	1.3	114
India	497	408	67	1.2	21	300	152	949
Indonesia	429	292	92	43	1.7	69	18	516
Kenya	75	65	9.0	1.7	0	16	3.2	94
Lesotho	10	8.5	1.1	<0.1	0.69	0.42	<0.1	11
Liberia	9.9	8.2	1.5	0.15	<0.1	<0.1	<0.1	9.9
Mozambique	26	14	8.6	3.2	0.73	6.8	0.59	34
Myanmar	79	61	16	2.1	0.11	3.8	0.77	84
Namibia	31	27	4.1	0.19	0.47	4.6	7.1	43
Nigeria	384	273	101	7.7	2.5	4.9	8.6	397
Pakistan	158	98	59	0.22	0	4.5	0.20	163
Papua New Guinea	34	18	8.4	7.5	<0.1	9.5	0.98	45
Philippines	217	199	13	3.9	1.0	100	8.3	325
Russian Federation ^{b,c}	1 571	367	1 195	0.23	8.5	—	—	1 571
Sierra Leone	9.4	6.1	2.9	0.30	<0.1	22	0.89	32
South Africa	197	177	16	0	3.6	16	22	235
Thailand ^a	31	20	11	<0.1	<0.1	7.3	8.9	48
UR Tanzania	76	61	5.6	3.9	5.4	4.5	1.4	82
Viet Nam ^a	71	58	11	1.8	<0.1	30	5.8	106
Zambia	49	29	8.8	2.2	9.1	2.5	1.5	53
Zimbabwe	32	22	1.7	5.2	2.5	1.0	0.23	33
30 HIGH TB BURDEN COUNTRIES	5 390	3 142	2 086	95	66	733	263	6 385

— indicates values that cannot be calculated.

^a In 2020, the budget data reported by Brazil were for the federal level only, and for Thailand and Viet Nam they were for the central level only.

^b No amounts for the additional resources required for inpatient and outpatient care are shown for China and the Russian Federation because the reported NTP budgets included budgets for inpatient and outpatient care.

^c In the Russian Federation, the staff and infrastructure reported for TB care and control were allocated to DS-TB (15.9%) and MDR-TB (84.1%) by WHO based on the proportion of beddays used by DS-TB and MDR-TB patients.

TABLE 7.2

Reported budget in national strategic plans for TB, available funding for this budget from domestic and international donor sources and funding gap, 30 high TB burden countries, 2020 (current US\$ millions)

COUNTRY	TOTAL 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 ^c
Angola	20	18	2.6	87%	13%	0
Bangladesh	135	31	72	30%	70%	32
Brazil ^a	34	34	<0.1	100%	<0.1%	0
Cambodia	33	6.2	11	37%	63%	16
Central African Republic	3.3	0.77	1.6	32%	68%	0.91
China	994	884	0.35	100%	<0.1%	109
Congo	6.5	0.10	6.0	1.6%	98%	0.48
DPR Korea	49	6.0	19	24%	76%	24
DR Congo	41	0.85	25	3.3%	97%	16
Ethiopia	85	9.3	28	25%	75%	47
India	497	420	77	85%	15%	0
Indonesia ^b	429	42	69	38%	62%	318
Kenya	75	18	19	49%	51%	38
Lesotho	10	5.5	5.7	49%	51%	0
Liberia	9.9	0.29	1.80	14%	86%	7.8
Mozambique	26	3.2	23	12%	88%	0
Myanmar	79	3.1	45	6.5%	93%	32
Namibia	31	8.1	5.1	61%	39%	18
Nigeria	384	27	89	23%	77%	268
Pakistan	158	3.4	50	6.4%	94%	104
Papua New Guinea	34	17	16	52%	48%	1.8
Philippines	217	40	25	62%	38%	152
Russian Federation	1 571	1 571	0	100%	0%	0
Sierra Leone	9.4	0.47	7.0	6.4%	94%	1.9
South Africa	197	152	45	77%	23%	0
Thailand ^a	31	26	5.4	83%	17%	0
UR Tanzania	76	12	29	30%	70%	35
Viet Nam ^a	71	4.9	19	20%	80%	46
Zambia	49	11	32	25%	75%	6.9
Zimbabwe	32	0.25	11	2.3%	98%	21
30 HIGH TB BURDEN COUNTRIES	5 390	3 356	736	82%	18%	1 298

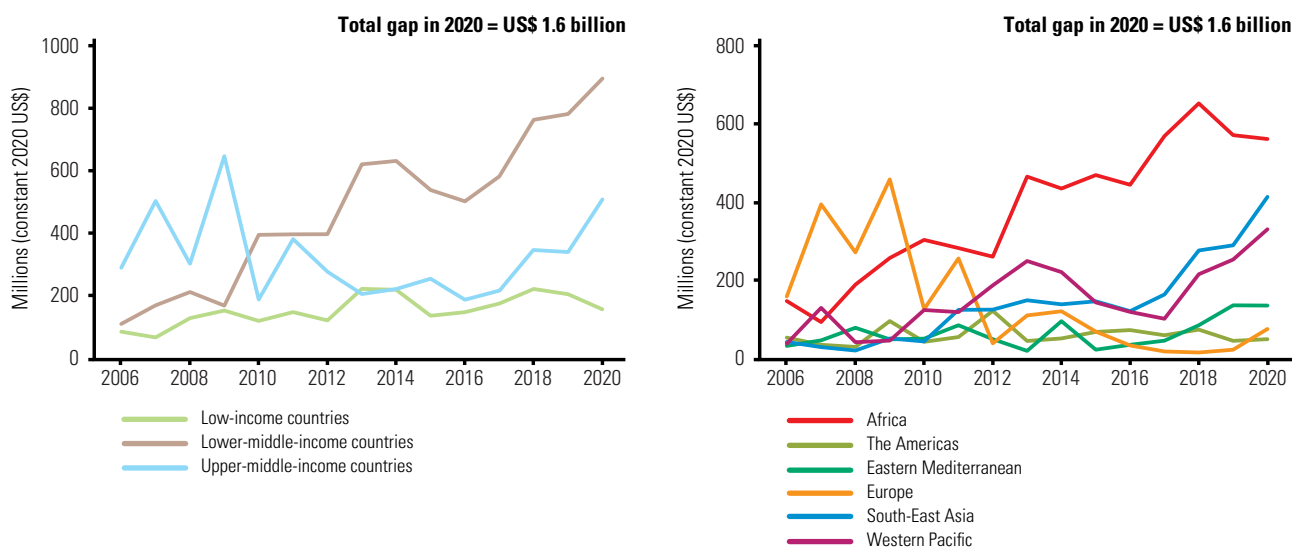
^a In 2020, the budget data reported by Brazil were for the federal level only, and for Thailand and Viet Nam they were for the central level only.

^b The funding gap in 2020 for Viet Nam and Indonesia reflects the fact that amounts of funding from provincial and district budgets are unknown at national level.

^c The funding gap reflects the anticipated gap for the year at the time a country reported data to WHO in the 2020 round of global TB data collection.

FIG. 7.10

Reported funding gaps for TB by income group and by WHO region, 2006–2020



ranges from less than 25% in Indonesia and Namibia¹ to 100% in Brazil and the Russian Federation.

Funding reported by NTPs to WHO does not capture all international donor funding for TB.² A complementary analysis based on donor reports to the Organisation for Economic Co-operation and Development (OECD) is provided in [Box 7.1](#).³

7.3 Funding gaps reported by NTPs, 2006–2020

Reported funding gaps are calculated as the difference between NTP assessments of funding needs for TB prevention, diagnosis and treatment in their national strategic plans, and the actual amounts of available funding reported by NTPs. Data for the period 2006–2020 are shown in [Fig. 7.9](#), [Fig. 7.10](#) and [Table 7.2](#).

Many NTPs continue to report funding gaps. The total reported gap in 2020 is US\$ 1.6 billion, the highest gap reported to date, up from US\$ 1.3 billion in 2019 and US\$ 0.9 billion in 2015. The most striking trends are the increases in the reported funding gap in lower-middle-income countries and the WHO African Region; recently, gaps in the South-East Asia and Western Pacific regions have also grown ([Fig. 7.10](#)). These increases suggest that, although national strategic plans and associated budgets for TB have become more ambitious, mobilization of funding has not kept pace. Overall, lower-middle-income countries accounted for 57% (US\$ 0.9 billion) of the total reported gap in 2020, with the largest gaps reported by Nigeria (US\$ 268 million), the Philippines (US\$ 152

million), Pakistan (US\$ 104 million), Ukraine (US\$ 73 million), Viet Nam (US\$ 46 million),⁴ Kenya (US\$ 38 million), the United Republic of Tanzania (US\$ 35 million), Bangladesh (US\$ 32 million), Myanmar (US\$ 32 million) and Zimbabwe (US\$ 21 million).

Reported funding gaps have been relatively stable in low-income countries and in the WHO European Region and Region of the Americas. Low-income countries that reported large funding gaps in 2020 include Ethiopia (US\$ 47 million), Democratic People’s Republic of Korea (US\$ 24 million), the Democratic Republic of the Congo (US\$ 16 million), Uganda (US\$ 14 million) and Malawi (US\$ 11 million) ([Table 7.2](#) and [Figure 7.9](#)).

Of the US\$ 1.6 billion funding gap reported by NTPs in 2020, US\$ 1.2 billion (75%) is for drug-susceptible TB and US\$ 0.4 billion (25%) is for MDR-TB. Relative to total funding needs, the funding gap is larger for drug-susceptible TB than for MDR-TB.

The total reported gap is less than a quarter of the gap that exists when available funding in 2020 (US\$ 6.5 billion) is compared with the Global Plan’s estimated requirement of US\$ 13 billion in 2020 ([Section 7.1](#)). 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. Some budgets have also been revised downwards in the context of the COVID-19 pandemic and reallocation of funds from TB to the COVID-19 response has been reported by several countries (e.g. in Georgia, Kenya, the Philippines, Somalia and Zambia).⁵

¹ The proportion in Namibia has fallen owing to austerity measures that have been put in place during a recession.

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

³ Out-of-pocket expenditures are also not included in the financing data reported by NTPs; these are discussed in [Chapter 8](#).

⁴ Funding gaps in Viet Nam and Indonesia are partly due to the difficulties faced by NTPs in tracking and reporting forecast expenditure at the provincial level.

⁵ The reductions reported to date have been relatively small (<US\$ 5 million) but may increase.

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 OECD’s creditor reporting system (CRS) is the most comprehensive source of information about international donor funding. The CRS Aid Activity database enables analysis of where aid goes, what purposes it serves and what policies it aims to implement, on a comparable basis for all members of the OECD’s Development Assistance Committee (DAC). Data are for developing countries or territories eligible to receive official development assistance (ODA), and are collected for individual projects and programmes. The focus is on financial data (<https://stats.oecd.org/>).

As of 2018, funding data (both commitments and disbursements) were provided by 37 multilateral donor organizations; members of the OECD’s DAC (which comprises 29 individual countries and the European Union) and a further 20 countries beyond the DAC that report to the OECD.

Disbursement data include both direct transfers to countries and the provision of goods and services, such as in-kind transfers or technical assistance. Data

were analysed on gross total official disbursements^a for TB (code 12263: Tuberculosis control) received by non-OECD countries during 2008–2018. Of note, the CRS does not capture 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 of Great Britain and Northern Ireland (United Kingdom). In addition, government contributions that are channelled through multilateral organizations are attributed to the multilateral organization, not to the government of origin.^b

Fig. B7.1.1 shows trends in international donor funding between 2008 and 2018, globally and for four of the world’s major regions as geographically organized by the OECD. The total from all sources in 2018 was US\$ 0.9 billion, slightly more than double the amount of US\$ 409 million in 2008. In 2018, the Global Fund provided 58% of international donor funding. The second-largest donor was the US government, which contributed US\$ 262 million (30% of the global total) in bilateral overseas development assistance.^c

FIG. B7.1.1
International donor funding for TB prevention, diagnosis and treatment by source, globally and by OECD region, 2008–2018

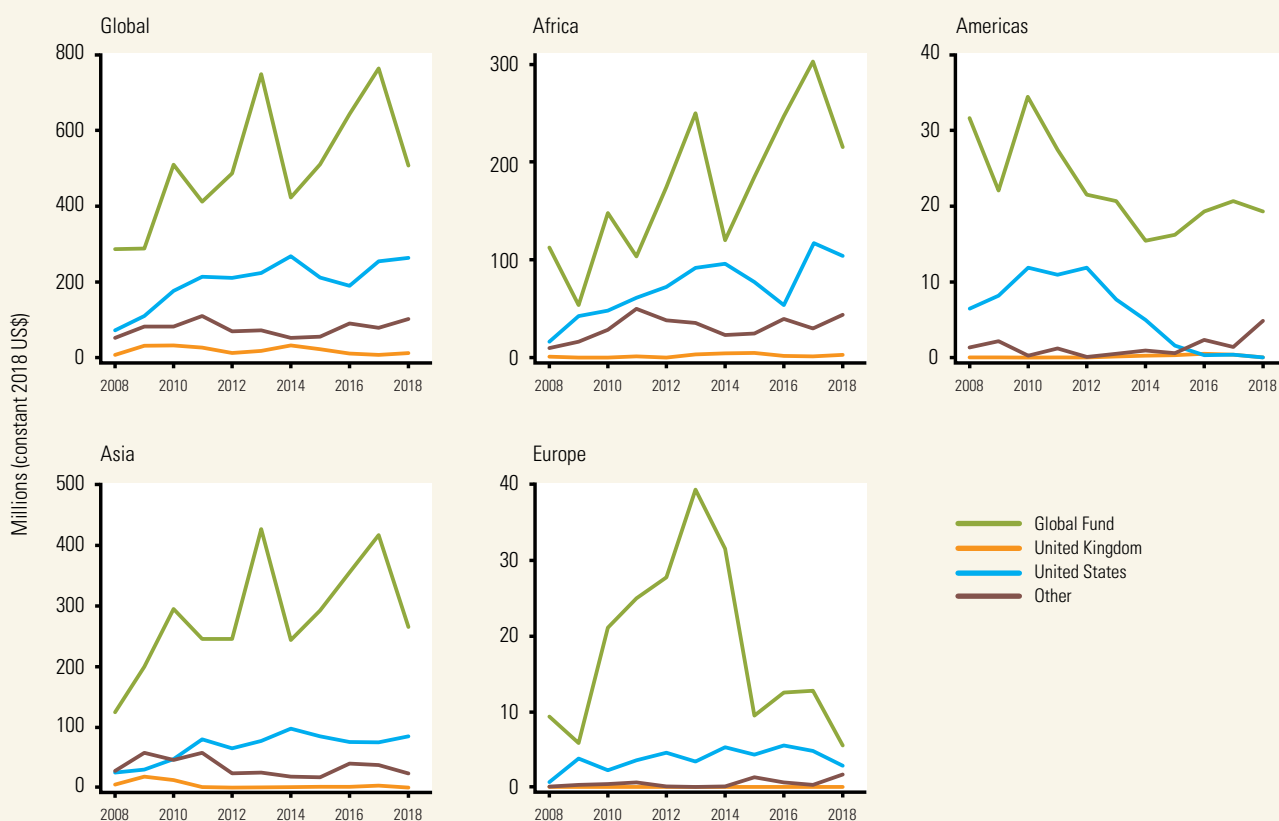
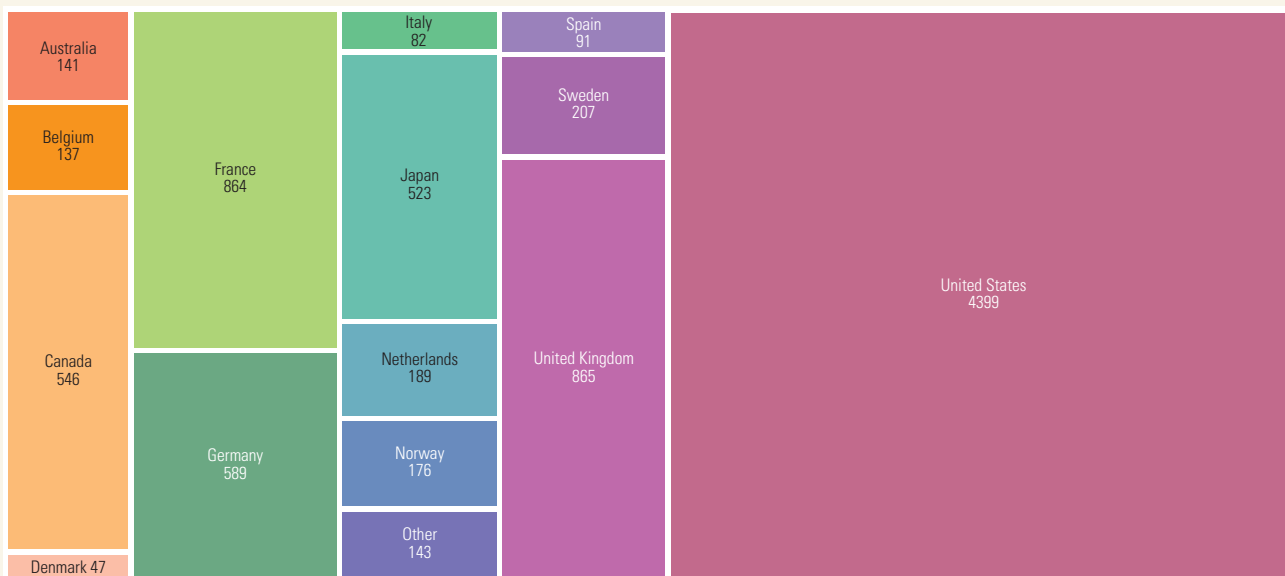


FIG. B7.1.2

International donor funding (in 2018 US\$ millions) for TB prevention, diagnosis and treatment from individual countries, 2008–2018



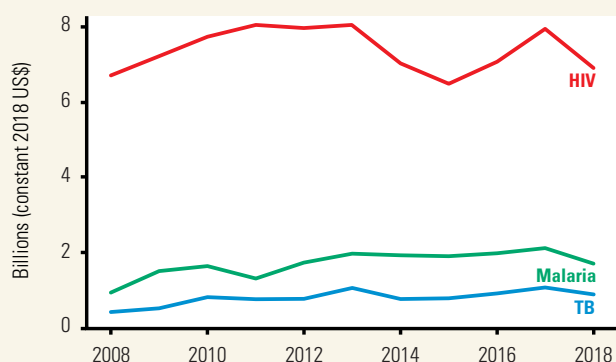
From 2008 to 2018, the Global Fund was consistently the largest provider of international donor funding, with the share averaging 63% in this period. However, its contributions to funding for TB declined noticeably between 2017 and 2018. In 2018, the total was US\$ 509 million. Disbursements from the US government steadily increased from 2006 to 2014, peaking at US\$ 263 million in 2014 before declining to US\$ 187 million in 2016, with a recovery to US\$ 255 million in 2017 and a further increase to US\$ 262 million in 2018.^c From 2017 to 2018, disbursements from the US government for TB increased in Asia and declined in Africa, while other donors increased their funding, particularly in Africa, the Americas and Europe. The regional panels show that most of the funding from international donors flows to Africa and Asia.^d

Fig. B7.1.2 shows the proportion and amounts of funding from 2008 to 2018 from individual DAC countries to non-OECD countries, including their estimated funding for TB via contributions to the Global Fund.^e During this period, 49% of funding came from the US. The next largest individual country contributors were the United Kingdom (10%), France (10%), Germany (7%), Canada (6%) and Japan (6%).

Fig. B7.1.3 shows that international funding for TB (US\$ 0.9 billion in 2018) is about half of that for malaria (US\$ 1.8 billion in 2018) and about 13% of that for HIV (US\$ 6.9 billion in 2018). To provide some context for these amounts, the disability-adjusted life-years (DALYs) lost to illness and death for these three diseases in 2018 were 49 million for HIV/AIDS, 46 million for malaria and 48 million for TB (9).

FIG. B7.1.3

International donor funding for TB, HIV and malaria, 2008–2018



^a These are the sum of ODA plus other official flows; that is, they are disbursements (as opposed to commitments, which may not materialize) by official sectors at large to the recipient country.

^b 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.

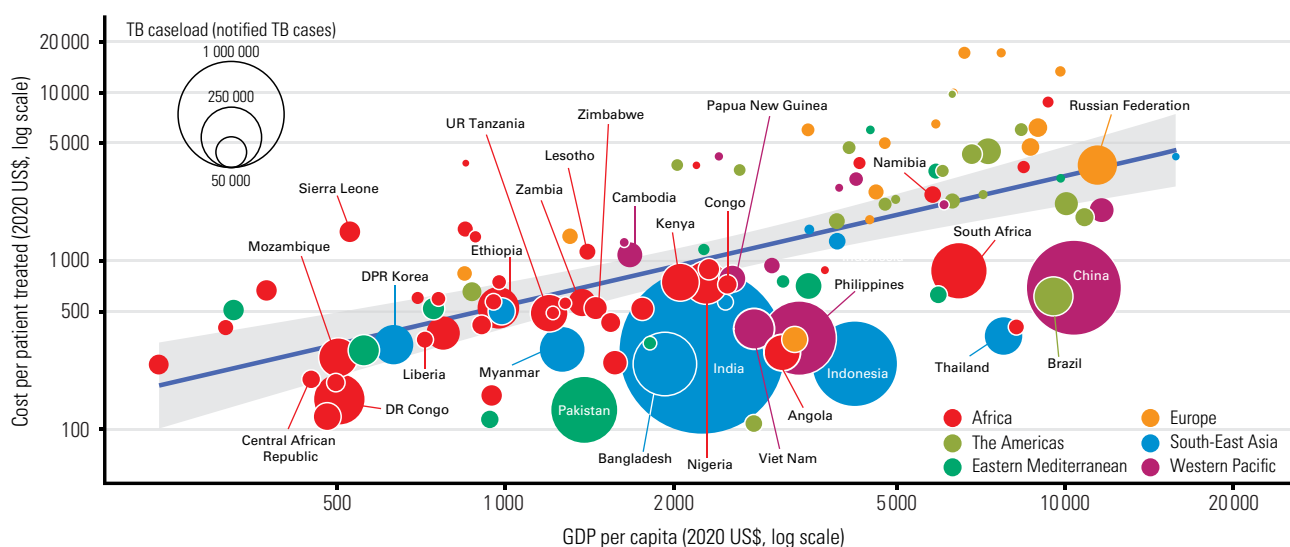
^c Disbursements from the US government captured in the OECD database are lower than official allocations.

^d Regional panels in **Fig. B7.1.1** exclude funding for Oceania as well as US\$ 99 million for TB that was “not allocated” (in the CRS classification) to a specific country or region. In 2018, the OECD reported US\$ 0.7 billion of international donor funding for TB that was allocated to countries and US\$ 149 million that was unallocated. The total of US\$ 0.9 billion in 2018 is captured in the global panel of **Fig. B7.1.1**.

^e Funding amounts include bilateral funding as well as estimated funding for TB via contributions to the Global Fund, with the assumption that 18% of Global Fund contributions are allocated to TB. A country’s contribution to TB funding provided by the Global Fund is assumed to be the same as its share of total contributions to the Global Fund (e.g. if a country provided 5% of the total contributions to the Global Fund, it was assumed to provide 5% of the TB funding attributed to the Global Fund).

FIG. 7.11

Estimated cost per patient treated for drug-susceptible TB in 112 countries,^a 2019



^a Limited to countries with at least 100 patients on first-line treatment in 2019.

7.4 Unit costs of treatment for drug-susceptible TB and MDR-TB, 2019

The cost per patient treated in 2019 for drug-susceptible TB and MDR-TB was estimated for 112 countries and 89 countries, respectively.¹ All 30 countries in the lists of high TB burden countries and high MDR-TB burden countries (except for Uzbekistan, which did not report data in 2020) were included in the analyses.² Unit cost estimates are shown in **Fig. 7.11** and **Fig. 7.12**, and analytical methods are described in the **online technical appendix**.³

7.4.1 Drug-susceptible TB

The median cost per person treated for drug-susceptible TB in 2019 was US\$ 860.⁴ In general, about 71% of this cost was accounted for by expenditures reported by NTPs, with the remainder being WHO-estimated costs for inpatient and outpatient care. There was a positive relationship between the cost per person treated and gross domestic product (GDP) per capita, and a negative relationship between the cost and the size of the patient caseload (indicating economies of scale; e.g. in China, India and Indonesia). In all but one of the 30 high TB burden countries included in the analysis, the cost per person treated for drug-susceptible TB was less than the GDP per capita; the exception was Sierra Leone.

In the 15 European countries included in the analysis, the cost per person treated for drug-susceptible TB was relatively high. These countries, which are all in Eastern Europe and Central Asia (EECA), have relatively high costs due to extensive use of hospitalization for patients in the intensive phase of treatment and a relatively long length of stay for people treated in hospital (an average of 58 days per person in 2019). High programme costs relative to a smaller pool of patients (i.e. <3000 people in 2019) also help to explain comparatively high per-person costs in some countries (e.g. in Belarus, Bulgaria and Serbia, the unit cost was US\$ 17 133, US\$ 13 254 and US\$ 10 018, respectively; in Bulgaria and Serbia, the cost was higher than GDP per capita).

It is also evident that some EECA countries have markedly reduced their use of hospitalization and have changed their model of care for people with drug-susceptible TB. From 2014 to 2019, 13 of the 15 EECA countries reduced the number of bed days per person. The size of the reduction (which is influenced by both the percentage of people with drug-susceptible TB who are hospitalized and the average length of stay if hospitalized) ranged from 21% in the Republic of Moldova to 81% in the Russian Federation (where the proportion of people with TB who were hospitalized fell from 93% to 69%, and the average length of stay if hospitalized fell from 75 to 19 days). In Kazakhstan, which has the second-highest number of cases among EECA countries after the Russian Federation, the number of bed days per person with drug-susceptible TB fell by 25%.

¹ Analysis for drug-susceptible TB was limited to countries that notified at least 100 TB cases in 2019; for MDR-TB, estimates were restricted to countries that reported at least 20 patients on second-line treatment for MDR-TB in 2019.

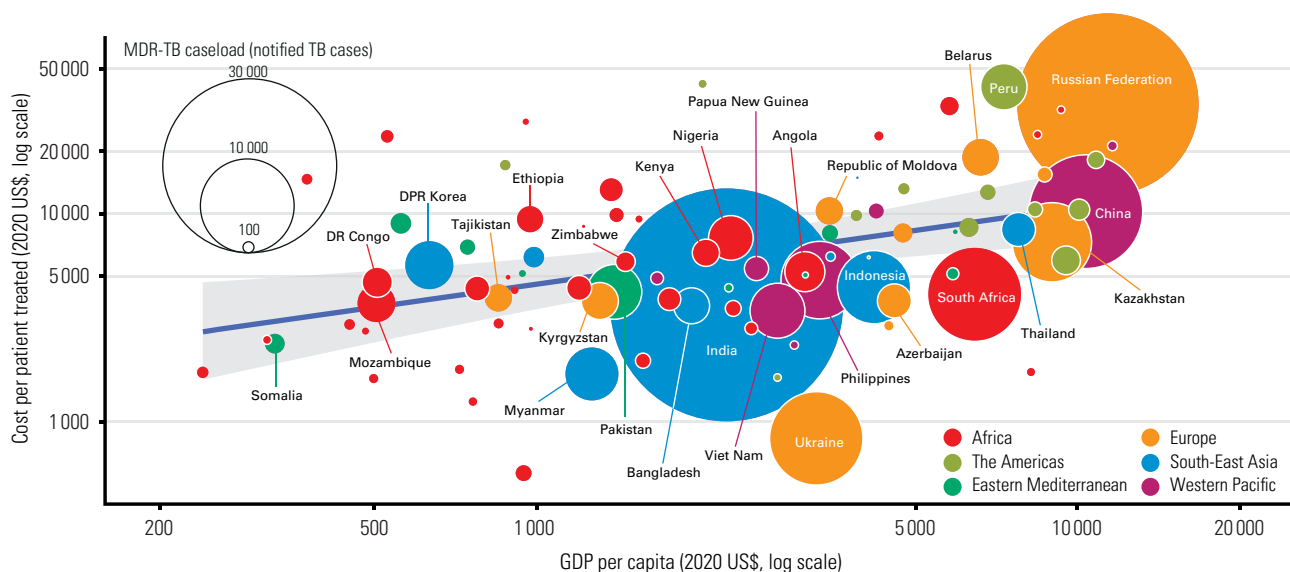
² For further details about both lists, see **Annex 2**.

³ The online appendix is available here: http://www.who.int/tb/publications/global_report/

⁴ Median values are cited rather than means because of a few countries with extreme values.

FIG. 7.12

Estimated cost per patient treated for MDR-TB in 89 countries,^a 2019



^a Limited to countries with at least 20 patients on second-line treatment in 2019.

7.4.2 Multidrug-resistant TB

In the 89 countries for which the unit cost of MDR-TB treatment was estimated, the median cost in 2019 was US\$ 5659, which was lower than in 2018, when it was more than US\$ 6400. This may reflect a general transition to using new treatment regimens for MDR-TB and a shift to models of care that are less reliant on inpatient care. As with drug-susceptible TB, the cost per person treated was positively correlated with GDP per capita.

Excluding China and the Russian Federation – for which inpatient and outpatient care costs are not reported separately from other components of TB diagnosis and treatment – in the remaining 87 countries, 44% of the unit cost was accounted for by second-line TB drugs and 31% was accounted for by inpatient care.

Between 2014 and 2019, the average length of hospital stay per person treated for MDR-TB fell from 120 to 81 days (the median also dropped from 90 to 60 days). The average length of stay fell in 72% (64/89) of countries. The most drastic reductions were in Nicaragua (–92%, from 180 days to 15 days), Pakistan (–85%, from 100 to 15 days), Mauritania (–88% from 120 days to 14 days) and Armenia (–85%, from 240 days to 36 days). In contrast, the average length of stay increased in several countries, including Kenya, Mozambique, Myanmar, Peru, Philippines and Thailand.

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A father and his young daughter being treated for severe malnutrition, Papua New Guinea.

Yoshi Shimizu/WHO

Chapter 8

Universal health coverage, TB determinants and multisectoral action

Key facts and messages

All countries have committed to global targets for reductions in tuberculosis (TB) disease burden, and improved access to TB prevention, diagnosis and treatment, through their adoption of the United Nations (UN) Sustainable Development Goals (SDGs), the End TB Strategy and the political declaration at the first UN high-level meeting on TB. Achieving these targets requires the provision of TB care and prevention services within the broader context of universal health coverage (UHC), and multisectoral action and accountability to address the broader social and economic determinants and consequences of TB.

UHC means that everyone can obtain the health services they need without suffering financial hardship. SDG Target 3.8 is to achieve UHC by 2030.

The two SDG indicators to monitor progress are a UHC service coverage index (SCI), and the percentage of the population experiencing household out-of-pocket expenditures on health care that are large in relation to total household expenditures or income.

The global SCI increased steadily between 2000 and 2017, from 45 (out of 100) in 2000 to 66 in 2017. Improvements were made in all World Health Organization (WHO) regions and all World Bank income groups. However, values of the SCI in 2017 in the 30 high TB burden countries were mostly in the range of 40–60.

In 2015, at least 930 million people, or 12.7% of the world's population, faced out-of-pocket expenditures on health care that accounted for 10% or more of their household expenditure or income (a threshold used within

the SDG framework to define direct expenditures on health in the general population as catastrophic), up from 9.4% in 2010.

Among high TB burden countries, Thailand stands out as having a high SCI of 80 and a low level of catastrophic health expenditures (2% of households). Brazil and China both had a relatively high SCI of 79.

The End TB Strategy includes a target that no TB patients and their households face total costs (including direct medical expenditures, non-medical expenditures and income losses) that are catastrophic (in this case, defined as costs equivalent to >20% of a TB-affected household's expenditure or income).^a Since 2016, 19 countries have completed a national facility-based survey of costs faced by TB patients and their households.

In the 17 countries (including 10 high TB burden countries) that have reported survey results, the percentage of TB patients and their households facing total costs that exceeded 20% of household expenditure or income ranged from 19% to 83%. The pooled average for all 17 countries, weighted for each country's number of notified cases, was 49% (95% confidence interval [CI]: 34–63%). Survey results have been used to inform approaches to health financing, service delivery and social protection that will reduce these costs.

Many new cases of TB are attributable to five risk factors: undernutrition, HIV infection, alcohol use disorders, smoking (especially among men) and diabetes. In 2019, the estimated

numbers of cases attributable to these risk factors were 2.2 million, 0.76 million, 0.72 million, 0.70 million and 0.35 million, respectively. In the context of the COVID-19 pandemic, multisectoral action to address these and other determinants of TB and its consequences, including poverty and social protection, is more important than ever.

A multisectoral accountability framework for TB (MAF-TB) was released by WHO in 2019. The framework has four major components: commitments; actions; monitoring and reporting; and review. These apply at the global/regional level, and at national (including subnational) level.

At global level, actions taken by WHO include: the development of a MAF-TB checklist; high-level missions; the WHO Director-General Initiative Find.Treat.All#EndTB; engagement of civil society and youth; updating of guidelines and tools; and development and release of a global strategy for TB research and innovation.

Since the UN high-level meeting on TB, 25/30 high TB burden countries have developed or updated a national strategic plan for TB, with countries reporting the involvement of civil society and affected communities in 29/30. Most high TB burden countries (27/30) reported that they produce an annual TB report. High-level review mechanisms were stated to be in place in 16/30 countries.

^a This TB-specific indicator is not comparable to the SDG indicator of catastrophic expenditures on health care. See [Box 8.1](#) for a full explanation of the differences.

The tuberculosis (TB) epidemic is strongly influenced by social and economic development, and by health-related risk factors. For example, numbers of TB cases and deaths started to decline in western Europe, North America and some other parts of the world around the turn of the 20th century, as incomes grew, and housing and nutrition improved (1, 2). The fastest declines in western Europe occurred in the 1950s and 1960s, in the context of progress towards universal health coverage (UHC), rapid social and economic development, and the availability of effective drug treatments. The links between TB and poverty, social protection, income per capita, indoor air pollution, undernutrition, diabetes, HIV, alcohol use disorders and smoking are well recognized and have been summarized elsewhere (3–6).

All countries have committed to global targets for reductions in TB disease burden and improved access to TB prevention, diagnosis and treatment through their adoption of the United Nations (UN) Sustainable Development Goals (SDGs), the End TB Strategy and the political declaration at the first UN high-level meeting on TB (Chapter 2) (7–9). Achieving these targets requires provision of TB care and prevention services within the broader context of UHC, and multisectoral action and accountability to address the broader social and economic determinants and consequences of TB. For example, the global target to reduce TB deaths by 90% between 2015 and 2030 is only feasible if everyone who develops TB can access high-quality treatment. The global target to reduce TB incidence by 80% between 2015 and 2030 is only feasible if the annual decline in TB incidence can be accelerated to 10% per year by 2025, which requires both progress towards UHC and action on the broader social and economic factors that strongly influence TB epidemics.

In 2020, the COVID-19 pandemic has caused enormous health, social and economic impacts, which are likely to persist in 2021 and beyond. There have been negative impacts on broader social and economic determinants that influence the TB epidemic (e.g. poverty and undernutrition), and access to and provision of health services. In combination, these impacts threaten to reverse recent progress towards global TB targets (Chapter 2, Chapter 3).

This chapter discusses UHC and a range of health, social and economic factors that influence the TB epidemic and the consequences of developing TB disease. Section 8.1 provides an overview of the status of progress towards UHC at global, regional and country levels. Section 8.2 synthesizes results from national surveys of costs faced by TB patients and their households completed in 2016–2020, and highlights the implications of these results for approaches to service delivery, financing and social protection that address TB-related considerations. Section 8.3 describes the status of 11 health, social and economic variables that are associated with TB incidence, based on a TB-SDG monitoring framework developed by the World Health Organization (WHO), and discusses how these variables are likely to be affected by the COVID-19 pandemic. Section 8.4 highlights progress made

in implementing key elements of the WHO multisectoral accountability framework for TB, following a request from Member States to develop such a framework and its finalization in May 2019 (10).

8.1 Global progress towards UHC

UHC means that everyone can obtain the health services they need without suffering financial hardship (11).

The SDG targets are for 2030, and SDG Target 3.8 is defined as “By 2030, 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”. In September 2019, UN Member States reaffirmed their commitment to this target at a UN General Assembly high-level meeting on UHC. A new target – that an additional 1 billion people have access to quality essential health services by 2023 – was also set (12).

Two SDG indicators have been defined to monitor progress towards SDG Target 3.8. The first (Indicator 3.8.1) is the coverage of essential health services, which is measured using a composite index (with values from 0 to 100) based on 16 tracer indicators (one of which is TB treatment). The second (Indicator 3.8.2) is the “proportion of the population with large household expenditures on health as a share of total household expenditure or income”.¹ The SDG framework includes two thresholds (10% and 25%) to define “large”. When these thresholds for household out-of-pocket expenditures on health² are surpassed, they are classified as “catastrophic”, because they may adversely affect a household’s ability to pay for other basic needs.

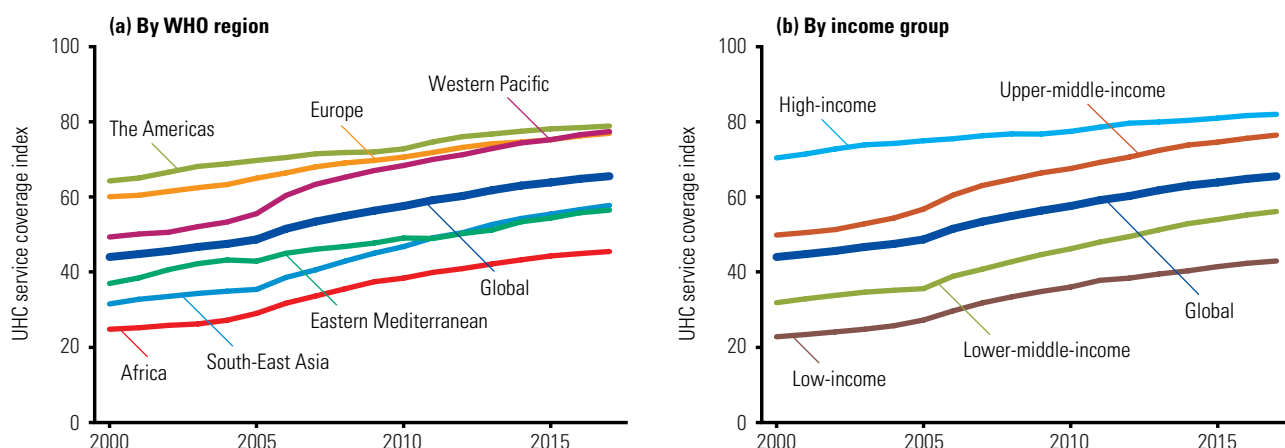
The latest WHO report on tracking progress towards UHC and a thematic report on financial protection jointly produced with the World Bank were both released in September 2019 (13, 14). These reports cover an assessment of the status of the two SDG indicators for UHC based on the latest available data, and key findings are summarized in this chapter. For catastrophic health expenditures, results based on the threshold of 10% of total household expenditure or income are provided.

8.1.1 UHC service coverage index

The service coverage index (SCI) increased steadily between 2000 and 2017, from a global value of 45 (out of 100) in 2000 to 66 in 2017 (Fig. 8.1). Improvements were made in all WHO regions (especially the Western Pacific Region) and all World Bank income groups. In both 2000 and 2017, low-income and lower-middle-income coun-

¹ This measure is population based, and therefore the denominator includes many people who either did not use health services or had only minor contact with the health system.

² Out-of-pocket health expenditures are defined as household spending on medicines, health products and health care services (outpatient, inpatient and other health services such as medical laboratory services) that are not reimbursed by a third party (e.g. the government, a health insurance fund or a private insurance company). They exclude household spending on health insurance premiums.

FIG. 8.1**Trends in the UHC service coverage index in WHO regions and World Bank income groups, 2000–2017**

Source: WHO Universal Health Coverage data portal (<http://apps.who.int/gho/portal/uhc-overview.jsp>, accessed 15 June 2020)

tries had the lowest SCI values; however, they also had the fastest rate of increase. There was little change over time in high-income countries.

National values for the SCI in 2017 are shown in Fig. 8.2. There was a great deal of variation among countries. The highest values were in high-income countries in Asia, Europe and North America. The lowest values were predominantly in countries in the WHO African Region; other countries with values below 40 were Afghanistan and Somalia. SCI values in 2017 in the 30 high TB burden countries were mostly in the range of 40–60 (Table 8.1), showing that much remains to be done to achieve UHC in these settings. However, higher values in Brazil (79), China (79) and Thailand (80) are encouraging.

8.1.2 Proportion of the general population incurring catastrophic expenditures on health

In contrast to improvements in the SCI, the proportion of the general population facing catastrophic expenditures on health has increased in recent years. Globally, the proportion of households that incurred expenditures on health that were above 10% of their income or expenditure rose from 9.4% in 2010 to 12.7% (927 million people) in 2015.¹ National values are shown in Fig. 8.3. More geographical variability is evident for this indicator than for the SCI, including within regions.

Countries in the highest category for catastrophic expenditures on health ($\geq 15\%$ of the general population) include those that rank first (India) and third (China) in terms of their total number of TB cases, as well as five other high TB burden countries: Bangladesh, Brazil, Cambodia, Nigeria and Sierra Leone. Overall, in high TB burden countries, the median value during the period 2007–2018 was 4.9% (Table 8.1).

¹ Global estimates for later years are not yet available.

Countries with the lowest levels of catastrophic expenditures on health (0–3%) include a mix of high-, middle- and low-income countries. One example of the latter is Mozambique, for which the value of the SCI was 46 while the estimated proportion of households facing catastrophic expenditures on health was 1.6% (based on data for 2014). Countries may have low levels of direct spending on health because there are geographic, financial or other barriers to access. Low levels of service coverage and low levels of catastrophic health spending are most likely a signal of high levels of unmet need rather than good financial protection.

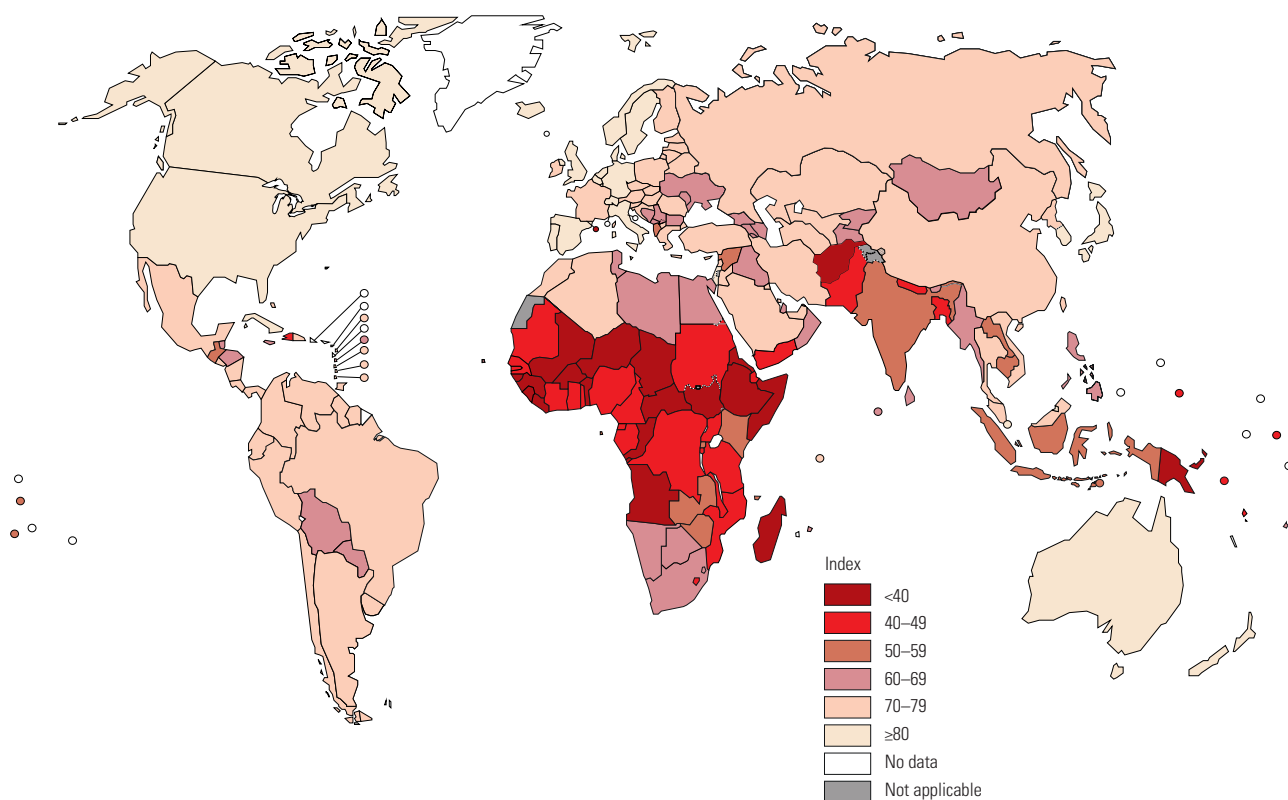
Thailand stands out as a high TB burden country with both a high SCI (80) and a low level of catastrophic health expenditures (2% of households). A UHC scheme was established in 2002, supported by domestic funding and a strong primary health care system (15).

8.1.3 Current health expenditure per capita

SDG Target 3.c urges Member States to substantially increase health financing and the recruitment, development, training and retention of the health workforce in developing countries. Without such investment, UHC will not be achieved.

Trends in health expenditure (from all sources) per capita over the period 2000–2017 in the 30 high TB burden countries are shown in Fig. 8.4. There was a striking increase in the absolute amount of spending per person in a few countries: Brazil, China, the Russian Federation, South Africa and Thailand. A steady upward trend was evident in India, Indonesia, the Philippines and Viet Nam; also, despite some year-to-year fluctuation, funding in Namibia doubled. Since about 2012, there has been a noticeable rise in health expenditure per capita in Myanmar. Elsewhere, levels of spending have been relatively stable, and at generally much lower levels.

FIG. 8.2
UHC service coverage index by country, 2017



Source: WHO Universal Health Coverage data portal (<http://apps.who.int/gho/portal/uhc-overview.jsp>, accessed 15 June 2020)

8.2 National surveys of costs faced by TB patients and their households (TB patient cost surveys)

The End TB Strategy includes a target that no TB patients or their households face catastrophic costs (including direct medical expenditures, non-medical expenditures and income losses) due to TB disease (Chapter 2). Monitoring of progress towards this target can inform monitoring of progress towards UHC. Box 8.1 explains the distinction between the indicator of catastrophic total costs among TB patients and their households and the broader indicator of catastrophic spending on health care in the general population (Section 8.1.2).

In 2015, WHO established a standardized protocol for conducting a national survey to assess the direct and indirect costs incurred by TB patients and their households (TB patient cost surveys). Based on the experience of countries that conducted the first surveys, the protocol was refined and expanded into a handbook in 2017 (16).

TB patient cost surveys have three primary objectives, which are to:

- ▶ document the magnitude and main drivers of different types of costs incurred by TB patients and their households;
- ▶ assess the percentage of TB patients and their households treated in the national TB programme (NTP) network who incur catastrophic total costs due to TB; and
- ▶ use survey findings as the basis for actions to reduce financial barriers for accessing care and to minimize the adverse socioeconomic impact of TB.

TABLE 8.1

UHC service coverage index (SDG 3.8.1)^a and percentage of the general population facing catastrophic health expenditures (SDG 3.8.2),^b 30 high TB burden countries, stratified by income group^c

COUNTRY	SERVICE COVERAGE INDEX	CATASTROPHIC HEALTH EXPENDITURE
LOW-INCOME		
Mozambique	46	1.6
DR Congo	41	4.8
Ethiopia	39	4.9
Central African Rep.	33	6.7
Sierra Leone	39	54
Liberia	39	–
DPR Korea	71	–
LOWER-MIDDLE-INCOME		
Zambia	53	0.3
Zimbabwe	54	2.1
UR Tanzania	43	3.8
Pakistan	45	4.5
Lesotho	48	4.5
Congo	39	4.6
Kenya	55	5.4
Philippines	61	6.3
Viet Nam	75	9.4
Angola	40	12
Myanmar	61	14
Nigeria	42	15
Cambodia	60	15
India	55	17
Bangladesh	48	25
Papua New Guinea	40	–
UPPER-MIDDLE-INCOME		
Namibia	62	1.2
South Africa	69	1.4
Thailand	80	2.2
Indonesia	57	2.7
Russian Federation	75	4.9
China	79	20
Brazil	79	26

– Data were not available.

^a Data are for 2017.

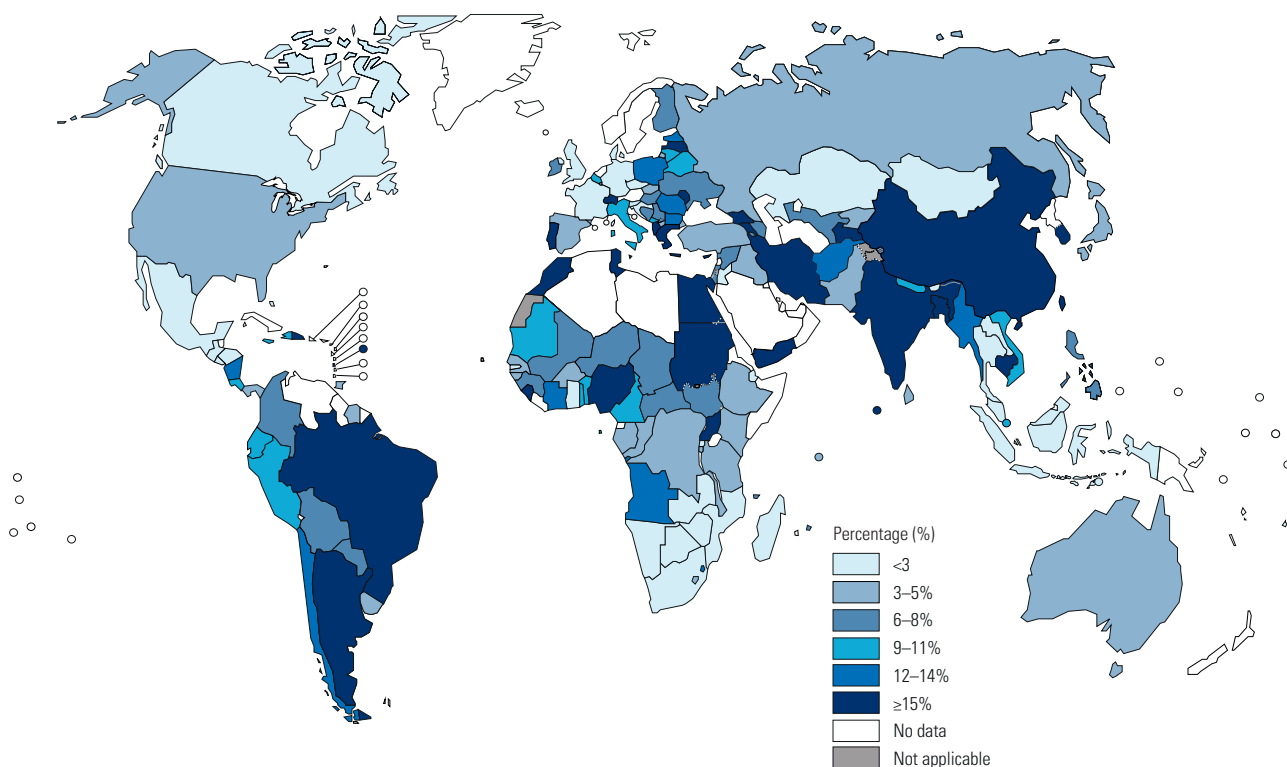
^b Defined as ≥10% of total household consumption or income. The latest available year ranges from 2007 to 2018 for the 30 high TB burden countries.

^c Countries are listed within each income group (as per the 2020 World Bank classification) according to the level of catastrophic health expenditure (from lowest to highest).

Source: WHO Universal Health Coverage data portal (<http://apps.who.int/gho/portal/uhc-financial-protection-v3.jsp>, accessed 15 June 2020)

FIG. 8.3

Percentage of the general population facing catastrophic health expenditure,^a latest available year of data^b



Source: WHO Universal Health Coverage data portal (<http://apps.who.int/gho/portal/uhc-overview.jsp>, accessed 15 June 2020)

^a Defined as $\geq 10\%$ of total household consumption or income.

^b The latest available year ranges from 2000 to 2018.

BOX 8.1

The difference between “catastrophic total costs” for TB patients and their households, and the SDG indicator of catastrophic expenditures on health care

It is important to distinguish between the indicator of “the proportion of the population with large household expenditures on health as a share of total household expenditure or income”, which is used within the SDG monitoring framework (SDG indicator 3.8.2), and the indicator of “the percentage of TB patients and their households facing catastrophic costs due to TB”, which is part of the WHO End TB Strategy.

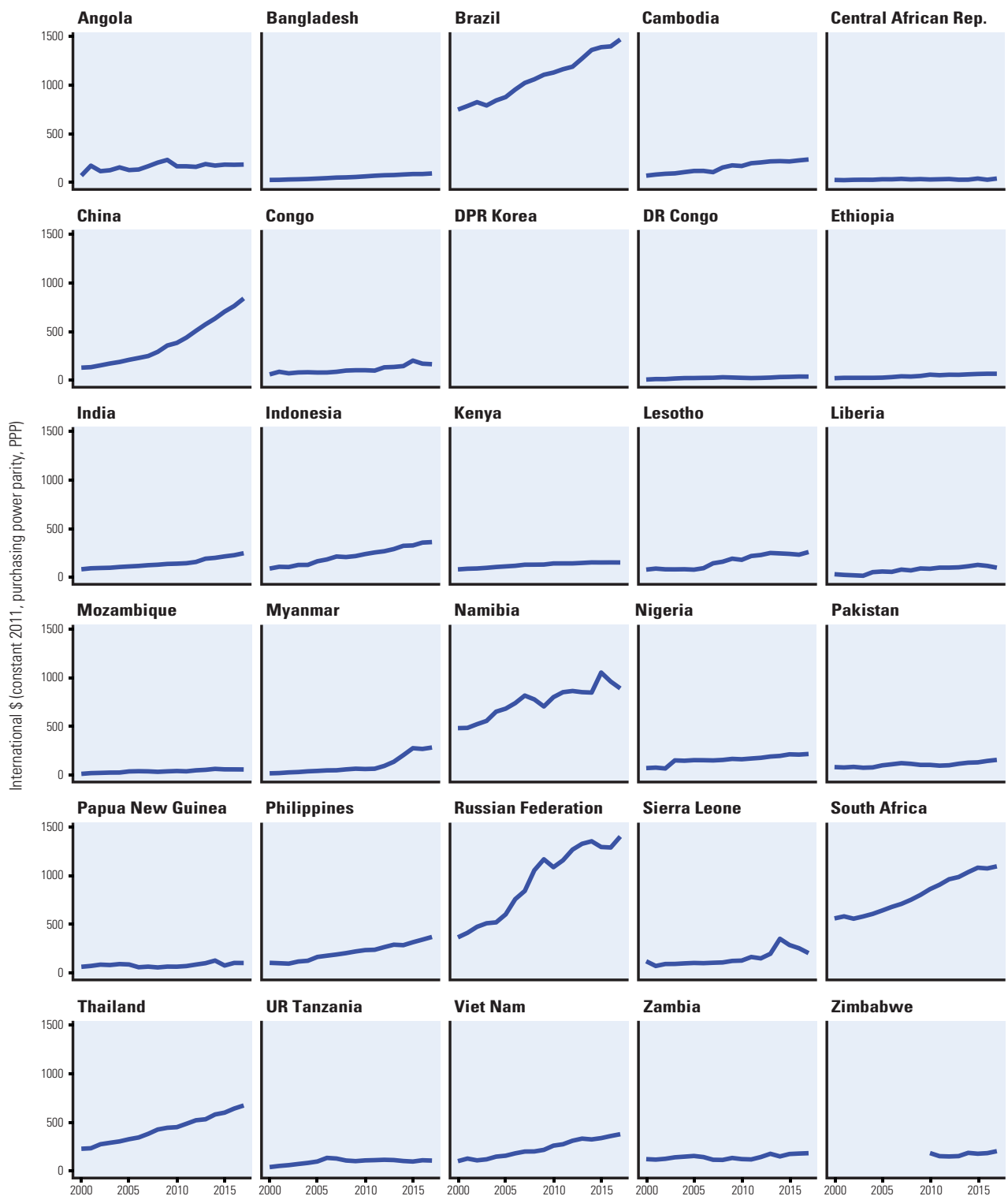
The SDG indicator is for the *general population*, and health expenditures are defined as *direct expenditures* on medical care. This indicator attempts to capture the impact of direct health spending on household ability to spend on other basic needs. The denominator includes many people who had no contact with the health system and thus had zero expenditures on health. Although these people did not experience financial hardship as a consequence of direct expenditures on health care, they may nonetheless have faced financial barriers to accessing health services that they needed.

Due to the nature of the illness, TB patients and their households can face severe direct and indirect financial and economic costs. These pose barriers that can greatly affect their ability to access diagnosis and treatment, and to complete treatment successfully. Costs included in the TB-specific indicator include not only *direct medical payments* for diagnosis and treatment, but also *direct non-medical payments* (e.g. transportation and lodging) and *indirect costs* (e.g. lost income). In contrast to SDG indicator 3.8.2, the TB-specific indicator is restricted to a particular population: *diagnosed TB patients who are users of health services that are part of NTP networks*.

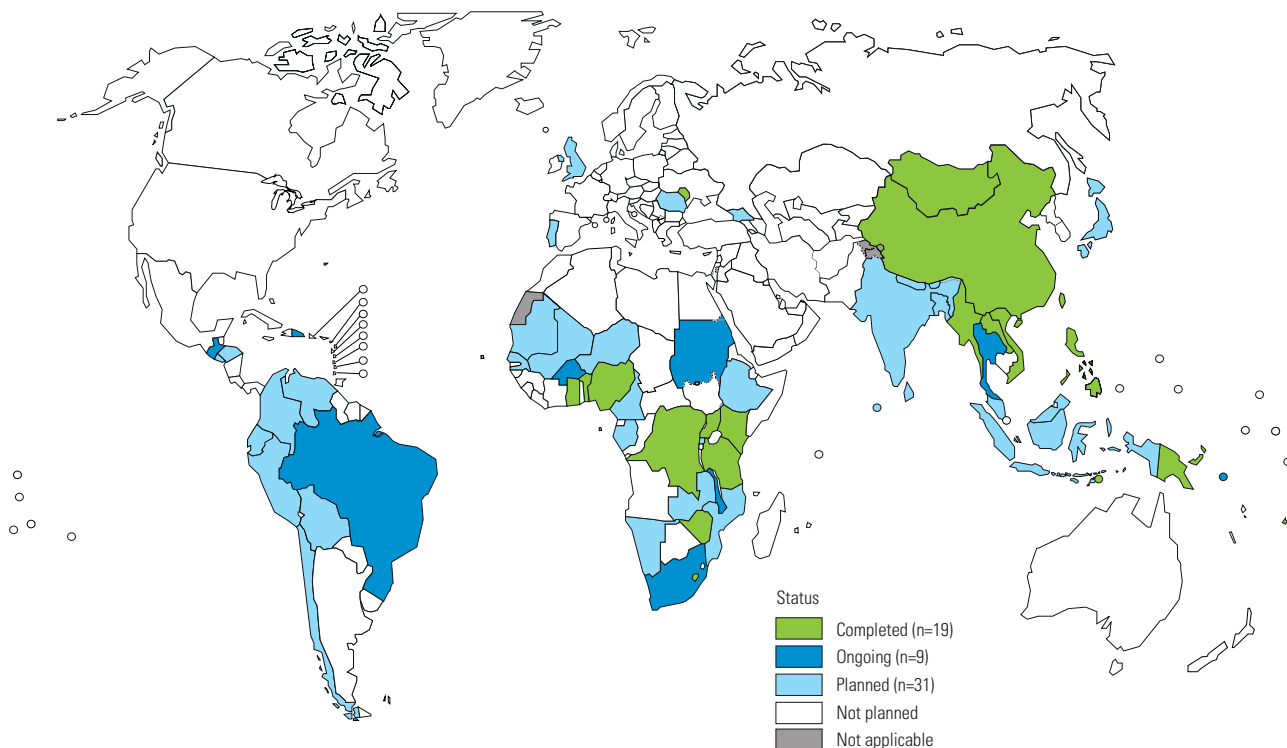
Given these conceptual differences, the percentage of TB patients facing “catastrophic total costs” (defined as costs that account for $>20\%$ of their household income) is expected to be much higher than the percentage of the general population facing catastrophic expenditures on health care. Hence, the two indicators cannot and should not be compared directly.

FIG. 8.4

Current health expenditure per capita, 30 high TB burden countries, 2000–2017



Sources: WHO Global Health Expenditure Database (<http://apps.who.int/nha/database/ViewData/Indicators/en>, accessed 15 June 2020)

FIG. 8.5**National surveys of costs faced by TB patients and their households since 2016: progress and plans (as of July 2020)**

Source: WHO Global TB Programme

In the context of TB patient cost surveys, catastrophic costs for TB patients and their households have been defined as direct medical and non-medical costs plus income losses that sum to more than 20% of household income (16). WHO recommends conducting a baseline survey by 2020, especially in high TB burden countries.

8.2.1 Global progress in implementation of surveys

The status of progress in planning and implementing national TB patient cost surveys is shown in Fig. 8.5. By July 2020, 19 countries had completed a survey:¹ Benin (2018), China (2016), the Democratic Republic of the Congo (2019), Fiji (2017), Ghana (2016), Kenya (2017), Lao People's Democratic Republic (2019), Lesotho (2019), Mongolia (2017), Myanmar (2015), Nigeria (2017), Papua New Guinea (2019), the Philippines (2016), Republic of Moldova (2016), Timor-Leste (2017), Uganda (2018), the United Republic of Tanzania (2019), Viet Nam (2016) and Zimbabwe (2018).²

In July 2020, national surveys were underway in nine countries: Brazil, Burkina Faso, Dominican Republic,

Guatemala, Malawi, Solomon Islands, South Africa, Sudan and Thailand. In a further 31 countries, surveys are scheduled to start in 2020 or 2021: Bangladesh, Bhutan, Bolivia, Cameroon, Colombia, El Salvador, Ethiopia, Gabon, Georgia, Honduras, India, Indonesia, Japan, Malaysia, Maldives, Mali, Mauritania, Mozambique, Namibia, Nepal, Niger, Peru, Portugal, Romania, Rwanda, Sao Tome and Principe, Senegal, Sri Lanka, the United Kingdom of Great Britain and Northern Ireland, Venezuela and Zambia.

The main survey results for 17 countries are shown in Fig. 8.6. The panel on the left shows the estimated percentage of TB patients and their households that faced catastrophic costs among all TB patients, and the associated 95% confidence intervals (CIs),³ together with a pooled average for all 17 countries (weighted for each country's number of notified cases). The plot on the right shows the same indicator for a subgroup of patients who were treated for drug-resistant TB.

The percentage of TB patients and their households that experienced catastrophic total costs ranged from 19% (95% CI: 15–25%) in Lesotho to 83% (95% CI: 80–86%) in Timor-Leste. The pooled average for all 17 countries,

¹ "Completed a survey" is defined as having completed survey field work, analysis of data, and documentation of results (e.g. in a report).

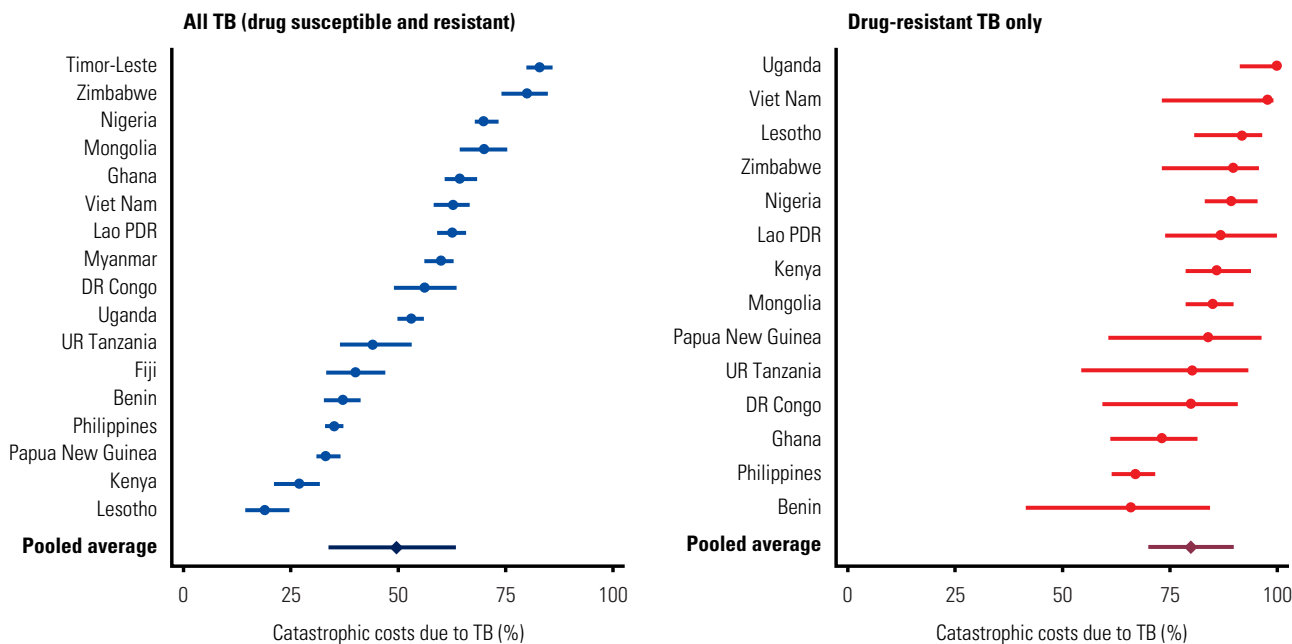
² The year indicates the year in which data were collected.

³ If available, 95% CIs were taken from the original survey reports. If they were not available in the reports, simple binomial CIs were calculated based on a given sample size.

FIG. 8.6

Estimates of the percentage of TB patients and their households facing catastrophic costs due to TB disease in 17 national surveys completed 2016–2020

Best estimates and uncertainty intervals are shown for all TB patients (left) and those with drug-resistant TB (right).^a



^a Estimates for all TB patients were based on 17 country surveys that have been completed and the data were reported. Among them, disaggregated estimates were available only for 14 countries.
Source: WHO Global TB Programme

weighted for each country’s number of notified cases, was 49% (95% CI: 34–63%).¹

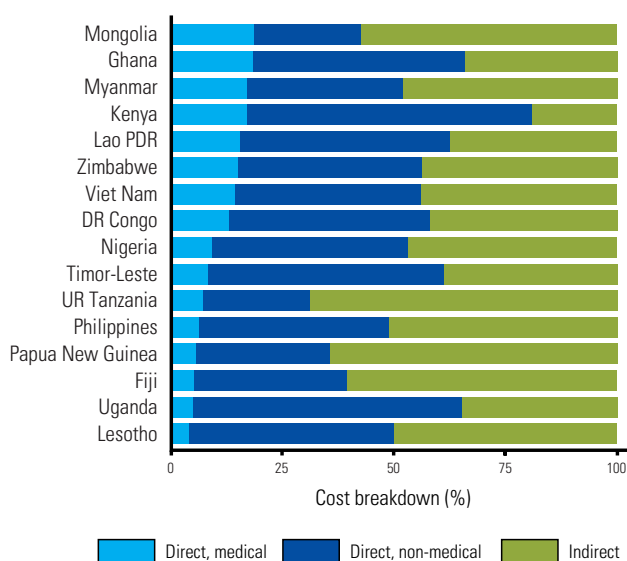
Among 14 countries that reported disaggregated data, the pooled averages were 44% (95% CI: 31–58%) for drug-susceptible TB and 80% (95% CI: 70–90%) for drug-resistant TB. The percentage of TB patients with drug-resistant TB and their households that experienced catastrophic total costs ranged from 67% (95% CI: 62–72%) in the Philippines and 67% (95% CI: 42–85%) in Benin to 100% (95% CI: 92–100%) in Uganda.

The distribution of costs for three major cost categories is illustrated in Fig. 8.7. Although the distribution varied among countries, it was evident that – despite the widespread norm of “free TB care” policies – TB-affected households still face direct medical costs.² Such costs accounted for a sizeable proportion of total costs in some countries (e.g. 19% in both Ghana and Mongolia). Minimizing direct medical costs borne by TB patients should be a high priority for NTPs and ministries of health.

The surveys also showed that actions are needed to eliminate non-medical costs and to reduce income losses. The combined cost of transportation, food, nutritional

FIG. 8.7

Distribution of costs faced by TB patients and their households in 16 national surveys completed 2016–2020^a



^a The distribution of costs by cost category was not available for Benin at the time of report publication.
Source: WHO Global TB Programme

¹ Pooled averages were derived from a random effects model weighted by the number of notified TB patients in each country.

² In most countries that have implemented surveys to date, costs after diagnosis were higher than costs before diagnosis.

supplements and other non-medical expenditures (“direct non-medical costs”) accounted for the largest share of total costs in the Democratic Republic of the Congo (45%), Ghana (47%), Kenya (64%), Lao People’s Democratic Republic (47%), Timor-Leste (53%) and Uganda (60%). Income losses associated with loss of employment or time lost while seeking or staying in care accounted for the largest single share of total costs in Fiji (60%), Mongolia (57%), Myanmar (48%), Nigeria (47%), Papua New Guinea (64%), the Philippines (52%), the United Republic of Tanzania (69%), Viet Nam (44%) and Zimbabwe (44%).

All cost categories are influenced by the model of TB care; for example, to what extent there is reliance on hospitalization or outpatient care, the frequency with which attendance at health facilities is requested and the level of service decentralization to bring the services close to the community. They are also influenced by ease of access to the health facilities used to provide care.

8.2.2 Policy and strategy implications of survey results

Results from TB patient cost surveys can show where approaches to health service delivery and financing need to be improved to reduce direct costs (e.g. by removing user fees and introducing more patient-centred models of care) for TB patients. They also show the extent to which there are costs that require mitigation through measures

such as social protection, in collaboration with stakeholders in various social sectors (especially in the social welfare, labour, poverty reduction and development sectors). Survey results should be used to stimulate multi-sectoral engagement and action to reduce costs faced by TB patients and their households, and to eliminate those costs as far as possible.

A multistakeholder consultation can be an effective way to initiate discussions about survey results and the actions needed in response. An early example was a meeting in Viet Nam in March 2017, which was used to disseminate findings and formulate a joint action plan with the country’s Ministry of Labour and Social Affairs (17). Subsequently, similar dissemination and stakeholder consultations have been held in Myanmar in 2017; in Ghana, Kenya and Mongolia in 2018; and in Lao People’s Democratic Republic, Nigeria, Uganda and Zimbabwe in 2019. These consultations resulted in identification of multisectoral actions required to improve social support for TB patients and their households. Recent country case studies from the Democratic Republic of the Congo and Lao People’s Democratic Republic are featured in **Box 8.2**.

The WHO handbook provides guidance on the dissemination of survey findings and policy translation (16); also, activities such as national TB programme reviews provide excellent opportunities for the periodic review of actions taken and progress achieved.

BOX 8.2

National surveys of costs faced by TB patients and their households in the Democratic Republic of the Congo and Lao People’s Democratic Republic

It is becoming clear that findings from national TB patient cost surveys convey powerful messages that draw political attention, raise public awareness and facilitate multisectoral engagement to strengthen the TB response. The socioeconomic hardships and social consequences faced by TB patients and their households are relatively easily understood, and messages can resonate with politicians, other high-level officials and the general public.

Examples featured in previous editions of the WHO global TB report include Ghana, Kenya, Mongolia, Myanmar, Nigeria and Viet Nam. Two new examples, from the Democratic Republic of the Congo^a and Lao People’s Democratic Republic, are featured here.

Democratic Republic of the Congo

In 2018, the economic and financial burden borne by TB patients and their households was unknown at national level. The NTP decided to implement a baseline survey to understand the composition and magnitude of costs being faced, and who was worst affected. The survey was implemented in 2019, and included 1118 people in 43 clusters.

The main findings were that:

- ▶ 56% (95% CI: 49–64%) of TB-affected households experienced costs (direct and indirect) that were greater than 20% of their annual household expenditure;
- ▶ the average cost per patient was US\$ 549;
- ▶ the largest drivers of mean costs (**Fig. 8.7**) were non-medical direct costs (i.e. travel, food, nutritional supplements and accommodation) at 45%, followed by lost income (42%) and direct medical costs (13%);
- ▶ the average annual expenditure of surveyed households was US\$ 1472;
- ▶ half of households resorted to dissaving strategies to overcome costs associated with TB, while 78% lost days of work and 23% lost their jobs;
- ▶ the risk of catastrophic costs was higher for people with drug-resistant TB and those in the lowest household expenditure quintile; and

^a Kayomo MK, Minga G, Nkiere NM, Mingiedi B, Eloko G, Nguhiu P, Baena IG. First national survey of the costs borne by households with tuberculosis in Democratic Republic of Congo, 2019. Abstract for presentation at the 51st Union World Conference on Lung Health in October 2020 (18).

BOX 8.2

- ▶ 94% of TB patients had no health insurance and 7.5% received social support (including travel vouchers and food support).

The findings have been used to identify actions needed to improve the delivery and funding of TB services, and social protection for people with TB, as outlined below.

Improving the delivery and funding of TB services

- ▶ Reduce the time taken for visits to health facilities for treatment or collection of anti-TB drugs by improving the availability of treatment observation at community level and in the workplace.
- ▶ Minimize diagnostic delays (on average 10 weeks between the onset of symptoms and care seeking) and shorten patient journeys by expanding access to quality services for TB diagnosis, in collaboration with local government authorities.

Overall, the aim is to reduce medical costs to US\$ 65 for people with drug-susceptible TB and to US\$ 115 for people with multidrug-resistant TB (MDR-TB).

Improving social protection for people with TB

- ▶ Expand patient support beyond the 7.5% covered in the survey.
- ▶ Protect the employment status of people with TB; for example, through legislation to prevent dismissals from work and to facilitate work absences required for visits to health facilities, and through collaboration with unions and businesses to improve workplace policies and services for people with TB.
- ▶ Establish a mechanism for simplified reimbursement for medical costs incurred by people with TB patients.

Survey results were presented at an international conference in October 2020.

Lao People's Democratic Republic

The NTP conducted a first national TB patient cost survey in 2018–2019. The objectives were to assess the magnitude and main drivers of costs incurred by TB patients and their households, and to establish a baseline against which to monitor progress towards the elimination of catastrophic costs due to TB.

The survey enrolled 848 TB patients across 12 provinces; of these, 818 had drug-susceptible TB and 30 had drug-resistant TB. The survey also enrolled an additional 123 TB patients who were living with HIV.

The main findings were that:

- ▶ 62% of people with drug-susceptible TB, 85% of people with drug-resistant TB and 81% of TB patients living with HIV faced catastrophic costs (>20% of household annual income);

- ▶ the total cost incurred by TB-affected households was US\$ 755 on average, which was more than three times the average monthly salary of TB patients in the survey;
- ▶ the main cost driver (47% of the total) was direct non-medical costs (e.g. travel, food and accommodation while seeking and receiving care, and nutritional supplements), followed by income losses due to TB (37%); patients spent a relatively large amount on the additional food required for their nutritional recovery;
- ▶ the proportion of people with TB living below the international poverty line increased from 9% to 25% during the period of treatment;
- ▶ the proportion of people with TB who were unemployed increased from 17% to 35% during their illness; patients who were working in the informal sector were more likely to lose their jobs;
- ▶ to cope with the economic and financial burden, half (50%) of TB patients had to rely on one or more of the following – savings (21%), borrowing money (26%) or selling assets (18%) – all of which caused prolonged negative impacts on their lives; and
- ▶ 20% of TB-affected households experienced food insecurity and 10% experienced social exclusion.

Survey results were officially disseminated in December 2019, with the participation of high-level officials and multisectoral partners. Before the dissemination, in July 2019, the NTP organized policy discussions with multisectoral partners – such as the State Authority for Social Security, the Social Security Organization and the National Nutrition Programme – to jointly identify collaborative actions to enhance social protection and support for TB patients and their families. Following discussions among stakeholders and partners, agreement was reached on recommendations to improve health service delivery and financing, and to enhance social protection for people with TB.

Improved health service delivery and financing in relation to TB

- ▶ Decentralize services and streamline patient pathways to care at all levels to minimize diagnostic delays and patient costs.
- ▶ Actively engage in discussions related to the inclusion of TB services within the national health insurance scheme, including the design and costing of TB services within the benefit package.
- ▶ Improve nutritional support for TB patients – including systematic assessment of nutritional status, counselling, and therapeutic and supplementary feeding for those in need – in coordination with the national nutrition centre and in line with the National Nutrition Strategy 2016–2020.

BOX 8.2

Enhanced social protection for people with TB

- ▶ Establish a streamlined claim mechanism for people with TB to access sickness and unemployment benefits, in collaboration with the National Social Security Fund.
- ▶ Explore collaboration with the labour and corporate sectors to improve workplace policies and services for people with TB, including mechanisms for protecting the employment status of TB patients.
- ▶ Strengthen advocacy and action by parliamentarians to end TB and poverty in Lao People's Democratic Republic.

8.3 Broader determinants of the TB epidemic

In 2017, WHO developed a TB-SDG monitoring framework as part of the preparations for a global ministerial conference on TB (19). The framework was based on previously published work that identified clear linkages between TB incidence and various indicators that are part of the SDG framework (3-6), and new analysis of the relationship between these indicators and TB incidence. The TB-SDG framework comprises 14 indicators under seven SDGs (Table 8.2). The relationship between two of the indicators (GDP per capita and the prevalence of undernutrition) and TB incidence is illustrated in Fig. 8.8.

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

- ▶ subindicators of indicators that have already been included (e.g. subindicators related to UHC, under SDG 3); and
- ▶ indicators that are only 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).

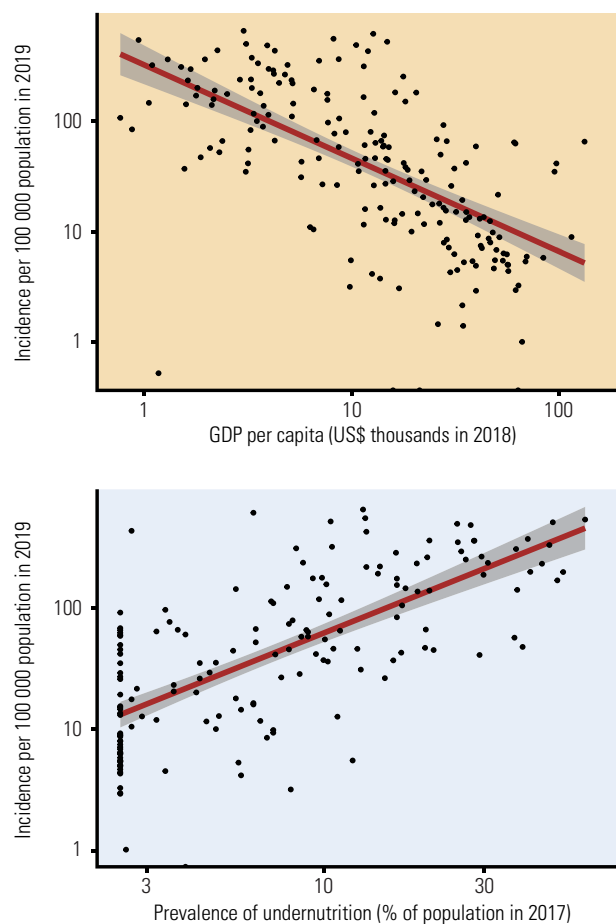
In some cases, the official SDG indicator was not considered the best metric, and a better (but closely related) alternative was identified and justified (five indicators under SDG 3, one under SDG 8 and one under SDG 10).

The most recent data on the prevalence of four health-related risk factors (diabetes, HIV infection, smoking and alcohol use disorders) under SDG 3 that are associated with TB incidence (Table 8.2a) as well as undernutrition (Table 8.2b) are shown for the 30 high TB burden countries in Table 8.3.¹ For all of the indicators shown, a lower level is more desirable.

¹ The three indicators relating to coverage of health services and health expenditure per capita are not included here because they are discussed in Section 8.1.

FIG. 8.8

The relationship between GDP per capita and the prevalence of undernutrition, and TB incidence per 100 000 population



The countries with generalized HIV epidemics (a prevalence of >1% in the general population) include 15 of the 16 high TB burden countries in the WHO African Region (the exception is the Democratic Republic of the Congo), with especially high levels in southern Africa (24% in Lesotho, 13% in Mozambique, 12% in Namibia, 20% in South Africa, 11% in Zambia and 13% in Zimbabwe).

The prevalence of smoking in adult men (aged ≥15 years) is above 40% in six of the 30 high TB burden countries and is exceptionally high (60%) in Indonesia and Lesotho; the only countries where it is below 20% are Brazil, Ethiopia, Liberia and Nigeria. Smoking is much less common among adult women, with levels below 5% in most high TB burden countries and exceeding 10% only in the Russian Federation. These striking differences between men and women contribute to the higher burden of TB disease among men (Chapter 4).

TABLE 8.2A

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	HIV prevalence	HIV is a strong risk factor for development of TB disease and is associated with poorer treatment outcomes. HIV prevalence is selected in preference to HIV incidence because it is directly measured.	UNAIDS	Yes, already routinely collected.
	3.3.2 TB incidence per 100 000 population			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 (defined as the average coverage of essential services based on 16 tracer interventions).	NA	Achieving UHC is required to achieve the three high-level targets of the End TB Strategy for reductions in the TB incidence rate, reductions in the number of TB deaths and elimination of catastrophic costs for TB patients and their households. TB treatment coverage has been monitored for years and is one of the 16 tracer indicators that have been selected to measure SDG indicator 3.8.1.	WHO	To assess progress in elimination of catastrophic costs for TB patients and their households, periodic facility-based surveys of TB patients are recommended.
	3.8.2 Proportion of population with large household expenditures on health as a share of total household expenditure or income	NA			
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).
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.c.1 Health worker density and distribution	Current health expenditure per capita	Health expenditure per capita is correlated with TB incidence.	WHO	No

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 8.2B

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, currently measured as people living on less than \$1.25 a day	1.1.1 Proportion of population living below the international poverty line	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
1.3 Implement nationally appropriate social protection systems and measures for all, including floors, and achieve substantial coverage of the poor and vulnerable	1.3.1 Proportion of population covered by social protection floors/ systems	NA			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, in particular the poor and people in vulnerable situations, including infants, to safe, nutritious and sufficient food year-round	2.1.1 Prevalence of undernourishment	NA	Undernutrition 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 in accordance with national circumstances and, in particular, at least 7% GDP growth 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. 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 undernutrition.	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.

TABLE 8.3

Status of selected SDG 3 indicators, 30 high TB burden countries, latest available year

COUNTRY	PREVALENCE OF UNDERNOURISHMENT (% OF POPULATION)	HIV PREVALENCE (% OF POPULATION AGED 15–49 YEARS)	SMOKING PREVALENCE (% OF POPULATION AGED ≥15 YEARS)		DIABETES PREVALENCE (% OF POPULATION AGED ≥18 YEARS)		ALCOHOL USE DISORDERS, 12 MONTH PREVALENCE (% OF POPULATION AGED ≥15 YEARS)	
			FEMALE	MALE	FEMALE	MALE	FEMALE	MALE
Angola	25	2.0	–	–	7.8	8.5	1.7	11
Bangladesh	15	0.1	1.0	41	9.3	10	0.3	1.4
Brazil	2.5	0.5	9.5	17	8.7	7.8	1.6	6.9
Cambodia	16	0.5	2.0	32	6.9	7.4	1.8	8.7
Central African Rep.	60	3.6	–	–	7.6	8.0	0.9	6.8
China	8.6	–	1.8	48	7.6	9.9	0.2	8.4
Congo	40	2.6	0.7	25	7.6	7.7	0.5	3.8
DPR Korea	48	–	0.0	38	5.9	5.8	1.0	6.2
DR Congo	–	0.8	–	–	6.1	6.2	1.0	9.1
Ethiopia	21	1.0	0.7	6.1	5.0	5.8	0.5	4.5
India	15	–	1.4	22	8.3	9.1	0.5	9.1
Indonesia	8.3	0.4	1.9	60	8.0	7.4	0.3	1.4
Kenya	29	4.7	1.0	20	6.2	5.8	0.9	7.1
Lesotho	13	24	0.3	60	9.9	7.3	1.3	9.3
Liberia	37	1.3	1.0	14	7.6	7.8	1.3	9.2
Mozambique	28	13	4.4	27	6.2	6.6	0.7	5.9
Myanmar	11	0.8	4.4	36	7.9	6.9	0.6	3.2
Namibia	27	12	8.1	34	7.5	7.3	2.1	11
Nigeria	13	1.5	0.3	7.9	6.0	6.3	0.1	1.1
Pakistan	20	0.1	3.0	38	12	13	0.1	0.6
Papua New Guinea	–	0.8	–	–	14	15	1.8	8.8
Philippines	13	0.1	7.0	42	7.3	7.1	1.8	8.8
Russian Federation	2.5	–	16	41	8.0	7.4	7.4	37
Sierra Leone	26	1.5	8.5	31	6.6	7.1	0.7	6.3
South Africa	6.2	20	7.1	34	13	9.7	1.8	12
Thailand	7.8	1.1	1.7	39	8.8	8.3	0.9	10
UR Tanzania	31	4.6	2.0	20	6.1	6.0	2.2	12
Viet Nam	9.3	0.3	–	–	5.1	5.5	1.2	9.8
Zambia	47	11	3.0	24	6.7	6.5	1.2	9.8
Zimbabwe	51	13	1.3	27	7.6	6.5	2.0	11

– Data were not available.

Sources: World Bank Sustainable Development Goals Database (<http://datatopics.worldbank.org/sdgs/>, accessed 15 June 2020) and WHO Global Health Observatory (<http://www.who.int/gho/en/>, accessed 15 June 2020)

TABLE 8.4

Global estimates of the number of TB cases attributable to selected risk factors, 2019

RISK FACTOR	RELATIVE RISK (UNCERTAINTY INTERVAL)		EXPOSED (MILLIONS)	POPULATION ATTRIBUTABLE FRACTION (%)	ATTRIBUTABLE TB CASES (MILLIONS, UNCERTAINTY INTERVAL)	
Alcohol use disorders	3.3	2.1–5.2	288	8.1	0.72	0.30–1.3
Diabetes	1.5	1.3–1.8	489	3.1	0.35	0.14–0.65
HIV infection	18	15–21	38	7.7	0.76	0.68–0.86
Smoking	1.6	1.2–2.1	1 040	7.1	0.70	0.23–1.4
Undernourishment	3.2	3.1–3.3	812	19	2.2	1.5–3.1

Sources: Imtiaz S et al. *Eur Resp Jour* (2017); Hayashi S et al. *Trop Med Int Health* (2018); Lönnroth K et al. *Lancet* (2010); World Bank Sustainable Development Goals Database (<http://datatopics.worldbank.org/sdgs/>, accessed 15 June 2020); WHO Global Health Observatory (<http://www.who.int/gho/en/>, accessed 15 June 2020); and WHO Global TB Programme.

The prevalence of diabetes in men and women is similar and is generally between 5% and 10%. The three countries with higher levels are Pakistan (13% among men and 12% among women), Papua New Guinea (15% among men and 14% among women) and South Africa (13% among women).

The prevalence of alcohol use disorders is generally low among adult women but is higher among men (1–12%, but 37% in the Russian Federation).

The prevalence of undernourishment is greater than 20% in 14 of the 30 high TB burden countries: the Democratic People’s Republic of Korea, Pakistan and 12 of the 16 high TB burden countries in the WHO African Region. The country with the highest value (60%) is Central African Republic.

Estimates of the number of incident TB cases attributable to these five health-related risk factors for TB in 2019 are shown in **Table 8.4**. An estimated 2.2 million cases were attributable to undernutrition, 0.76 million to HIV infection, 0.72 million to alcohol use disorders, 0.70 million to smoking and 0.35 million to diabetes. Country-specific estimates are shown in **Fig. 8.9**. There is considerable variation among countries in the relative contribution of the five factors, and thus also variation in which of these factors need to be prioritized as part of national efforts to reduce the burden of TB disease.

The most recent data for six of the seven indicators associated with TB incidence listed in **Table 8.2b** are shown for the 30 high TB burden countries in **Fig. 8.10**.¹ In this figure, the outer edge of the hexagon (100) is the ideal value for each indicator. Therefore, better performance corresponds to a larger shaded region. To represent this situation visually, the indicators “proportion of the urban population living in slums” and “proportion of the population living below the international poverty line” are inverted in **Fig. 8.10**. All indicator values in **Fig. 8.10** are for the general population, as opposed to people with TB; values for TB patients specifically (e.g. out-of-pocket expenditure and access to social protection) may differ from these general values.

¹ GDP per capita is not included in **Fig. 8.9** 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 **Fig. 8.10**.

Although some upper-middle-income and lower-middle-income countries (e.g. Brazil, China, India, Indonesia, South Africa and Thailand) are performing relatively well, many high TB burden countries, especially those in the low-income category, still face significant challenges in achieving a range of TB-related SDG targets. Furthermore, values for poor populations and vulnerable groups most at risk of developing TB are likely to be worse than national averages.

Fig. 8.11 shows trends since 2000 in four SDG-related indicators in the 30 high TB burden countries: (a) gross domestic product (GDP) per capita, (b) proportion of the population living below the international poverty line, (c) prevalence of undernourishment and (d) prevalence of diabetes. Although rapid growth in GDP per capita has occurred in several countries, many others show slow growth or stagnation. In general, poverty levels have been falling, but the proportion of the population living below the international poverty line is still elevated in many high TB burden countries, especially in the WHO African Region. It is encouraging that the prevalence of undernutrition has fallen substantially in some countries in the past decade (e.g. Angola, Ethiopia, Myanmar and Sierra Leone). However, the trend of increasing undernutrition observed in Central African Republic, the Democratic People’s Republic of Korea, Kenya and Zimbabwe is concerning, as is the rising prevalence of diabetes prevalence in all countries.

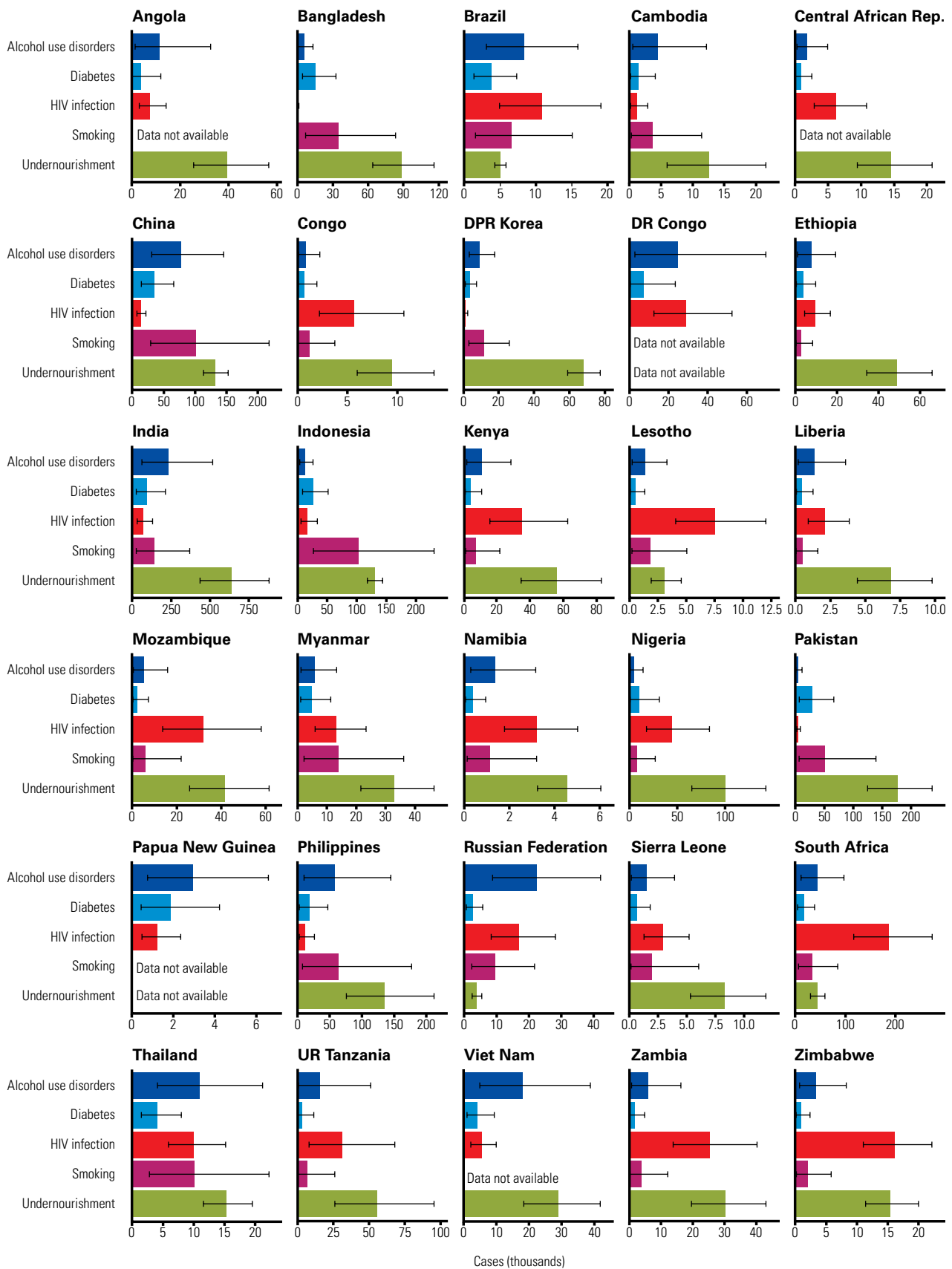
The latest status and recent trends in all of the 14 indicators in **Table 8.2** are shown for the 30 high TB burden countries in country profiles available on the WHO website² and in the Global TB Report 2020 mobile app (**Annex 3**).

Although there have been positive trends in recent years in some of the indicators associated with TB incidence, the major threat posed by the COVID-19 pandemic could slow or reverse progress. The impact is difficult to predict at this stage, but the potential impact of the COVID-19 pandemic on TB determinants and TB disease burden is highlighted in **Box 8.3**.

² See <http://www.who.int/tb/data/en/>.

FIG. 8.9

Estimated number of TB cases attributable to five risk factors, 30 high TB burden countries, 2019
 Best estimates (in colour) and uncertainty intervals (black) are shown.



Sources: Intiazi S et al. Eur Resp Jour (2017); Hayashi S et al. Trop Med Int Health (2018); Lönnroth K et al. Lancet (2010); World Bank Sustainable Development Goals Database (<http://datatopics.worldbank.org/sdgs/>, accessed 15 June 2020); WHO Global Health Observatory (<http://www.who.int/gho/en/>, accessed 15 June 2020); and WHO Global TB Programme.

FIG. 8.10

Status of selected SDG indicators beyond SDG 3 that are associated with TB incidence, 30 high TB burden countries, latest available year



Income equality: An inverse GINI index is shown where 0 is perfect inequality and 100 is perfect equality.

Not in poverty: Percentage of population living above the international poverty line.

Social protection: Percentage of population covered by social protection and labour programmes.

Not in slums: Percentage of urban population not living in slums.

Nutrition: Percentage of population not undernourished.

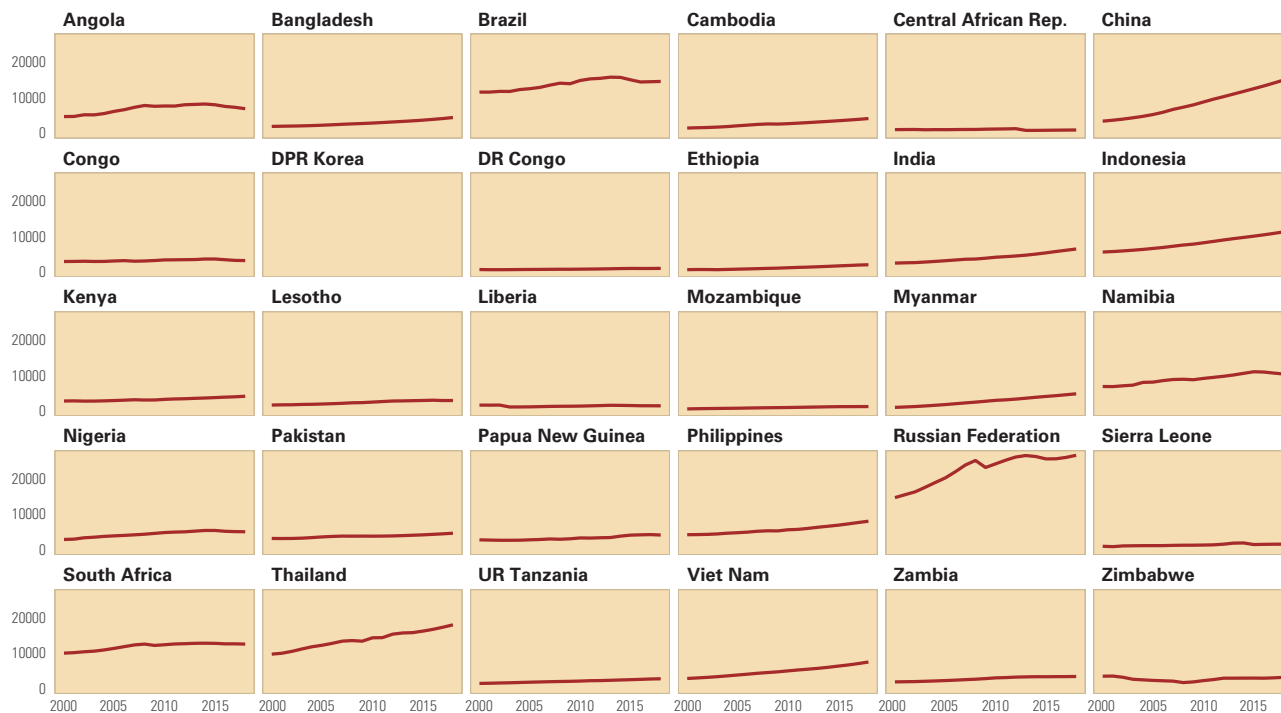
Clean fuels: Percentage of population with access to clean fuels and technologies for cooking.

Source: World Bank Sustainable Development Goals Database (<http://datatopics.worldbank.org/sdgs/>, accessed 15 June 2020).

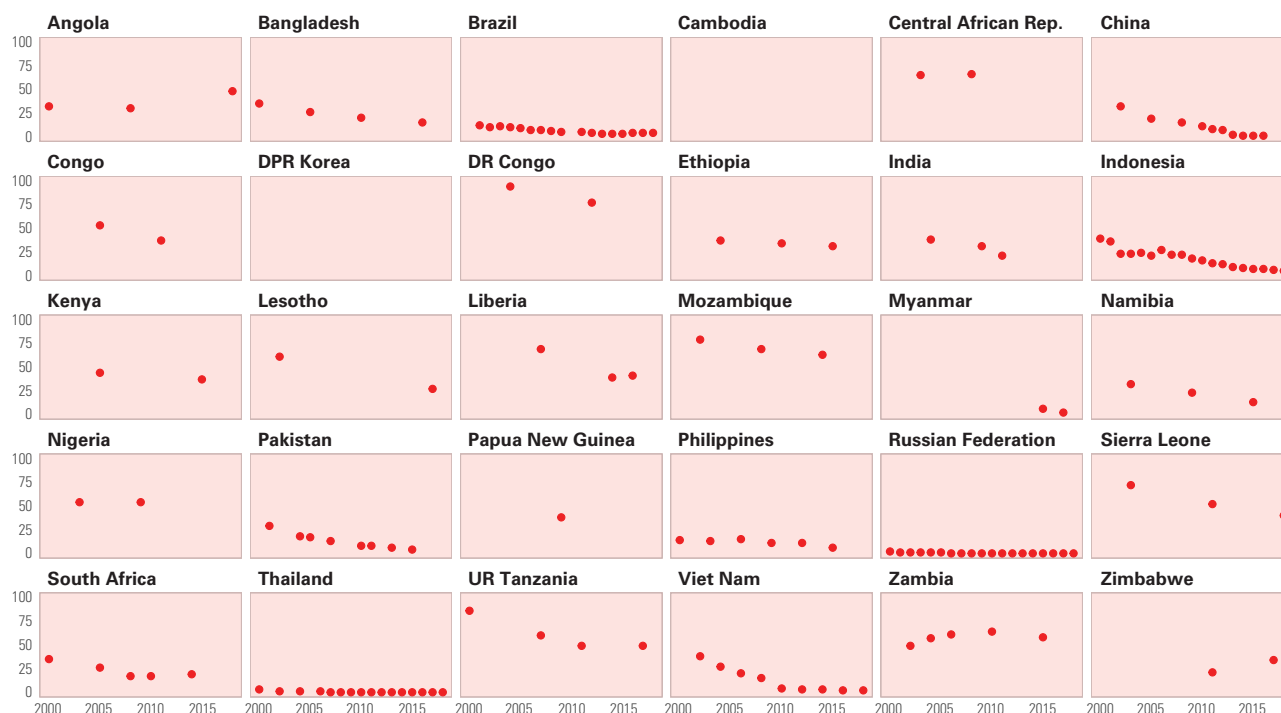
FIG. 8.11 (A, B)

Trends in four indicators associated with TB incidence, 30 high TB burden countries

(a) GDP per capita, PPP (constant 2011 international \$), 2000–2018



b) Population living below the international poverty line (%), 2000–2018

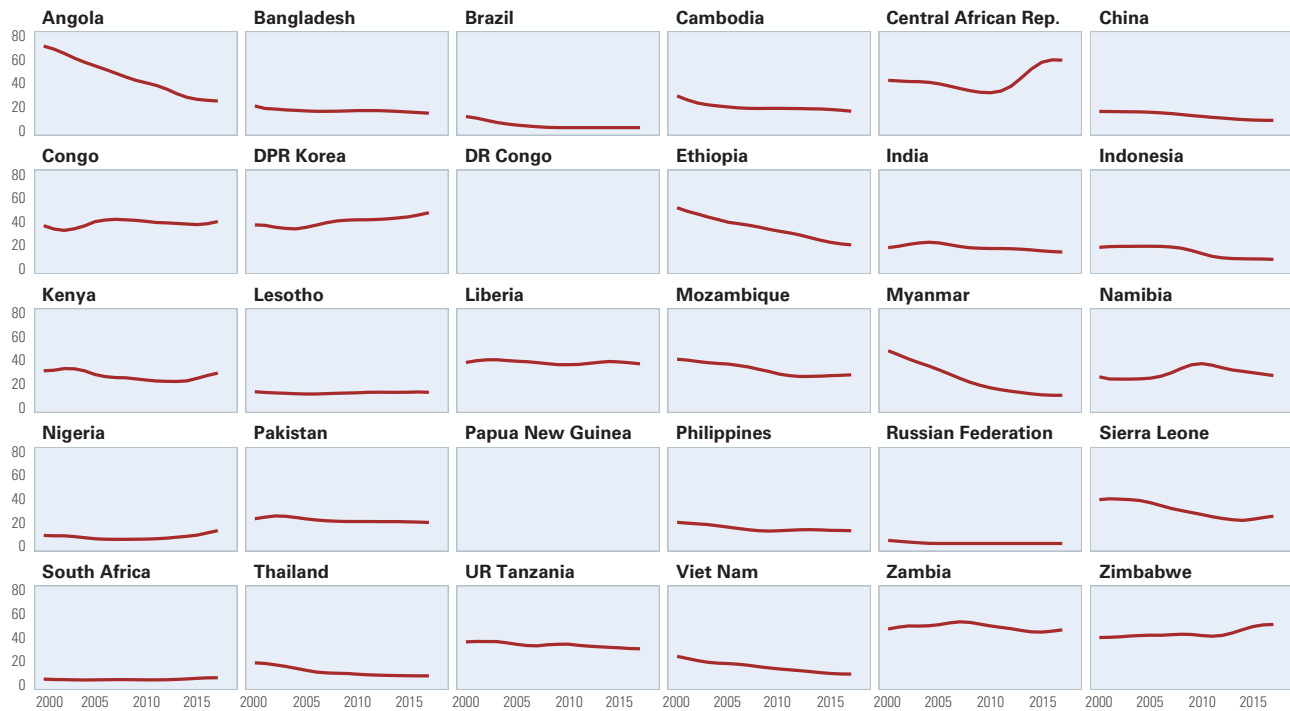


Sources: World Bank Sustainable Development Goals Database (<http://datatopics.worldbank.org/sdgs/>, accessed 15 June 2020) and WHO Global Health Observatory (<http://www.who.int/gho/en/>, accessed 15 June 2020)

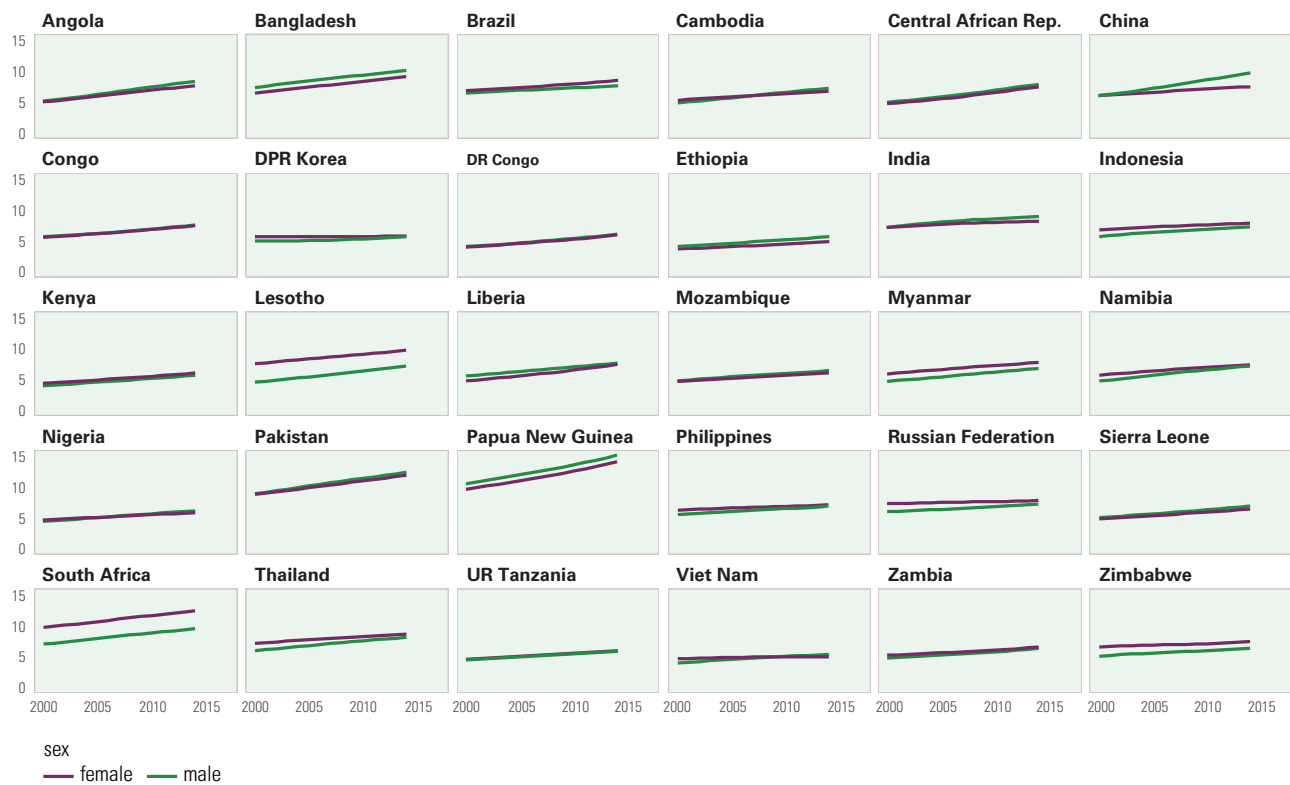
FIG. 8.11 (C, D)

Trends in four indicators associated with TB incidence, 30 high TB burden countries

(c) Prevalence of undernourishment (%), 2000–2017



(d) Diabetes prevalence (% of population aged ≥18 years), 2000–2014



Sources: World Bank Sustainable Development Goals Database (<http://datatopics.worldbank.org/sdgs/>, accessed 15 June 2020) and WHO Global Health Observatory (<http://www.who.int/gho/en/>, accessed 15 June 2020)

TB determinants and TB disease burden: potential impact of the COVID-19 pandemic

The COVID-19 pandemic has already caused enormous health, social and economic impacts, which are likely to persist for some time. The World Bank has estimated that global GDP could contract by 5.2% in 2020, with much more severe economic recessions already occurring in many countries.^a Among other consequences, income per capita will fall and levels of unemployment will rise, in turn damaging livelihoods, worsening poverty and risking increased levels of undernutrition.

Globally, the proportion of the population living below the international poverty line of \$1.90 per day is forecast to increase from 8.2% in 2019 to 8.8–9.2% in 2020, the first increase since 1998.^b This is equivalent to an extra 71–100 million people being pushed into extreme poverty due to the COVID-19 pandemic. Many of the countries most affected will be those already struggling with high poverty rates, including those with a high burden of TB. Almost half of the projected COVID-induced poor will be in the World Bank region of South Asia (especially in India), and more than one third in Sub-Saharan Africa. Three high TB burden countries – the Democratic Republic of the Congo, India and Nigeria – are home to more than one third of the world's poor.

The UN World Food Programme has estimated that the COVID-19 pandemic will double the number of people suffering from acute hunger: 270 million people by the end of 2020, compared with 135 million in 2019.^c The proportion of the population experiencing acute food insecurity is forecast to be very serious in some high TB burden countries, notably the Democratic Republic of the Congo (7.1%) and Nigeria (14%).^d Sharp increases in the number of people experiencing food insecurity are also predicted in West and Central Africa (+135%) and Southern Africa (+90%). In Zimbabwe, the number of people facing food insecurity in urban areas alone is projected to increase by more than 1 million (from 2.2 million to 3.3 million) during 2020.

While economic recessions, poverty, food insecurity and undernutrition are all determinants that fuel the TB epidemic, the effects of the COVID-19 pandemic on health-related risk factors such as HIV, diabetes, smoking, and alcohol use disorders are uncertain. However, considering the ongoing disruptions of essential health services due to the pandemic, negative impacts are likely.

The worsening levels of these TB determinants are likely to have short- and medium-term negative impacts on the TB epidemic at global and national levels. This is in addition to the impact on TB deaths in 2020 that is estimated to be due to reductions in TB case detection associated with the COVID-19 pandemic (**Chapter 3**). Early and rapid restoration of essential TB services is critical, but will not be enough to remedy the impact on broader TB determinants. In the context of the COVID-19 pandemic, addressing the socioeconomic determinants of TB and its consequences, as well as health-related risk factors for TB infection and disease, is more important than ever.

^a Global economic prospects, June 2020. Washington, DC: World Bank; 2020 (<https://www.worldbank.org/en/publication/global-economic-prospects>, accessed 20 July 2020) (20).

^b Projected poverty impacts of COVID-19 (coronavirus). Washington, DC: World Bank; 2020 (<http://pubdocs.worldbank.org/en/461601591649316722/Projected-poverty-impacts-of-COVID-19.pdf>, accessed 20 July 2020) (21).

^c Coronavirus and hunger: WFP ready to assist largest number of people ever. Rome: World Food Programme; 2020 (<https://insight.wfp.org/coronavirus-and-hunger-wfp-ready-to-assist-largest-number-of-people-ever-23aea919e87d>, accessed 20 July 2020) (22).

^d 2020 – Global report on food crises. Rome: World Food Programme; 2020 (<https://www.wfp.org/publications/2020-global-report-food-crises>, accessed 20 July 2020) (23).

8.4 Multisectoral accountability framework

Addressing broader determinants of the TB epidemic requires multisectoral action and accountability. In November 2017, WHO and the Ministry of Health of the Russian Federation co-hosted the first global ministerial conference on TB, titled *Ending TB in the sustainable development era: a multisectoral response*. In the resulting Moscow Declaration, multisectoral accountability was one of four key areas for action (24). Member States committed to “supporting the development of a multisectoral accountability framework” in advance of the first UN high-level meeting on TB in September 2018, and called on WHO to develop such a framework, working in close cooperation with Member States and partners.

8.4.1 Global progress

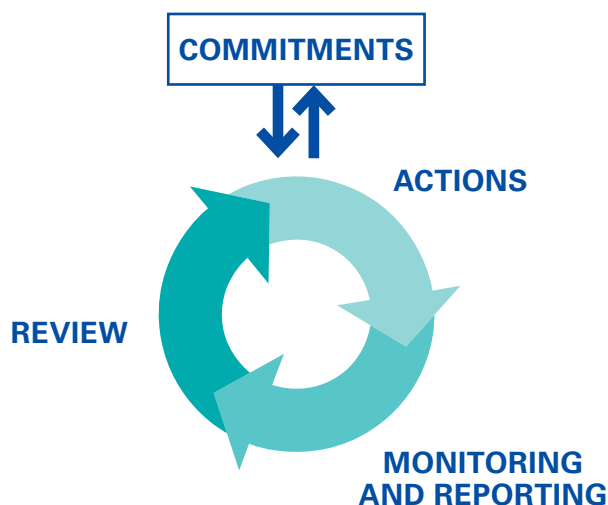
Commitments

The political declaration at the UN high-level meeting on TB asked the WHO Director-General to continue to develop the multisectoral accountability framework for TB (MAF-TB) and ensure its timely implementation (no later than 2019) (8). Following extensive preparatory and development work, WHO finalized the framework and published it in May 2019, shortly in advance of the 2019 World Health Assembly (10).

The MAF-TB has two parts: one focused on multisectoral engagement and accountability at national (including local) level; and the other on multisectoral engagement and accountability at global and regional levels, which applies to countries collectively. There are four critical components of accountability at all levels: commitments, actions, monitoring and reporting, and review (Fig. 8.12).

FIG. 8.12

Essential components of an accountability framework



Actions

To support efforts in adaptation and use of the MAF-TB at country level, WHO has developed a baseline assessment checklist (25). This can be used to assess the status of core elements of the MAF-TB and to inform related efforts, including stakeholder consultations to develop a national MAF-TB, NTP reviews, updating of national strategic plans and civil society audits.

In 2019 and 2020, WHO worked with high TB burden countries to ensure the development or strengthening of accountability mechanisms. Examples include joint reviews of NTPs with independent and civil society representatives, and support for high-level collaboration and review mechanisms, broad stakeholder forums and head-of state or government initiatives (e.g. those in India, Indonesia, and Viet Nam).

Civil society has been closely engaged in efforts to strengthen accountability. An example is the establishment of a WHO Civil Society Task Force on TB in 2018 (Box 8.4). The task force contributed to the development of the MAF-TB baseline assessment checklist (25) and is helping to advocate and provide support for its use at national level.

Since the UN high-level meeting on TB, WHO has undertaken high-level missions to Bangladesh, Brazil, Cambodia, India, Indonesia, Iran, Nigeria, Oman, Pakistan, the Philippines and the Russian Federation, with leadership from the Director of the WHO Global TB Programme. These were used to urge the translation of commitments made by heads of state and government into high-level action, accountability and investment at national and subnational levels; and to promote the WHO Director-General Flagship Initiative called FIND.TREAT.ALL#TB, together with the Stop TB Partnership and The Global Fund.

An accelerator package of WHO guidance and tools to help countries to implement their commitments to ending TB was released in 2019, and updated WHO guidelines on key topics including infection prevention and control, TB preventive treatment, drug-resistant TB treatment and TB diagnostics were issued in 2019–2020. Following commitments and requests in the Moscow Declaration and the political declaration at the UN high-level meeting related to advancing research and innovation through global collaboration, including through WHO mechanisms and networks, WHO has also published a global strategy for TB research and innovation. This was adopted by WHO Member States at the World Health Assembly in August 2020.¹ The strategy was developed using a broad consultation process that included the engagement of Member States and partners such as civil society and research networks (e.g. the BRICS TB research network).

¹ Further details are provided in Chapter 9.

The WHO Civil Society Task Force on TB

Building on the End TB Strategy, in 2018 the political declaration at the UN high-level meeting on TB called for prioritizing the strong and meaningful engagement of civil society and affected communities in all aspects of the TB response.

The WHO Civil Society Task Force on TB provides a platform for discussion and exchange with WHO, building on the commitments made by the WHO Director-General during the first WHO global ministerial conference on TB (in November 2017) and several consultations.^a It aims to harness the untapped potential for engagement with civil society and affected communities at all levels.

The current mandate of the Task Force is for the period January 2019 to December 2020. Priorities include:

- ▶ helping to translate the End TB Strategy and associated WHO guidance into practice by mainstreaming the voices of communities affected by TB and their networks at global, regional and country levels;
- ▶ catalysing greater collaboration between civil society organizations, NTPs and WHO at all levels, including through meaningful engagement of civil society and affected communities in policy development;
- ▶ contributing to the implementation of WHO guidance on TB, with a particular focus on multisectoral action for social protection and universal health coverage, and advocating for their inclusion in national TB strategies and plans, national social programmes, national political platforms (e.g. parliaments) and regional and global platforms for policy dialogue;

- ▶ promoting and nurturing strong and effective links between community-based actors and NTPs or their equivalent, as well as promoting demand for TB prevention, diagnosis, care and treatment services;
- ▶ developing a framework for monitoring and evaluation of collaboration among civil society organizations, NTPs and WHO at all levels;
- ▶ promoting capacity-building for civil society members and representatives of communities affected by TB to intensify information-sharing, dialogue and consultation on the implementation of WHO guidance;
- ▶ advocating for increased domestic funding and donor commitments for the TB response at all levels.

Fifteen civil society members were selected, with input from an independent selection panel. Selection was based on assessments of individual competencies and experience, and the process aimed to balance geography, gender and the diversity of communities and civil society representatives.

^a WHO Civil Society Task Force on TB: Engagement with civil society as the driver for change (<https://www.who.int/publications/i/item/who-civil-society-task-force-on-tb>, accessed 20 September 2020)

Recognizing young people as a powerful but underused ally in the fight to end TB, especially to scale up multisectoral action and accountability, WHO launched the 1+1 Youth Initiative in 2019. This was followed by the adoption of a Youth Declaration to End TB at the first-ever Global Youth Townhall on Ending TB. The 1+1 Initiative has expanded to include over ten thousand young people across the world in countries including Bangladesh, India, Indonesia, Kenya, Nepal, the Philippines and Viet Nam. Social media platforms set up as part of the 1+1 Youth Initiative and social media posts are followed by over 20 000 people, with the number growing each day. More than 100 youth-led activities and events on ending TB have been conducted worldwide. This includes peer education in schools and universities, sensitizing young people, encouraging them to become TB advocates, and supporting TB patients in the community with resources and advice.

Monitoring, reporting and review

Regular reports and reviews of progress towards ending TB by the UN General Assembly and World Health Assembly are essential to global and national accountability. The World Health Assembly reviewed progress on TB in follow-up to the UN high-level meeting in 2019 and 2020, based on WHO's global monitoring and reporting on the status of the TB epidemic and progress in the response.¹

¹ The two key components are the annual rounds of global TB data collection and series of annual WHO global TB reports described in [Chapter 1](#).

In 2020, a report of the UN Secretary-General on progress towards achieving global TB targets and implementation of other commitments in the political declaration of the UN high-level meeting on TB was prepared with WHO support.

The next review of progress by the World Health Assembly is expected in 2022, in advance of a comprehensive review at a high-level meeting of the General Assembly in 2023.

As part of the monitoring and reporting component of the MAF-TB, WHO has launched a collaborative multi-stakeholder and multisectoral platform to coordinate the TB response and review progress at the global level.

8.4.2 Regional progress

There is accelerated action in all WHO regions to strengthen accountability to end TB.

Recent examples include:

- ▶ establishment of high-level reviews by the African Union in collaboration with the WHO Regional Office for Africa and the Stop TB Partnership, based on an annual Continental Scorecard to End TB;
- ▶ creation of a UN common position on ending HIV, TB and viral hepatitis through intersectoral collaboration, under the leadership of the WHO Regional Office for Europe;
- ▶ organization of a ministerial meeting on ending TB by the WHO Regional Office for South-East Asia in 2018, with a follow-up meeting in 2019;
- ▶ subregional mechanisms to support progress towards global TB targets in the Americas, including the Council of Ministers of Health of Central America and Dominican Republic (COMSICA);
- ▶ discussion of TB elimination strategies by the Gulf Coordination Council, in the Eastern Mediterranean Region; and
- ▶ high-level missions to high TB burden countries in the Western Pacific Region, including the launch of initiatives called “Race to End TB” in the Philippines and Viet Nam.

8.4.3 National progress

Examples of national high-level leadership on multisectoral accountability include Presidential or Head of State End TB initiatives and formalized mechanisms for the engagement and accountability of stakeholders in India, Indonesia, Pakistan, Philippines and Viet Nam, as well as national campaigns to drive progress such as the “Race to End TB”.

In the 2020 round of TB data collection, WHO requested information from all countries and territories (n=215) on three key elements of multisectoral accountability in the national TB response: national strategic plans (NSPs) for TB, annual TB reports, and multisectoral and multi-stakeholder review mechanisms under high-level leadership (**Table 8.5**). This request was in line with the political declaration at the UN high-level meeting on TB and the content of the MAF-TB. In the political declaration, UN Member States committed to:

develop or strengthen, as appropriate, national tuberculosis strategic plans ... including through national multisectoral mechanisms to monitor and review progress ... with high-level leadership, preferably under the direction of the Head of State or Government, and with the active involvement of civil society and affected communities.

All of the 30 high TB burden countries have an NSP and, in 25 of those 30 countries, the current plan was developed or updated since the high-level meeting in September 2018. In developing the plan, almost all countries (29/30) involved civil society and affected communities.

Globally, 148 of 215 countries and territories reported having an NSP for TB; of these, 116 were developed with the engagement of civil society and affected communities, and 97 were developed or updated since the UN high-level meeting.

Most high TB burden countries (27/30) and 134 (62%) countries in total stated that they produce an annual TB report. WHO is working with countries to review report content and learn lessons, such as about how epidemiological and programmatic issues are addressed, stakeholders are engaged, and reports are promoted and used.

Of the three elements of accountability for which data were collected, the one that is least well-established to date is high-level review. Only 16 of the 30 high TB burden countries reported having a mechanism for high-level review, and globally, less than half of countries reported having one (86/215, 40%). Examples of progress in terms of high-level engagement, coordination or review bodies, and legislation in high TB burden countries, are provided in **Box 8.5**.

In some eastern European countries, civil society organizations are among those advocating for conversion of the existing Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) country coordination mechanisms (CCMs) into national commissions to address TB, or TB, HIV and hepatitis. This reflects the transition from Global Fund financing to domestic financing, and the critical need for high-level engagement.

TABLE 8.5
Status of core elements of multisectoral accountability in 2020 for 30 high TB burden countries, WHO regions and globally
a) National strategic plan (NSP) for TB and annual TB report

HIGH TB BURDEN COUNTRIES AND WHO REGIONS	NUMBER OF COUNTRIES AND TERRITORIES	NSP EXISTS		REPRESENTATIVES OF CIVIL SOCIETY AND AFFECTED COMMUNITIES WERE ACTIVELY INVOLVED IN NSP DEVELOPMENT		NSP WAS DEVELOPED OR UPDATED SINCE THE UN HIGH-LEVEL MEETING ON TB IN SEPTEMBER 2018		ANNUAL TB REPORT AVAILABLE PUBLICLY	
High TB burden countries	30	30	100%	29	97%	25	83%	27	90%
Africa	47	42	89%	40	85%	32	68%	39	83%
The Americas	45	32	71%	21	47%	16	36%	21	47%
Eastern Mediterranean	22	17	77%	11	50%	12	55%	16	73%
Europe	54	25	46%	21	39%	14	26%	30	56%
South-East Asia	11	11	100%	9	82%	8	73%	9	82%
Western Pacific	36	21	58%	14	39%	15	42%	19	53%
Total	215	148	69%	116	54%	97	45%	134	62%

b) High-level review mechanism(s)

HIGH TB BURDEN COUNTRIES AND WHO REGIONS	NUMBER OF COUNTRIES AND TERRITORIES	NATIONAL MULTISECTORAL AND MULTI-STAKEHOLDER ACCOUNTABILITY/REVIEW MECHANISM(S) IN PLACE		REPRESENTATIVES OF CIVIL SOCIETY AND AFFECTED COMMUNITIES PARTICIPATE IN THE MECHANISM(S)		DOCUMENTATION AVAILABLE DESCRIBING OR EXPLAINING THE MECHANISM(S)		RECOMMENDATIONS PROVIDED VIA THE MECHANISM(S) MADE AVAILABLE PUBLICLY	
High TB burden countries	30	16	53%	12	40%	15	50%	7	23%
Africa	47	26	55%	24	51%	22	47%	11	23%
The Americas	45	13	29%	6	13%	8	18%	2	4%
Eastern Mediterranean	22	6	27%	3	14%	5	23%	1	5%
Europe	54	19	35%	14	26%	16	30%	7	13%
South-East Asia	11	7	64%	4	36%	6	55%	3	27%
Western Pacific	36	15	42%	11	31%	12	33%	6	17%
Total	215	86	40%	62	29%	69	32%	30	14%

High-level mechanisms and initiatives to end TB: country examples

The WHO MAF-TB identifies three key elements of a national-level review mechanism:

- ▶ high-level leadership, preferably under the direction of the head of government or head of state, especially in countries with a high burden of TB;
- ▶ a multisectoral perspective; and
- ▶ engagement of key stakeholders, as appropriate; stakeholders include government ministries and institutes, local governments, civil society, TB-affected communities, patient groups, parliamentarians, the private sector, public-private partnerships (including product development partnerships), research institutes and universities (and associated research networks), professional associations and other constituencies.

In the political declaration of the UN high-level meeting on TB in 2018, countries committed to use national multisectoral mechanisms to monitor and review progress to end TB.

A high-level coordination and review mechanism for TB can be constituted in different ways. Examples include a stand-alone TB-specific committee, similar to a national AIDS commission, or an existing high-level government health committee that addresses TB substantively on a periodic basis and involves outside stakeholders. A body or mechanism could result from a head-of-state decree or legislation, or could form part of a presidential or head-of-state initiative.

Recent examples in high TB burden countries are profiled here.

China

China has issued a new National Action Plan for TB Control for 2019–2022 in which the responsibilities of key ministries in the TB response are clearly identified. These responsibilities were also defined in the Healthy China Action Plan (2019–2030) issued by the State Council. The China State Council has established an Inter-ministerial Coordinating Mechanism for the Prevention and Control of Major Diseases, which will address TB regularly. In this mechanism, the National Health Commission (equivalent of a Ministry of Health) will play the coordination role among the other ministries and entities identified and involved in the TB response (e.g. Ministry of Education, Ministry of Civil Affairs, Ministry of Science and Technology, Ministry of Finance, National Healthcare Security Administration, the State Council Leading Group Office of Poverty Alleviation and Development, among others).

India

In 2017, the Prime Minister set the target of ending TB in India by 2025. The following year, he presided over a ministerial meeting on ending TB that was organized by the WHO Regional Office for South-East Asia. He has included TB in his quarterly discussions with the chief ministers of the country's 28 states. In 2019, national, state and district TB forums, and a large inter-ministerial committee, were established. Several chief ministers have developed their own state TB elimination plans and special initiatives, and TB-free *panchayats* (villages) are being promoted across the country. In 2020, the Revised National TB Control Programme was renamed the National TB Elimination Programme and a strategic plan for the period 2020–2025, which emphasizes the centrality of multisectoral action to end the epidemic, is being implemented.

Indonesia

High-level engagement was boosted by the UN high-level meeting on TB in 2018 and by high-profile global and national TB meetings held in 2019, which were organized with WHO and the Stop TB Partnership Indonesia.

In January 2020, the President held an event with officials from across the country to launch a "TB Elimination Movement". As part of the national response to the COVID-19 pandemic, a protocol was issued to help ensure ongoing TB care and prevention, and the President has repeatedly issued public warnings about the ongoing urgency of TB detection and care.

In April 2020, the Secretary of State formally announced work on a Presidential Decree on TB Elimination. In July 2020, the President held a meeting with the Vice-President and several ministers (e.g. of Health, Planning, Social Affairs, Justice and Human Rights, Public Works and Human Settlements) and announced the decree's key aims. These include strengthening active case finding, ensuring effective treatment services and an intensified focus on prevention. The decree is intended to include high-level monitoring and review. Completion of the official processing of the decree, including via formal consultations, is expected in 2020.

Myanmar

The Global Fund country coordinating mechanism has been transformed into the Myanmar Health Sector Coordination Committee, under the leadership of the Ministry of Health and Sport. Its roles include guiding the implementation of the Essential Package of Health Services (including TB), and contributing to tracking sectoral progress related

BOX 8.5

to the Myanmar Sustainable Development Plan via the Development Assistance Coordination Unit. As part of the national TB strategic plan for 2021–2025, there will be a national multisectoral accountability framework for TB and additional multisectoral coordination committees, including one dedicated to the Yangon Region. The framework will build on recent successes, such as standards of practice for screening with the Prison Department in the Ministry of Home Affairs, and mandatory TB case notification from services provided by multiple sectors.

Philippines

A cross-governmental mechanism to address TB prevention and care was first established through a Presidential Executive Order in 2003, engaging 17 government agencies and five private sector organizations to work together to implement harmonized policies for TB prevention and care. The mechanism covers a range of social sectors such as health, labour, welfare, development, poverty reduction, justice, social insurance, education, agriculture and the private and corporate sectors. In 2016, building on these foundations, the Congress of the Philippines passed a Comprehensive Tuberculosis Elimination Plan Act (Republic Act 10767). This strengthens the mandate and capacity of the National Coordination Committee and the regional coordination committees to coordinate stakeholder efforts in the public and private sectors. These national and subnational mechanisms serve as venues for coordination, monitoring and review of multisectoral actions to end TB.

Russian Federation

A 2001 federal law and 2019 order of the Ministry of Health provide the main legal foundation for the roles and responsibilities of federal and subnational authorities and institutions in the fight against TB.

A high-level working group on TB was established 20 years ago and is co-chaired by WHO and the Ministry of Health. The working group is multisectoral and multistakeholder in nature. It includes representatives from the penitentiary services; a body responsible for surveillance related to protection of consumer rights and human well-being; people affected by TB; research institutes; and international agencies, including the World Bank, International Labour Organization and International Organization of Migration. The group has served as a model for a more recently established high-level working group for HIV/AIDS.

In 2016, the President directed national action to dramatically reduce the top 10 causes of adult deaths, one of which was TB, with regular high-level monitoring and review of progress. Between 2015 (the baseline year of the WHO End TB Strategy) and

2019, the number of TB deaths fell at a rate of 10% per year; the country is one of only seven high TB burden countries to have achieved the 2020 milestone of the End TB Strategy (a 35% reduction 2015–2020) ahead of schedule (**Chapter 2, Chapter 4**). Measures to combat TB in the Russian Federation include a combination of medical and non-medical multisectoral measures, such as social support for TB patients (job retention and paid sick leave, preferential disability pensions, provision of housing), as well as free drug provision from the federal and regional budgets, treatment and rehabilitation.

The President hosted WHO's first global ministerial conference on ending TB in November 2017, which resulted in the Moscow Declaration.

The Russian Federation is also supporting the implementation of the MAF-TB at global and national levels.

South Africa

The mandate of the high-level South Africa National AIDS Council (SANAC) was expanded to include TB in 2009, more than a decade ago. SANAC is chaired by the country's Deputy President, with membership including representatives from civil society, affected communities and the private sector. It also serves as the country coordinating mechanism for proposals to and grant agreements with the Global Fund. There is one strategic plan for both the HIV and TB epidemics, and the respective national programmes are coordinated by one deputy director-general in the Department of Health.

Viet Nam

A National Commission to End TB was established in 2019, as part of a Prime Ministerial decree to consolidate the system for TB prevention and control. The Commission is chaired by the Deputy Prime Minister and aims to guide and coordinate implementation of the National Action Plan through engagement of multiple sectors, in line with the WHO MAF-TB. The first meeting of the Commission was held in March 2020 with representatives from several government ministries (finance, health, information and communication, planning and investment, public security, and science and technology) as well as associations and related commissions. In the next national TB strategic plan for 2021–2025, under an overall Action Programme to 2030, sector roles and responsibilities are being defined, 15 provinces are being targeted for a strengthened managerial structure to provide oversight of TB-related services, and domestic financing for TB drugs is being strengthened. A revised national law on infectious diseases, including TB, is being formulated.

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Maxim Dondyuk/WHO

Chapter 9

TB research and innovation

Key facts and messages

Tuberculosis (TB) research and innovation is essential to achieve the global TB targets set in the United Nations (UN) Sustainable Development Goals (SDGs) and the World Health Organization (WHO) End TB Strategy. A major technological breakthrough is required by 2025, so that the rate at which TB incidence falls can be dramatically accelerated compared with historic levels, to an average of 17% per year between 2025 and 2035.

“Intensified research and innovation” is the third pillar of the End TB Strategy; also, Target 3b of the SDGs includes supporting research and development related to vaccines and medicines for “communicable and non-communicable diseases that primarily affect developing countries”.

To end the TB epidemic, the world needs affordable and accessible rapid point-of-care tests for diagnosing TB infection and TB disease, and for detecting drug resistance; shorter, safer and more effective regimens for treating TB infection, drug-susceptible TB and drug-resistant TB; a TB vaccine that is effective before and after exposure, as well as across a range of age groups and geographical settings; and innovative strategies to address broader determinants of TB, such as poverty, undernutrition, HIV infection, smoking and diabetes.

Following a request from Member States at the World Health Assembly in 2018, WHO has developed a global strategy for TB research and innovation. The strategy aims to support countries and relevant stakeholders to translate the commitments to research and

innovation made in the Moscow Declaration of the first global ministerial conference on TB (held in November 2017), and the political declaration of the first UN high-level meeting on TB (held in September 2018) into concrete actions.

One of the objectives of the global strategy is to double the funding for TB research to reach the UN high-level meeting target of US\$ 2 billion per year. In 2018, only US\$ 906 million was available.

The role of digital technologies in the delivery of TB services (e.g. for remote advice and support) has gained prominence in the context of the COVID-19 pandemic. In 2020, WHO launched an implementation research toolkit to support greater use of digital technologies across the TB continuum of care. To facilitate information sharing and evidence-based decision-making, WHO has also established a compendium for research projects and publications related to TB and COVID-19.

Despite challenges (e.g. mobilization of funding), progress in the research and development pipeline for TB has been made in recent years.

The diagnostic pipeline appears robust in terms of the number of tests, products or methods in development. These include several cartridge-based technologies for the detection of isoniazid and second-line drug resistance; broth micro-dilution methods for drug-susceptibility testing (DST); amplification-based targeted next-generation sequencing (NGS) assays for detecting drug-resistant TB directly from sputum specimens;

a next-generation lateral-flow lipoarabinomannan assay that has significant performance improvements over currently marketed assays (particularly in terms of sensitivity); newer skin tests for TB infection based on recombinant ESAT-6 and CFP-10 antigens derived from *Mycobacterium tuberculosis* (which have significant performance improvements compared with tuberculin skin tests, particularly in terms of specificity); an expanding pipeline of new interferon gamma release assays (IGRA) to test for TB infection; and computer-aided detection (CAD) software that employs artificial intelligence to help screen for TB and other pathologies on digital chest radiographs.

Currently, 22 drugs for the treatment of drug-susceptible TB, multidrug-resistant TB (MDR-TB) or TB infection are in Phase I, II or III trials. These comprise 13 new compounds, two drugs that have received accelerated regulatory approval, one drug that was recently approved by the United States (US) Food and Drug Administration under the limited population pathway for antibacterial and antifungal drugs, and six repurposed drugs. Various combination regimens with new or repurposed drugs are in Phase II or III trials.

There are 14 vaccine candidates in clinical trials: three in Phase I, nine in Phase II and two in Phase III. They include candidates to prevent TB infection and TB disease, and candidates to help improve the outcomes of treatment for TB disease.

The global tuberculosis (TB) targets set in the United Nations (UN) Sustainable Development Goals (SDGs) and the World Health Organization (WHO) End TB Strategy can only be achieved with TB research and innovation. The SDG target is to “end the epidemic” by 2030; more specific targets for 2030 set in the End TB Strategy are a 90% reduction in TB deaths and an 80% reduction in TB incidence compared with 2015 levels, with targets for further reductions (95% and 90%, respectively) by 2035 (Chapter 2). Reaching these targets requires a major technological breakthrough by 2025, so that the rate at which TB incidence falls can be dramatically accelerated compared with historic levels, to an average of 17% per year from 2025 to 2035.

“Intensified research and innovation” is the third pillar of the WHO End TB Strategy, and Target 3b of the SDGs includes supporting research related to vaccines and medicines for “communicable and non-communicable diseases that primarily affect developing countries”. The third pillar of the End TB Strategy recognizes that substantial reductions in TB incidence and mortality require the development and use of innovative tools and strategies, as well as universal access to and better use of existing technologies. Top priorities are rapid point-of-care tests for diagnosing TB infection and TB disease, and for detecting drug resistance; shorter and safer regimens for treating TB infection and drug-susceptible TB; shorter, safer and more effective treatment for drug-resistant TB; a TB vaccine that is effective before and after exposure, and across a range of age groups and geographical settings; innovative strategies to address the broader determinants of TB, such as poverty, undernutrition, HIV infection, diabetes and smoking;¹ and expanded use of digital technologies.

Building on the SDGs and End TB Strategy, commitments to TB research and innovation were included in both the Moscow Declaration to End TB at the first global ministerial conference on TB, held in November 2017 (1), and the political declaration at the first UN high-level meeting on TB, held in September 2018 (2). The political declaration at the UN high-level meeting included the first global financing target for TB research to be agreed by all UN Member States (Chapter 2). In 2018 and 2019, WHO developed a global strategy for TB research and innovation, which aims to support countries and relevant stakeholders to translate these commitments into concrete actions.

This chapter provides an overview of the WHO global strategy for TB research and innovation, and profiles two related products that were made available by the WHO Global TB Programme in 2020, and that are directly or closely related to the COVID-19 pandemic (Section 9.1). As in previous global TB reports, this chapter also provides an overview of the status of the pipelines for new TB diagnostics (Section 9.2), new drugs and regimens for the treatment of TB disease (Section 9.3), new drugs and regimens for the treatment of TB infection (Section 9.4), and

new TB vaccines (Section 9.5). It describes their status in August 2020, based on recent publications as well as communications with the secretariats of the relevant working groups of the Stop TB Partnership and other stakeholders.

This chapter is not intended to be an exhaustive overview of current or recently completed TB research.

9.1 A new WHO global strategy for TB research and innovation

At the World Health Assembly in 2018, Member States passed a TB resolution that included a request to the WHO Director-General to develop a global strategy for TB research and innovation (3). The rationale for such a strategy was “to make further progress in enhancing cooperation and coordination in respect of tuberculosis research and development”.

In 2018 and 2019, WHO led a wide consultative process to develop a strategy, building on a review of the TB research landscape (4). The strategy set out four major areas for action: creating an enabling environment for TB research and innovation, increasing financial investments in TB research and innovation, promoting and improving approaches to data sharing, and promoting equitable access to the benefits of research and innovation.

In August 2020, Member States adopted the global strategy for TB research and innovation in a written silence procedure of the 73rd session of the World Health Assembly (5). The strategy was adopted through a resolution, which includes the following commitments, calls and requests:

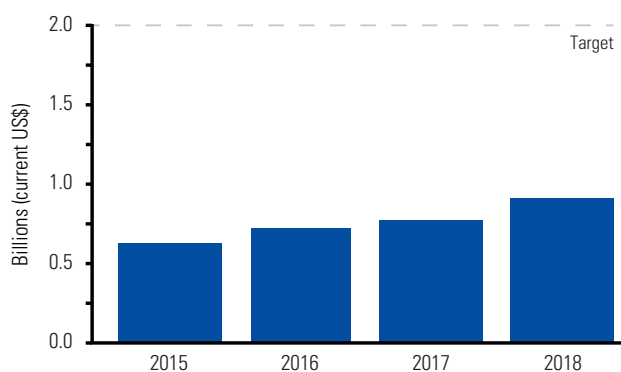
- ▶ Member States commit to implement the strategy by providing adequate resources, establishing or strengthening TB research networks, sharing scientific data, and amplifying financing for TB research.
- ▶ Member States call for the support of the scientific community, international partners and other relevant stakeholders to undertake research and innovation aligned to the needs of those countries most affected by TB, to strengthen public–private partnerships and to facilitate knowledge sharing.
- ▶ Member States request WHO to provide them with all the necessary technical and strategic assistance to address their TB research needs, including by promoting collaboration across agencies and sectors, and to report every 2 years to the World Health Assembly on strategy implementation from 2022 to 2030.

Recently, the Ministry of Health of Brazil committed US\$ 4 million in grants for an open call for collaborative TB research projects among researchers in the BRICS group of countries (Brazil, the Russian Federation, India, China and South Africa) (6). An additional US\$ 500 000 will also be made available to encourage collaboration between research institutes in at least two of the BRICS group of countries.

One of the objectives of the global strategy is to double global funding for TB research to reach the UN high-level meeting target of US\$ 2 billion per year

¹ These determinants are discussed in Chapter 8.

FIG. 9.1
Funding for TB research, 2015–2018



Source: Treatment Action Group, Stop TB Partnership. Tuberculosis research funding trends 2005–2018. New York: Treatment Action Group; 2019 (<https://www.treatmentactiongroup.org/resources/tbrd-report/tbrd-report-2019/>, accessed 22 July 2020)

(Chapter 2). Funding for TB research, which is tracked by the Treatment Action Group (7), has been slowly increasing (Fig. 9.1). However, the latest published data show that only US\$ 906 million was available in 2018, which is less than half of the US\$ 2 billion annual investment needed to address unmet research needs in TB prevention and care.

The two largest investors in 2018 were the US government and the Bill & Melinda Gates Foundation which, in combination, accounted for 56% of total funding. The 30 largest funders accounted for 90% of the total. About 37%

of TB research funding was for drug research, followed by 20% for basic science, 13% for operational research, 12% for vaccines, and 9% each for diagnostics and infrastructure or unspecified research. Strong government leadership is needed to mobilize more domestic funding, foster public–private partnerships and incentivize the engagement of pharmaceutical companies, biotechnology firms and other health product developers.

In line with WHO’s global strategy for TB research and innovation, the WHO Global TB Programme has recently developed two other resources. One is a compendium of research related to TB and COVID-19 (Box 9.1); the other is a toolkit to support the implementation and scale-up of digital technologies across the TB continuum of care (Box 9.2). Both the compendium and the toolkit are expected to contribute to mitigating the impact of the COVID-19 pandemic on TB services.

9.2 New diagnostics for TB

This section provides an overview of the TB diagnostics pipeline and describes diagnostic tests, products and methods that WHO has evaluated in 2020, or that are scheduled for assessment within the next year. It also discusses the latest status of technologies that can assist with TB screening, tests for TB infection and use of DNA sequencing to diagnose drug-resistant TB.

9.2.1 An overview of the diagnostics pipeline

An overview of the TB diagnostics pipeline in August 2020 is shown in Fig. 9.2. The pipeline is robust and actively

BOX 9.1

Compendium for research on TB and COVID-19

The COVID-19 pandemic is generating many questions about the co-management of TB and COVID-19. To facilitate information sharing and inform evidence-based decision-making, WHO has established a compendium of publications and research projects related to TB and COVID-19.^a

The compendium includes a digital library of TB/COVID-19 publications with full-text articles, covering topics such as prevention, screening, clinical observation, treatment and modelling. This was developed by screening both pre-print and peer-reviewed publications from PubMed, medRxiv and WHO databases. Articles are categorized by their date of publication, journal name, study site, type of data source(s) and topic.

The compendium also includes a list of TB/COVID-19 research projects, self-reported by research

investigators, and a list of clinical trials testing the use of the bacille Calmette–Guérin (BCG) vaccine against COVID-19. It also maps multicountry efforts related to the co-management of TB and COVID-19, with a view to stimulating cooperation between scientists, funding institutions, policy-makers and civil society.

The WHO Global TB Programme is monitoring all research findings to support national TB programmes (NTPs) to address TB in the context of COVID-19. It is also supporting partner efforts to compile individual patient-level data on people with COVID-19 with past or concurrent TB, to better understand the disease profile and outcomes of COVID-19 in this subpopulation.

^a Compendium of TB/COVID-19 studies. Geneva: World Health Organization; 2020 (<https://www.who.int/teams/global-tuberculosis-programme/covid-19/compendium>, accessed 29 July 2020) (8).

Expanding the use of digital technologies in TB service delivery: an implementation research toolkit

The COVID-19 pandemic has drawn attention to the role of digital technologies in health care and, in the context of TB, how such technologies can help to mitigate impacts on and address persistent gaps in TB services. Many countries have already expanded the use of remote advice and support for people with TB (Chapter 3).

To help drive the use of evidence-based and context-appropriate digital technologies to improve approaches to TB prevention and care, in 2015, WHO released the publication *Digital health for the End TB Strategy: an agenda for action*.^a However, context-specific barriers to implementation and scale-up of digital innovations persist.

Implementation research (IR) is a systematic approach to recognizing, understanding and addressing barriers to implementation and scale-up of effective and quality health interventions, strategies and policies.

The Special Programme for Research and Training in Tropical Diseases (TDR) and the WHO Global TB Programme (WHO/GTB) have jointly developed a toolkit to help NTP managers and

other partners to conduct IR projects to evaluate digital technologies in routine programmatic conditions.^b The toolkit covers key steps in the process (Fig. B9.2.1) and four thematic areas: patient care, programme management, e-Learning, and surveillance and monitoring. It also aims to generate new evidence to inform future WHO guidance.

The toolkit has a modular structure and includes practical exercises as well as illustrative case studies of existing applications of digital technologies within NTPs. It was built on the foundations of the TDR IR toolkit^c and will be complemented by an online course.

^a Digital health for the End TB Strategy: an agenda for action. Geneva: World Health Organization; 2015 (<https://www.who.int/tb/publications/digitalhealth-TB-agenda/en/>, accessed 29 July 2020) (9).

^b Implementation Research for digital technologies and TB (IR4DTB): A toolkit for evaluating the implementation and scale-up of digital innovations across the TB continuum of care. Geneva: TDR; 2020 (<https://www.ir4dtb.org/>, under construction, accessed 15 September 2020) (10).

^c Implementation research toolkit. Geneva: TDR; 2014 (<https://www.who.int/tdr/publications/topics/ir-toolkit/en/>, accessed 5 August 2020) (11).

FIG. B9.2.1

Key steps in the conduct of implementation research on digital technologies for TB



developing in terms of the number of tests, products or methods, as shown by the following examples:

- ▶ several cartridge-based technologies for the detection of resistance to isoniazid and second-line drugs, one of which is close to being ready for WHO evaluation;
- ▶ broth micro-dilution methods for drug susceptibility testing (DST);
- ▶ amplification-based targeted next-generation sequencing (NGS) assays for detecting drug-resistant TB directly from sputum specimens;
- ▶ a next-generation lateral-flow lipoarabinomannan assay, which has significant performance improve-

ments over currently marketed assays (particularly in terms of sensitivity);

- ▶ an increasing number of newer interferon gamma release assays (IGRAs) and skin-based tests for detection of TB infection, both in development and on the market; and
- ▶ computer-aided detection (CAD) software that employs artificial intelligence to help screen for TB and other pathologies on digital chest radiographs – the number of commercially available CAD systems have increased substantially in recent years.

FIG. 9.2

An overview of progress in the development of TB diagnostics, August 2020

TECHNOLOGIES IN DEVELOPMENT	
<p>Molecular detection of TB and drug resistance</p> <ul style="list-style-type: none"> ■ Gendrive MTB/RIF ID, Epistem, UK ■ TruArray MDR-TB, Akkoni, USA ■ INFINITIMTB Assay, AutoGenomics, USA ■ FluoroType XDR-TB assay, Hain Lifescience, Germany ■ MeltPro TB assay, Zeesan Biotech, China ■ QuantuMDx, POC, UK ■ Truenat MTB-INH/MTB-FQ, Molbio, India ■ AccuPower XDR-TB RT PCR, Bioneer, Republic of Korea 	<p>Interferon gamma release assays (IGRAs) for TB infection</p> <ul style="list-style-type: none"> ■ Access QuantiFERON®-TB, QIAGEN, USA ■ IP-10 IGRA elisa/lateral flow, rBioPharm, Germany ■ ichroma™ IGRA-TB, Boditech Med Inc., Republic of Korea ■ T-Track(R) TB, Lophius Biosciences GmbH, Germany ■ VIDAS TB-IGRA, bioMérieux, France <p>Skin tests for TB infection</p> <ul style="list-style-type: none"> ■ c-Tb skin test, Serum Institute of India, India ■ EC-Test, Anhui Zhifei Longcom Biopharmaceutical Co. Ltd, China
ON THE MARKET (NOT YET EVALUATED BY WHO)	
<p>Molecular detection of TB and drug resistance</p> <ul style="list-style-type: none"> ■ iCubate System, iCubate, USA ■ Genechip, TB drug resistance array, Capital Bio, China ■ EasyNAT TB Diagnostic kit, Ustar Biotechnologies, China ■ Amplification-based tNGS assays: Next Gen-RDST assay, TGen, USA; Deeplex-MycTB assay, GenoScreen, France 	<p>Interferon gamma release assays (IGRAs) for TB infection</p> <ul style="list-style-type: none"> ■ Lioferon TB/LTBI, LIONEX Diagnostics & Therapeutics GmbH, Germany ■ STANDARD E TB-Feron ELISA, SD Biosensor, Republic of Korea ■ Advansure TB IGRA, LG chem, Republic of Korea <p>Skin tests for TB infection</p> <ul style="list-style-type: none"> ■ Diaskintest, JSC Generium, Russian Federation
TECHNOLOGIES ENDORSED BY WHO	
<p>Molecular detection of TB and drug resistance</p> <ul style="list-style-type: none"> ■ Xpert MTB/RIF and Xpert Ultra as the initial diagnostic test for TB and rifampicin resistance, Cepheid, USA ■ 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 ■ Line probe assays for the detection of resistance to fluoroquinolones and second-line injectable agents (SL-LPA), Hain Lifescience, Germany ■ TB LAMP for detection of TB, Eiken, Japan ■ Truenat MTB, MTB Plus and MTB-RIF Dx assays as initial diagnostic tests for TB and rifampicin resistance, Molbio Diagnostics, India 	<p>Interferon gamma release assays (IGRAs) for TB infection</p> <ul style="list-style-type: none"> ■ T-SPOT.TB, Oxford Immunotec, UK ■ QuantiFERON-TB Gold Plus (QFT-Plus), Qiagen, USA <p>Culture-based technologies</p> <ul style="list-style-type: none"> ■ Commercial liquid culture systems and rapid speciation ■ Culture-based phenotypic DST using 1% critical proportion in LJ,7H10,7H11 and MGIT media <p>Microscopy</p> <ul style="list-style-type: none"> ■ Light and light-emitting diode microscopy (diagnosis and treatment monitoring) <p>Biomarker based assays</p> <ul style="list-style-type: none"> ■ Alere Determine TB-LAM, Alere, USA for TB detection in HIV infected people
UNDER EVALUATION BY WHO	
<p>Molecular detection of TB and drug resistance</p> <ul style="list-style-type: none"> ■ Molecular technologies for genotypic drug resistance testing (including sequencing technologies) ■ FluoroType MTBDR, Hain Lifescience, Germany ■ m2000 RealTime MTB System, Abbott, USA ■ BD Max MDR-TB, Becton Dickinson, USA ■ Roche cobas® MTB system, Roche Diagnostics, Switzerland ■ AccuPower TB & MDR RT PCR, Bioneer, Republic of Korea ■ Genoscholar PZA TB II, Nipro, Japan ■ Xpert XDR-TB cartridge, Cepheid, USA 	<p>Computer-aided detection (CAD) for digital chest radiography</p> <ul style="list-style-type: none"> ■ CAD4TB, Delft Imaging, Netherlands ■ Lunit INSIGHT CXR, Lunit, South Korea ■ qXR, qure.ai, India ■ DxTB, Deeptek, USA ■ XrayAME, Epcon, Belgium ■ InterRead DR Chest, Inter VISION, China ■ T-Xnet, Artelius, India ■ Dr CADx, Dr CADx, Zimbabwe ■ RediSen, AXIR, South Korea ■ JF CXR-1, JF HEALTHCARE, China <p>Culture-based drug susceptibility testing</p> <ul style="list-style-type: none"> ■ Sensititre™ MYCOTBI plate; ThermoFisher Scientific Inc., USA

XDR-TB = combined resistance to rifampicin, isoniazid, a fluoroquinolone and an injectable agent

Some of the marketed nucleic-acid amplification tests (NAATs) have battery options (e.g. GeneXpert Edge® and Truenat®) to enable their use in decentralized settings. Nonetheless, there is still a significant gap in the development of diagnostics suitable for use at the point of care. There is an urgent need for new technologies to minimize barriers to a timely diagnosis for people with TB, ensure quality testing for difficult-to-diagnose groups, expand the spectrum of DST, and reduce the costs of diagnostic platforms and their maintenance.

9.2.2 TB diagnostic tests, products and methods evaluated by WHO in 2020 or scheduled for evaluation within the next year

Molecular assays intended as initial tests for the diagnosis of pulmonary and extrapulmonary TB and rifampicin resistance in adults and children

The development of the Xpert® MTB/RIF assay (Cepheid, Sunnyvale, USA), which was endorsed by WHO in 2010, was a major step forward in improving the diagnosis of TB and rifampicin-resistant TB (RR-TB) globally. Compared with the reference standard of culture, however, it still had suboptimal sensitivity (particularly among people with smear-negative TB and people living with HIV) and specificity. In 2017, WHO evaluated and recommended a next-generation assay with improved sensitivity, Xpert® MTB/RIF Ultra (hereafter referred to as “Xpert Ultra”). This assay uses the same GeneXpert® platform as Xpert MTB/RIF.

New molecular assays called Truenat® MTB, MTB Plus and MTB-RIF Dx (Molbio Diagnostics, Goa, India, hereafter referred to as “Truenat”) were developed in India, and may potentially be used at the same level of the health system as Xpert MTB/RIF and Xpert Ultra. The MTB and MTB Plus assays are initial diagnostic tests for TB, whereas the MTB-RIF Dx assay is a test for rifampicin resistance among those with positive results on the initial tests.

In December 2019, WHO convened a guideline development group (GDG) to review evidence about the use of Xpert MTB/RIF, Xpert Ultra and Truenat. The key recommendations agreed upon are as follows:

- ▶ Xpert MTB/RIF, Xpert Ultra and two Truenat assays (MTB and MTB Plus) are recommended as initial tests to diagnose pulmonary TB and to detect rifampicin resistance;
- ▶ Xpert MTB/RIF and Xpert Ultra are recommended to improve the diagnosis of TB and rifampicin resistance in children, using sputum, stool, nasopharyngeal and gastric specimens; and
- ▶ Xpert MTB/RIF and Xpert Ultra are recommended to improve the diagnosis of TB and rifampicin resistance in patients with various forms of extrapulmonary TB.

These recommendations have been published as part of WHO’s consolidated guidelines for TB that were released in June 2020 (12).

Other rapid tests and platforms for the detection of TB disease and drug resistance

Progress is being made with the Cepheid close-to-care platform, GeneXpert® Omni® (Omni). This platform is undergoing field evaluation to assess bioequivalence with the GeneXpert instrument. If equivalence is demonstrated, it will initially be available for testing for TB and RR-TB using the next-generation Xpert Ultra cartridge.¹

The Omni is expected to complement existing multi-module GeneXpert instruments, including the GeneXpert Edge® (Edge) – a single-module GeneXpert instrument connected to a tablet device for transfer of data, whose specific features include an auxiliary battery that allows for operation in decentralized settings, at the same level as microscopy. Both tests, the Omni and the Edge, have been developed to facilitate wider access to rapid molecular testing for TB and rifampicin resistance, and virology parameters for HIV and hepatitis C virus. WHO will evaluate the Omni once sufficient data are available for policy formulation.

Centralized high-throughput testing platforms

In July 2019, WHO convened a technical group to assess the performance of four centralized testing platforms based on polymerase chain reaction, suitable for high-throughput laboratories. The platforms reviewed were the RealTime MTB assay (Abbott), the Roche Cobas MTB assay (Roche), the FluoroType MTBDR assay (Hain Lifescience) and the BD Max MDR-TB assay (Becton Dickinson). The evidence available for this first evaluation phase was limited.

WHO plans to convene a GDG to undertake a second evaluation of centralized testing platforms in December 2020. WHO issued a public call for data in June 2020 and has commissioned systematic reviews of the evidence about the diagnostic accuracy of several centralized high-throughput testing platforms.

Cartridge-based technology for isoniazid and second-line drug resistance detection

Cepheid has developed the Xpert MTB/XDR assay to detect resistance to isoniazid as well as second-line drugs (fluoroquinolones and amikacin). The Foundation for Innovative New Diagnostics (FIND) is conducting a large-scale, multicentre clinical trial to evaluate its diagnostic accuracy when used as a follow-on test to a positive Xpert MTB/RIF or Xpert MTB/RIF Ultra result. Similar products from Molbio and Bioneer are at earlier stages of development. The evidence will be reviewed by a GDG convened by WHO in December 2020.

¹ The Omni platform requires cartridges with near-field communication chips; hence, it will not be compatible with the current Xpert MTB/RIF and Ultra cartridges.

Hybridization-based technology for pyrazinamide resistance detection

Nipro (Osaka, Japan) has developed and marketed a hybridization-based technology (Genoscholar PZA TB II) for the detection of resistance to pyrazinamide. WHO, FIND and the Supranational Reference Laboratory network are conducting multicentre validation studies to measure the test's diagnostic accuracy and reproducibility. The evidence will be reviewed by a GDG convened by WHO in December 2020.

Microbroth dilution method for DST

The development of a microbroth dilution plate is a promising option for reducing the cost of phenotypic DST (pDST) for drug-resistant strains of *Mycobacterium tuberculosis* complex (MTBC), through which a large number of drugs can be tested simultaneously to individualize patient treatment. The Sensititre MYCOTBI *M. tuberculosis* MIC [minimum inhibitory concentration] Plate by Thermo Fisher (Waltham, USA) does not meet current clinical needs, owing to an outdated selection of drugs; also, the concentrations tested for some drugs do not span the full range required for quality control, and the test's performance has never been evaluated systematically.

WHO convened a technical expert group in February 2020, which reached agreement on the optimal choice of drugs to meet short- and medium-term clinical priorities, and on the choice of drug concentrations and their arrangement on the plate to meet clinical needs. The technical report from the meeting is expected towards the end of 2020.

Critical concentrations of anti-TB medicines used for DST

Culture-based pDST methods are currently the reference standard for detection of drug resistance. They use critical concentrations (CCs) of anti-TB agents to distinguish between susceptibility and resistance.

The CC is defined as the lowest concentration of an anti-TB agent in vitro that will inhibit the growth of 99% of phenotypically wild-type strains of MTBC. The clinical breakpoint (CB) is the concentration or concentrations that distinguish a likely response to treatment from an unlikely one.

WHO commissioned FIND to perform a systematic review of available MIC data for both phenotypically wild-type and non-wild-type strains, including associated sequencing data for relevant resistance genes. The medicines included in the review were isoniazid and rifamycins (rifampicin, rifabutin and rifapentine), and the media considered were Löwenstein Jensen, Middlebrook 7H10/7H11 and BACTEC™ Mycobacterial Growth Indicator Tube™ 960.

WHO convened a technical expert group in February 2020 to review the results from the FIND evaluation. The outcome was that the CC for rifampicin pDST was updated, whereas the CC for isoniazid was retained. The technical report from the meeting is expected towards the end of 2020.

9.2.3 TB screening tests

Systematic screening for TB is one of the interventions that can enable progress towards the global target of treating 40 million people for TB disease between 2018 and 2022, which was set at the UN high-level meeting on TB in 2018 (Chapter 2). In 2020, WHO convened a GDG to update its 2013 guidance on systematic screening for TB. Updated recommendations will provide guidance on the implementation of screening activities, including the use of screening tools and algorithms; this is scheduled for finalization and publication in early 2021.

CAD software

Chest radiography or chest X-ray (CXR) is an important tool for TB triaging and screening; it is also a useful aid in TB diagnosis. A major limitation of CXR is that it requires experienced interpreters (usually radiologists or trained technicians) to interpret the images. The accuracy of TB screening when reading CXRs varies markedly, even among specialists. In many countries, few experienced CXR readers are available. The last WHO guidance on CXR was issued in 2016 (13).

In recent years, several CAD software products have been developed to interpret digital chest radiographs for abnormalities suggestive of TB or other diseases. These CAD systems incorporate machine-learning algorithms that analyse a CXR image and produce a standardized interpretation of the image. A score or report is generated that estimates the likelihood that the CXR image is consistent with TB. CAD systems are trained on thousands of images, using machine-learning techniques.

The GDG on TB screening convened in 2020 reviewed data on the use of CAD software products for TB screening and triage. Recommendations are scheduled for publication in early 2021.

FIND and the Stop TB Partnership have collated information on CAD products for TB detection, to summarize what is available on the market and allow for comparisons of the products.¹

9.2.4 Tests for TB infection

There are currently two methods to test for TB infection: skin tests – including tuberculin skin tests (TSTs) – and IGRAs. Both methods depend on cell-mediated immunity (memory T-cell response), but neither test can accurately distinguish between TB infection and active TB disease.

¹ See <https://www.ai4hlth.org/>.

Skin tests

The TST is commonly performed using the Mantoux technique, which consists of intradermal placement of two tuberculin units (TU) of RT-23 or five TU of purified protein derivative S (PPD-S); the result is reported as millimetres of induration in the transverse diameter. However, the PPD-S TST has relatively low specificity, lacks sensitivity in immunosuppressed individuals (e.g. people living with HIV) and requires two clinic visits (one to administer the test and one to read the result). A further challenge is that failure to attend the clinic for evaluation of test results within 48–72 hours renders the results invalid.

Newer skin tests for infection are emerging. These aim to maximize the advantages of current implementation platforms, and they have the potential to improve uptake of diagnosis and treatment for TB infection.

A new commercial skin test that is on the market is Diaskintest (Generium). Another test, C-Tb (Serum Institute of India), is planned for market entry in 2020 or 2021, and a third, EC-Test (Anhui Zhifei Longcom Biopharmaceutical Co., Ltd), is in the late stages of development. All three tests contain recombinant ESAT-6 (dimer) and CFP-10 (monomer) antigens derived from *M. tuberculosis*, and may perform better than TST (particularly with respect to specificity). They may also provide accurate, acceptable and cheaper alternatives to existing IGRA tests. Compared with IGRAs, emerging evidence suggests that these new skin tests may have similar specificity and provide comparable results in children and people living with HIV.

IGRAs

There are two approaches to IGRAs: the enzyme-linked immunosorbent assay (ELISA)-based method and the enzyme-linked immunosorbent spot (ELISPOT) assay. The ELISA is a whole-blood test that uses peptides from the RD1 antigens ESAT-6 and CFP-10, and peptides from one additional antigen that is not an RD1 antigen, in an in-tube format. The result is reported as a quantification of interferon gamma (IFN-gamma) in international units (IU) per millilitre.

The ELISPOT assay is performed on separated and counted peripheral blood mononuclear cells that are incubated with ESAT-6 and CFP-10 peptides. The result is reported as the number of IFN-gamma-producing T cells (spot-forming cells). In contrast to the TST, IGRAs are not affected by bacille Calmette-Guérin (BCG) vaccination status; thus, they are useful for the evaluation of TB infection in BCG-vaccinated individuals, particularly in countries where BCG vaccination is administered after infancy or repeated vaccinations are given (Chapter 6). However, the IGRA platforms are more expensive to run, have specific time and temperature requirements for transport, and require specialized kits, a qualified technician and an accredited laboratory.

The pipeline for IGRAs is rich, with five products in development: T-Track(R) TB (Lophius Biosciences GmbH), VIDAS TB-IGRA (bioMérieux), Access

QuantiFERON®-TB (Boditech Med Inc.), ichroma™ IGRA-TB (Boditech Med Inc.) and IP-10 IGRA elisa/lateral flow (rBioPharm). In addition, five products are already on the market: STANDARD E TB-Feron ELISA/STANDARD and F TB-Feron FIA (IFN-gamma) (both SD Biosensor), LIOFERON TB/LTBI (LIONEX Diagnostics & Therapeutics GmbH), and Advansure TB IGRA and Avansure i3 TB-IGRA (both LG Chem).

9.2.5 DNA-sequencing technologies for diagnosis of drug-resistant TB

Conventionally, the diagnosis of drug resistance in *M. tuberculosis* strains has relied heavily upon culture and DST in liquid or solid media in TB containment laboratories. However, phenotypic results are only obtained after weeks to months of incubation, and it is a challenge to establish the stringent laboratory biosafety conditions required for these culture-based methods. Because drug resistance in the MTBC is mainly conferred through point mutations in specific gene targets in the bacterial genome, molecular tests are increasingly being used to allow more rapid testing and thus earlier initiation of appropriate treatment for drug-resistant TB.

Compared with the rapid molecular tests currently available, DNA sequencing can provide detailed information on resistance across multiple gene regions. Amplification-based targeted NGS assays for detecting drug-resistant TB directly from sputum specimens are in the pipeline. The Next Gen-RDST assay (Translational Genomics Research Institute, Phoenix, Arizona, USA) can detect mutations associated with resistance to at least seven drugs, and the Deeplex®-MycTB assay (GenoScreen, Lille, France) can detect mutations in gene regions associated with resistance to at least 13 drugs. WHO has not yet reviewed or approved these assays.

Recognizing the added value offered by NGS, WHO supports the work of FIND for the development and validation of novel molecular diagnostic tools.

9.3 New drugs and drug regimens to treat TB disease

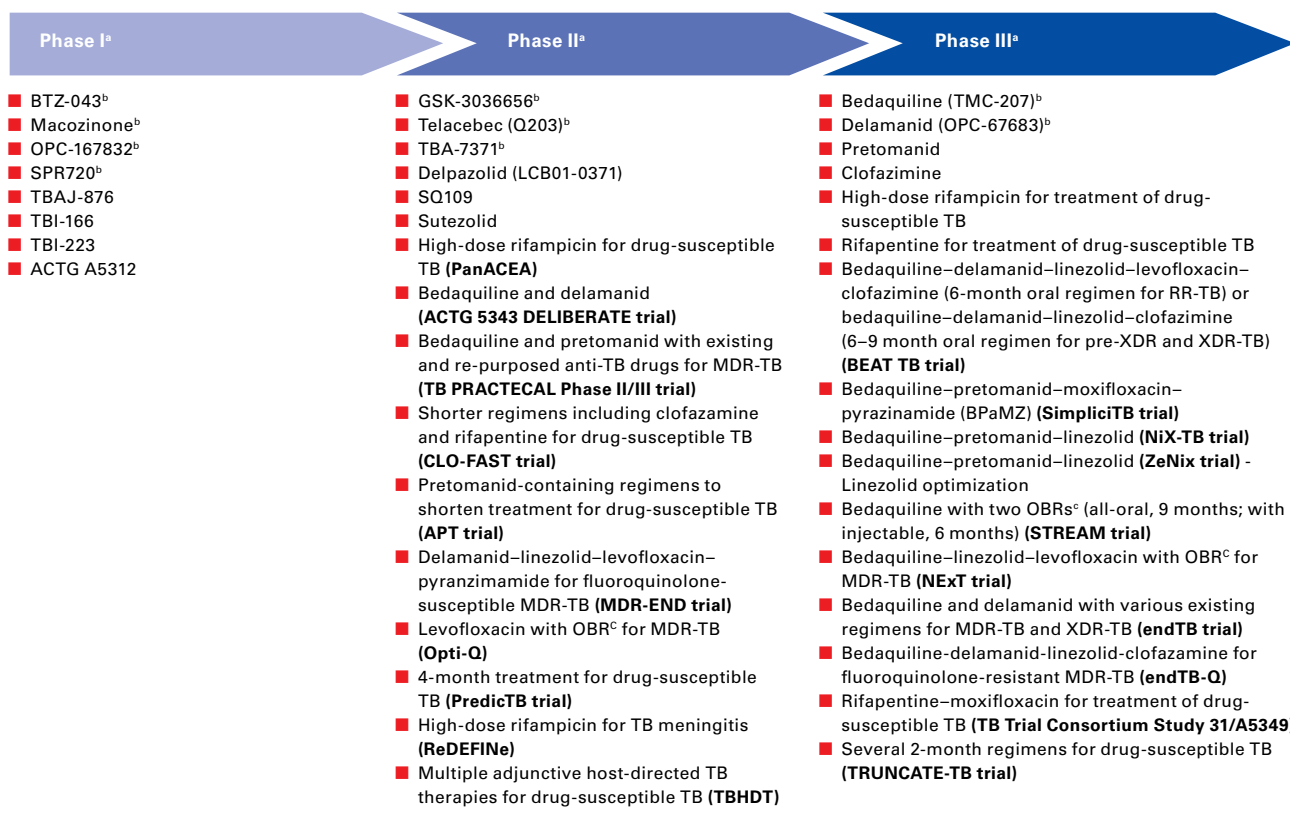
Current treatment regimens for TB disease require combinations of multiple drugs, ranging from a duration of 6 months for drug-susceptible TB to typically 6–20 months for multidrug-resistant TB (MDR-TB) or RR-TB (i.e. MDR/RR-TB),¹ but possibly longer if there is additional drug resistance, or if clinical and laboratory outcomes at the end of treatment are unsatisfactory. Globally, the latest available data (published in this report) show a treatment success rate of 85% for drug-susceptible TB and 57% for MDR/RR-TB.

The main challenges in treatment of TB disease are the duration and complexity of drug regimens, both of which affect adherence; toxicity, especially of second-line drugs used to treat drug-resistant TB; and the limited availabil-

¹ MDR-TB is defined as resistance to at least isoniazid and rifampicin.

FIG. 9.3

The global clinical development pipeline for new anti-TB drugs and drug regimens to treat TB disease, August 2020



XDR-TB = combined resistance to rifampicin, isoniazid, a fluoroquinolone and an injectable agent

^a New drug compounds are listed first, followed by repurposed drugs and then by regimens.

^b New chemical class.

^c Optimized background regimen.

Source: Adapted from the Working Group on New TB Drugs pipeline. More information on these products and other ongoing projects can be found at <http://www.newtbdrugs.org/pipeline.php>

ity of paediatric drug formulations for second-line treatment. The reasons for the latter are complex; they include lack of market forces, reluctance to include children and pregnant women in clinical trials, and insufficient funding for paediatric research. TB treatment for people living with HIV is further complicated by drug–drug interactions between anti-TB drugs and antiretroviral therapies. There is a pressing need for regimens that are more effective, more affordable and nontoxic, and that shorten the duration of treatment, particularly for drug-resistant TB.

The pipeline for new anti-TB drugs in August 2020 is shown in Fig. 9.3. There are 22 drugs in Phase I, II or III trials. They include 13 new compounds: BTZ-043, delpazolid, GSK-3036656, macozinone, OPC-167832, Q203, SQ109, SPR720, sutezolid, TBAJ-876, TBA-7371, TBI-166 and TBI-223.¹ Two other drugs (bedaquiline and delamanid) received accelerated regulatory approval, and

¹ Most of the new compounds are being developed by not-for-profit organizations, academic institutions, small businesses or government agencies, which lack the secure funding and resources available to major pharmaceutical companies. This makes the process of progression through trials and registration uncertain.

another, pretomanid, was recently approved by the US Food and Drug Administration (FDA), under the limited population pathway for antibacterial and antifungal drugs. Six approved antimicrobial drugs are undergoing further testing against TB: clofazimine, levofloxacin, linezolid, moxifloxacin, rifampicin (high dose) and rifapentine. Host-directed therapies such as auronofin, CC-11050 (AMG 634) and everolimus are also being evaluated.

New TB regimens are also being tested. These are described in Section 9.3.3.

9.3.1 New compounds

Bedaquiline

WHO first issued policy guidance on the use of bedaquiline for the treatment of adults with MDR-TB in 2013, based on Phase IIb trial results (14). The recommendation to use bedaquiline as part of longer treatment regimens for MDR-TB was conditional upon proper patient selection, a regimen design following WHO recommendations, close monitoring of treatment, active TB drug safety monitoring and management, and informed consent according

to local requirements. The recommendation was maintained, following a review of data from observational studies in 2016 (15). In 2018 and 2019, additional data for patients treated with bedaquiline-containing regimens were analysed as part of an update to WHO consolidated guidance on TB (drug-resistant TB treatment); bedaquiline was recommended as one of the priority medicines (group A) to design all-oral longer regimens of 9–12 months to treat MDR/RR-TB (16). A 6-month all-oral regimen – combining bedaquiline, pretomanid and linezolid – was recommended for treating people with fluoroquinolone-resistant MDR-TB under operational research conditions.

The safety and efficacy of bedaquiline when used as part of short MDR-TB treatment regimens (i.e. 6 and 9 months duration) compared with the updated current standard of care recommended by WHO (i.e. a 9–12-month regimen) is being investigated in the second stage of the Phase III trial Standardised Treatment Regimen of Anti-TB Drugs for Patients with MDR-TB (STREAM) (17). Recruitment started in March 2016 and the first results are expected in 2020.

A study of 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, and investigation of its use in the treatment of drug-susceptible TB in the bedaquiline, pretomanid, moxifloxacin and pyrazinamide (BPamZ) trial is ongoing (Section 9.3.3).

BTZ-043

BTZ-043 is a benzothiazinone compound that acts by inhibiting the DprE1 enzyme, which is necessary for the synthesis of D-arabinofuranose, a constituent of the *M. tuberculosis* cell wall. A Phase Ib/IIa study to evaluate the safety, tolerability, extended early bactericidal activity and pharmacokinetics of multiple oral doses of BTZ-043 in people with smear-positive, drug-susceptible TB is underway in South Africa.

Delamanid

WHO issued interim policy guidance on the use of delamanid for the treatment of adults with MDR-TB in 2014, based on Phase IIb trial results (18). A conditional recommendation was made to use delamanid as part of longer MDR-TB treatment regimens for adults. This recommendation was conditional on proper patient selection, a regimen design following WHO recommendations, close monitoring of treatment, active TB drug safety monitoring and management, and informed consent according to local requirements. Following the release of results for children and adolescents treated for MDR-TB using delamanid in 2016, WHO's guidance on the use of delamanid in adults was expanded to include patients aged 6–17 years (19).

In 2017, final results from a Phase III trial assessing the safety and efficacy of delamanid as an addition to an optimized background regimen for adults with MDR-TB were

reported to WHO by the manufacturer, Otsuka Pharmaceutical, Japan. WHO conducted an expedited external expert review of the new data, and in January 2018 issued a position statement (20), which stated that the conditional guidance on delamanid remained valid, but that delamanid should only be added to a longer MDR-TB treatment regimen when the regimen cannot otherwise be composed according to WHO recommendations. In 2018 and 2019, WHO analysed additional data from the Phase III trials alongside data from other studies of patients treated with delamanid-containing regimens, as part of an update to WHO consolidated guidance on TB (drug-resistant TB treatment). Based on these findings, delamanid may now be included in longer treatment regimens for treating people aged 3 years or older with MDR/RR-TB (16).

As with bedaquiline, delamanid is being used in trials of all-oral treatment regimens (Section 9.3.3). The use of delamanid in addition to an optimized background regimen to treat children aged under 6 years is also being investigated in other trials. 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. A Phase II trial to assess early bactericidal activity, safety and tolerability is underway in the Republic of Korea.

GSK-3036656

GSK-3036656 belongs to a new chemical class of oxaborole compounds developed by GlaxoSmithKline. A Phase IIa trial assessing its early bactericidal activity, safety and tolerability is underway in South Africa.

Macozinone

Macozinone (formerly PBTZ169) is a benzothiazinone developed by Innovative Medicines for Tuberculosis and Nearmedic Plus. One Phase I trial has been completed and another Phase I study with a new formulation began in 2018 in Switzerland.

OPC-167832

OPC-167832 is a carbostyryl derivative developed by Otsuka that is bactericidal against both growing and intracellular bacilli. A single ascending dose study has been completed. A Phase I/II multiple ascending dose and early bactericidal activity study of OPC-167832, alone and in combination with delamanid, is being implemented in South Africa.

Pretomanid

Pretomanid is a nitroimidazole, developed by the Global Alliance for TB Drug Development (TB Alliance). It was recently recommended by WHO for treating fluoroquinolone-resistant MDR-TB (in combination with

bedaquiline and linezolid) in people with no or less than 2 weeks exposure to bedaquiline and linezolid, under operational research conditions (16). It is currently being further tested as part of combination regimens for the treatment of both drug-susceptible and drug-resistant TB (Section 9.3.3).

Telacebec (Q203)

Telacebec (Q203) is an imidazopyridine that has been developed by Qurient (Republic of Korea). Single doses of various sizes have been tested in Phase I trials, and recruitment has been completed in South Africa as part of a Phase IIa trial assessing its early bactericidal activity in sputum smear-positive patients with drug-susceptible pulmonary TB.

SPR720

SPR720 is an orally administered antibiotic being developed by Spero Therapeutics for the treatment of pulmonary nontuberculous mycobacterial infections. A Phase I trial is ongoing in the United Kingdom of Great Britain and Northern Ireland (United Kingdom). The Bill & Melinda Gates Medical Research Institute (Gates MRI) has recently obtained a license to further develop the drug.

SQ109

SQ109 is a novel drug that was discovered by scientists at Sequella Inc (USA) and the US National Institutes of Health (NIH). 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. A press release in March 2017 reported positive results in terms of safety, efficacy and tolerability. A Phase II trial in the USA is in the planning stages.

Sutezolid

Sutezolid (PNU-100480) is an oxazolidinone and analogue of linezolid. Results from a study of early bactericidal activity 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 had signed a license 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 Medicines Patent Pool announced a licensing agreement for the clinical development of sutezolid. In partnership with the Gates MRI, a Phase IIb dose-finding study is being planned in South Africa and the United Republic of Tanzania.

TBA-7371

TBA-7371 is an inhibitor of the enzyme DprE1, which is essential in the synthesis of components of mycobacterial cell walls. This inhibitor has been shown to be active against strains of *M. tuberculosis* resistant to known TB

drugs. The TB Alliance has completed a Phase I study in the USA, and a Phase II study, sponsored by the Gates MRI, is underway in South Africa.

TBI-166

TBI-166, which belongs to the same clinical class as clofazimine, was identified through a lead optimization effort by the TB Alliance, in partnership with the Institute of Materia Medica, the Chinese Academy of Medical Sciences and the Peking Union Medical College in Beijing. This rimonophenazine compound has improved physicochemical and pharmacokinetic properties (to avoid skin discolouration), and its efficacy is similar to that of clofazimine. A Phase I trial is being implemented in China, led by the Institute of Materia Medica.

TBI-223

TBI-223 was identified through a lead optimization effort by the TB Alliance, in partnership with the Institute of Materia Medica. This oxazolidinone compound works as a protein synthesis inhibitor, targeting an early step that involves the binding of N-formylmethionyl-tRNA to the ribosome. A Phase I trial in the USA is ongoing.

TBAJ-876

TBAJ-876 is a next-generation diarylquinoline. In animal models, this compound exhibits efficacious and potent activity against TB (compared with bedaquiline), with a lower predicted clinical dose and improved safety properties. TBAJ-876 is currently in a Phase I trial.

9.3.2 Approved drugs being tested for new purposes

Clofazimine

Clofazimine is a rimonophenazine that is used to treat leprosy and is also recommended as one of the medicines (group B) that can be used to design all-oral longer regimens to treat people with MDR/RR-TB. Its use in treatment for MDR-TB is being further 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 in Phase III trials (Section 9.3.3).

Levofloxacin

Levofloxacin is recommended as part of the regimen for treating isoniazid-resistant TB, and is one of the priority medicines (group A) used in the design of longer regimens to treat people with MDR/RR-TB. It is being further tested in a Phase II study called Opti-Q, which is investigating the best dose of levofloxacin to use for treatment of MDR-TB in adults with smear- and culture-positive pulmonary TB. Four different dosages are being tested as part of an optimized background regimen. Trial enrolment and follow-up (in Peru and South Africa) have been

completed and data analysis is underway. Levofloxacin continues to be tested as part of treatment regimens for drug-resistant-TB ([Section 9.3.3](#)).

Linezolid

Linezolid is a marketed oxazolidinone with potent activity against TB. It is currently recommended as one of the priority medicines (group A) that can be used in the design of longer regimens to treat people with MDR/RR-TB. Further use of linezolid is being explored in other Phase II and III trials ([Section 9.3.3](#)).

Moxifloxacin

Moxifloxacin is recommended as one of the priority medicines (group A) that can be used in the design of longer regimens for treatment of people with MDR/RR-TB. Its use is being further explored in several trials of new regimens for treatment of both drug-susceptible and drug-resistant TB, including in the BPamZ, endTB, TB-PRACTICAL and TB Trial Consortium (TBTC) Study 31 trials ([Section 9.3.3](#)).

Rifampicin (high dose)

Findings from the Multi-Arm, Multi-Stage TB (MAMS-TB) trial of the Pan-African Consortium for the Evaluation of Antituberculosis Antibiotics (PanACEA) were published in 2017 (21). The trial found that 35 mg/kg of rifampicin given over 12 weeks is safe and shortens 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 were taken into consideration, the trial suggested that a 35 mg/kg dose of rifampicin given for 12 weeks is likely to improve treatment outcomes. This trial was 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. Another study (RIFASHORT) is assessing the added benefit and safety of giving an increased dose of rifampicin to patients receiving standard treatment for drug-susceptible TB. For TB meningitis, a Phase II dose-finding study (ReDEFINE) has indicated an added value of using high-dose rifampicin to improve survival (22).

Rifapentine

The effectiveness of rifapentine in the treatment of drug-susceptible TB is being studied in several trials. The TBTC Study 31/ACTG A5349 is a Phase III trial that is investigating the use of rifapentine, with or without moxifloxacin, to shorten the treatment of drug-susceptible pulmonary TB to 4 months. TBTC Study 35, a Phase II study of the pharmacokinetics of new water-dispersible paediatric formulations of rifapentine, is being implemented in South Africa ([Section 9.4](#)).

9.3.3 New regimens for the treatment of drug-susceptible or drug-resistant TB disease

New combinations of drugs are being tested in Phase II or Phase III trials.

ACTG A5343 DELIBERATE

The ACTG A5343 DELIBERATE was a Phase II trial that evaluated the cardiotoxicity of regimens containing delamanid and bedaquiline, alone and in combination, in pharmacokinetic and drug–drug interaction studies. Preliminary results from this trial were presented at a WHO-convened GDG meeting in November 2019; also, the results informed statements on the concurrent use of bedaquiline and delamanid that have been included in the updated WHO consolidated guidelines on TB (in the module for treatment of drug-resistant TB) (16).

ACTG A5312

ACTG A5312 is a Phase I trial in South Africa that is assessing the safety and efficacy of high-dose isoniazid for treating different genetic variants of isoniazid-resistant TB.

APT trial

APT is a Phase II trial testing the bactericidal activity of pretomanid when substituted for ethambutol in first-line therapy for drug-susceptible TB.

BEAT TB

BEAT TB is a research programme being implemented in India and South Africa with funding from USAID. It has the overall aim of reducing side-effects and treatment duration for patients with drug-resistant TB. In India, the safety and efficacy of a 6–9-month oral regimen (consisting of bedaquiline, delamanid, linezolid and clofazimine) is being tested to treat adults with MDR-TB as well as resistance to fluoroquinolones or injectable agents. In South Africa, a Phase III trial is assessing the safety and efficacy of a 6-month oral regimen for MDR-TB (consisting of bedaquiline, delamanid, linezolid, levofloxacin and clofazimine) compared with the national standard of care (i.e. a 9-month regimen).

CLO-FAST trial

CLO-FAST is a Phase II trial assessing whether a regimen containing clofazimine and rifapentine can shorten the treatment duration of drug-susceptible TB, compared with the standard of care.

endTB

The endTB trial started in 2017. It is a Phase III study comparing several shorter treatment regimens for MDR-TB with the current standard-of-care treatment for MDR-TB 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.

endTB-Q

endTB-Q is a Phase III trial evaluating the safety and efficacy of new combination regimens (including bedaquiline, delamanid, linezolid and clofazimine) to shorten treatment for people with fluoroquinolone-resistant MDR-TB.

MDR-END

The MDR-END trial is investigating a 9–12-month regimen of delamanid, linezolid, levofloxacin and pyrazinamide for the treatment of MDR-TB among people without resistance to fluoroquinolones. It is being implemented in the Republic of Korea.

NeXT

NeXT is a Phase III trial evaluating a 6–9-month regimen of bedaquiline, ethionamide or high-dose isoniazid, linezolid, levofloxacin and pyrazinamide for patients with MDR-TB. It is being undertaken in South Africa.

NiX-TB, ZeNix

The Phase III NiX-TB trial informed WHO's guidance on the use of a 6-month all-oral regimen combining bedaquiline, pretomanid and linezolid for treating fluoroquinolone-resistant MDR-TB, under operational research conditions in people with no or less than 2 weeks exposure to bedaquiline and linezolid. A follow-on trial (called ZeNix) is exploring lower doses and shorter durations of linezolid to minimize toxicity.

SimpliciTB

SimpliciTB is a Phase III trial evaluating the efficacy, safety and tolerability of BPamZ in people with drug-susceptible TB or MDR/RR-TB. It is being implemented in 27 sites in eight countries globally. The primary end-point is relapse-free cure 12 months after initiation of therapy. A previous Phase IIb study of BPamZ regimen showed almost 100% culture conversion at 2 months in patients with MDR-TB.

PredictTB trial

The Phase II PredictTB trial is investigating the possibility of shortening the treatment duration for “less-severe” cases of drug-susceptible TB (as determined by the baseline radiographic extent of disease) to 4 months instead of the standard 6 months of treatment. The primary end-point will be a comparison of the treatment success rate at 18 months between the experimental and standard-of-care cohorts. This trial is being implemented in China.

STREAM

STREAM Stage 1 was a Phase III, randomized, non-inferiority trial that compared a standardized 9–11-month regimen for the treatment of MDR-TB with longer regimens of 18–24 months in Ethiopia, Mongolia, South Africa and Viet Nam. The final trial results showed that the shorter regimen was non-inferior to the control (longer

regimen (23). Current WHO guidelines on the treatment of drug-resistant TB treatment recommend that NTPs and other stakeholders continue to use the shorter MDR-TB regimen under programmatic conditions, as described in the guidance (16).

STREAM Stage 2 is assessing whether an all-oral 40-week regimen including bedaquiline, and a 28-week regimen including both bedaquiline and an injectable agent, are as effective as the 9-month regimen studied in STREAM Stage 1. It is funded by USAID and implemented by the Union.¹

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 adult patients with MDR-TB (including those with resistance to additional drugs). Primary outcomes include 8-week culture conversion, and the development of unfavourable outcomes (treatment failure or recurrence, death, discontinuation or loss to follow-up during a 72-week follow-up period). The trial is being implemented in Belarus, South Africa and Uzbekistan.

TBHDT trial

The TBHDT trial is a Phase II trial examining the safety and preliminary efficacy of host-directed therapies – CC-11050 (AMG 634), auronofin and everolimus – in shortening TB treatment or preventing permanent lung damage (or both), when co-administered with rifabutin-modified standard therapy in people with drug-susceptible smear-positive TB.

TRUNCATE-TB

The TRUNCATE-TB trial is a Phase II/III randomized, open-label, multi-arm, multi-stage trial to evaluate the safety and efficacy of 2-month regimens (compared with standard care) for the treatment of adults with drug-susceptible TB; the regimens contain isoniazid, pyrazinamide ethambutol, linezolid and rifampicin; isoniazid, pyrazinamide, linezolid, rifapentine and levofloxacin; or isoniazid, pyrazinamide, ethambutol, linezolid and bedaquiline. The primary outcome is an unsatisfactory clinical outcome at 96 weeks after randomization, which is defined as an ongoing requirement for TB treatment, or ongoing TB disease activity at week 96. The trial is being implemented in Indonesia, the Philippines, Singapore and Thailand.

9.4 New drugs and drug regimens to treat TB infection

At the UN high-level meeting on TB in 2018, Member States committed to provide TB preventive treatment to at least 30 million people globally between 2018 and 2022 (Chapter 2). Achieving this target will require program-

¹ See <https://www.theunion.org/>

matic reach to be expanded and access to medicines such as rifapentine to be widened (Chapter 6).

The reduced price agreement for rifapentine signed among Unitaid, the Global Fund and Sanofi in 2019 has improved the prospects for expanded use of shorter treatment options for TB infection (24). Progress towards the global target would also be facilitated by improved diagnostics for TB infection and better treatment options (i.e. treatments that are easier to take, shorter in length, have longer-lasting effect, are less toxic and are effective against drug-resistant strains). Such tools will probably increase acceptability and feasibility, and improve the cost-effectiveness of preventive treatment under programmatic conditions.

To facilitate the development of and sustainable access to better preventive treatment options, WHO has recently launched target product profiles to inform drug manufacturers about the attributes that prospective users wish to see in future regimens, aligning the preferences of affected communities, NTPs, scientists, funding agencies and other stakeholders (25).

Translating these needs into viable tools requires increased financing, better clinical trial site capacity, public-private partnerships, and more responsive regulatory capacity and policies for research and development. IR could enhance evidence-informed delivery and scale-up of preventive treatment to the populations that need them most. Unitaid is currently supporting multicountry IR projects to increase evidence-based uptake of shorter TB preventive treatment in collaboration with countries, partners and WHO (26).

The status of the pipeline in August 2020 for new TB preventive treatments is shown in Fig. 9.4. Delamanid, levofloxacin and rifapentine (with or without isoniazid) are currently being studied in Phase I/II and III trials.

9.4.1 Phase I/II trials

DOLPHIN and DOLPHIN TOO

DOLPHIN was a Phase I/II trial that assessed the pharmacokinetics, safety and tolerability of 3 months of a weekly dose of isoniazid and rifapentine (3HP) for people living

with HIV, taking dolutegravir (DTG) based antiretroviral therapy (ART). The results showed that 3HP can be used for people living with HIV taking DTG-based ART without dose adjustments (27). A similar study is being planned among infants, children and adolescents (DOLPHIN KIDS).

The DOLPHIN study has also been extended to include additional trial arms to compare the pharmacokinetics, safety and tolerability of standard isoniazid preventive treatment (IPT) versus 3HP among people living with HIV who have not started ART (DOLPHIN TOO). IPT or 3HP are initiated at the same time as ART (DTG with lamivudine/tenofovir); the safety and effect of isoniazid and rifapentine on the pharmacokinetics of DTG are being evaluated. The study is also measuring the proportion of HIV treatment-naive participants who achieve virologic suppression at 12 and 24 weeks under these circumstances. DOLPHIN TOO is being implemented in South Africa, through the IMPAACT4TB platform.

Impact of 3HP on the pharmacokinetics of tenofovir alafenamide (YODA)

YODA is a Phase I study to assess the effect of weekly administration of rifapentine and isoniazid on the steady state pharmacokinetics of the antiretroviral medicine tenofovir alafenamide among healthy adults in the USA. The study is sponsored by the US NIH Clinical Center.

Impact of 3HP on the pharmacokinetics of dolutegravir and darunavir, with cobicistat

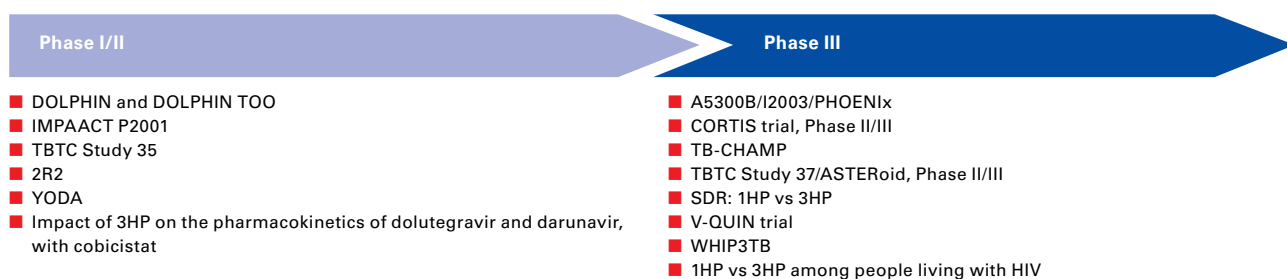
This is a Phase I study designed to assess the effect of weekly administration of rifapentine and isoniazid on the steady state pharmacokinetics of the antiretroviral medicines DTG and darunavir, boosted with cobicistat, among healthy adults in the USA. The study is sponsored by the US NIH Clinical Center.

IMPAACT P2001

Currently, the 3HP regimen is not recommended for pregnant women or women planning pregnancy during the treatment period. IMPAACT P2001 is a Phase I/II trial designed to evaluate the pharmacokinetics and safety of

FIG. 9.4

The global clinical development pipeline for new drugs and drug regimens to treat TB infection, August 2020



3HP among HIV-positive and HIV-negative pregnant and postpartum women with *M. tuberculosis* infection. The study is sponsored by US NIH/National Institute of Allergy and Infectious Diseases (NIAID), and is being implemented in Haiti, Kenya, Malawi, Thailand and Zimbabwe.

TBTC Study 35

TBTC Study 35 is a single-arm, open-label Phase I/II dose-finding and safety study of 3HP (with rifapentine given as a water-dispersible monolayer or as a fixed-dose combination with isoniazid) for children aged 12 years or under, for whom treatment for TB infection is recommended. The study is sponsored by the US Centers for Disease Control and Prevention (CDC) and IMPAACT4TB (Unitaid).

2R2: Higher-dose rifampin for 2 months versus standard-dose rifampin

2R2 is a Phase IIb study evaluating the safety and efficacy of 2 months of daily rifampin (at double or triple the standard dose) compared with the standard 4 months of daily rifampin to treat TB infection. The study is being implemented in Canada by McGill University Health Centre.

9.4.2 Phase III trials

A5300B/I2003/PHOENIX

PHOENIX is a Phase III trial, randomized by household, to assess the efficacy of 26 weeks of daily delamanid compared with 26 weeks of isoniazid among high-risk household contacts of adults diagnosed with MDR-TB. The study is sponsored by USNIH/NIAID and is being implemented in Botswana, Brazil, Haiti, India, Kenya, Peru, the Philippines, Thailand, South Africa, Uganda, the United Republic of Tanzania and Zimbabwe.

Correlate of Risk Targeted Intervention Study

Correlate of Risk Targeted Intervention Study (CORTIS) is a Phase II/III trial to assess the diagnostic and prognostic performance of an 11-gene signature of risk (also known as prognostic correlate of risk, COR), to identify individuals who are most likely to progress to active TB disease and individuals with TB disease who have not yet presented for medical care. The study randomizes eligible HIV-negative COR test-positive and COR test-negative adults into 3HP treatment or standard of care; participants are monitored for progression to active TB. The primary objectives are to assess whether preventive treatment reduces TB incidence compared with the standard of care in people who are COR test-positive, and to measure the performance of the biomarker. The study is sponsored by the University of Cape Town and is being implemented in South Africa.

TB-CHAMP

TB-CHAMP is a Phase III trial to assess the safety and efficacy of 6 months of daily levofloxacin for the prevention

of TB in child contacts of adults with MDR-TB in South Africa. The study's sponsors include the Global Health Trials Scheme of the United Kingdom and Unitaid.

TBTC Study 37/ASTERoid

TBTC Study 37/ASTERoid is a Phase II/III non-inferiority trial to compare the safety and efficacy of a 6-week regimen of daily rifapentine with a comparator arm of 12–16 weeks of rifamycin-based treatment (standard care). The study is sponsored by the US CDC and the United Kingdom Medical Research Council. It is being implemented in the United Kingdom, USA and other countries with a low to moderate incidence of TB.

The risk of systemic drug reaction (SDR): 1HP versus 3HP

The SDR is a Phase III head-to-head study to compare the safety (the risk of systemic drug reaction) of the 1HP and 3HP regimens, when used to treat TB infection among people living with HIV. The study is sponsored by the National Taiwan University Hospital.

V-QUIN trial

V-QUIN is a Phase III trial assessing 6 months of daily levofloxacin among household contacts of adults with MDR-TB. The trial is sponsored by the Australian Woolcock Institute of Medical Research and is being implemented in Viet Nam.

WHIP3TB

WHIP3TB is a Phase III trial designed to assess the durability of protection, as well as the safety and adherence of periodic 3HP (given once a year for 2 years), compared with a single round of 3HP (given once) or 6 months of daily isoniazid (6H) among people living with HIV. The trial is funded by USAID and is being implemented by the Aurum Institute in Ethiopia, Mozambique and South Africa.

1HP versus 3HP among people living with HIV

This is a Phase III non-inferiority trial comparing the safety and effectiveness of 1HP and 3HP for treating TB infection among people living with HIV. The study will also monitor adherence to treatment and patterns of antibiotic resistance in those for whom treatment fails. It is sponsored by the HIV Netherlands Australia Thailand Research Collaboration, and is being implemented in Thailand.

9.5 New TB vaccines

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 6), 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.

Roadmap for the research and development of new TB vaccines

The Amsterdam Institute for Global Health and Development, in collaboration with WHO and with support from the European & Developing Countries Clinical Trials Partnership (EDCTP), is developing a roadmap for research and development of new TB vaccines. The vision of the roadmap is the licensing of safe and effective vaccines that prevent TB infection or disease, and that dramatically reduce transmission and TB deaths in line with SDG and End TB Strategy targets.

To make this vision a reality, the roadmap takes stock of progress to date and identifies the path forward for development, licensing and equitable access to new TB vaccines. In particular, it identifies:

- ▶ knowledge gaps and actionable recommendations to advance the science required to develop new TB vaccines that meet WHO preferred-product characteristics;^a and

- ▶ strategic priorities that vaccine developers, funders and implementers can take forward, in the short, medium and long-term, to foster collaboration, enable harmonized vaccine introduction, and enable equitable and affordable access to new TB vaccines.

The roadmap reflects the consensus reached by the world’s leading scientists, funders, research institutes, product development partnerships, civil society and representatives of high TB burden countries during a series of consultations convened between October 2019 and April 2020. The roadmap will be launched in 2020.

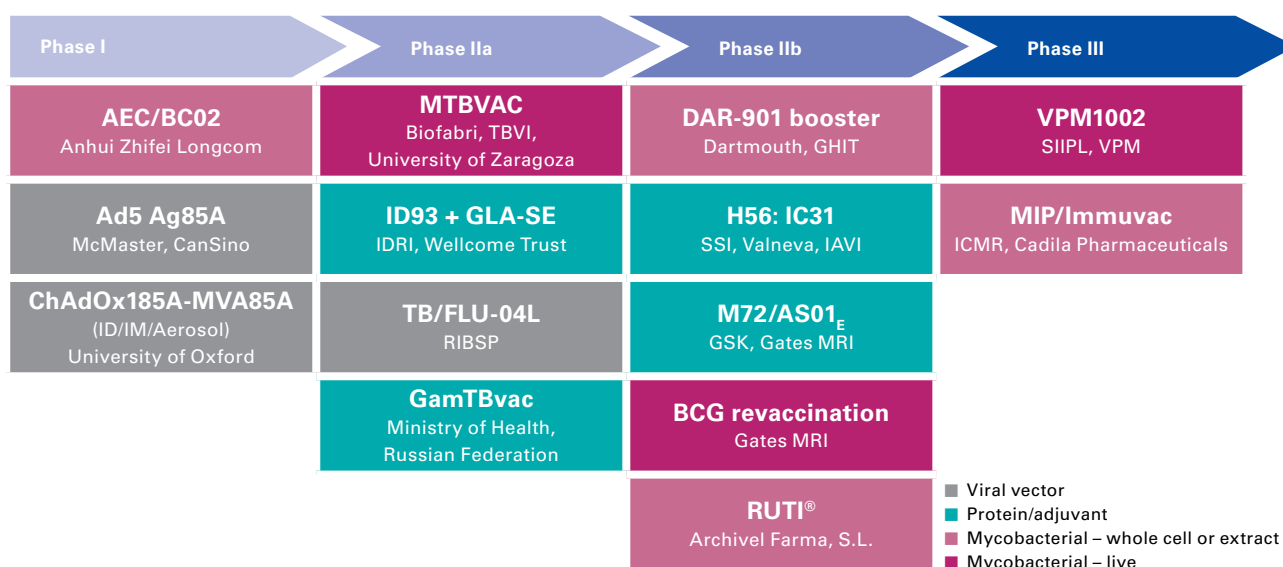
^a WHO preferred product characteristics for new tuberculosis vaccines. Geneva: WHO; 2018 (http://www.who.int/immunization/documents/who_ivb_18.06/en/, accessed 5 August 2020) (29).

In 2019, the experimental TB vaccine candidate M72/AS01_E (Section 9.5.2) was reported to protect against TB disease in a Phase IIB trial. The vaccine efficacy was 50% (90% confidence interval [CI]: 12–71%) after about 3 years of follow-up (28). If these findings are confirmed in a larger study, it could transform TB prevention approaches. At the same time, the fight against TB will probably require more than one type of vaccine, with the different vaccines working in multiple ways to prevent the establishment of an initial infection (pre-exposure) or to prevent progression to disease (post-exposure).

Prioritization and alignment of efforts, collaboration, data sharing, improved regulatory processes and increased financing are needed to shorten the time to the availability of effective vaccines. Beyond discovery, broader research in areas of social, economic and population-health impact are also needed to guide vaccine introduction and implementation. WHO is supporting the development of a comprehensive roadmap for the research and development of new TB vaccines (Box 9.3).

The status of the pipeline for new TB vaccines in August 2020 is shown in Fig. 9.5. There are 14 vaccines in Phase I, II or III trials; their main characteristics are summarized below.

FIG. 9.5
The global clinical development pipeline for new TB vaccines, August 2020^a



^a Information was self-reported by vaccine sponsors, and the Stop TB Partnership Working Group on New TB Vaccines supported the review of the pipeline.

9.5.1 Phase I trials

There are currently 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 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.

AEC/BC02

AEC/BC02 is a freeze-dried recombinant vaccine expressing Ag85B and fusion protein ESAT-6 and CFP-10, together with CpG (from BCG) and an alum salt-based adjuvant. A Phase I study assessing safety and immunogenicity is underway in China, with sponsorship from Anhui Zhifei Longcom Biologic Pharmacy Co., Ltd.

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 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. A Phase I trial of aerosol administration of ChAdOx185A in BCG-vaccinated adults is underway in Switzerland. Two studies of aerosol administration of MVA85A in BCG-vaccinated individuals have been completed, as has a further study in people with TB infection. A Phase IIa study of intramuscular administration of ChAdOx185A and MVA85A among adults and adolescents is ongoing in Uganda.

9.5.2 Phase II and Phase III trials

There are currently 11 vaccines in Phase II or Phase III trials.

BCG revaccination (Gates MRI-TBV01-201)

Gates MRI-TBV01-201 is a Phase IIb trial to evaluate the efficacy, safety and immunogenicity of BCG revaccination in healthy adolescents for “prevention of sustained QFT conversion”, as a surrogate for sustained infection with *M. tuberculosis*. The study, sponsored by the Gates MRI, intends to confirm that BCG revaccination protects against sustained *M. tuberculosis* infection; assess the duration of protection 48 months post-revaccination; and identify or validate biomarkers that correlate with risk for or protection against transient or sustained *M. tuberculosis*

infection, as assessed by the QuantiFERON-TB Gold Plus (QFT-Plus) assay.

DAR-901 booster

DAR-901 is a whole-cell, heat-inactivated, nontuberculous mycobacterial vaccine booster. It represents a new scalable manufacturing method for SRL172, a candidate vaccine that showed efficacy among adults living with HIV in a Phase III trial in the United Republic of Tanzania. It is now being tested in a Phase IIb prevention of infection trial among BCG-primed adolescents, also in the United Republic of Tanzania. The trial is scheduled for completion in 2020.

GamTBvac

GamTBvac is a recombinant subunit vaccine containing dextran-binding domain-modified Ag85a and ESAT6-CFP10 MTB antigens and CpG ODN adjuvant, formulated with dextrans. It is intended for use as a BCG booster vaccine to prevent TB. A Phase I study among healthy volunteers in the Russian Federation has found the candidate vaccine to be safe and immunogenic. A Phase II study is currently ongoing to further assess safety and immunogenicity. The trial is sponsored by the Russian Ministry of Health.

H56:IC31

H56:IC31 is an adjuvanted subunit vaccine that combines three *M. tuberculosis* antigens (Ag85B, ESAT-6 and Rv2660c) with the IC31[®] adjuvant from Valneva Austria GmbH (Vienna Austria). Five 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 TB infection, and without a history or any evidence of TB disease. Two trials enrolled HIV-negative participants with pulmonary TB, who were vaccinated at different time points during TB treatment. Finally, analyses of a Phase Ib trial evaluating the safety and immunogenicity of H4:IC31, H56:IC31 and BCG revaccination in adolescents have recently been published (30). The results showed that the vaccine had an acceptable safety profile and was immunogenic at all studied doses.

A Phase IIb trial assessing H56:IC31 for prevention of recurrence of TB is ongoing in the United Republic of Tanzania and South Africa, co-sponsored by the Statens Serum Institut and Aeras, with support from the EDCTP.

ID93 + GLA-SE

The ID93 + GLA-SE vaccine comprises four *M. tuberculosis* antigens associated with either virulence (Rv2608, Rv3619 and Rv3620) or latency (Rv1813), and the adjuvant GLA-SE. A Phase IIa trial in HIV-negative TB patients, who have recently completed treatment for pulmonary TB disease, has been completed in South Africa, in preparation for two Phase II studies that will establish the safety and immunogenicity of ID93 in TB patients undergoing active therapy. Currently underway are a Phase IIa trial

in BCG-vaccinated healthy adult health care workers, to assess prevention of infection, and a Phase I age-de-escalation trial in BCG-vaccinated healthy adolescents to assess safety and immunogenicity.

M72/AS01_E

M72/AS01_E is a subunit vaccine that pairs two *M. tuberculosis* antigens (32A and 39A) with an adjuvant (AS01_E). It was tested in a Phase IIb efficacy trial in HIV-negative adults already infected with *M. tuberculosis* in Kenya, South Africa and Zambia, with the primary end-point being the number of incident cases of active laboratory-confirmed pulmonary TB disease not associated with HIV infection.

The final analysis of this trial showed a 50% (90% CI: 12–71%) point estimate for vaccine efficacy after 3 years of follow-up (28). In terms of the clinical significance and strength of evidence, this result is unprecedented in decades of TB vaccine research. If the findings are confirmed in a Phase III trial, this vaccine has the potential to transform global TB prevention efforts.

In 2020, the Gates MRI obtained a license to develop M72/AS01_E for use in low-income countries, paving the way for continued development and potential use of the vaccine candidate in countries with a high TB burden. The first M72/AS01_E trial that the Gates MRI intends to conduct is a safety and immunogenicity study in 400 people living with HIV in South Africa.

WHO has highlighted the importance of accelerated progress towards a well-designed, Phase III programme, with priorities such as a more precise estimation of vaccine efficacy in different geographical settings and further evaluation of safety. The effect of vaccination also needs to be characterized in people who are not infected with *M. tuberculosis*, in children and in specific risk groups such as people living with HIV. This will require adequate vaccine manufacturing and financing. WHO calls on all relevant stakeholders – including the pharmaceutical industry, funders, governments, civil society, health care practitioners, policy-makers and international agencies – to work with a sense of urgency, in a spirit of collaboration and with a sense of responsibility towards public health, to advance the development of this investigational vaccine in the fight against TB.

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 populations are adolescents and adults (as a booster vaccine). A Phase Ib trial in neonates was completed in 2018. Phase IIa trials in both target populations are ongoing.

RUTI®

RUTI is a non-live, polyantigenic vaccine based on cell wall fragments of *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 TB infection have demonstrated a good safety profile and found the vaccine to be immunogenic at all studied doses. A Phase IIa study in patients with MDR-TB is ongoing in Eastern Europe, and a Phase IIb study in patients with drug-susceptible TB and MDR-TB has been authorized in India.

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 TB infection is being implemented.

VPM1002

VPM1002 is a live recombinant vaccine. A Phase II trial to assess the safety and immunogenicity of the vaccine in HIV-exposed and unexposed neonates in South Africa has been completed successfully, and a subsequent Phase III trial is currently underway. A Phase II/III trial for prevention of TB recurrence in adults is being implemented in India. A Phase III trial in India to evaluate the efficacy and safety of VPM1002 in preventing pulmonary TB among healthy household contacts of sputum smear-positive TB patients is also underway.

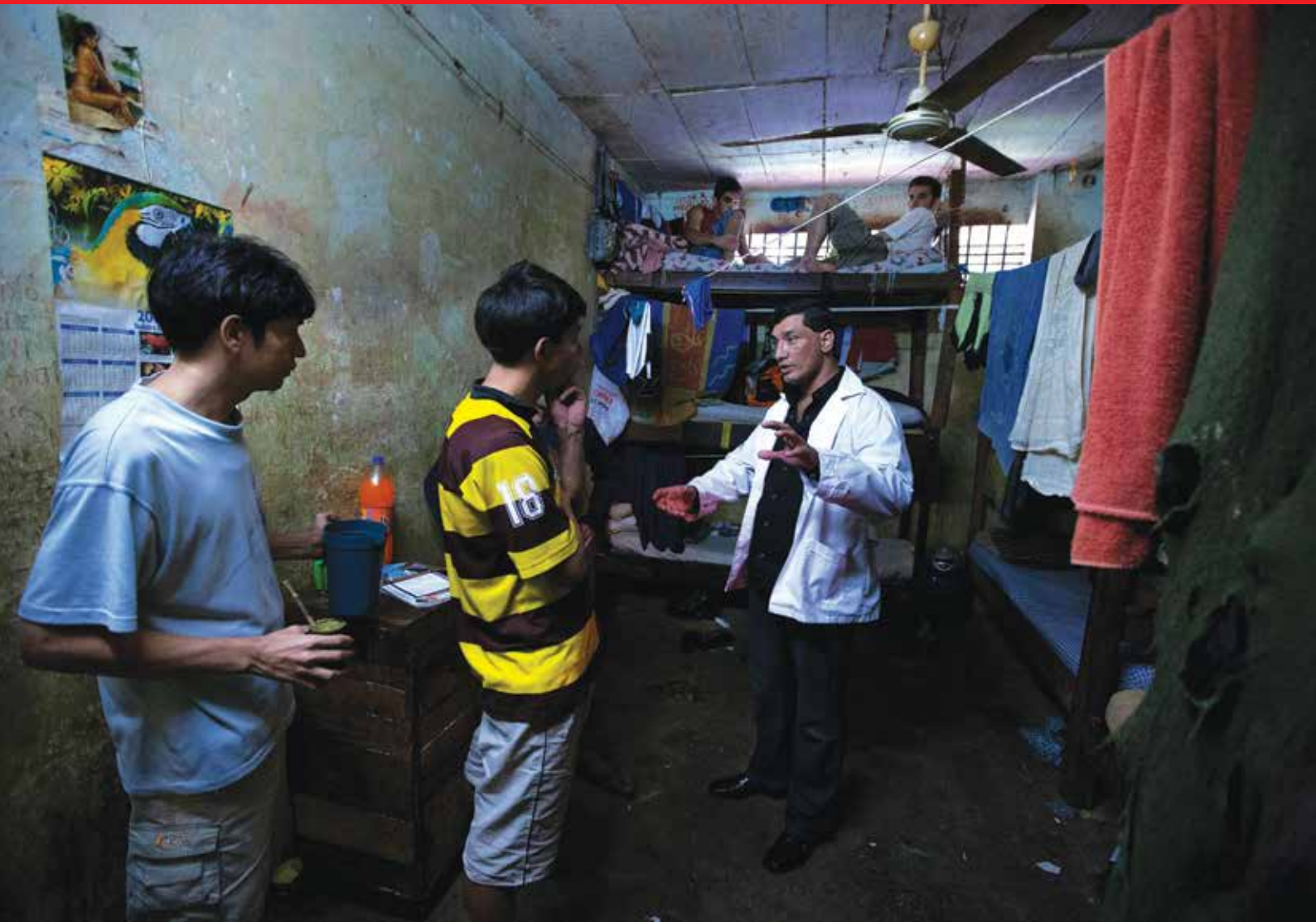
MIP/Immuvac

MIP, also known as Immuvac, is a heat-killed *M. indicus pranii* vaccine. It has been approved by the drug controller general of India and the FDA as an immunotherapeutic and immunoprophylactic agent for treating multibacillary leprosy patients (as an adjunct to standard multidrug therapy), and for preventing the development of leprosy among close contacts of leprosy patients. A Phase III trial to assess the efficacy and safety of Immuvac in preventing pulmonary TB among healthy household contacts of sputum smear-positive TB patients is being implemented in India by the Indian Council of Medical Research.

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An ex-inmate undertaking TB outreach in a prison, Paraguay.

John Rae Photography

Annex 1

The WHO global TB database

A1.1 Database contents

The 2020 global tuberculosis (TB) report is based on data collected annually from 215 countries and territories, including all 194 World Health Organization (WHO) Member States. The Global TB Programme has implemented annual rounds of data collection since 1995, with an online system used since 2009. Data are stored in a global TB database that is managed by the TB monitoring, evaluation and strategic information unit of the Global TB Programme, at WHO headquarters.

The topics on which data have been collected have been consistent for many years. In 2020, as in previous years, data were collected on the following: TB case notifications and treatment outcomes, including breakdowns by TB case type, age, sex, HIV status and drug resistance; laboratory diagnostic services; monitoring and evaluation, including surveillance and surveys specifically related to drug-resistant TB; TB preventive therapy; digital systems; TB infection control; palliative care; engagement of all public and private care providers in TB prevention and care; community engagement; budgets of national TB control programmes (NTPs); use of general health services (hospitalization and outpatient visits) during treatment; and NTP expenditures. A shortened version of the online questionnaire was used for high-income countries (i.e. countries with a gross national income per capita of \geq US\$ 12 376 in 2018, as defined by the World Bank)¹ or low-incidence countries (defined as countries with an incidence rate of $<$ 20 cases per 100 000 population or $<$ 10 cases in total in 2018).

Data were also collected from all countries and territories on two new topics in 2020: the impact of the COVID-19 pandemic on TB services; and specific elements of the WHO multisectoral accountability framework for TB that were included in the political declaration at the 2018 UN high-level meeting on TB.

The main round of data collection was implemented in April and May. At the end of July, the 30 high TB burden countries and selected other regional priority countries in the WHO regions of the Americas and Western Pacific were asked to report monthly notification data for the period January–June 2020, to allow assessment of trends in the context of the COVID-19 pandemic.

Countries reported data via a dedicated website,² which was opened for reporting in April 2020. Countries in the European Union submitted data on notifications and treatment outcomes to the TESSy system managed by the European Centre for Disease Prevention and Control (ECDC). Data from TESSy were uploaded into the global TB database.

Additional data about the provision of treatment for latent TB infection to people newly or currently enrolled in HIV care, detection of TB among people newly enrolled in HIV care, and provision of antiretroviral therapy for HIV-positive TB patients were collected by the Joint United Nations Programme on HIV/AIDS (UNAIDS). These data were jointly validated by UNAIDS and the WHO's Global TB Programme and HIV department, and were uploaded into the global TB database.

Following review and follow-up with countries, the data used for the main part of this report were those that were available on **10 August 2020**. **Table A1.1** shows the number of countries and territories that had reported data by 10 August 2020.

TABLE A1.1

Reporting of data in the 2020 round of global TB data collection

WHO REGION	COUNTRIES AND TERRITORIES		WHO MEMBER STATES	
	NUMBER	NUMBER THAT REPORTED DATA	NUMBER	NUMBER THAT REPORTED DATA
Africa	47	46	47	46
The Americas	45	39	35	33
Eastern Mediterranean	22	22	21	21
Europe	54	46	53	45
South-East Asia	11	11	11	11
Western Pacific	36	34	27	27
Global	215	198	194	183

Indicators in the Sustainable Development Goals associated with TB incidence were imported into the global TB database on **15 June 2020**. **Table A1.2** shows the data sources used.

¹ <http://data.worldbank.org/about/country-classifications>

² <https://extranet.who.int/tme>

TABLE A1.2
Data sources for indicators in the Sustainable Development Goals associated with TB incidence

SDG INDICATOR	DISPLAY NAME IN PROFILE	DATA SOURCE	NAME AT SOURCE	SOURCE URL
1.1.1	Population living below the international poverty line (% of population)	UN SDG database	Proportion of population below the international poverty line of US\$1.90 per day	https://unstats.un.org/SDGAPI/v1/sdg/Series/Data?seriesCode=SI_POV_DAY1
1.3.1	Population covered by social protection floors/systems (% of population)	World Bank	Coverage of social protection and labor programs (% of population)	http://data.worldbank.org/indicator/per_allsp.cov_pop_tot
2.1.1	Prevalence of undernourishment (% of population)	World Bank	Prevalence of undernourishment (% of population)	http://data.worldbank.org/indicator/SN.ITK.DEFC.ZS
3.3.1 (alternative)	HIV prevalence (% of population aged 15-49 years)	WHO-GHO	Prevalence of HIV among adults aged 15 to 49 (%)	https://ghoapi.azureedge.net/api/MDG_0000000029
3.4.1 (alternative)	Diabetes prevalence (% of population aged ≥18 years)	WHO-GHO	Raised fasting blood glucose (≥7.0 mmol/L or on medication) (age-standardized estimate)	https://ghoapi.azureedge.net/api/NCD_GLUC_04
3.5.2 (alternative)	Alcohol use disorders, 12 month prevalence (% of population aged ≥15 years)	WHO-GHO	Alcohol use disorders (15+), 12 month prevalence (%) with 95%	https://ghoapi.azureedge.net/api/SA_0000001462
3.a.1 (alternative)	Smoking prevalence (% of population aged ≥15 years)	WHO-GHO	Estimate of current tobacco smoking prevalence (%) (age-standardized rate)	https://ghoapi.azureedge.net/api/M_Est_smk_curr_std
3.8.1	UHC index of essential service coverage (based on 14 tracer indicators including TB treatment)	WHO-GHO	UHC index of essential service coverage	https://ghoapi.azureedge.net/api/UHC_INDEX_REPORTED
3.8.2	Greater than 10% of total household expenditure or income on health (% of population)	WHO-GHO	Catastrophic out-of-pocket health spending (SDG indicator 3.8.2)	https://ghoapi.azureedge.net/api/FINPROTECTION_CATA_TOT_10_POP
3.8.2 (alternative)	Health expenditure per capita, PPP (current international \$)	WHO-GHO	Current health expenditure (CHE) per capita in PPP int\$	https://ghoapi.azureedge.net/api/GHED_CHE_pc_PPP_SHA2011
7.1.2	Access to clean fuels and technologies for cooking (% of population)	World Bank	Access to clean fuels and technologies for cooking (% of population)	http://data.worldbank.org/indicator/EG.CFT.ACCS.ZS
8.1.1 (alternative)	GDP per capita, PPP (constant 2011 international \$)	World Bank	GDP per capita, PPP (constant 2011 international \$)	http://data.worldbank.org/indicator/NY.GDP.PCAP.PP.KD
10.1.1 (alternative)	GINI index (0=perfect equality, 100=perfect inequality)	World Bank	GINI index (World Bank estimate)	http://data.worldbank.org/indicator/SI.POV.GINI
11.1.1	Population living in slums (% of urban population)	UN SDG database	Proportion of urban population living in slums (%)	https://unstats.un.org/SDGAPI/v1/sdg/Series/Data?seriesCode=EN_LND_SLUM

A1.2 Accessing TB data using the WHO Global TB Programme website

Most of the data held in the global TB database are available online.¹ The web page provides access to comma-separated value (CSV) data files and data visualizations, as well as country profiles (**Annex 3**).

The CSV data files are the primary resource for anyone interested in conducting their own analyses of the records in the global TB database. Data reported by countries (e.g. time series for case notifications and treatment outcomes) and WHO's estimates of TB disease burden can be downloaded as CSV files covering all years for which data are available. These CSV files can be imported into many applications (e.g. spreadsheets, databases and statistical analysis software).

A data dictionary that defines each of the variables available in the CSV files is also available and can be downloaded.

The CSV files are generated on-demand directly from the global TB database, and may therefore include updates received after publication of the global TB report.

¹ www.who.int/tb/data

A1.3 Accessing TB data using the WHO Global Health Observatory

The WHO Global Health Observatory (GHO)¹ is a portal that provides access to data and analyses for monitoring the global health situation; it includes a data repository.

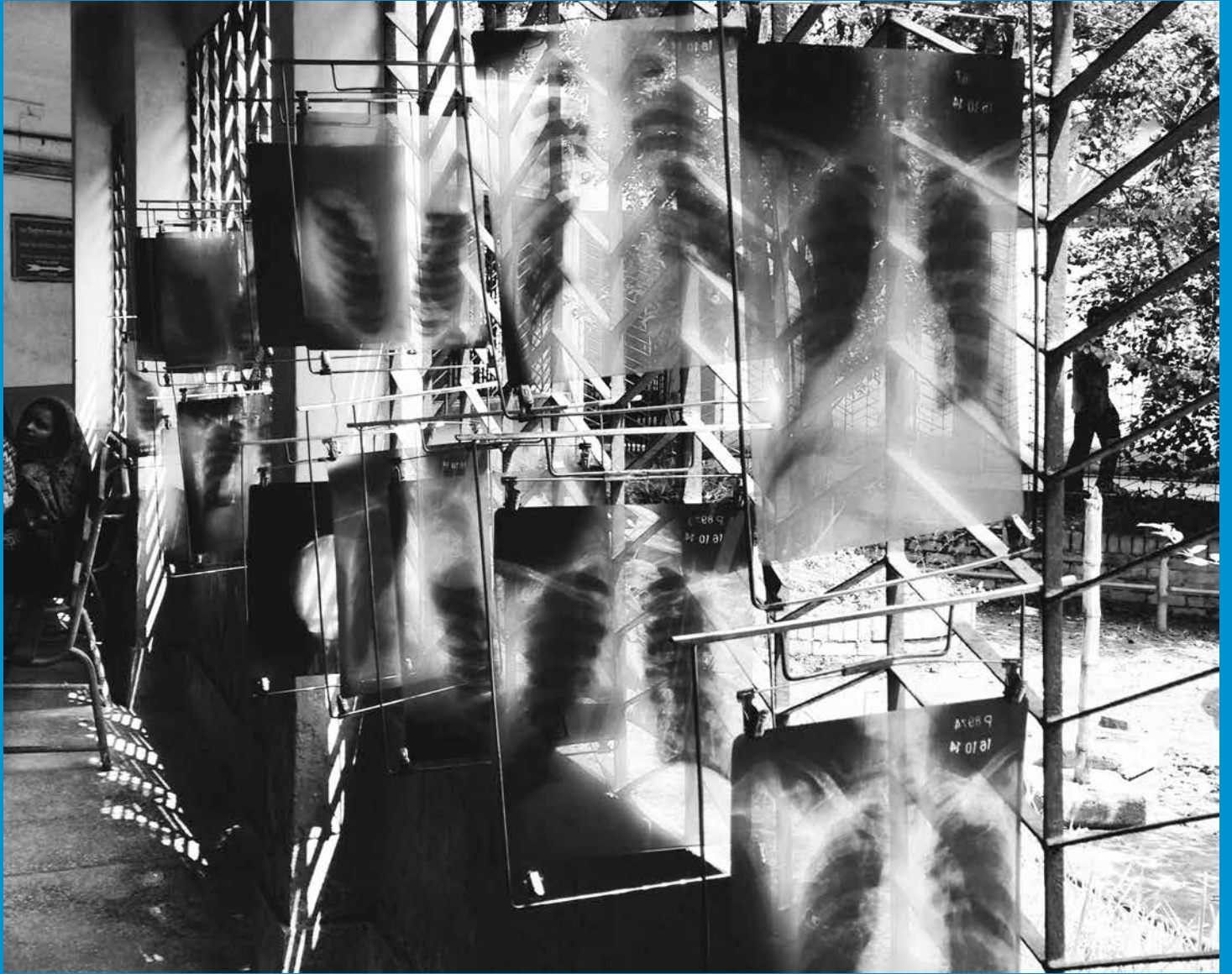
Data from WHO's global TB database can be viewed, filtered, aggregated and downloaded from within the GHO data repository.²

There is also an application programme interface (API)³ using the open data protocol. The API allows analysts and programmers to use GHO data directly in their software applications.

¹ www.who.int/data/gho

² www.who.int/data/gho/data/themes/tuberculosis

³ www.who.int/data/gho/info/gho-odata-api



Chest X-ray sheets drying in a corridor in a TB hospital in Dhaka, Bangladesh.

Irwin Law/WHO

Annex 2

Lists of high-burden countries defined by WHO for the period 2016–2020

During the period 1998–2015, the concept of a high burden country (HBC) became familiar and widely used in the context of TB. In 2015, three HBC lists – for TB, HIV-associated TB and MDR-TB – were in use.

In 2015, as part of the transition from the Millennium Development Goals (2000–2015) and Stop TB Strategy (2006–2016) to a new era of the Sustainable Development Goals (2016–2030) and End TB Strategy (2016–2035), the lists were revisited and updated. Following a wide consultation process (1), three new HBC lists were defined for the period 2016–2020: one for TB, one for MDR-TB and one for HIV-associated TB (Fig. A2.1, Table A2.1).

Each list contains 30 countries (Table A2.1). These are defined as the top 20 countries 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 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 HIV-associated TB and MDR-TB). The lists were defined using the 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.

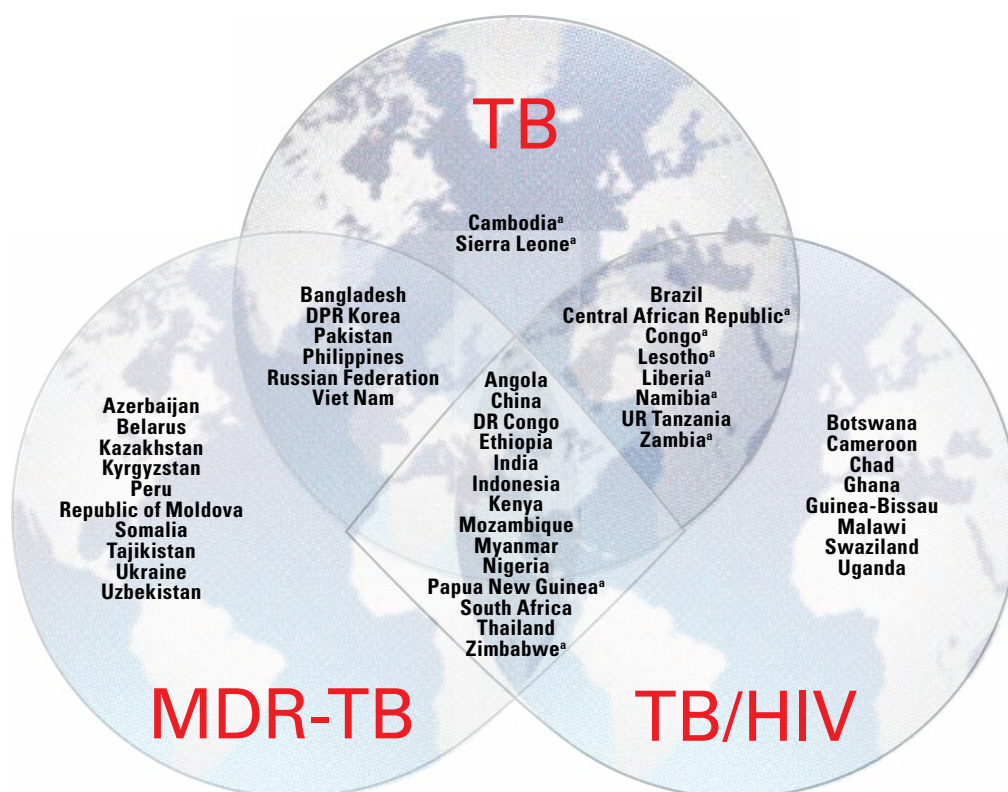
There is overlap among the three lists, but 48 countries appear in at least one of them. The 14 countries that are in all three lists (shown in the central diamond in Fig. A2.1) are Angola, China, the Democratic Republic of the Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Papua New Guinea, South Africa, Thailand and Zimbabwe. These 14 countries accounted for 63% of the estimated global number of incident TB cases in 2019.

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 HIV-associated TB or MDR-TB specifically, the countries in the other two lists are given particular attention. Country profiles for all countries are available online, including in the mobile app that accompanies the report (Annex 3).

The lists will be reviewed and updated for the period 2021–2025.

FIG. A2.1

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.

^a 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 incident cases 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. See also Table A2.1.

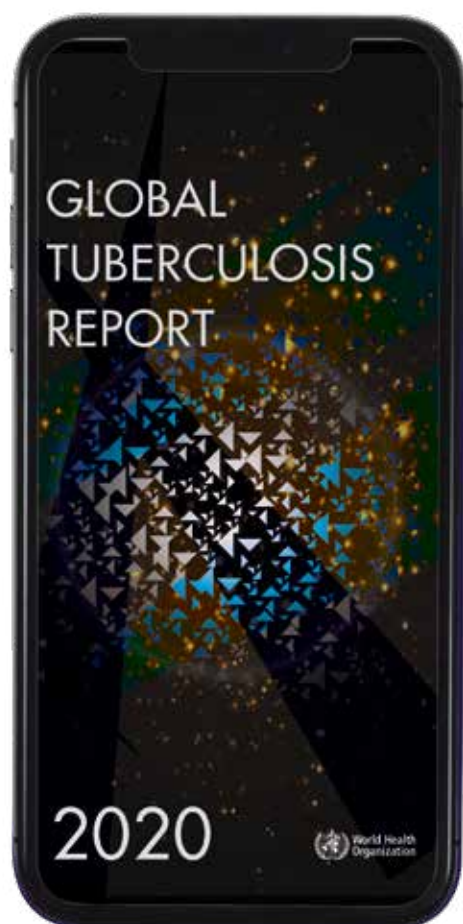
TABLE A2.1
The three high-burden country lists for TB, TB/HIV and MDR-TB defined by WHO for the period 2016–2020

LIST	THE 30 HIGH TB BURDEN COUNTRIES		THE 30 HIGH TB/HIV BURDEN COUNTRIES		THE 30 HIGH MDR-TB BURDEN COUNTRIES	
Purpose and target audience	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.	
Definition	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).	
Countries in the list	<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 Eswatini Ghana Guinea-Bissau Liberia Namibia Papua New Guinea	<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
Share of global incidence in 2019 (%)	84%	2.9%	81%	5.0%	85%	5.0%
Lifetime of list	5 years (review criteria and included countries in 2020).		5 years (review criteria and included countries in 2020).		5 years (review criteria and included countries in 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.

Reference

- World Health Organization. Use of high burden country lists for TB by WHO in the post-2015 era (discussion paper). Geneva: World Health Organization; 2015 (https://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020.pdf, accessed 28 July 2020).



Global, regional and country data (including profiles) are available at your fingertips with the Global TB Report app. It can be downloaded free of charge and content is available in multiple languages.



Annex 3

Country, regional and global profiles

Previous editions of the WHO global tuberculosis (TB) report have included annexes with TB profiles for the 30 high TB burden countries, WHO regions and the world. They have also included detailed data tables showing selected indicators for all countries, for the latest available year.

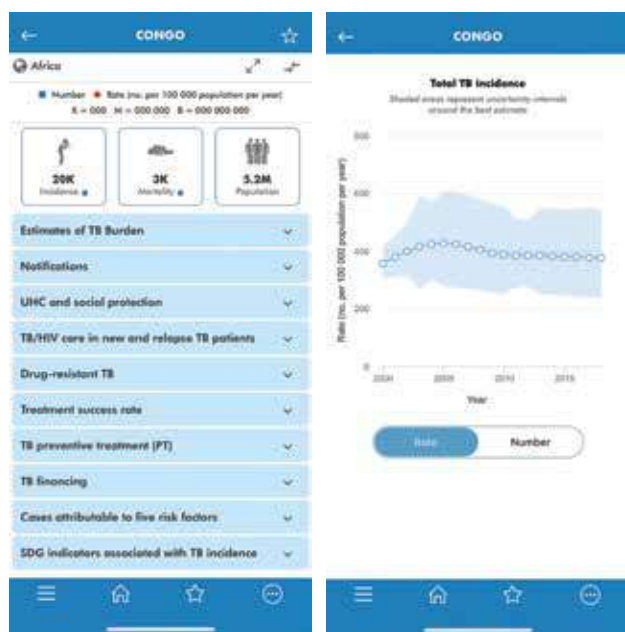
Following the development of new resources, in particular the WHO TB Report mobile app and infographic-style country profiles, this 2020 report no longer includes these annexes of TB profiles and data tables. Instead, readers are encouraged to use the new resources to access country, regional and global profiles as well as data for all key indicators for all countries. These new resources are more comprehensive in scope and include additional features.

A3.1 The WHO TB Report mobile app

The free WHO TB Report mobile app includes country, regional and global profiles from the global TB database, as well as a summary of the key facts and messages from the report and an overview of progress towards global TB targets. The app includes all the information that previously appeared in country, regional and global profiles in the annexes of the global TB report, but it is also more comprehensive in scope (covering all countries), includes some better visualizations (particularly of trends) and allows users to easily view, query and visualize data. Users can also define queries, including those for specific country groups.

Once installed, the app works offline so that users can access the data without an ongoing internet connection.

The app is available for Android devices through Google Play¹ and for iOS devices, such as iPhones and iPads,



¹ <https://play.google.com/store/apps/details?id=uk.co.adappt.whotbreport>

through the Apple Store.² It is available in English, French and Russian and will soon be available in Spanish.

A3.2 Infographic-style country profiles

Infographic-style country profiles are available online for the 48 high TB, high TB/HIV and high MDR-TB burden countries (for the countries in these lists, see [Annex 2](#)).



A3.3 Online country profiles and other reports

As in previous years, country profiles are available online for all 215 countries and territories that report TB data to WHO each year.³ The profiles are available in English, French, Spanish and Russian. They are generated on-demand directly from the global TB database ([Annex 1](#)) and may therefore include updates received after publication of the global TB report.

Estimates of TB cases attributable to five risk factors and indicators in the Sustainable Development Goals that are associated with TB incidence are available for all 215 countries and territories.

TB financial profiles are available for more than 100 countries and territories that report detailed TB financial data to WHO.

² <https://apps.apple.com/us/app/tb-report/id1483112411>

³ <https://www.who.int/tb/country/data/profiles/en/>



www.who.int/tb/data

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