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The cover design is based on a chest X-ray from a participant who was found to have MDR-TB during a national TB prevalence survey. The colour scheme and motifs aim to represent all people who are affected by TB. The cover was designed by Irwin Law based on an idea by Tom Hiatt.

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Abbreviations

AFB	acid-fast bacilli	NTP	national tuberculosis [control] programme
AIDS	acquired immunodeficiency syndrome	OECD	Organisation for Economic Co-operation and Development
ART	antiretroviral therapy	PEPFAR	US President's Emergency Plan for AIDS Relief
BCG	Bacille-Calmette-Guérin	PK	pharmacokinetic
BRICS	Brazil, Russian Federation, India, China, South Africa	PMDT	Programmatic Management of Drug-resistant TB
CDR	case detection rate	PPM	public-private mix
CFR	case fatality rate	PTB	pulmonary TB
CFU	colony forming units	rGLC	Regional Green Light Committee
CI	confidence interval	RR-TB	rifampicin-resistant tuberculosis
CPT	co-trimoxazole preventive therapy	SDG	Sustainable Development Goal
DR-TB	drug-resistant tuberculosis	SRL	supranational reference laboratory
DST	drug susceptibility testing	SRL-CE	SRL National Centre of Excellence
EBA	early bactericidal activity	STAG-TB	WHO's Strategy and Technical Advisory Group for TB
EPTB	extrapulmonary TB	STEP-TB	Speeding Treatments to End Pediatric Tuberculosis
EQA	external quality assessment	TAG	Treatment Action Group
FDA	US Food and Drug Administration	TB	tuberculosis
GDI	Global Drug-resistant TB Initiative	TBTC	TB Trials Consortium
GDP	gross domestic product	TBVI	Tuberculosis Vaccine Initiative
GLC	Green Light Committee	TPP	target product profile
GLI	Global Laboratory Initiative	TST	tuberculin skin test
HBC	high-burden country	UHC	universal health coverage
HIV	human immunodeficiency virus	UN	United Nations
ICD-10	International Classification of Diseases (10th revision)	UNAIDS	Joint United Nations Programme on HIV/AIDS
IHME	Institute for Health Metrics and Evaluation	UNITAID	international facility for the purchase of diagnostics and drugs for diagnosis and treatment of HIV/AIDS, malaria and TB
IGRA	interferon-gamma release assay	USAID	United States Agency for International Development
IPT	isoniazid preventive therapy	VR	vital registration
IRR	incidence rate ratio	WHA	World Health Assembly
ITT	intention-to-treat	WHO	World Health Organization
LED	light-emitting diode	XDR-TB	extensively drug-resistant tuberculosis, defined as MDR-TB plus resistance to at least one fluoroquinolone and a second-line injectable
LPA	line-probe assay	ZN	Ziehl-Neelsen
LTBI	latent TB infection		
MDG	Millennium Development Goal		
MDR-TB	multidrug-resistant tuberculosis, defined as resistance to at least isoniazid and rifampicin, the two most powerful anti-TB drugs		
MGIT	Mycobacteria Growth Indicator Tube		
MNCH	maternal, newborn and child health		
NAAT	nucleic acid amplification test		
NDWG	New Diagnostics Working Group		
NGO	nongovernmental organization		
NIAID	US National Institute of Allergy and Infectious Diseases		

Acknowledgements

DEDICATION

This global tuberculosis (TB) report is dedicated to Glenn Thomas and Amal Bassili.

Glenn Thomas died in the Malaysian Airlines tragedy on 17 July 2014, on his way to the 2014 International AIDS conference in Melbourne, Australia. Glenn worked with the Global TB Programme in WHO headquarters as TB Communications Adviser for nearly a decade before joining the WHO Department of Communications in 2012. He was a passionate TB communicator, advocate and liaison with the media community. He contributed significantly to raising global awareness of and attention to the TB/HIV co-epidemic and the emergence and spread of M/XDR-TB, to spreading the news on WHO policies, findings and new tools, and to the launch of ten global TB reports.

Amal Bassili died in August 2014. She was the focal point for Tropical Disease Research in the Eastern Mediterranean Regional Office (EMRO) from 2000–2013 and the surveillance officer within EMRO's TB unit from 2007–2013. She made an outstanding contribution to TB surveillance and operational research in the Eastern Mediterranean Region and globally, including improving country staff capacity in data management, promotion of and strong support to inventory/capture-recapture studies to improve estimates of TB disease burden, technical assistance for the design, implementation and analysis of national TB prevalence surveys, and essential support for the reporting of data featured in global TB reports.

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The writing of the main part of the report was led by Katherine Floyd. Chapter 2, on the burden of TB disease, was written by Katherine Floyd, Philippe Glaziou and Charalambos Sismanidis, with contributions from Irwin Law and Ikushi Onozaki. Chapter 3, on the “countdown to 2015”, was written by Katherine Floyd and Irwin Law. Chapter 4, on notifications and treatment outcomes, was written by Katherine Floyd, with contributions from Hannah Monica Dias, Haileyesus Getahun, Thomas Joseph, Nathalie Likhite and Mukund Uplekar. Chapter 5, on drug-resistant TB, was prepared by Anna Dean, Dennis Falzon, Linh Nguyen, Karin Weyer and Matteo Zignol, with input from Vineet Bhatia, Katherine Floyd, Philippe Glaziou, Fraser Wares and Charalambos Sismanidis. Chapter 6, on diagnostics and laboratory strengthening, was prepared by Wayne van Gemert, with input from Christopher Gilpin, Fuad Mirzayev and Karin Weyer. Chapter 7 was prepared by Annabel Baddeley, with input from Haileyesus Getahun, Alberto Matteelli and Katherine Floyd. Chapter 8, on TB financing, was written by Katherine Floyd with inputs from Inés Garcia, Knut Lönnroth and Andrew Siroka. Chapter 9, on research and development, was written by Christian Lienhardt (new TB drugs and new TB vaccines) and Christopher Gilpin (new TB diagnostics), with input from Karin Weyer. Chapter 9 was carefully reviewed by the chairs and secretariats of the Working Groups of the Stop TB Partnership. Particular thanks are due to Daniela Cirillo and Tom Shinnick (new TB diagnostics); Andrew Vernon, Carl Mendel, Cherise Scott, Chidi Akusobi and Mel Spigelman (new TB drugs); and Jennifer Woolley, Lewis Schrage, Ann Ginsberg, Tom Evans, Kari Stoeber and Daniel Yeboah-Kordieh (new TB vaccines). The report team is also grateful to various internal and external reviewers for useful comments and sug-

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Executive summary

Tuberculosis (TB) remains one of the world's deadliest communicable diseases. In 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease, 360 000 of whom were HIV-positive. TB is slowly declining each year and it is estimated that 37 million lives were saved between 2000 and 2013 through effective diagnosis and treatment. However, given that most deaths from TB are preventable, the death toll from the disease is still unacceptably high and efforts to combat it must be accelerated if 2015 global targets, set within the context of the Millennium Development Goals (MDGs), are to be met.

TB is present in all regions of the world and the *Global Tuberculosis Report 2014* includes data compiled from 202 countries and territories. This year's report shows higher global totals for new TB cases and deaths in 2013 than previously, reflecting use of increased and improved national data.

A special supplement to the 2014 report highlights the progress that has been made in surveillance of drug-resistant TB over the last two decades, and the response at global and national levels in recent years. Worldwide, the proportion of new cases with multidrug-resistant TB (MDR-TB) was 3.5% in 2013 and has not changed compared with recent years. However, much higher levels of resistance and poor treatment outcomes are of major concern in some parts of the world. The supplement, *Drug Resistant TB: Surveillance and Response*, defines priority actions needed, from prevention to cure.

Burden of disease and progress towards 2015 global targets

Improved data give a clearer global picture of TB burden; an acceleration in current rates of decline is needed to meet all targets.

- The data available to estimate TB disease burden continue to improve. In 2013, direct measurements of TB mortality were available from 126 countries and since 2009 there has been an unprecedented increase in the number of direct measurements of TB prevalence from nationwide population-based surveys. Survey results were finalized for five new countries in 2013: Gambia, Lao PDR, Nigeria, Pakistan and Rwanda. When new data become available they can affect global TB estimates for the current year and retrospectively.¹

- Of the estimated 9 million people who developed TB in 2013, more than half (56%) were in the South-East Asia and Western Pacific Regions. A further one quarter were in the African Region, which also had the highest rates of cases and deaths relative to population. India and China alone accounted for 24% and 11% of total cases, respectively.
- About 60% of TB cases and deaths occur among men, but the burden of disease among women is also high. In 2013, an estimated 510 000 women died as a result of TB, more than one third of whom were HIV-positive. There were 80 000 deaths from TB among HIV-negative children in the same year.
- An estimated 1.1 million (13%) of the 9 million people who developed TB in 2013 were HIV-positive. The number of people dying from HIV-associated TB has been falling for almost a decade. The African Region accounts for about four out of every five HIV-positive TB cases and TB deaths among people who were HIV-positive.
- The 2015 Millennium Development Goal (MDG) of halting and reversing TB incidence has been achieved globally, in all six WHO regions and in most of the 22 high TB burden countries (HBCs). Worldwide, TB incidence fell at an average rate of about 1.5% per year between 2000 and 2013.
- Globally, the TB mortality rate fell by an estimated 45% between 1990 and 2013 and the TB prevalence rate fell by 41% during the same period. Progress needs to accelerate to reach the Stop TB Partnership targets of a 50% reduction by 2015.
- Two out of six WHO regions have achieved all three 2015 targets for reductions in TB disease burden (incidence, prevalence, mortality): the Region of the Americas and the Western Pacific Region. The South-East Asia Region appears on track to meet all three targets. Incidence, prevalence and mortality rates are all falling in the African, Eastern Mediterranean and European Regions but not fast enough to meet targets.

¹ Currently WHO produces estimates back to 1990 since this is the baseline year for 2015 global targets for TB mortality and prevalence.

TB detection and treatment outcomes

The treatment success rate among new cases of TB continues to be high, but major efforts are needed to ensure all cases are detected, notified and treated.

- In 2013, 6.1 million TB cases were reported to WHO. Of these, 5.7 million were people newly diagnosed and another 0.4 million were already on treatment.
- Notification of TB cases has stabilized in recent years. In 2013, about 64% of the estimated 9 million people who developed TB were notified as newly diagnosed cases. This is estimated to have left about 3 million cases that were either not diagnosed, or diagnosed but not reported to national TB programmes (NTPs). Major efforts are needed to close this gap.
- In 2013, the treatment success rate continued to be high at 86% among all new TB cases.
- Although treatment success rates in the European Region have improved since 2011, they were still below average in 2012 at 75%.

MDR-TB detection and treatment outcomes

Increased use of new diagnostics is ensuring that significantly more TB patients are correctly diagnosed, but major treatment gaps remain and funding is insufficient.

- Globally, 3.5% of new and 20.5% of previously treated TB cases were estimated to have had MDR-TB in 2013. This translates into an estimated 480 000 people having developed MDR-TB in 2013.
- On average, an estimated 9.0% of patients with MDR-TB had extensively drug resistant TB (XDR-TB).
- If all notified TB patients (6.1 million, new and previously treated) had been tested for drug resistance in 2013, an estimated 300 000 cases of MDR-TB would have been detected, more than half of these in three countries alone: India, China and the Russian Federation.
- In 2013, 136 000 of the estimated 300 000 MDR-TB patients who could have been detected were diagnosed and notified. This was equivalent to almost one in two (45%), and up from one in six in 2009. Progress in the detection of drug-resistant TB has been facilitated by the use of new rapid diagnostics.
- A total of 97 000 patients were started on MDR-TB treatment in 2013, a three-fold increase compared with 2009. However, 39 000 patients (plus an unknown number detected in previous years) were on waiting lists, and the gap between diagnosis and treatment widened between 2012 and 2013 in several countries.
- The most recent treatment outcome data are for patients started on MDR-TB treatment in 2011. Globally the success rate was 48%. Five of the 27 high MDR-TB burden countries achieved a treatment success rate of

≥70%: Ethiopia, Kazakhstan, Myanmar, Pakistan and Viet Nam. Health system weaknesses, lack of effective regimens and other treatment challenges are responsible for unacceptably low cure rates, and the MDR-TB response is seriously hampered by insufficient funding. These barriers must be urgently addressed.

- Five priority actions – from prevention to cure – are needed to address the MDR-TB epidemic. These are: 1) high-quality treatment of drug-susceptible TB to prevent MDR-TB; 2) expansion of rapid testing and detection of MDR-TB cases; 3) immediate access to quality care; 4) infection control; and 5) increased political commitment, including adequate funding for current interventions as well as research to develop new diagnostics, drugs and treatment regimens.

TB diagnostics and laboratory strengthening

The successful roll out of new diagnostics is ensuring more TB cases are correctly diagnosed and treated.

- Laboratory confirmation of TB and drug resistance is key to ensuring that individuals with TB signs and symptoms are correctly diagnosed and treated. In 2013, 58% of the 4.9 million pulmonary TB patients notified globally were bacteriologically confirmed via a WHO-recommended test, including rapid tests such as Xpert MTB/RIF.
- By June 2014, 108 countries with access to Xpert MTB/RIF at concessional prices had started to use the technology, and more than one million test cartridges were being procured each quarter.
- In late 2013, WHO expanded its recommendations on the use of Xpert MTB/RIF to include the diagnosis of TB in children and some forms of extrapulmonary TB.

Addressing the co-epidemics of TB and HIV

There has been continued progress in the implementation of collaborative TB/HIV activities but intensified efforts are needed, especially to ensure universal access to antiretroviral therapy (ART).

- The first key intervention for reducing the burden of HIV-associated TB is HIV testing for TB patients. In 2013, 48% of TB patients globally had a documented HIV test result, but progress in increasing coverage has slowed. In the African Region, 76% of TB patients knew their HIV status.
- The most important intervention to reduce mortality among HIV-positive TB patients is ART. In 2013, 70% of TB patients known to be HIV-positive were on ART. This level, however, falls short of the 100% target set for 2015.

- Besides early initiation of ART, the main intervention to prevent TB in people living with HIV is isoniazid preventive therapy (IPT). In 2013, only 21% of countries globally and 14 of the 41 high TB/HIV burden countries reported provision of IPT to people living with HIV.

TB Financing

Despite substantial growth in funding for TB prevention, diagnosis and treatment since 2002, an annual gap of around US\$ 2 billion still needs to be filled.

- An estimated US\$ 8 billion per year is required to ensure a full response to the global TB epidemic: about two thirds for detection and treatment of drug susceptible TB; 20% for treatment of MDR-TB; 10% for rapid diagnostic tests and associated laboratory testing; and 5% for collaborative TB/HIV activities. The amount excludes resources required for research and development for new TB diagnostics, drugs and vaccines, which is estimated at about US\$ 2 billion per year.
- Based on reports to WHO from the 122 countries that account for 95% of reported TB cases, funding for TB prevention, diagnosis and treatment reached a total of US\$ 6.3 billion in 2014. This left a gap of almost US\$ 2 billion per year compared with the required total of US\$ 8 billion.
- Brazil, the Russian Federation, India, China and South Africa (BRICS), which collectively account for almost 50% of global TB cases, are in a position to mobilize all or a large share of their required funding from domestic sources. International donor funding remains critical for many other countries. For example, in the group of 17 HBCs excluding BRICS, international donor funding accounted for more than 50% of total funding in 2014. In several countries, more than 90% of the funding available in 2014 was from international donor sources. The Global Fund and the US government are the two main sources of international donor funding.
- The cost per patient treated for drug-susceptible TB in 2013 was in the range of US\$ 100–US\$ 500 in most countries with a high burden of TB. The cost per patient treated for MDR-TB ranged from an average of US\$ 9 235 in low-income countries to US\$ 48 553 in upper middle-income countries.

TB Research and Development

New tools are emerging from the pipeline but much more investment is required.

- Many new diagnostic technologies are under development or are available on the market, but the funding required to rapidly evaluate whether these tests are accurate and ready for implementation is far from adequate.
- There are 10 new or repurposed anti-TB drugs currently in the late phases of clinical development and, in the last two years, two new drugs have been approved for the treatment of MDR-TB under specific conditions: bedaquiline and delamanid.
- Trials of four-month treatment regimens for drug-susceptible TB found that they were inferior to the six-month standard of care regimen currently recommended by WHO. However, a series of new combination regimens are currently being tested and show encouraging prospects for treatment of both drug-susceptible and drug-resistant TB.
- There are currently 15 vaccine candidates in clinical trials.

Beyond 2015

- The end of 2015 marks a transition from the MDGs to a post-2015 development framework. Within this broader context, WHO has developed a post-2015 global TB strategy (the End TB Strategy) that was approved by all Member States at the May 2014 World Health Assembly.
- The overall goal of the strategy is to end the global TB epidemic, with corresponding 2035 targets of a 95% reduction in TB deaths and a 90% reduction in TB incidence (both compared with 2015). The strategy also includes a target of zero catastrophic costs for TB-affected families by 2020.

Introduction

BOX 1.1

Basic facts about TB

TB is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extrapulmonary TB). The disease is spread in the air when people who are sick with pulmonary TB expel bacteria, for example by coughing. Overall, a relatively small proportion of people infected with *M. tuberculosis* will develop TB disease. However, the probability of developing TB is much higher among people infected with HIV. TB is also more common among men than women, and affects mainly adults in the most economically productive age groups.

The most common method for diagnosing TB worldwide is sputum smear microscopy (developed more than 100 years ago), in which bacteria are observed in sputum samples examined under a microscope. Following recent breakthroughs in TB diagnostics, the use of rapid molecular tests to diagnose TB and drug-resistant TB is increasing. In countries with more developed laboratory capacity, cases of TB are also diagnosed via culture methods (the current reference standard).

Without treatment, TB mortality rates are high. In studies of the natural history of the disease among sputum smear-positive/HIV-negative cases of pulmonary TB, around 70% died within 10 years; among culture-positive (but smear-negative) cases, 20% died within 10 years.^a

Effective drug treatments were first developed in the 1940s. The most effective first-line anti-TB drug, rifampicin, became available in the 1960s. The currently recommended treatment for new cases of drug-susceptible TB is a six-month regimen of four first-line drugs: isoniazid, rifampicin, ethambutol and pyrazinamide. Treatment success rates of 85% or more for new cases are regularly reported to WHO by its Member States. Treatment for multidrug-resistant TB (MDR-TB), defined as resistance to isoniazid and rifampicin (the two most powerful anti-TB drugs) is longer, and requires more expensive and more toxic drugs. For most patients with MDR-TB, the current regimens recommended by WHO last 20 months, and treatment success rates are much lower.

For the first time in four decades, new TB drugs are starting to emerge from the pipeline, and combination regimens that include new compounds are being tested in clinical trials. There are several TB vaccines in Phase I or Phase II trials. For the time being, however, a vaccine that is effective in preventing TB in adults remains elusive.

^a Tiemersma EW et al. Natural history of tuberculosis: duration and fatality of untreated pulmonary tuberculosis in HIV-negative patients: A systematic review. *PLoS ONE*, 2011, 6(4): e17601.

Tuberculosis (TB) remains a major global health problem, responsible for ill health among millions of people each year. TB ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV). The latest estimates included in this report are that there were 9.0 million new TB cases in 2013 and 1.5 million TB deaths (1.1 million among HIV-negative people and 0.4 million among HIV-positive people). These totals are higher than those included in the 2013 global TB report, primarily because of upward revisions to estimates of the number of TB cases and deaths in Nigeria following the finalization of results from the country's first-ever national TB prevalence survey (completed in 2012). Given the size of the population and the high TB burden in Nigeria, these revisions have affected global estimates.

Though most TB cases and deaths occur among men, the burden of disease among women is also high. In 2013, there were an estimated 3.3 million cases and 510 000 TB deaths among women, as well as an estimated 550 000 cases and 80 000 deaths among children.¹ TB mortality is unacceptably high given that most deaths are preventable if people can access health care for a diagnosis and the correct treatment is provided. Short-course regimens of first-line drugs that can cure around 90% of cases have been available for decades. Basic facts about TB are summarized in **Box 1.1**.

These large numbers of TB cases and deaths notwithstanding, 21 years on from the 1993 World Health Organization (WHO) declaration of TB as a global public health emergency, major progress has been made. Globally, the TB mortality rate (deaths per 100 000 population per year) has fallen by 45% since 1990 and TB incidence rates (new cases per 100 000 population per year) are decreasing in most parts of the world. Between 2000 and 2013, an estimated 37 million lives were saved through effective diagnosis and treatment.

The global TB strategy developed by WHO for the period 2006–2015 is the *Stop TB Strategy* (**Box 1.2**).²

¹ The estimated number of deaths among children excludes TB deaths in HIV-positive children, for which estimates are not yet available. Further details are provided in **Chapter 2**.

² Raviglione M, Uplekar M. WHO's new Stop TB strategy. *The Lancet*, 2006, 367: 952–5.

BOX 1.2

The Stop TB Strategy at a glance

VISION	A TB-free world
GOAL	To dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goals (MDGs) and the Stop TB Partnership targets
OBJECTIVES	<ul style="list-style-type: none">■ Achieve universal access to high-quality care for all people with TB■ Reduce the human suffering and socioeconomic burden associated with TB■ Protect vulnerable populations from TB, TB/HIV and drug-resistant TB■ Support development of new tools and enable their timely and effective use■ Protect and promote human rights in TB prevention, care and control
TARGETS	<ul style="list-style-type: none">■ MDG 6, Target 6.c: Halt and begin to reverse the incidence of TB by 2015■ Targets linked to the MDGs and endorsed by the Stop TB Partnership:<ul style="list-style-type: none">— 2015: reduce prevalence of and deaths due to TB by 50% compared with a baseline of 1990— 2050: eliminate TB as a public health problem (defined as <1 case per 1 million population per year)

COMPONENTS

1. Pursue high-quality DOTS expansion and enhancement

- a. Secure political commitment, with adequate and sustained financing
- b. Ensure early case detection, and diagnosis through quality-assured bacteriology
- c. Provide standardized treatment with supervision, and patient support
- d. Ensure effective drug supply and management
- e. Monitor and evaluate performance and impact

2. Address TB/HIV, MDR-TB, and the needs of poor and vulnerable populations

- a. Scale up collaborative TB/HIV activities
- b. Scale up prevention and management of MDR-TB
- c. Address the needs of TB contacts, and of poor and vulnerable populations

3. Contribute to health system strengthening based on primary health care

- a. Help improve health policies, human resource development, financing, supplies, service delivery and information
- b. Strengthen infection control in health services, other congregate settings and households
- c. Upgrade laboratory networks, and implement the Practical Approach to Lung Health
- d. Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health

4. Engage all care providers

- a. Involve all public, voluntary, corporate and private providers through public-private mix approaches
- b. Promote use of the *International Standards for Tuberculosis Care*

5. Empower people with TB, and communities through partnership

- a. Pursue advocacy, communication and social mobilization
- b. Foster community participation in TB care, prevention and health promotion
- c. Promote use of the *Patients' Charter for Tuberculosis Care*

6. Enable and promote research

- a. Conduct programme-based operational research
- b. Advocate for and participate in research to develop new diagnostics, drugs and vaccines

The overarching goal of this strategy is to achieve 2015 global targets for reductions in the burden of disease caused by TB. These targets are that incidence should be falling, and that prevalence and incidence rates should be halved by 2015 compared with 1990 levels.

The end of 2015 is significant, representing a transition between the Millennium Development Goals (MDGs) established in 2000 and a post-2015 development framework. By July 2014, following the work of a high-level

panel and ongoing consultations, a set of 17 Sustainable Development Goals (SDGs) with targets set for 2030 had been proposed.¹ The third of these goals, “Ensure healthy lives and promote well-being for all at all ages”, includes a target to “end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases”

¹ <http://sustainabledevelopment.un.org/focussdgs.html>

BOX 1.3

The post-2015 global TB strategy at a glance

VISION	A TB-free world — zero deaths, disease and suffering due to TB
GOAL	End the global tuberculosis epidemic
MILESTONES FOR 2025	— 75% reduction in TB deaths (compared with 2015) — 50% reduction in TB incidence rate (less than 55 TB cases per 100 000 population) — No affected families facing catastrophic costs due to TB
TARGETS FOR 2035	— 95% reduction in TB deaths (compared with 2015) — 90% reduction in TB incidence rate (less than 10 TB cases per 100 000 population) — No affected families facing catastrophic costs due to TB

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 co-morbidities
- 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

by 2030. It is anticipated that the SDGs will be finalized by September 2015.

Within this broader context and contributing to the development of health-related SDGs, in 2012 WHO initiated the development of a post-2015 global TB strategy. Following an extensive consultation process, the strategy was endorsed by all Member States at the 2014 World Health Assembly in resolution WHA 67.1.¹ The overarching goal of the post-2015 strategy is to end the global TB epidemic by 2035, with corresponding global targets for a 95% reduction in the number of TB deaths and a 90% reduction in the number of cases by 2035, compared with a baseline of 2015 (Box 1.3). Milestones for 2020, 2025 and 2030 are also included; examples are a 75% reduction in TB deaths by 2025 (compared with 2015), and that by 2020 no TB patients or their households experience cata-

strophic costs as a result of their disease. Achieving the proposed targets is based on three strategic pillars: integrated, patient-centred care and prevention; bold policies and supportive systems; and intensified research and innovation.

In the context of global TB strategies and targets, WHO has published a global TB report every year since 1997 (Figure 1.1). The main aim of the report is to provide a comprehensive and up-to-date assessment of the TB epidemic and progress in prevention, diagnosis and treatment of the disease at global, regional and country levels, based primarily on data that are reported by countries and territories to WHO in annual rounds of global TB data collection (Box 1.4). This 2014 global TB report is the nineteenth in the series of annual reports, and uses data reported by a total of 202 countries and territories including 183 Member States that account for over 99% of the world's estimated cases of TB (Table 1.1).

¹ http://www.who.int/tb/post2015_TBstrategy.pdf?ua=1

BOX 1.4

Data collected in WHO 2014 round of global TB data collection

Data were requested on the following topics: TB case notifications and treatment outcomes, including breakdowns by TB case type, age, sex and HIV status; an overview of services for the diagnosis and treatment of TB; laboratory diagnostic services; drug management; monitoring and evaluation; surveillance and surveys of drug-resistant TB; management of drug-resistant TB; collaborative TB/HIV activities; TB infection control; engagement of all care providers in TB control; the budgets of national TB control programmes (NTPs) in 2014; utilization of general health services (hospitalization and outpatient visits) during treatment; and NTP expenditures in 2013. A shortened version of the online questionnaire was used for high-income countries (that is, countries with a gross national income per capita of \geq US\$ 12 746 in 2013, as defined by the World Bank^a and/or low-incidence countries (defined as countries with an incidence rate of <20 cases per 100 000 population or <10 cases in total).

Countries reported data using an online web-based system (<https://extranet.who.int/tme>). The system was opened for reporting on 19 March, with a deadline of 14 May for all WHO regions except for the Region of the Americas and the European Region (these had a deadline of 30 May). Countries in the European Union submitted notification data to a system managed by the European Centre for Disease Prevention and Control (ECDC). Data from the ECDC system were uploaded into the WHO online system.

Data were reviewed, and, where appropriate, followed up with countries by a team of reviewers. Validation of data by respondents was also encouraged via a series of real-time checks of submitted data. Following corrections and updates by countries, the data used for the main part of this report for most countries were those available on 29 July 2014; for a few countries that corrected their data when country profiles were sent for review, the data available on 11 August were used. The detailed data tables for key indicators provided alongside the report were produced using data available on 6 October, and include additional data from a few European countries.^b

In addition to the data reported through the online global TB data collection system, data about TB screening and the provision of isoniazid preventive therapy (IPT) to people living with HIV and antiretroviral therapy (ART) for HIV-positive TB patients were collected by the HIV department in WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS). The data were jointly validated by the WHO's Global TB Programme and HIV department, and UNAIDS.

^a <http://data.worldbank.org/about/country-classifications>

^b For this reason, there may be slight discrepancies between the main part of the report and the data on the accompanying CD-rom and online global TB database.

FIGURE 1.1

Eighteen annual WHO global TB reports, 1997–2013

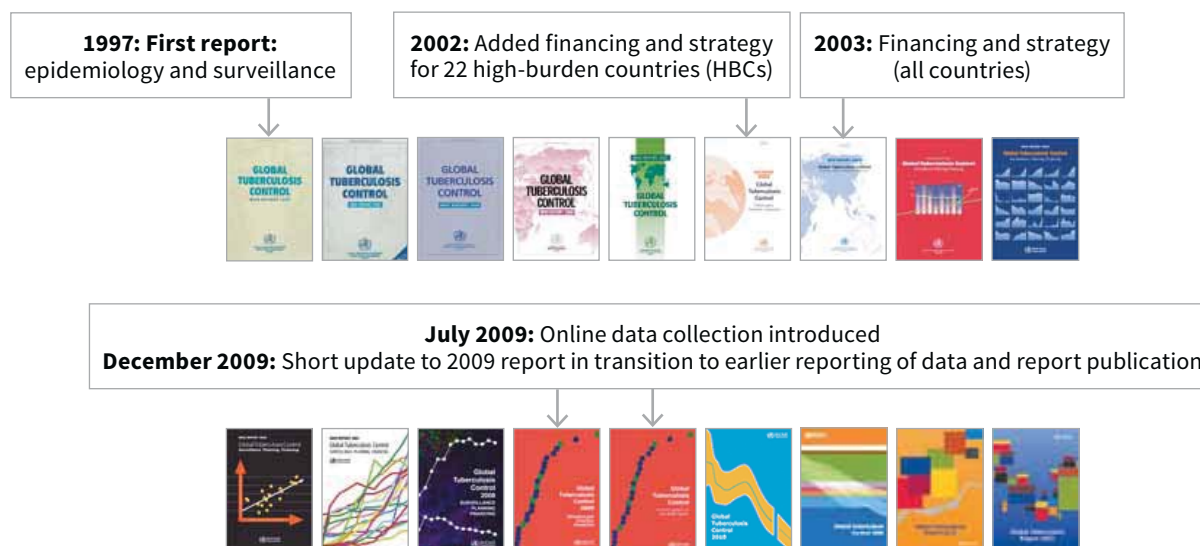


TABLE 1.1

Reporting of data in the 2014 round of global TB data collection

WHO REGION OR SET OF COUNTRIES	COUNTRIES AND TERRITORIES		WHO MEMBER STATES	
	NUMBER	NUMBER THAT REPORTED DATA	NUMBER	NUMBER THAT REPORTED DATA
African Region	47	46	47	46
Eastern Mediterranean Region	22	20	21	20
European Region ^a	54	47	53	46
Region of the Americas	46	46	35	35
South-East Asia Region	11	11	11	11
Western Pacific Region	36	32	27	25
High-burden countries (HBCs) ^b	22	22	22	22
World	216	202	194	183

^a Countries that did not report by the deadlines were mostly low-incidence countries in Western Europe.

^b The HBCs are Afghanistan, Bangladesh, Brazil, Cambodia, China, the Democratic Republic of the Congo, Ethiopia, India, Indonesia, Kenya, Mozambique, Myanmar, Nigeria, Pakistan, the Philippines, the Russian Federation, South Africa, Thailand, Uganda, the United Republic of Tanzania, Viet Nam and Zimbabwe.

The main part of the report contains eight major chapters. Each chapter is intended to stand alone, but links to other chapters are highlighted where appropriate.

Chapter 2 contains the latest estimates of the burden of disease caused by TB and assessment of progress towards the 2015 targets at global, regional and country levels. Estimates for women and children specifically, and the results and lessons learned from the recent national TB prevalence survey in Nigeria, are given particular attention. The latest status of efforts to improve the measurement of TB cases and deaths at country level, with guidance and support from the WHO Global Task Force on TB Impact Measurement, is described.

With the end of 2015 just one year away, **Chapter 3** provides a snapshot of the status of progress towards 2015 global targets in the 22 high-burden countries (HBCs) that account for 80% of the world's TB cases, in WHO's six regions, and globally. This covers progress towards the overarching targets for reductions in disease burden (incidence, prevalence, mortality). It also summarizes progress towards related 2015 targets for TB detection and treatment that have been set for two additional indicators included in the MDG framework (the case detection rate¹ and the treatment success rate for new TB cases) and targets set for the response to the epidemics of TB/HIV and multidrug-resistant TB (MDR-TB) as part of the latest Global Plan to Stop TB.²

Chapter 4 presents data on the numbers of cases notified to NTPs and reported to WHO, and their treatment

outcomes, including breakdowns of TB cases by type, sex and age. The chapter highlights recent progress in the contribution of community health workers and volunteers to the referral of TB cases and treatment support, and the role of public-private mix interventions in the post-2015 global TB strategy.

Chapter 5 focuses on drug-resistant TB. The first part of the chapter covers progress in drug resistance surveillance and associated estimates of the absolute number and proportion of TB patients that have MDR-TB and extensively drug-resistant TB (XDR-TB). The second part of the chapter presents and discusses the latest data on the programmatic response to MDR-TB, including the coverage of testing for drug resistance among new and previously treated TB patients; the number of cases detected with MDR-TB and enrolled on treatment; and treatment outcomes.

Chapter 6, on TB diagnostics and laboratory strengthening, covers two main topics. These are the status of laboratory capacity and incorporation of WHO guidance into national policy in 2013, and recent progress in strengthening laboratories and associated diagnostic capacity. It includes the latest data on the roll-out of the rapid molecular test Xpert MTB/RIF since it was recommended in 2010, a multinational project to strengthen laboratory capacity worldwide (EXPAND-TB).

Chapter 7 contains the most recent data on progress in implementing collaborative TB/HIV activities to jointly address the epidemics of TB and HIV. These include HIV testing for TB patients, provision of antiretroviral therapy (ART) to HIV-positive TB patients, TB screening and isoniazid preventive therapy (IPT) for people living with HIV.

Chapter 8 assesses financing for TB prevention, diagnosis and treatment. It starts by summarizing estimates of the funding required for a full response to the global TB epidemic up to 2015, which were produced in early 2013 as

¹ The case detection rate, or CDR, is calculated as the number of new cases reported to NTPs in a given year divided by estimated incidence for the same year. The CDR is thus a ratio rather than a rate, but in the context of this indicator the term 'rate' has become standard terminology.

² *The Global Plan to Stop TB, 2011–2015*. Geneva, World Health Organization, 2010 (WHO/HTM/STB/2010.2). Available at http://www.stoptb.org/assets/documents/global/plan/TB_GlobalPlanToStopTB2011-2015.pdf

part of preparatory work undertaken to inform the replenishment of the Global Fund. The chapter then assesses trends in funding and funding gaps since 2006 based on data reported by NTPs to WHO, including breakdowns by category of expenditure and sources of funding both overall and for country groups defined according to income level, geography and TB burden. Estimates of the cost per patient treated for drug-susceptible and MDR-TB and a new analysis of donor funded using the Organization for Economic Cooperation and Development's creditor reporting system are also featured.

Chapter 9 discusses research and development for new TB diagnostics, drugs and vaccines. The development pipelines in August 2014 are described and discussed.

The report has three annexes. **Annex 1** explains how to use the online WHO global TB database, which is the best source of the latest data reported to and estimates produced by WHO (data for key indicators as of 6 October are

also available on the CD-ROM provided with the report). **Annex 2** contains country profiles for the 22 HBCs (profiles for other countries are available online¹) and **Annex 3** contains regional profiles.

The methods used to produce the estimates of disease burden shown in **Chapter 2** are available in an online technical appendix (www.who.int/tb/data).

The report is also accompanied by a **special supplement**. Marking the twenty years since the establishment of the Global Project on Surveillance of anti-TB Drug Resistance, the supplement provides the latest status of progress in surveillance of drug-resistant TB and a new analysis of trends in the burden of drug-resistant TB worldwide. One year on from the 2013 global report's description of MDR-TB as a "public health crisis", the supplement also highlights the latest status of the response to the MDR-TB epidemic.

¹ www.who.int/tb/data.

The burden of disease caused by TB

KEY FACTS AND MESSAGES

WHO updates estimates of the burden of disease caused by TB annually, using the latest available data and analytical methods that are explained in a technical appendix and periodically reviewed by an expert group. Estimates are extended to include the most recent calendar year and updates affect the entire time-series back to 1990. For this reason, estimates presented in this chapter for 1990–2012 supersede those of previous reports and direct comparisons (for example, 2012 estimates in this report and 2012 estimates in the last report) are not appropriate.

The data available to estimate TB disease burden continue to improve. In 2013, data from vital registration (VR) systems were used to estimate TB mortality in 126 countries (up from 3 countries in 2008). There has been substantial progress in the implementation of national TB prevalence surveys since 2008, with 16 surveys completed from 2009–2014 and a further 12 underway or planned for 2014–2016.

Final results from national TB prevalence surveys completed from 2011–2013 in Gambia, Lao PDR, Nigeria, Pakistan and Rwanda became available at the end of 2013. Results have provided a recent and direct measure of TB burden at population level in these countries, in four instances for the first time, and used to update estimates of TB prevalence as well as TB incidence and mortality. Upward revisions to estimates of the absolute number of TB cases and deaths in Nigeria have affected global estimates of the absolute number of TB cases and deaths, given the size of the country's population and TB burden.

In 2013, there were an estimated 9.0 million incident cases of TB and 1.5 million people died from the disease (1.1 million deaths among people who were HIV-negative and 360 000 among people who were HIV-positive). Among these deaths there were an estimated 210 000 from MDR-TB, a relatively high total compared with 480 000 incident cases of MDR-TB. An estimated 13% of new TB cases were HIV-positive in 2013.

The South-East Asia and Western Pacific Regions collectively accounted for 56% of the world's TB cases in 2013. The African Region had approximately one quarter of the world's cases, and the highest rates of cases and deaths relative to population (280 incident cases per 100 000 on average, more than double the global average of 126). India and China had the largest number of cases (24% and 11% of the global total, respectively).

The MDG target of halting and reversing TB incidence by 2015 has already been achieved globally. The TB incidence rate fell at an average rate of 1.5% per year between 2000 and 2013. Globally by 2013, the TB mortality rate had fallen by 45% since 1990 and the TB prevalence rate had fallen by 41% since 1990. To achieve the Stop TB Partnership targets of halving TB mortality and prevalence rates by 2015 compared with a baseline of 1990, an acceleration in the current rates of decline is required.

The Region of the Americas and the Western Pacific Region have already met the three 2015 targets for reductions in TB disease burden; the South-East Asia Region appears on track to do so. The other three regions are unlikely to meet the 2015 targets, although incidence, prevalence and mortality rates are falling. Among the 22 high burden countries (HBCs) that account for over 80% of the world's TB cases, 10 appear on track to achieve all three global targets.

Between 2000 and 2013, TB diagnostic and treatment interventions saved an estimated 37 million lives.

Although most TB cases and deaths occur among men, the burden of disease is also high among women. In 2013, an estimated 510 000 women died from TB (330 000 among HIV-negative women and 180 000 among HIV-positive women). An estimated 80 000 HIV-negative children died from TB (estimates for HIV-positive children are not yet available).

The burden of disease caused by TB can be measured in terms of incidence (defined as the number of new and relapse cases of TB arising in a given time period, usually one year), prevalence (defined as the number of cases of TB at a given point in time) and mortality (defined as the number of deaths caused by TB in a given time period, usually one year).

This chapter presents estimates of TB incidence, prevalence and mortality (absolute numbers and rates) between

1990 and 2013 and forecasts up to 2015 for prevalence and mortality (in [sections 2.1–2.3](#)). These data are used to assess progress towards achieving the global targets for reductions in TB disease burden set for 2015: that incidence should be decreasing (MDG Target 6.c) and that prevalence and mortality rates should be halved by 2015 compared with 1990 ([Box 1.2 in Chapter 1](#)). Key aspects of the methods used to produce the estimates are provided at the beginning of each section; these methods are

periodically reviewed by an expert group and details are provided in an [online technical appendix](#).¹ Estimates of the number of incident TB cases among people living with HIV, the number of incident cases of MDR-TB, mortality due to MDR-TB and TB deaths disaggregated by HIV status are included in the relevant sections. Estimates are presented globally, for the six WHO Regions, and at country level with particular focus on the 22 HBCs. In response to increasing demand and global attention to maternal and child health, special consideration is given to estimates of TB disease burden among women and children.

A summary of key updates to data sources and methods used to produce the estimates of TB disease burden presented in this chapter compared with those used in 2013, and associated results, is provided in [Box 2.1](#). Among these, the results from the first-ever survey of the national prevalence of TB disease in Nigeria have affected global estimates of TB burden. The main findings and programmatic implications of this survey are highlighted in [Box 2.2](#).

There is uncertainty in all estimates of the burden of disease caused by TB, whether published by WHO or other sources. The final section of the chapter ([Section 2.4](#)) profiles efforts to improve measurement of the burden of disease caused by TB under the umbrella of the WHO Global Task Force on TB Impact Measurement. The recent and unprecedented progress in implementing national TB prevalence surveys is described and expanding efforts to strengthen surveillance of cases and deaths via notification and vital registration (VR) systems are discussed. [Section 2.4](#) also includes a comparison of the latest WHO estimates contained in this report with other estimates that were published in peer-reviewed journals in 2014.

2.1 TB incidence

TB incidence has never been measured at national level because this would require long-term studies among large cohorts of people (hundreds of thousands), involving high costs and challenging logistics. Notifications of TB cases provide a good proxy indication of TB incidence in countries that have both high-performance surveillance systems (for example, there is little underreporting of diagnosed cases) and where the quality of and access to health care means that few cases are not diagnosed. In the large number of countries where these criteria are not yet met, better estimates of TB incidence can be obtained from an inventory study (an inventory study is a survey to quantify the level of underreporting).² To date, such studies have been undertaken in only a few countries: examples include Egypt, Iraq, Pakistan and Yemen (see [section 2.4](#)).

The ultimate goal is to directly measure TB incidence from TB notifications in all countries. This requires a combination of strengthened surveillance, better quantification of underreporting (i.e. the number of cases that

are missed by surveillance systems) and universal access to health care. A *TB surveillance checklist* developed by the WHO Global Task Force on TB Impact Measurement defines the standards that need to be met for notification data to provide a direct measure of TB incidence (further details in [section 2.4](#)).

For most countries, incidence estimates are currently based on notification data combined with country consultations in which in-depth analyses of the available surveillance, survey and programmatic data are undertaken, and expert opinion about the fraction of cases diagnosed but not reported, or not diagnosed at all, is elicited and documented. The 96 countries (with 89% of estimated TB cases) covered by such consultations since 2008 are shown in [Figure 2.1](#). For remaining countries not covered in workshops and in which notifications do not provide a good proxy indication of TB incidence, estimates are based on extending previously published time series, mortality data from VR systems combined with evidence about the case fatality rate, or ecological modelling (details are provided in the [online technical appendix](#)).

In 2013, there were an estimated 9.0 million incident cases of TB (range, 8.6 million–9.4 million) globally, equivalent to 126 cases per 100 000 population ([Table 2.1](#), [Table 2.2](#)). The absolute number of incident cases is falling slowly ([Figure 2.2](#)), at an average rate of 1.5% per year 2000–2013 and 0.6% between 2012 and 2013.

Most of the estimated number of cases in 2013 occurred in Asia (56%) and the African Region (29%);³ smaller proportions of cases occurred in the Eastern Mediterranean Region (8%), the European Region (4%) and the Region of the Americas (3%). The 22 HBCs that have been given highest priority at the global level since 2000 (listed in [Table 2.1](#) and [Table 2.2](#)) accounted for 82% of all estimated incident cases worldwide. The six countries that stand out as having the largest number of incident cases in 2013 were India (2.0 million–2.3 million), China (0.9 million–1.1 million), Nigeria (340 000–880 000), Pakistan (370 000–650 000), Indonesia (410 000–520 000) and South Africa (410 000–520 000); these and the other five countries that make up the top ten in terms of numbers of cases are highlighted in [Figure 2.3](#). India and China alone accounted for 24% and 11% of global cases, respectively. Of the 9.0 million incident cases, an estimated 550 000 were children and 3.3 million (range, 3.2–3.5 million) occurred among women ([Box 2.3](#)).

The 9.0 million incident TB cases in 2013 included 1.0 million–1.2 million (11–14%) among people living with

¹ The online technical appendix is available at www.who.int/tb/data.

² Inventory studies can be used to measure the number of cases that are diagnosed but not reported. If certain conditions are met, results can also be used to estimate TB incidence using capture-recapture methods. A guide on inventory studies is available at: www.who.int/tb/publications/inventory_studies/en/index.html.

³ Asia refers to the WHO Regions of South-East Asia and the Western Pacific.

Updates to estimates of TB disease burden in this report and updates that are anticipated in the near future

Each year, new data become available for the estimation of TB disease burden. Periodically, methods for using surveillance and survey data as well as other sources of information to estimate TB disease burden are reviewed and updated. This box provides a summary of updates that were made in 2014. Updates for specific countries that are expected in the near future, pending the finalization of results from recently completed national prevalence surveys, are also highlighted.

Updates in this report

1. Updates based on new data from national TB prevalence surveys

At the end of 2013, final results became available from national TB prevalence surveys implemented between 2011 and 2013 in five countries: Gambia, Lao PDR, Nigeria, Pakistan and Rwanda. Survey results have been used to update estimates of TB burden in these countries (Figure 2.1.1; this also shows results for five other countries where surveys were implemented between 2007 and 2010). In Pakistan and Rwanda, updated estimates are similar to those published in previous global TB reports. In the Gambia, burden estimates have been revised downwards. In Lao PDR and Nigeria, burden estimates have been revised upwards. In Nigeria, the best estimate of the burden of prevalent TB based on survey results is approximately two times higher than the previous estimate. Given the size of Nigeria's population and TB burden, this upward revision in burden estimates affects global estimates of the absolute number of TB cases and deaths (but not overall global trends).

2. Expanded use of the Spectrum software programme

For the first time in 2013, estimates of TB incidence among people living with HIV and TB mortality among HIV-positive people were generated using the Spectrum software programme.^a Spectrum has been used for more than a decade to produce estimates of the burden of disease caused by HIV, to build projections about

the future course of the HIV epidemic and to assess the potential impact of TB prevention and treatment interventions. A TB module was developed in 2012 and 2013 through a collaboration among the Futures Institute, the TB Modelling and Analysis Consortium (TB-MAC) hosted at the London School of Hygiene and Tropical Medicine, UNAIDS and WHO. In 2014, the use of Spectrum was expanded to generate not only estimates of HIV-positive TB incidence and mortality but also indirect estimates of HIV-negative TB mortality for countries without VR or mortality survey data. Details are provided in the [online technical appendix](#).

3. Newly reported data

There are some relatively small changes to estimates of TB incidence, mortality and prevalence for many countries that reflect new VR data reported to WHO between mid-2013 and mid-2014, updated WHO estimates of the total number of deaths from all causes (that provide overall mortality envelopes), updates to estimates of the burden of HIV-associated TB and new TB notification data including corrections made to historical data. In most instances, changes are well within the uncertainty intervals of previously published estimates of TB burden and time trends are generally consistent. Newly-reported data are the reason for small changes to estimates of the number of TB deaths among women and children and to the number of incident MDR-TB cases.

4. In-depth epidemiological reviews

Updates to burden estimates have drawn on new analyses undertaken as part of in-depth epidemiological reviews. These have increased in frequency since 2013, linked to the requirements of the Global Fund's new funding model. Epidemiological reviews are also helping to identify performance gaps in TB surveillance and form the basis of detailed and costed monitoring and evaluation plans.

Updates anticipated in the near future

Updates to estimates of disease burden are expected in several countries that have recently completed or will soon complete national TB prevalence surveys. These include: Ghana, Indonesia, Malawi, Mongolia, Sudan, the United Republic of Tanzania, Thailand, Zambia and Zimbabwe. Future updates will be made available in online country profiles and associated data sets. It is anticipated that updated estimates for Indonesia will have an impact on global estimates.

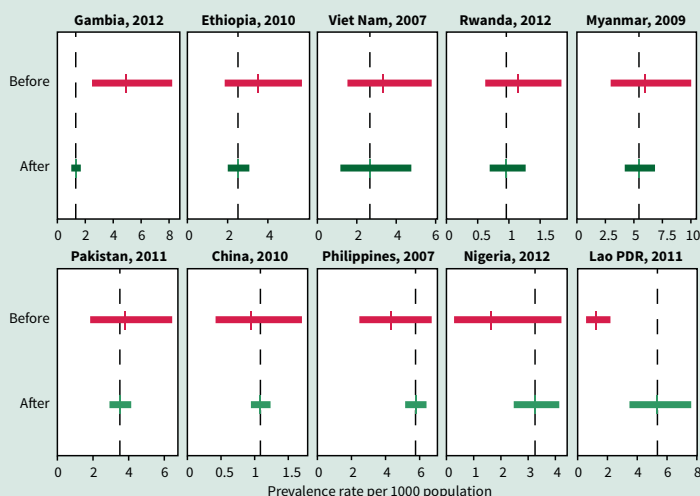
There is increasing country interest in inventory studies to directly measure under-reporting of cases (i.e. the number of cases that is detected but not reported to NTPs). If such studies are implemented, they may result in updates to estimates of TB burden, especially TB incidence.

In early 2015, following extensive preparations, a thorough review of the current epidemiological and modelling methods used to estimate TB disease burden will be conducted by an expert group convened by the WHO Global Task Force on TB Impact Measurement (see also section 2.4). The recommendations may result in some further updates in the 2015 global TB report.

^a <http://www.futuresinstitute.org/spectrum.aspx>

FIGURE B2.1.1

Estimates of TB prevalence (all ages, all forms of TB) for 10 countries, before and after results from national TB prevalence surveys became available. Panels are ordered by the size of the before-after difference. Crosses mark the best estimate and the horizontal lines mark 95% uncertainty intervals.



The first-ever national TB prevalence survey in Nigeria: main results and their implications

The first-ever national survey of the prevalence of TB disease in Nigeria was implemented in 2012, under the leadership of the National TB and Leprosy Control Programme (NTLCP). The main objective of the survey was to estimate the prevalence of pulmonary TB (bacteriologically confirmed i.e. sputum smear and/or culture positive) among the general population aged ≥15 years old.

Methods and main results

Survey design and overall methods followed the international recommendations of the WHO Global Task Force on TB Impact Measurement.^a All survey participants were screened for symptoms by interview and by chest X-ray examination. Participants with any current symptom suggestive of TB or radiological lesion(s) in the lung were requested to submit two sputum specimens (one spot and one early-morning) that were examined by microscopy (AFB) and culture (LJ solid media) in one of three laboratories – the Nigeria Institute of Medical Research (NMIR),

FIGURE B2.2.1

Consort diagram of the 2012 national TB prevalence survey in Nigeria

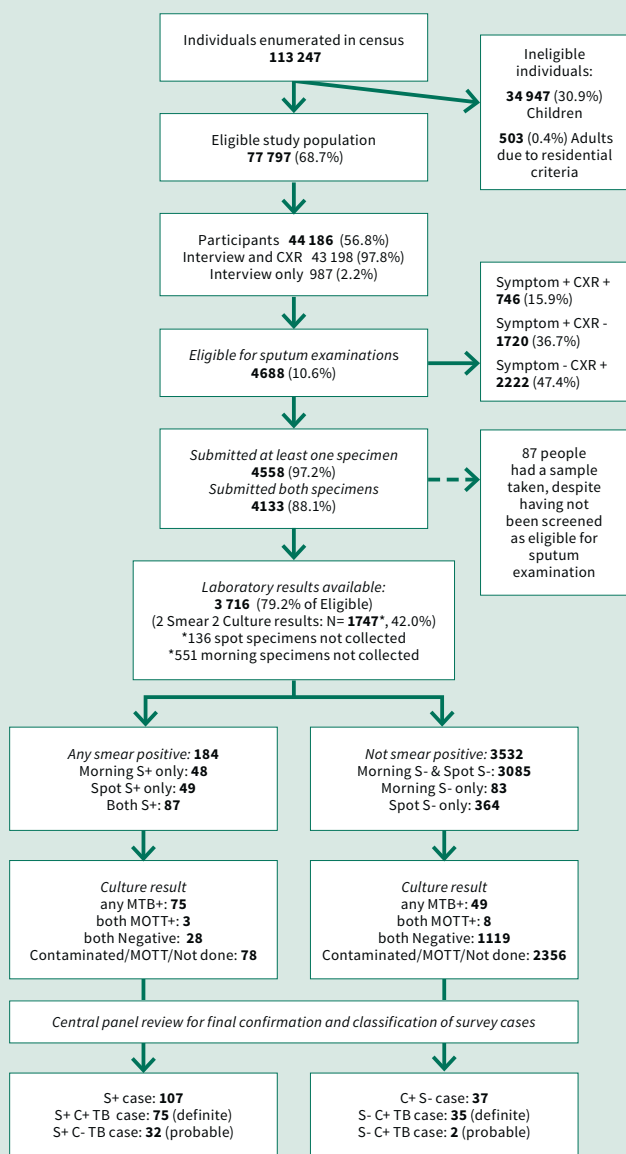
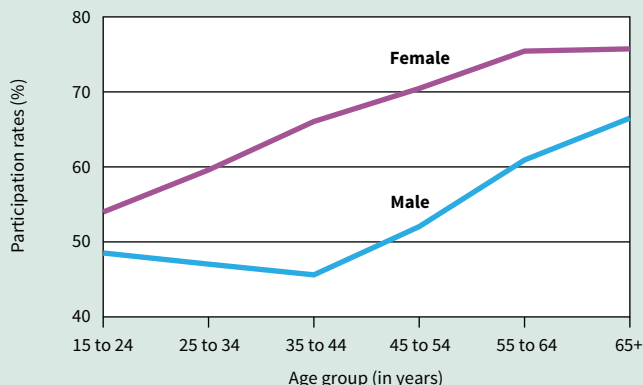


FIGURE B2.2.2

Survey participation rate by age group and sex



the National Tuberculosis and Leprosy Training Centre (NTBLTC), and the Zankli Medical Centre in Abuja.

A total of 113 247 people of all ages were enumerated during the survey, which covered 70 randomly selected clusters. Of these, 77 797 (69%) were eligible and invited to participate in the survey based on age (≥15 years old) and residency status (residents were defined as having slept in the household for 14 days or more at the day of the survey census). Of those who were eligible, 44 186 persons (57%) participated in the survey’s cluster operations, and of these 4 688 (10.6%) screened positive for TB (based on reported symptoms and/or chest X-ray result) and submitted at least one sputum specimen for bacteriological examination (Figure B2.2.1). The average number of participants per cluster was 631 (with a range of 279–819). Female participation was higher (59%) compared with male participation (41%) (Figure B2.2.2).

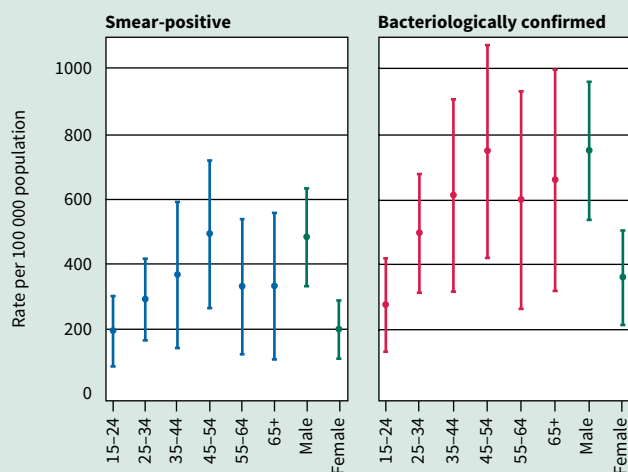
Among participants whose sputum specimens were processed, there were 107 smear-positive TB and 37 smear-negative/culture-positive TB cases, giving a total of 144 bacteriologically confirmed pulmonary TB cases. Among the 107 smear-positive TB cases, 80 (75%) reported TB symptoms during the screening process and 94 (88%) had a positive chest X-ray. Of the 144 bacteriologically confirmed cases, 92 (64%) reported TB symptoms during the screening process and 128 (89%) had a positive chest X-ray.

The crude prevalence of smear-positive TB among participants aged 15 years or older was 256 per 100 000 population (95% CI: 178–333) while the case notification rate of smear-positive TB cases (2012) in this age group was approximately 50 per 100 000 population, giving a prevalence:notification (P:N) ratio of 5.

Best-practice analytical methods were used to estimate TB prevalence accounting for clustered sampling, as well as non-participation and other missing data. TB prevalence rates per 100 000 population aged ≥15 years old were estimated to be 318 (95% CI: 225–412) for smear-positive TB, and 524 (95% CI: 378–670) for bacteriologically confirmed TB. Smear-positive TB prevalence among men was 484 (95% CI: 333–635) per 100 000 population, and 198 (95% CI: 108–289) per 100 000 population among women (Figure B2.2.3). For bacteriologically confirmed TB, the figures were 751 (95% CI: 538–965) and 359 (95% CI: 213–505) per 100 000 for men and women, respectively. An age differential in TB prevalence was also observed, with the highest burden of disease among the those aged 35–54 years old i.e. the most economically productive age groups.

FIGURE B2.2.3

Age and sex-specific TB prevalence rates, for both smear-positive and bacteriologically confirmed TB, per 100 000 and associated 95% confidence intervals



The prevalence of TB disease varied geographically, and was considerably higher in urban compared with rural areas (Figure B2.2.4).

A total of 82 survey participants (0.2%) reported being on TB treatment at the time of the survey (37 men and 45 women, with 39 residing in urban areas). There were 552 (1.2%) survey participants who reported a past history of TB treatment (281 men and 271 women). Most of these people reported taking treatment in general hospitals (49%), followed by health centres/primary health centres (22%), teaching hospitals (11%), and private hospitals (10%). Only one person reported taking treatment at a pharmacy.

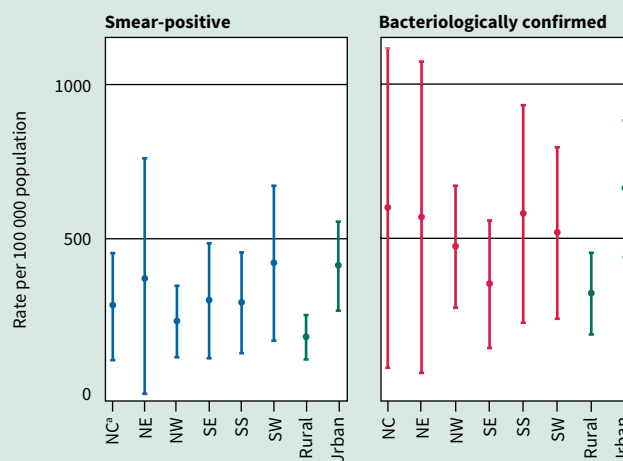
Lessons learned and programmatic implications

Notwithstanding the challenges of a low participation rate along with issues of security in some districts, the survey results are of high quality and have contributed towards a much better understanding and robust measurement of the burden of TB disease in Nigeria.

Amongst all national TB prevalence surveys since 2001 (data not shown), Nigeria has the highest prevalence to annual case notification ratio, at approximately 5 to 1. Such a high ratio was typically observed in national TB prevalence surveys in Asia before TB diagnostic and treatment services had been fully expanded and decentralized to the lowest levels of the health system. The high proportion (75%) of prevalent smear-positive cases in the community that reported typical TB symptoms also shows that TB diagnostic and treatment services of high quality still need to be made more accessible. Building on the past decade of efforts by the NTLCP and its partners to improve TB diagnosis and treatment, further strengthening and decentralization of TB diagnostic and treatment services are required. This should lead to a reduction in the proportion of prevalent cases that report TB symptoms. The geographical variation in the

FIGURE B2.2.4

Zonal and urban/rural TB prevalence rates, for both smear-positive and bacteriologically confirmed TB, per 100 000 and associated 95% confidence intervals



^a NC=North Central; NE=North East; NW=North West; SE=South East; SS=South South; SW=South West

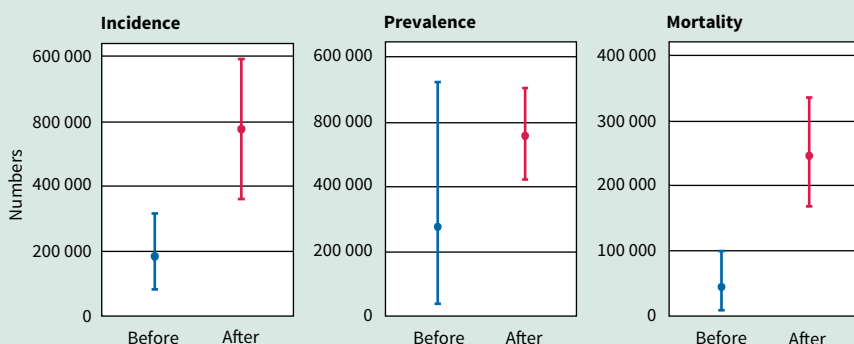
burden of disease also suggests that intensified case finding activities are a particular priority in urban slum areas.

Implications of survey results for national, regional and global estimates of TB disease burden

Results from the national TB prevalence survey in Nigeria have provided a robust direct measurement of TB disease burden in the country for the first time. Before survey results became available, indirect estimates of TB disease burden were calculated based mainly on reported TB case notification data and expert opinion about the levels of underreporting and underdiagnosis of cases. Case notification data were known to underestimate the true burden due to recognized problems with case detection.^b Based on the new prevalence survey results, burden estimates have been updated (see also Box 2.1) not only for prevalence (with appropriate adjustments for children and extra-pulmonary TB) but also for incidence (indirectly estimated from prevalence using plausible distributions of disease duration) and mortality (indirectly estimated from prevalence using case fatality ratios estimated from literature reviews). More details are provided in the [online technical appendix](#). These updates have resulted in large upward revisions to estimates of TB disease burden in

FIGURE B2.2.5

2012 TB disease burden estimates for Nigeria in absolute numbers, before and after TB prevalence survey results



BOX 2.2 (CONTINUED)

Nigeria (Figure B2.2.5). Compared with the previously published best estimates for 2012, the new estimates in this report are 200% higher for incidence, 100% higher for prevalence and 400% higher for mortality (the greater impact on estimated mortality is due to the larger than previously estimated number of untreated cases). The estimated case detection rate (notifications of new and relapse cases divided by estimated incidence) has also decreased and the estimate for 2013 is 16% (95% uncertainty interval 11–30%).

Due to the size of the country's population, these increases to estimates of TB disease burden in Nigeria also affect global es-

timates and estimates for the African Region. TB mortality in the African Region in 2013 is now estimated to be 44% higher than the previously published estimate for 2012. Global estimates of the absolute number of TB cases and deaths have also been revised upwards.

^a *Tuberculosis prevalence surveys: a handbook*. Geneva: World Health Organization; 2010 (WHO/HTM/TB/2010.17). Available at: http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/resources_documents/thelimebook/en/

^b *Joint External mid-term evaluation of the Nigeria national tuberculosis and leprosy control strategic plan 2010–2015*. 8–18 April 2013.

FIGURE 2.1

Coverage of country consultations on estimates of TB disease burden, 2008–2014

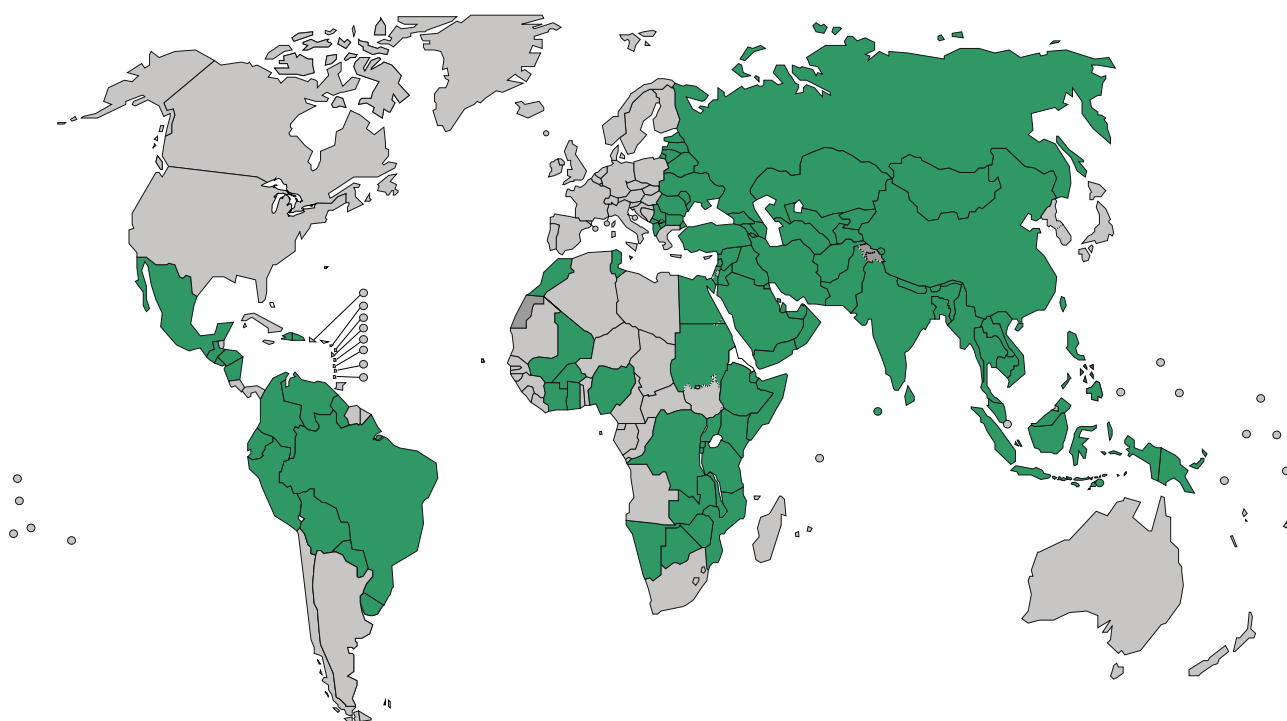
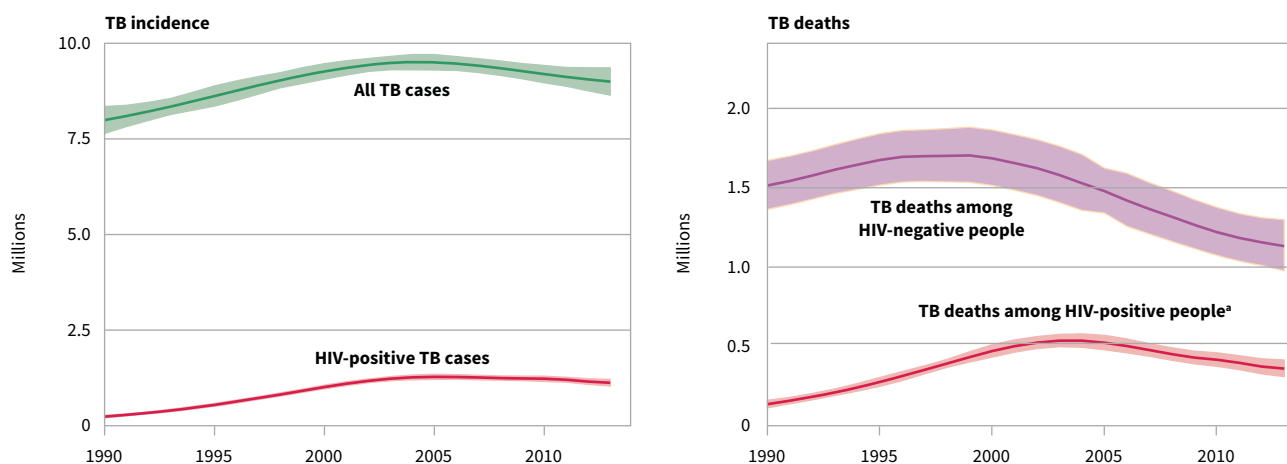


FIGURE 2.2

Estimated absolute numbers of TB cases and deaths (in millions per year), 1990–2013



^a HIV-associated TB deaths are classified as HIV deaths according to ICD-10.

TABLE 2.1

Estimated epidemiological burden of TB, 2013. Best estimates are followed by the lower and upper bounds of the 95% uncertainty interval. Numbers in thousands^a

	POPULATION	MORTALITY ^b		HIV-POSITIVE TB MORTALITY		PREVALENCE		INCIDENCE		HIV-POSITIVE INCIDENT TB CASES	
Afghanistan	30 552	13	8.4–16	<0.1	<0.1–0.1	100	54–170	58	51–65	0.2	0.2–0.2
Bangladesh ^c	156 595	80	51–110	0.2	0.1–0.2	630	330–1 000	350	310–400	0.4	0.2–0.5
Brazil	200 362	4.4	2.5–6.8	2.1	1.5–2.7	110	54–200	93	83–110	13	13–13
Cambodia	15 135	10	6.3–14	0.6	0.5–0.8	110	91–130	61	55–67	2.3	2.1–2.6
China	1 385 567	41	40–43	0.7	0.2–1.3	1 300	1 100–1 500	980	910–1 100	4.5	4.3–9.9
DR Congo	67 514	46	22–53	6.4	0.2–24	370	190–610	220	200–240	16	9.8–75
Ethiopia	94 101	30	16–47	5.6	3.6–8.0	200	160–240	210	180–260	22	19–32
India ^d	1 252 140	240	150–350	38	31–44	2 600	1 800–3 700	2 100	2 000–2 300	120	100–140
Indonesia ^e	249 866	64	36–93	3.9	2.2–6.2	680	340–1 100	460	410–520	15	8.7–20
Kenya	44 354	9.1	5.5–12	9.5	7.5–12	130	69–200	120	120–120	48	47–50
Mozambique	25 834	18	9.4–26	38	27–51	140	78–230	140	110–180	81	64–100
Myanmar	53 259	26	16–38	4.3	3.3–5.3	250	190–320	200	180–220	17	16–18
Nigeria	173 615	160	68–270	85	47–140	570	430–730	590	340–880	140	81–220
Pakistan	182 143	100	45–170	1.0	0.5–1.6	620	520–740	500	370–650	2.6	1.2–3.4
Philippines	98 394	27	25–29	<0.1	<0.1–<0.1	430	380–490	290	260–330	0.3	0.2–0.3
Russian Federation	142 834	17	17–18	1.4	1.0–1.9	160	74–290	130	120–140	7.9	6.9–9.1
South Africa	52 776	25	15–38	64	47–83	380	210–590	450	410–520	270	240–310
Thailand	67 011	8.1	4.9–12	1.9	1.3–2.4	100	48–170	80	71–90	12	10–13
Uganda	37 579	4.1	2.2–6.6	7.2	5.0–9.9	58	32–91	62	56–73	32	29–38
UR Tanzania	49 253	6.0	3.4–8.2	6.1	4.8–7.5	85	45–140	81	77–84	30	29–31
Viet Nam	91 680	17	12–24	2.0	1.2–2.9	190	79–350	130	110–160	9.4	8.0–12
Zimbabwe	14 150	5.7	3.6–7.4	22	17–27	58	33–89	78	67–91	56	48–66
High-burden countries	4 484 710	960	810–1 100	300	250–350	9 300	8 200–11 000	7 400	7 100–7 800	910	820–990
AFR	927 371	390	300–500	300	250–350	2 800	2 400–3 200	2 600	2 300–2 900	870	790–960
AMR	970 821	14	12–17	6.1	5.5–6.8	370	290–460	280	270–300	32	31–33
EMR	616 906	140	90–210	1.8	1.3–2.4	1 000	880–1 200	750	620–890	5.1	4.0–6.4
EUR	907 053	38	37–39	3.8	3.2–4.4	460	350–590	360	340–370	21	20–22
SEAR	1 855 068	440	330–550	48	42–55	4 500	3 500–5 700	3 400	3 200–3 600	170	150–190
WPR	1 858 410	110	100–120	4.8	3.7–5.9	2 300	2 000–2 500	1 600	1 500–1 700	23	19–26
Global	7 135 628	1 100	980–1 300	360	310–410	11 000	10 000–13 000	9 000	8 600–9 400	1 100	1 000–1 200

^a Numbers for mortality, prevalence and incidence shown to two significant figures. Totals (HBCs, regional and global) are computed prior to rounding.

^b Mortality excludes deaths among HIV-positive TB cases. Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD-10 and are shown separately in this table.

^c Estimates of TB disease burden have not been approved by the national TB programme in Bangladesh and a joint reassessment will be undertaken following completion of the prevalence survey planned for 2015.

^d Estimates for India have not yet been officially approved by the Ministry of Health & Family Welfare, Government of India, and should therefore be considered provisional.

^e As this report went to press, estimates for Indonesia were being revised based on the results of the 2013–2014 national TB prevalence survey. Updated estimates will be published online. See also [Box 2.1](#).

HIV, with a best estimate of 1.1 million (13%) ([Table 2.1](#), [Table 2.2](#)). The proportion of TB cases co-infected with HIV was highest in countries in the African Region ([Figure 2.4](#)). Overall, 34% of TB cases were estimated to be co-infected with HIV in this region, which accounted for 78% of TB cases among people living with HIV worldwide. In parts of southern Africa, more than 50% of TB cases were co-infected with HIV ([Figure 2.4](#)).

Following a systematic review of evidence about mortality caused by MDR-TB undertaken in 2013 (featured in the 2013 global TB report) and consensus about what

indicators to use for reporting on the burden of MDR-TB ([Chapter 5](#), [Box 5.3](#)), this report includes updated global estimates of MDR-TB incidence and mortality. The best estimate is that there were 480 000 (range, 350 000–610 000) new cases of MDR-TB worldwide in 2013. This total includes cases of primary and acquired MDR-TB.

The number of incident TB cases relative to population size (the incidence rate) varies widely among countries ([Figure 2.5](#)). The lowest rates are found predominantly in high-income countries including most countries in western Europe, Canada, the United States of America,

The burden of TB disease among women and children

With increasing global attention to maternal and child health, there has been growing demand for and interest in estimates of TB disease burden among women and children. Estimates of the global burden of TB disease among children (defined as people aged <15 years) have been published in this report since 2012 and this is the second year in which the report includes estimates of the burden among women (defined as females aged ≥15 years) disaggregated by WHO region and HIV status.

There were an estimated 3.3 million new cases of TB and 510 000 deaths from the disease among women in 2013. Among children, there were an estimated 550 000 new cases in 2013 and 80 000 deaths among children who were HIV-negative. The estimates of TB morbidity and mortality among women are slightly higher than those published in the 2013 global TB report, due to upward revisions in estimates of the total number of incident TB cases and TB deaths (Box 2.1). The estimates of TB morbidity and mortality among children are slightly higher than those published in the 2013 global TB report, reflecting the use of an ensemble approach to combine two different independent calculations of incidence among children globally, and new VR data. Methods used to produce these estimates and further details about results are provided below.

The burden of TB in women: estimates of TB incidence and mortality, 2013

Incidence

Regional estimates of the women:men ratio for new and relapse TB case notifications in 2013 were generated and assumed to be the same as the ratio among incident TB cases in 2013 (see [online technical appendix](#) for further details). The resulting global and regional estimates of incidence are shown in [Table B2.3.1](#). Women account for 37% of the total of 9.0 million incident cases in 2013. The African and South-East Asia regions account for 69% of the cases among women.

TABLE B2.3.1

Total number of new and relapse TB case notifications (among countries reporting notification data disaggregated by sex) and estimated incident cases among women in 2013, globally and for WHO regions

WHO REGION	NUMBER OF TB CASE NOTIFICATIONS AMONG WOMEN	ESTIMATED TB INCIDENCE AMONG WOMEN	
		BEST ESTIMATE	UNCERTAINTY INTERVAL
AFR	390 808	990 000	880 000–1 100 000
AMR	73 905	100 000	96 000–110 000
EMR	180 917	330 000	270 000–390 000
EUR	84 508	120 000	110 000–130 000
SEAR	234 190	1 300 000	1 200 000–1 400 000
WPR	346 537	510 000	480 000–530 000
Global	1 310 865	3 300 000	3 200 000–3 500 000

Mortality

In total, there were an estimated 510 000 TB deaths among women in 2013. This includes 330 000 (range, 290 000–380 000) TB deaths among HIV-negative women (30% of all TB deaths among HIV-negative adults) and 180 000 (range, 160 000–210 000) HIV-associated TB deaths (50% of all HIV-associated TB deaths). Newly reported data and upward revisions to the total estimated number of TB deaths (Box 2.1) are the reason why numbers are higher compared with those published in 2013.

Mortality data disaggregated by age and sex from VR systems were used to produce estimates of TB deaths among HIV-negative adults for 111 countries. TB deaths were calculated for women and men, after adjustment for incomplete coverage and ill-defined causes (see [online technical appendix](#) for further details). For countries without VR data, the ratio of the adjusted male:female number of deaths due to TB was estimated using an imputation model that included risk factors known to be associated with TB mortality. Globally, there were an estimated 2.14 (range, 1.56–2.73) male deaths among HIV-negative adults for every female death ([Figure B2.3.1](#)). Regional differences are evident ([Table B2.3.2](#)), with the African and South-East Asia regions accounting for 73% of total deaths. The main limitation in the methods used is that the 111 countries reporting usable VR data were all middle- or high-income countries. Predictions for low-income countries had to be extrapolated from these countries.

TB deaths among HIV-positive people were disaggregated by sex using the assumption that the male to female sex ratio is similar to the sex ratio of AIDS deaths estimated by UNAIDS. Globally, the numbers of HIV-associated TB deaths were similar among men and women ([Figure B2.3.2](#)). However, there were striking regional variations ([Table B2.3.2](#)). In the African Region, more deaths occurred among women than men, while in other regions more deaths were estimated to have occurred among men.

TABLE B2.3.2

Estimated number of TB deaths among women in 2013, globally and for WHO regions

	HIV-NEGATIVE		HIV-POSITIVE	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	BEST ESTIMATE	UNCERTAINTY INTERVAL
AFR	110 000	79 000–130 000	160 000	140 000–190 000
AMR	4 300	3 600–5 000	2 100	1 900–2 300
EMR	44 000	33 000–54 000	990	840–1 200
EUR	11 000	10 000–11 000	990	850–1 100
SEAR	130 000	100 000–170 000	17 000	14 000–20 000
WPR	36 000	33 000–39 000	1 200	1 000–1 400
Global	330 000	290 000–380 000	180 000	160 000–210 000

The burden of TB in children: estimates of TB notifications, incidence and mortality (among those HIV-negative), 2013

A global consultation on estimates of TB disease burden among children was held in September 2013. Outcomes of the consultation included the further development of analytical methods, strengthening of collaboration between WHO and research groups and the definition and prioritization of actions needed to obtain more and better data.

TB notifications and incidence

Among countries that reported age-disaggregated notification data for 2013 ([Figure B2.3.3](#)), the total number of new and relapse cases among children was 275 000. Compared with 2012, fewer cases were notified in India (about 15 000 less) and the Democratic Republic of the Congo (about 10 000 less). For countries that did not report age-disaggregated data,^a the ratio of child to adult notified cases was assumed to be the same as in those countries that did report notifications disaggregated by age. The estimated global number of TB case notifications among chil-

dren in 2013, after accounting for countries that did not report age-disaggregated data, was 300 000.

To estimate TB incidence among children, an ensemble approach was used to combine results from two independent methods (see [online technical appendix](#) for further details). The first method calculated child:adult ratios for new and relapse TB case notifications in 2013 and assumed those to be the same as the ratio among incident TB cases in 2013. These ratios were then used to disaggregate global TB incidence among children and adults. The second method was a mechanistic mathematical model, which estimated incidence in children using adult TB prevalence estimates and parameters related to the natural history of paediatric TB.^b The resulting estimate of global TB incidence among children in 2013, based on the combination of findings from two independent methods, is 550 000 (range, 470 000–640 000), equivalent to about 6% of the total number of 9.0 million incident cases.

Limitations of the methods used include:

- The assumption that reported cases were true cases of TB. Misdiagnosis is possible, especially given the difficulties of diagnosing TB in children.
- The assumption that the case detection rate is the same for adults and children, in the absence of any data on levels of underreporting of diagnosed cases for children and adults separately.
- The proportion of cases among children may be different in countries for which age-disaggregated data were not available. However, this is becoming less of a problem as the reporting of cases disaggregated by age has been improving and the number of countries not reporting age-disaggregated data was low in 2013 ([Figure B2.3.3](#)).

Mortality among HIV-negative children

Mortality data reported to WHO from VR systems that were disaggregated by age were available for 111 countries. These data were used to calculate TB death rates per 100 000 population for children and adults, after adjustment for incomplete coverage and ill-defined causes (see [online technical appendix](#) for further details). For countries without VR data, the adjusted child:adult ratio of the number of TB deaths was imputed using a model that included risk factors that are known to be associated with TB mortality. The estimated total number of deaths from TB among HIV-negative children in 2013 was 80 000 (range, 64 000–97 000), equivalent to about 7% of the total number of 1 100 000 TB deaths among HIV-negative people in 2013.

FIGURE B2.3.1

The male:female ratio for HIV-negative TB deaths among adults (aged ≥15 years), globally and for WHO regions

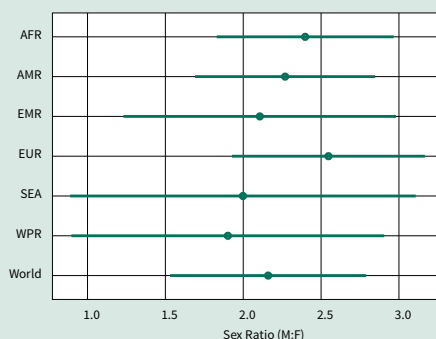
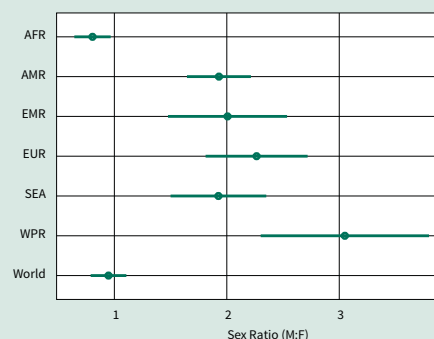


FIGURE B2.3.2

The male:female ratio for HIV-associated TB deaths among adults (aged ≥15 years), globally and for WHO regions



An estimate of TB mortality among HIV-positive children is not yet available, due to the difficulties arising from the miscoding of HIV deaths as TB deaths. Age-disaggregation of HIV-associated TB mortality will be one of the future outcomes of the TB component of Spectrum ([Box 2.1](#)).

Steps to improve estimation of TB cases among children include:

- promotion of case-based electronic recording and reporting systems that facilitate compilation and analysis of age-disaggregated data;
- nationwide inventory surveys to measure underreporting of childhood TB;
- more contact-tracing studies and the integration of TB activities in maternal, newborn and child health services to find childhood cases that might otherwise not be diagnosed.

^a In the updated recording and reporting framework issued by WHO in 2013 ([Chapter 4](#)), it is recommended that age-disaggregated data are reported for all new and relapse cases.

^b Dodd PJ, Gardiner E, Coghlan E, Seddon JA. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Global Health* 2014: [http://dx.doi.org/10.1016/S2214-109X\(14\)70245-1](http://dx.doi.org/10.1016/S2214-109X(14)70245-1).

FIGURE B2.3.3

Reporting of new and relapse TB case notifications disaggregated by age, 2013

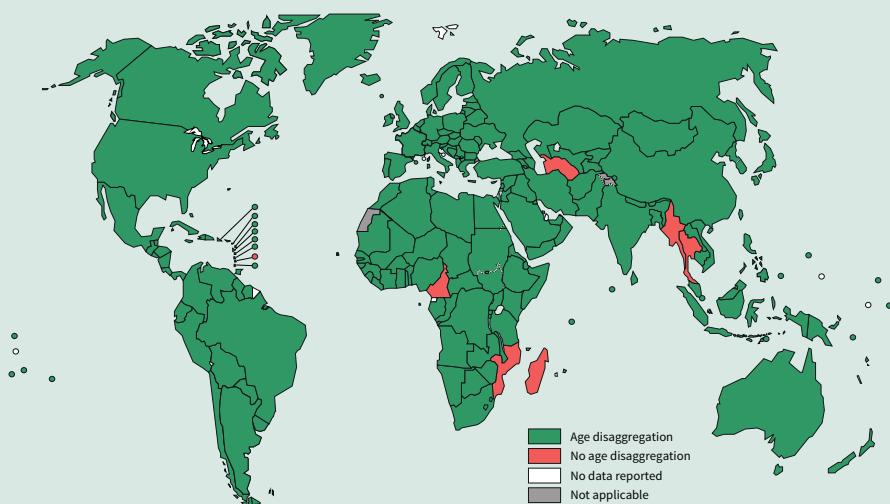


TABLE 2.2

Estimated epidemiological burden of TB, 2013. Best estimates are followed by the lower and upper bounds of the 95% uncertainty interval. Rates per 100 000 population except where indicated.

	POPULATION (THOUSANDS)	MORTALITY ^a		HIV-POSITIVE TB MORTALITY		PREVALENCE		INCIDENCE		HIV PREVALENCE IN INCIDENT TB CASES (%)	
Afghanistan	30 552	42	27–53	0.3	0.2–0.3	340	178–554	189	167–212	0.34	0.29–0.40
Bangladesh ^b	156 595	51	33–69	0.1	<0.1–0.2	402	210–656	224	199–253	0.12	<0.1–0.16
Brazil	200 362	2.2	1.3–3.4	1.0	0.8–1.4	57	27–99	46	41–52	14	13–16
Cambodia	15 135	66	42–92	3.9	3.0–5.0	715	604–834	400	366–444	3.9	3.4–4.4
China	1 385 567	3.0	2.9–3.1	<0.1	<0.1–0.1	94	82–107	70	66–77	0.46	0.22–0.79
DR Congo	67 514	68	33–78	9.5	0.3–35	549	285–898	326	297–356	7.5	0.13–27
Ethiopia	94 101	32	17–50	5.9	3.8–8.5	211	170–257	224	188–276	11	7.4–14
India ^c	1 252 140	19	12–28	3.0	2.5–3.5	211	143–294	171	162–184	5.7	4.8–6.6
Indonesia ^d	249 866	25	14–37	1.6	0.9–2.5	272	138–450	183	164–207	3.2	2.1–4.5
Kenya	44 354	20	12–27	21	17–27	283	156–447	268	261–275	41	39–42
Mozambique	25 834	69	36–101	148	105–198	559	303–893	552	442–680	57	39–74
Myanmar	53 259	49	29–71	8.0	6.3–9.9	473	364–595	373	340–413	8.8	7.8–9.8
Nigeria	173 615	94	39–156	49	27–78	326	246–418	338	194–506	25	10–44
Pakistan	182 143	56	25–92	0.5	0.3–0.9	342	284–406	275	205–357	0.53	0.3–0.83
Philippines	98 394	27	25–29	<0.1	<0.1–<0.1	438	385–495	292	261–331	0.11	<0.1–0.14
Russian Federation	142 834	12	12–13	1.0	0.7–1.3	114	51–201	89	82–100	6.2	5.2–7.3
South Africa	52 776	48	28–73	121	90–158	715	396–1 130	860	776–980	61	50–71
Thailand	67 011	12	7.3–18	2.8	2.0–3.6	149	72–252	119	106–134	15	12–17
Uganda	37 579	11	5.8–18	19	13–26	154	85–243	166	149–193	52	42–62
UR Tanzania	49 253	12	7.0–17	12	9.8–15	172	92–277	164	157–170	37	35–39
Viet Nam	91 680	19	13–26	2.1	1.3–3.2	209	86–384	144	121–174	7.2	5.4–9.1
Zimbabwe	14 150	40	25–52	153	121–189	409	235–630	552	474–643	72	55–86
High-burden countries	4 484 710	21	18–25	6.7	5.6–7.9	208	183–235	165	158–173	12	11–14
AFR	927 371	42	32–54	32	27–38	300	263–341	280	251–311	34	29–39
AMR	970 821	1.5	1.2–1.7	0.6	0.6–0.7	38	30–48	29	28–31	11	11–12
EMR	616 906	23	15–34	0.3	0.2–0.4	165	143–189	121	100–144	0.94	0.67–1.2
EUR	907 053	4.1	4.0–4.2	0.4	0.4–0.5	51	39–65	39	38–41	6.0	5.6–6.4
SEAR	1 855 068	23	18–30	2.6	2.2–3.0	244	188–307	183	175–192	4.9	4.4–5.5
WPR	1 858 410	5.8	5.4–6.3	0.3	0.2–0.3	121	109–134	87	82–92	1.4	1.2–1.6
Global	7 135 628	16	14–18	5.0	4.3–5.8	159	143–176	126	121–131	13	12–14

^a Mortality excludes deaths among HIV-positive TB cases. Deaths among HIV-positive TB cases are classified as HIV deaths according to ICD-10 and are shown separately in this table.

^b Estimates of TB disease burden have not been approved by the national TB programme in Bangladesh and a joint reassessment will be undertaken following completion of the prevalence survey planned for 2015.

^c Estimates for India have not yet been officially approved by the Ministry of Health & Family Welfare, Government of India, and should therefore be considered provisional.

^d As this report went to press, estimates for Indonesia were being revised based on the results of the 2013–2014 national TB prevalence survey. Updated estimates will be published online. See also [Box 2.1](#).

Japan, Australia and New Zealand. In these countries, the incidence rate is less than 10 cases per 100 000 population per year. Most countries in the Region of the Americas have rates below 50 per 100 000 population per year and this is the region with the lowest burden of TB on average. Most of the HBCs have rates of around 150–300 cases per 100 000 population per year ([Table 2.2](#)); HBCs with markedly lower rates in 2013 were Brazil, China and the Russian Federation, while rates were above 500 per 100 000 population in Mozambique, South Africa and Zimbabwe. Other countries in the top ten worldwide in terms of inci-

dence rates in 2013 were mostly in Africa ([Figure 2.3](#)). In Lesotho, South Africa and Swaziland, the best estimates suggest that about 1 person in every 100 (1000 per 100 000 population) develops active TB each year.

Globally, the incidence rate was relatively stable from 1990 up until around 2000, and then started to fall ([Figure 2.6](#)), achieving the MDG target ahead of the 2015 deadline. Between 2000 and 2013, the average rate of decline per year was 1.5%. This downward trend needs to be sustained to ensure that the MDG target is met in 2015. Incidence rates are also declining in all of six WHO

FIGURE 2.3

Estimated TB incidence: top-ten countries, 2013

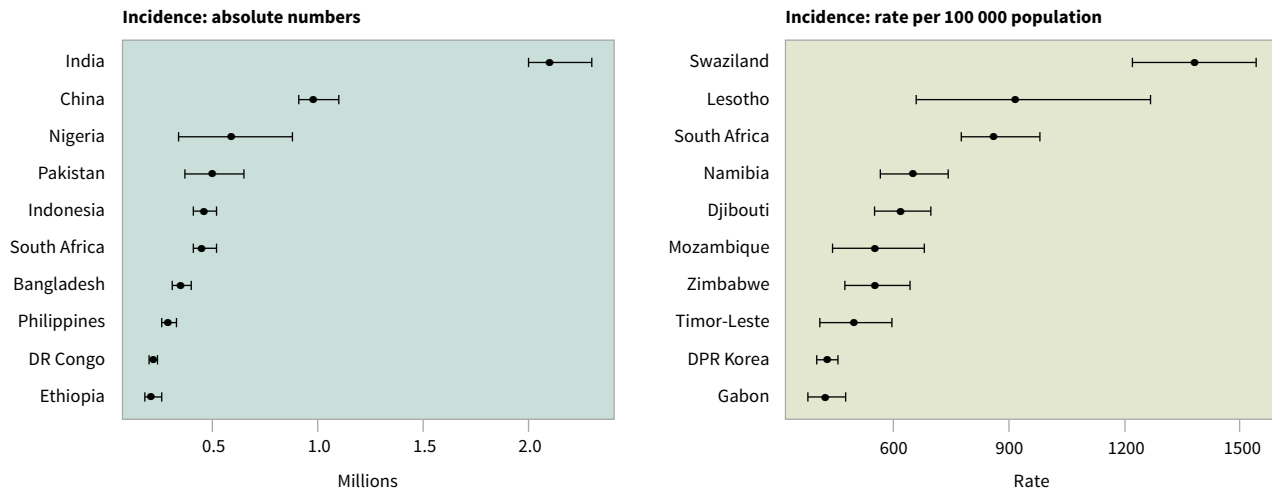
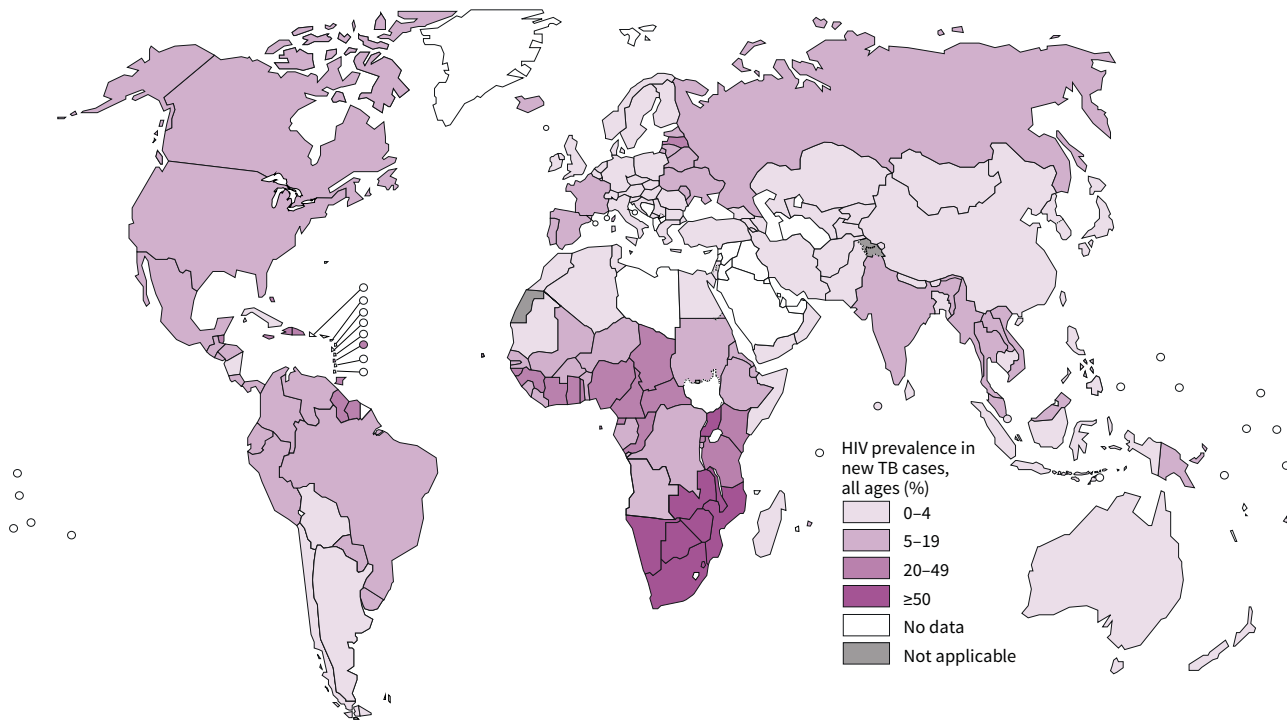


FIGURE 2.4

Estimated HIV prevalence in new and relapse TB cases, 2013



regions (Figure 2.7), fastest in the European Region (4.5% per year) and slowest in the Eastern Mediterranean and South-East Asia Regions (less than 1% per year and 1.5% per year, respectively). Incidence rates have been falling since around 2000 in the South-East Asia Region; they peaked around 1999 in the European Region and around 2003 in the African region, and have been falling since 1990 in Eastern Mediterranean Region, the Region of the Americas and the Western Pacific Region. The latest assessment for the 22 HBCs suggests that incidence rates are falling in most countries (Figure 2.8).

2.2 TB prevalence

In countries with a relatively high burden of TB (around 100 cases per 100 000 population or more), the prevalence of bacteriologically confirmed pulmonary TB can be directly measured in nationwide population-based surveys using sample sizes of around 50 000 people. Survey results can be used to produce a national estimate of TB prevalence that includes all forms of TB. The cost of a survey usually ranges from US\$ 1 to 4 million, and comprehensive theoretical and practical guidance on survey design, implementation, analysis and reporting of results

FIGURE 2.5

Estimated TB incidence rates, 2013

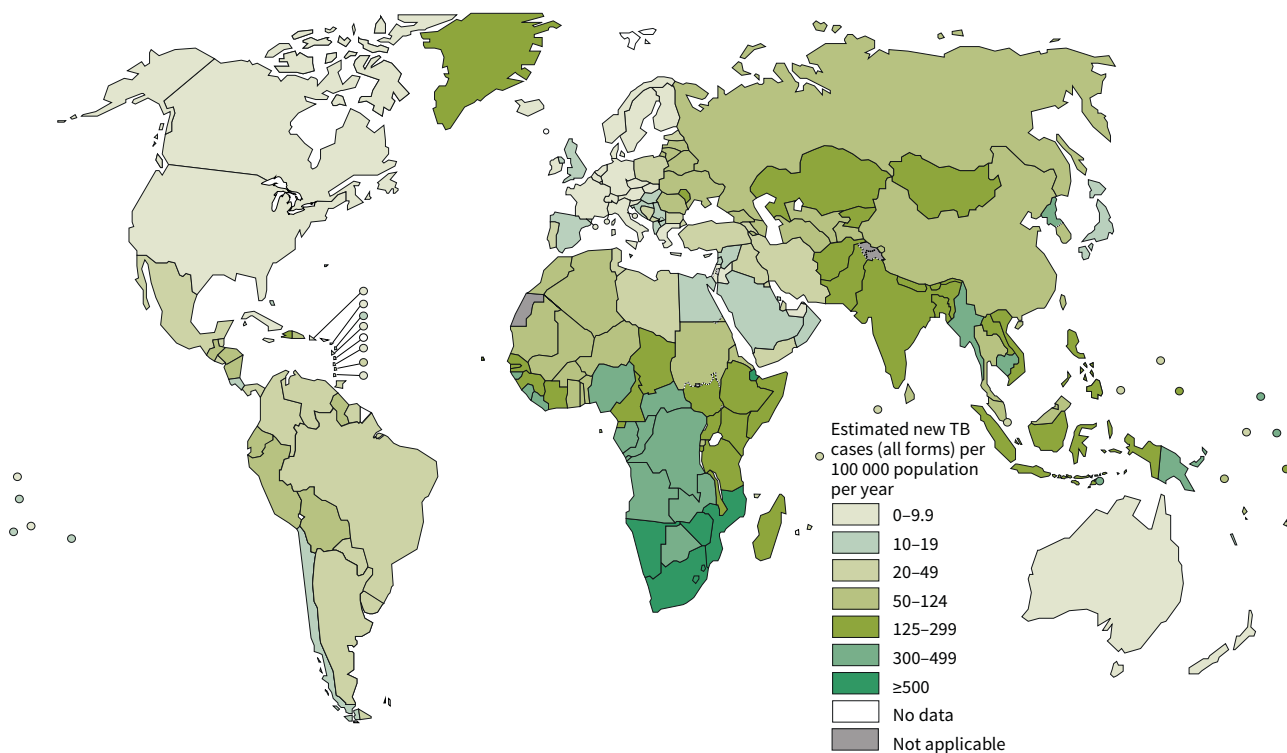


FIGURE 2.6

Global trends in estimated rates of TB incidence, prevalence and mortality. Left: Global trends in estimated incidence rate including HIV-positive TB (green) and estimated incidence rate of HIV-positive TB (red). Centre and right: Trends in estimated TB prevalence and mortality rates 1990–2013 and forecast TB prevalence and mortality rates 2014–2015. The horizontal dashed lines represent the Stop TB Partnership targets of a 50% reduction in prevalence and mortality rates by 2015 compared with 1990. Shaded areas represent uncertainty bands. Mortality excludes TB deaths among HIV-positive people.

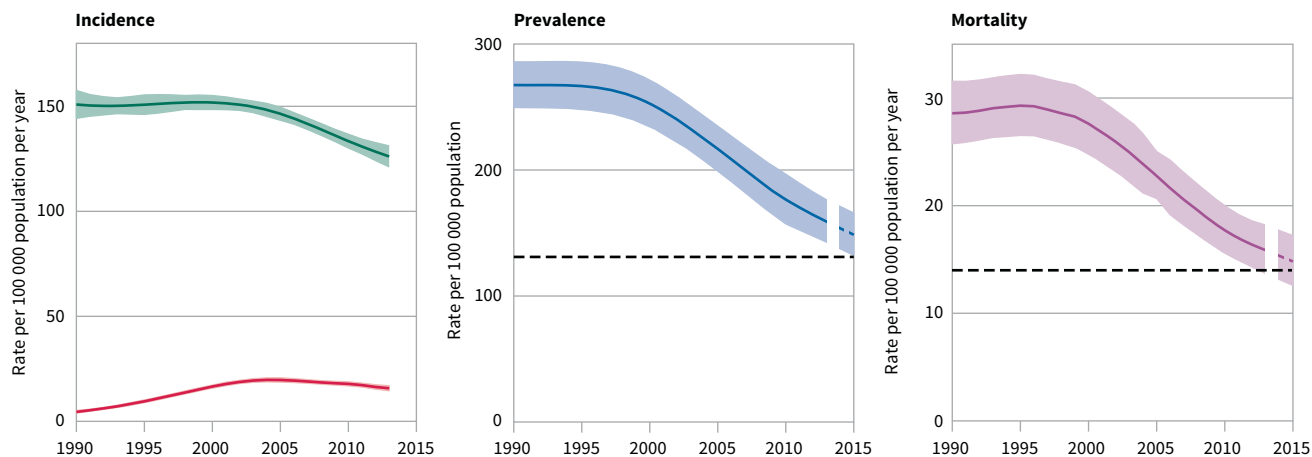
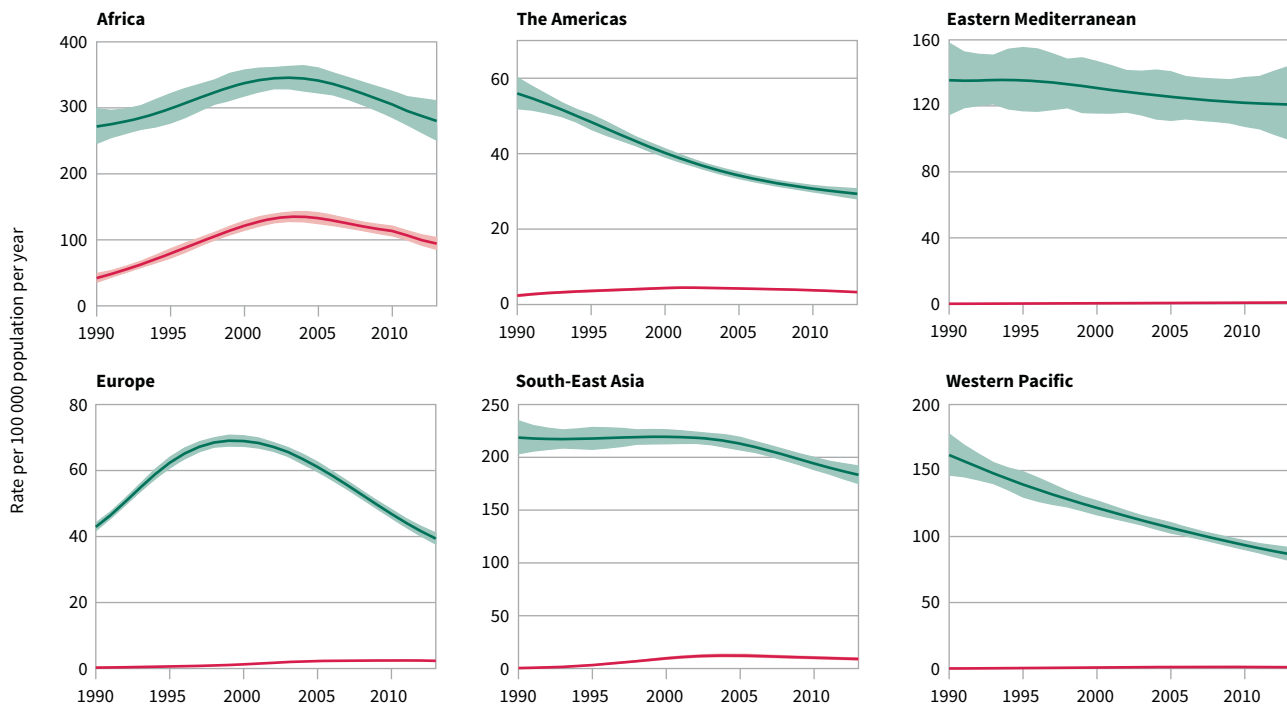


FIGURE 2.7

Estimated TB incidence rates by WHO region, 1990–2013. Regional trends in estimated TB incidence rates (green) and estimated incidence rates of HIV-positive TB (red). Shaded areas represent uncertainty bands.



is available.¹ Repeat surveys conducted about every 10 years allow trends in disease burden to be assessed. HBCs that have completed repeat surveys in the last 10 years include Cambodia, China, the Philippines and Thailand. Repeat surveys are planned in Myanmar and Viet Nam around 2015, and a fourth survey is planned in the Philippines in 2015. Countries in which surveys have been implemented or are planned in the near future are shown in **Figure 2.9**. Between 2008 and 2016, an unprecedented number of national TB prevalence surveys have been or will be conducted (see also **section 2.4**).

In low- and medium-burden countries, sample sizes and costs for surveys become prohibitively large. If survey data are not available, prevalence can be indirectly estimated as the product of incidence and the average duration of disease, but with considerable uncertainty (see the **online technical appendix**). Without a survey, TB prevalence can be estimated only indirectly.

There were an estimated 11 million prevalent cases (range, 10 million–13 million) of TB in 2013 (**Table 2.1**), equivalent to 159 cases per 100 000 population (**Table 2.2**). By 2013, the prevalence rate had fallen 41% globally since 1990. Current forecasts suggest that the Stop TB Partnership target of halving TB prevalence by 2015 compared with a baseline of 1990 will not be met world-

wide (**Figure 2.6**). Regionally, prevalence rates are declining in all six WHO regions (**Figure 2.10**). The Region of the Americas halved the 1990 level of TB prevalence by around 2005, well in advance of the target year of 2015, and the best estimate suggests that the Western Pacific Region achieved the 50% reduction target in 2012. Reaching the 50% reduction target by 2015 appears feasible in the South-East Asia Region. The target appears out of reach in the African, European and Eastern Mediterranean regions.

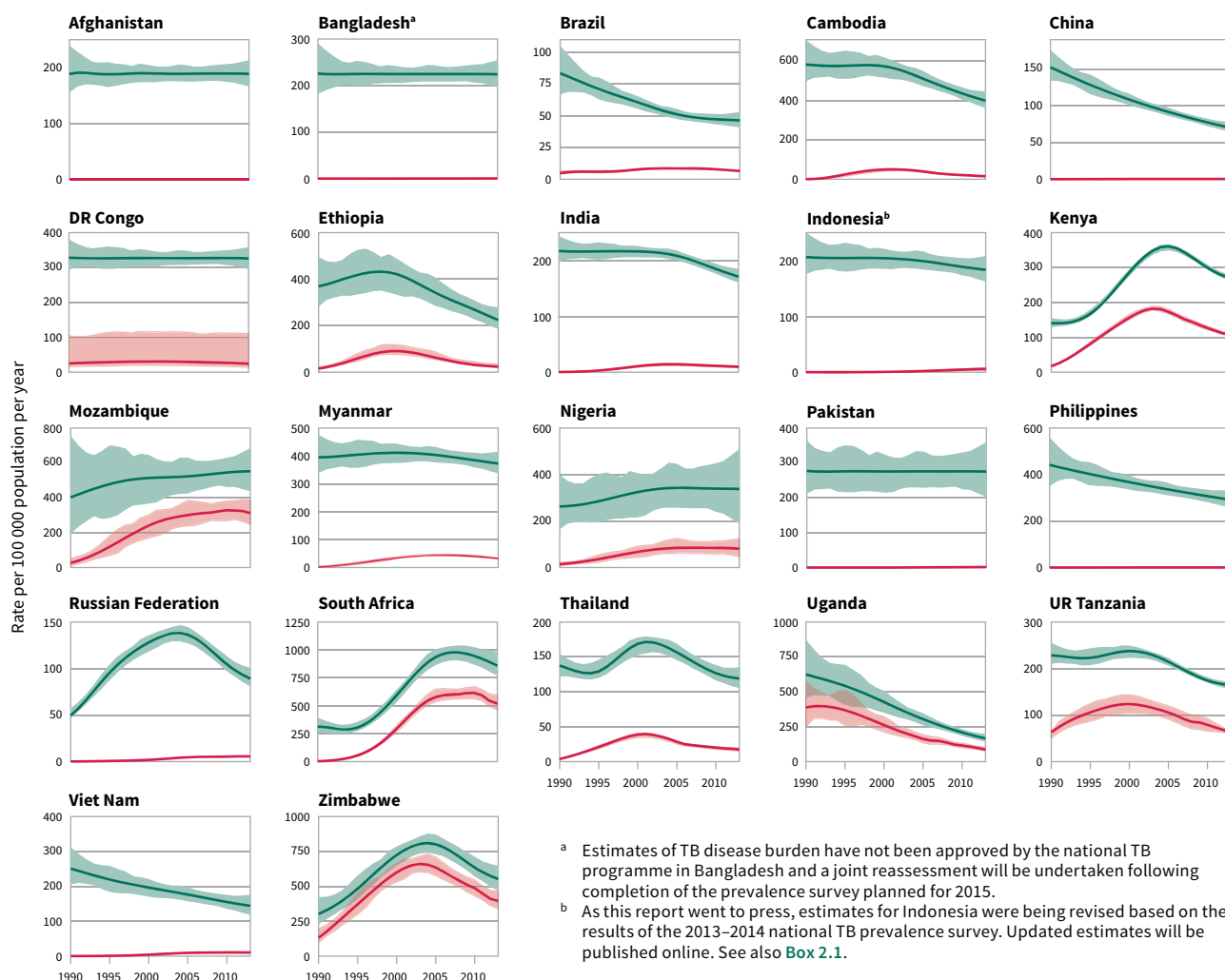
2.3 TB mortality

TB mortality among HIV-negative people can be directly measured using data from national VR systems, provided that these systems have high coverage and causes of death are accurately coded according to the latest revision of the *International classification of diseases* (ICD-10). Sample VR systems covering representative areas of the country (e.g. as in China) provide an interim solution. Mortality surveys can also be used to estimate deaths caused by TB. In 2013, most countries with a high burden of TB lacked national or sample VR systems and few had conducted mortality surveys. In the absence of VR systems or mortality surveys, TB mortality can be estimated as the product of TB incidence and the case fatality rate, or from ecological modelling based on 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

¹ *TB prevalence surveys: a handbook*. Geneva, World Health Organization, 2011 (WHO/HTM/TB/2010.17). Available at www.who.int/tb/advisory_bodies/impact_measurement_taskforce/resources_documents/thelimebook/

FIGURE 2.8

Estimated TB incidence rates, 22 high-burden countries, 1990–2013. Trends in estimated TB incidence rates (green) and estimated incidence rates of HIV-positive TB (red). Shaded areas represent uncertainty bands.



are coded as HIV deaths and contributory causes (such as TB) are often not reliably recorded. For this 2014 report, country-specific estimates of TB deaths among HIV-positive people were produced using the Spectrum software that has been used for HIV burden estimates for over a decade ([Box 2.1](#)).

Until 2008, WHO estimates of TB mortality used VR data for only three countries. This was substantially improved to 89 countries in 2009; however most of the data were from countries in the European Region and the Region of the Americas, which accounted for less than 10% of the world’s TB cases. In 2011, the first use of sample VR data from China and survey data from India enabled a further major improvement to estimates of TB mortality. For the current report, VR data of sufficient coverage and quality were available for 124 countries. Combined with survey data from India and Viet Nam, this means that estimates of TB mortality are based on direct measurements of TB mortality in 126 countries (shown in [Figure 2.11](#)). Collectively, these 126 countries account for 36% of

the estimated number of TB deaths globally. The parts of the world where there are major gaps in the availability of VR data are the African Region and parts of the South-East Asia Region; in the latter, Indonesia is currently building a sample VR system.

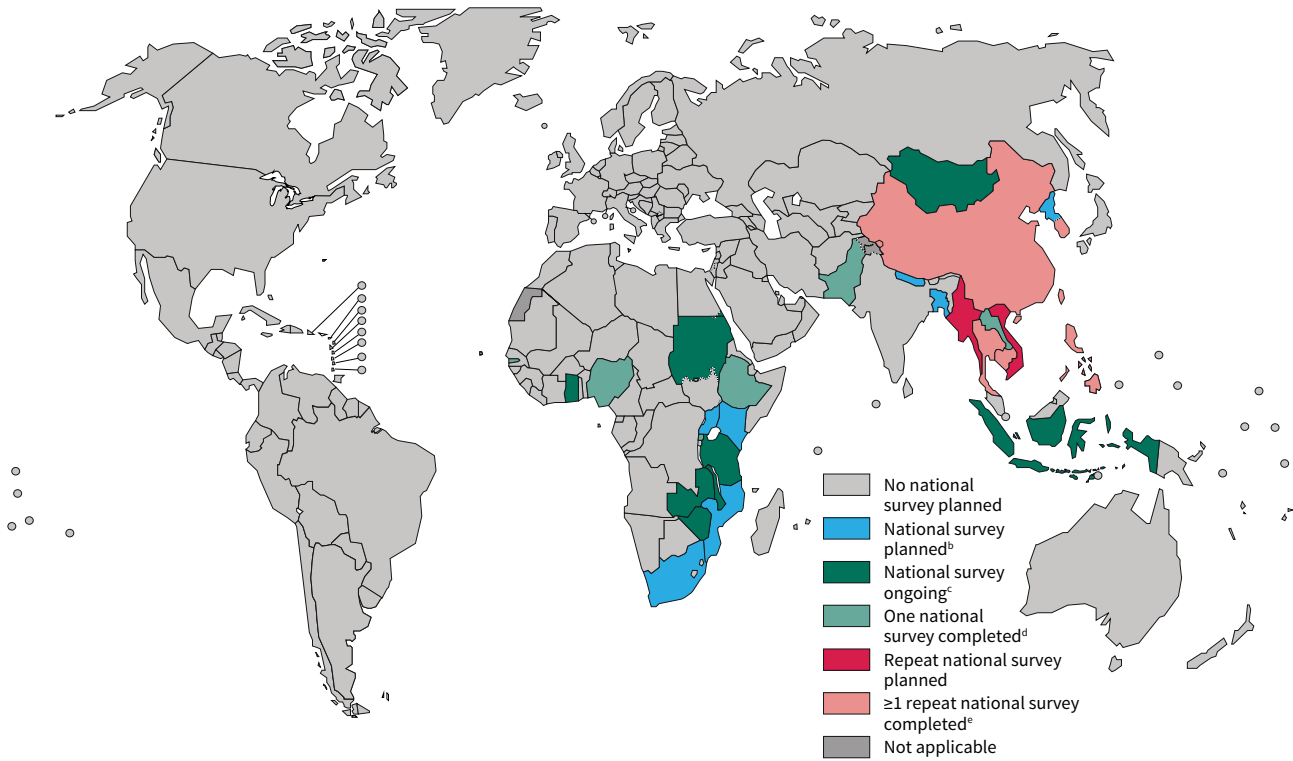
There were an estimated 1.5 million TB deaths in 2013 ([Table 2.1](#), [Figure 2.2](#)): 1.1 million among HIV-negative people and 360 000 among HIV-positive people (TB deaths among HIV-positive people are classified as HIV deaths in ICD-10).¹ These deaths included 510 000 among women and 80 000 among children ([Box 2.3](#)). There were approximately 210 000 deaths from MDR-TB (range, 130 000–290 000).

Approximately 78% of total TB deaths and 73% of TB deaths among HIV-negative people occurred in the African and South-East Asia Regions in 2013. India and Nigeria accounted for about one-third of global TB deaths.

¹ *International statistical classification of diseases and related health problems, 10th revision (ICD-10)*, 2nd ed. Geneva, World Health Organization, 2007.

FIGURE 2.9

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 1990 or are planned in the near future: status in July 2014



- ^a Screening methods include field chest X-ray; culture is used to confirm diagnosis.
- ^b A country has submitted at least a draft survey protocol and a budget plan to the WHO Global Task Force for TB Impact Measurement.
- ^c Countries were implementing field operations in July 2014 or were undertaking data cleaning and analysis.
- ^d A survey was conducted in accordance with WHO recommendations as outlined in “Tuberculosis prevalence surveys: a handbook (2011)” and at least a preliminary report has been published.
- ^e A repeat national survey is one in which participants were screened with chest X-ray, and culture examination was used to diagnose TB cases. In the Philippines, a repeat survey is planned in 2015–2016.

The number of TB deaths per 100 000 population averaged 15 globally in 2013 (Table 2.2) and 21 when TB deaths among HIV-positive people are included. There is considerable variation among countries (Figure 2.12), ranging from under 1 TB death per 100 000 population (examples include most countries in western Europe, Canada, the United States of America, Australia and New Zealand) to more than 40 deaths per 100 000 population in much of the African Region as well as three HBCs in Asia (Bangladesh, Cambodia and Myanmar) and the two HBCs in the Eastern Mediterranean Region (Afghanistan and Pakistan).

Globally, the mortality rate (excluding deaths among HIV-positive people)¹ has fallen by 45% between 1990 and 2013. The current rate of decline will need to accelerate to reach the Stop TB Partnership target of a 50% reduction by 2015 (Figure 2.6).

¹ Trends in TB mortality rates are restricted to TB deaths among HIV-negative people, given that TB deaths among HIV-positive people are classified as HIV deaths in ICD-10.

Regionally, mortality rates are declining in all six WHO regions (Figure 2.13). The 2015 target has already been surpassed in the Region of the Americas (since 2004) and the Western Pacific Region (since 2002), and may have been reached in 2013 in the South-East Asia Region. The target appears out of reach in the other three regions, although rates are falling fast in the European Region. Mortality rates appear to be falling in most of the 22 HBCs (Figure 2.14), although there is considerable uncertainty about the level of and trends in mortality in some countries, especially Nigeria where mortality estimates are indirectly derived from incidence (see technical appendix) and Thailand where the quality of cause of death data available from the national VR system needs improvement.

Between 2000 and 2013, TB diagnostic and treatment interventions saved an estimated 37 million lives (Box 2.4).

FIGURE 2.10

Trends in estimated TB prevalence rates 1990–2013 and forecast TB prevalence rates 2014–2015, by WHO region. Shaded areas represent uncertainty bands. The horizontal dashed lines represent the Stop TB Partnership target of a 50% reduction in the prevalence rate by 2015 compared with 1990. The other dashed lines show projections up to 2015.

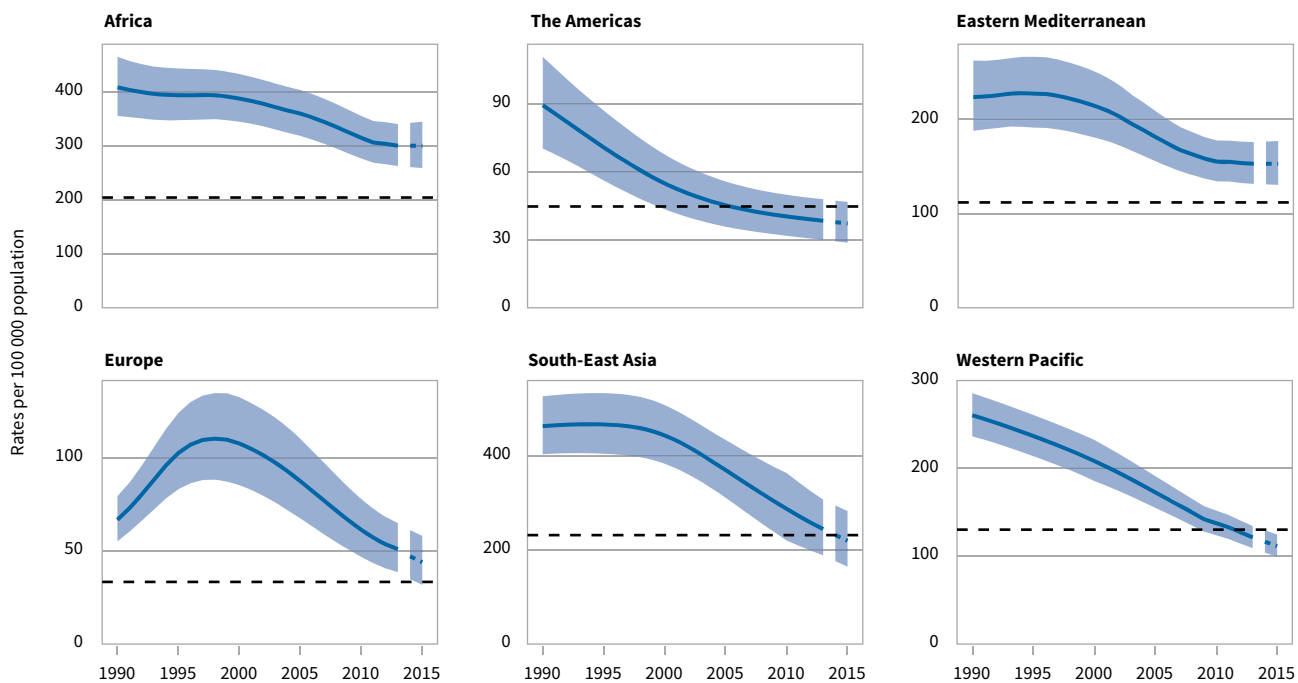
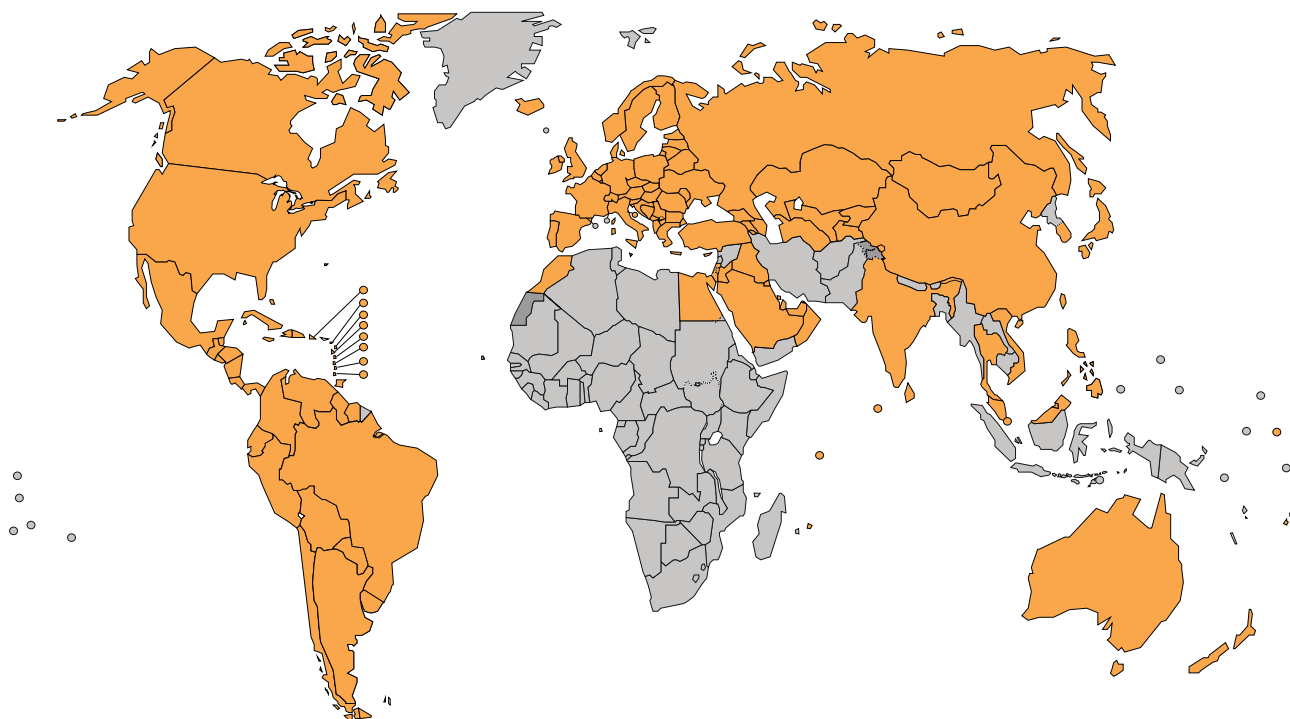


FIGURE 2.11

Countries (in orange) for which TB mortality is estimated using measurements from vital registration systems (n=124) and/or mortality surveys (n=2, India and Viet Nam)



BOX 2.4

Estimates of lives saved by TB interventions, 2000–2013

In July 2014, the Global Fund convened an expert meeting to discuss methods for estimating the lives saved by HIV, TB and malaria interventions. This followed concerns about methods used previously.^a For TB, it was agreed that lives saved should be estimated with respect to a counterfactual scenario of no TB treatment and no ART for HIV-positive TB cases. For the counterfactual scenario, it was further agreed that the number of TB deaths each year should be calculated as the estimated number of incident TB cases among HIV-negative and HIV-positive people each year (as presented in this chapter) multiplied by the case fatality ratios (CFR) for HIV-negative and HIV-positive TB that would apply in the absence of treatment (Table B2.4.1). The number of lives saved is then the difference between the estimated actual number of TB deaths each year (as presented in this chapter) and the number of deaths that would have occurred in the absence of treatment.

TABLE B2.4.1

Case fatality ratios (CFRs) in the absence of treatment

TB CASES	CFR (RANGE)
HIV negative not on TB treatment	0.43 (0.28–0.53)
HIV positive not on ART, not on TB treatment	0.78 (0.65–0.94)

Using these methods, globally an estimated 37 million lives were saved by TB prevention, diagnosis and treatment interventions 2000–2013 (Table B2.4.2).

TABLE B2.4.2

Cumulative lives saved by TB prevention, diagnosis and treatment interventions 2000–2013, globally and by WHO region (in millions). Best estimates are followed by uncertainty intervals.

REGION	HIV-NEGATIVE		HIV-POSITIVE		TOTAL	
AFR	4.0	3.3–4.8	5.0	4.5–5.6	9.1	8.1–10
AMR	1.4	1.2–1.5	0.28	0.26–0.30	1.6	1.5–1.8
EMR	2.6	2.1–3.0	0.03	0.026–0.034	2.6	2.2–3.1
EUR	2.1	1.8–2.3	0.15	0.14–0.16	2.2	2.0–2.4
SEAR	11	9.7–13	1.0	0.91–1.1	12	11–14
WPR	8.7	7.9–9.6	0.14	0.13–0.16	8.9	8.0–9.7
Global	30	26–34	7.0	6.3–7.7	37	33–41

A limitation of these methods is that they do not account for the impact of TB interventions on TB incidence or the impact of ART on TB incidence. They also do not account for the downstream impact of TB treatment and other interventions on the level of TB transmission and the future number of TB infections, cases and deaths. Methods that can incorporate these impacts are in development.

^a McCoy D, Jensen N, Kranzer K, Ferrand RA, Korenromp EL. Methodological and policy limitations of quantifying the saving of lives: a case study of the Global Fund's approach. *PLoS Med.* 2013;10(10):e1001522.

FIGURE 2.12

Estimated TB mortality rates excluding TB deaths among HIV-positive people, 2013

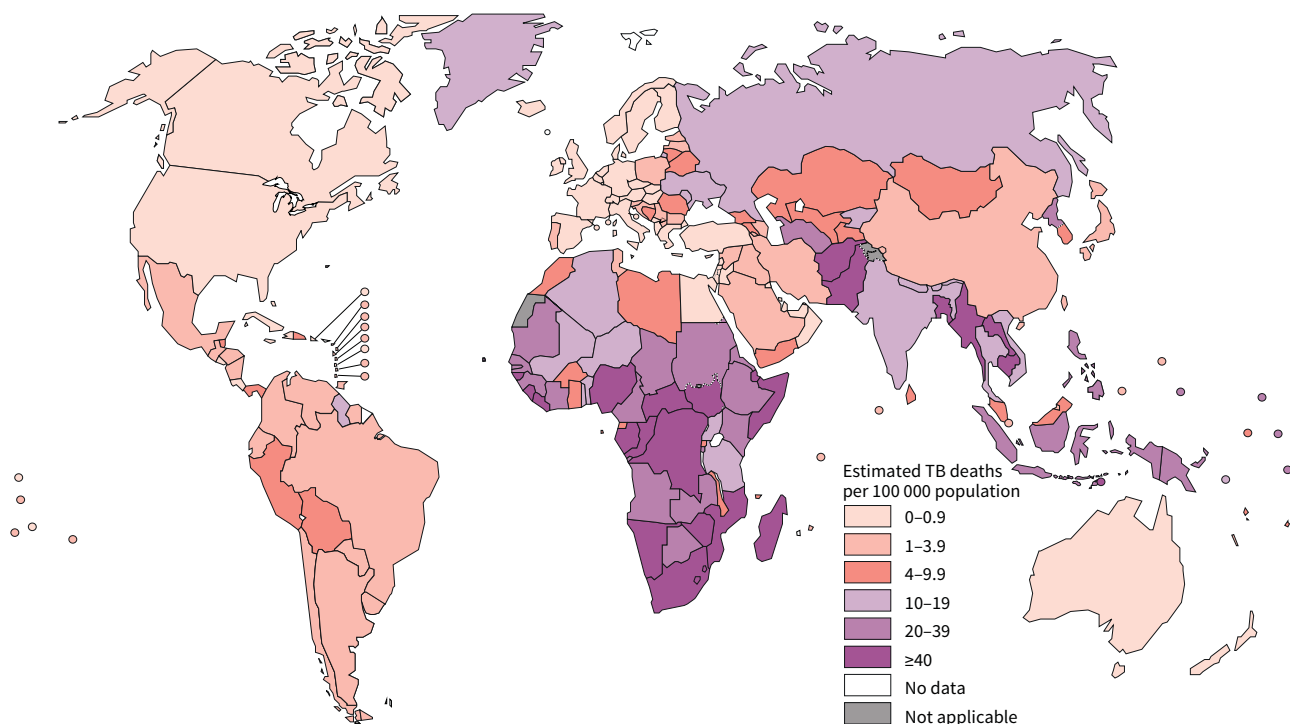
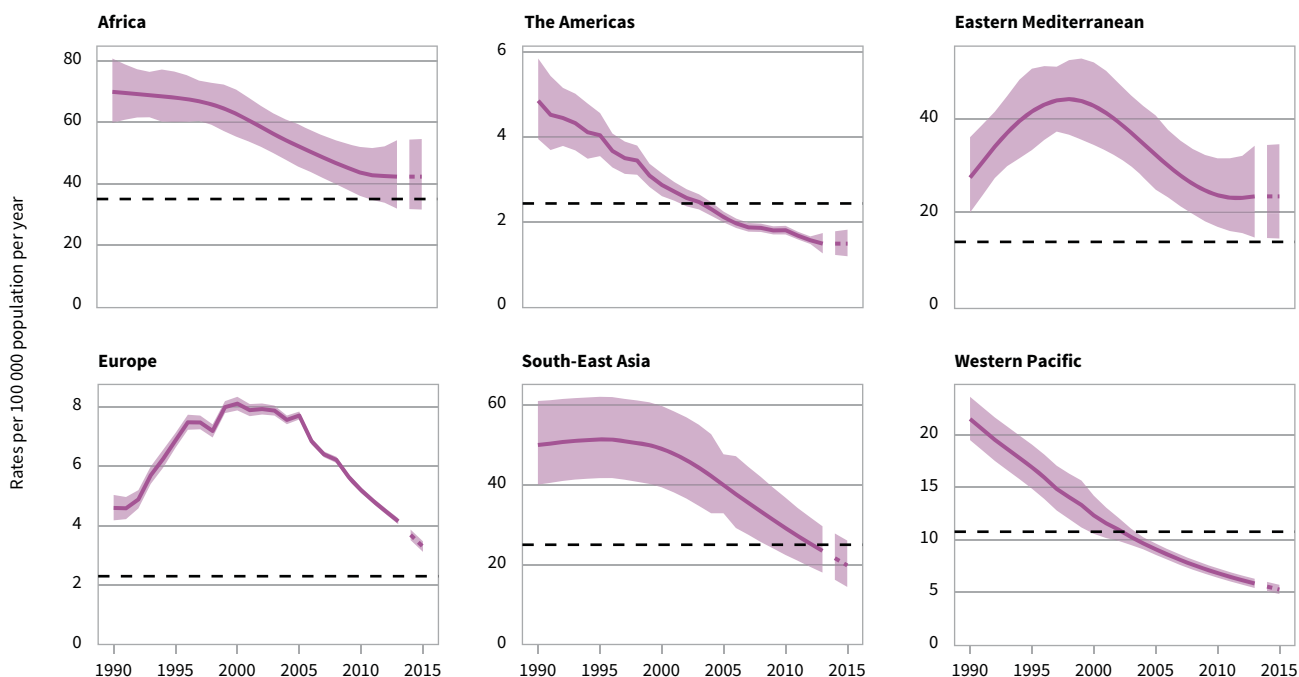


FIGURE 2.13

Trends in estimated TB mortality rates 1990–2013 and forecast TB mortality rates 2014–2015, by WHO region. Estimated TB mortality excludes TB deaths among HIV-positive people. Shaded areas represent uncertainty bands.^a The horizontal dashed lines represent the Stop TB Partnership target of a 50% reduction in the mortality rate by 2015 compared with 1990. The other dashed lines show projections up to 2015.



a The width of an uncertainty band narrows as the proportion of regional mortality estimated using vital registration data increases or the quality and completeness of the vital registration data improves.

2.4 Strengthening measurement of the burden of disease caused by TB: the WHO Global Task Force on TB Impact Measurement

The estimates of TB incidence, prevalence and mortality and their trends presented in sections 2.1–2.3 are based on the best available data and analytical methods, which are periodically reviewed by an expert group (Box 2.5). Nonetheless, there remains considerable scope to improve measurement of the burden and trends in TB disease. This final section of the chapter describes the latest status of efforts to improve measurement of the burden of disease caused by TB, under the umbrella of the WHO Global Task Force on TB Impact Measurement. This task force was established in 2006 and includes representatives from leading technical and financial partners and countries with a high burden of TB.¹

At its second meeting in December 2007, the Global Task Force on TB Impact Measurement defined three strategic areas of work:²

- strengthening surveillance towards the ultimate goal of direct measurement of incidence and mortality from notification and VR systems, respectively;
- conducting surveys of the prevalence of TB disease in a set of global focus countries that meet epidemiological and other relevant criteria; and

- periodic review and updating of the methods used to translate surveillance and survey data into estimates of TB incidence, prevalence and mortality.

In 2008 and 2009, methods were thoroughly reviewed and updated by an expert group convened by the task force. Updates were discussed and endorsed by the full task force in March 2010. Current methods are described in detail in the **online technical appendix**, and an updated review is planned in early 2015 (Box 2.1, Box 2.5). The following sections focus on the other two strategic areas of work: strengthened surveillance and national TB prevalence surveys. Further details are available on the task force's web site.³

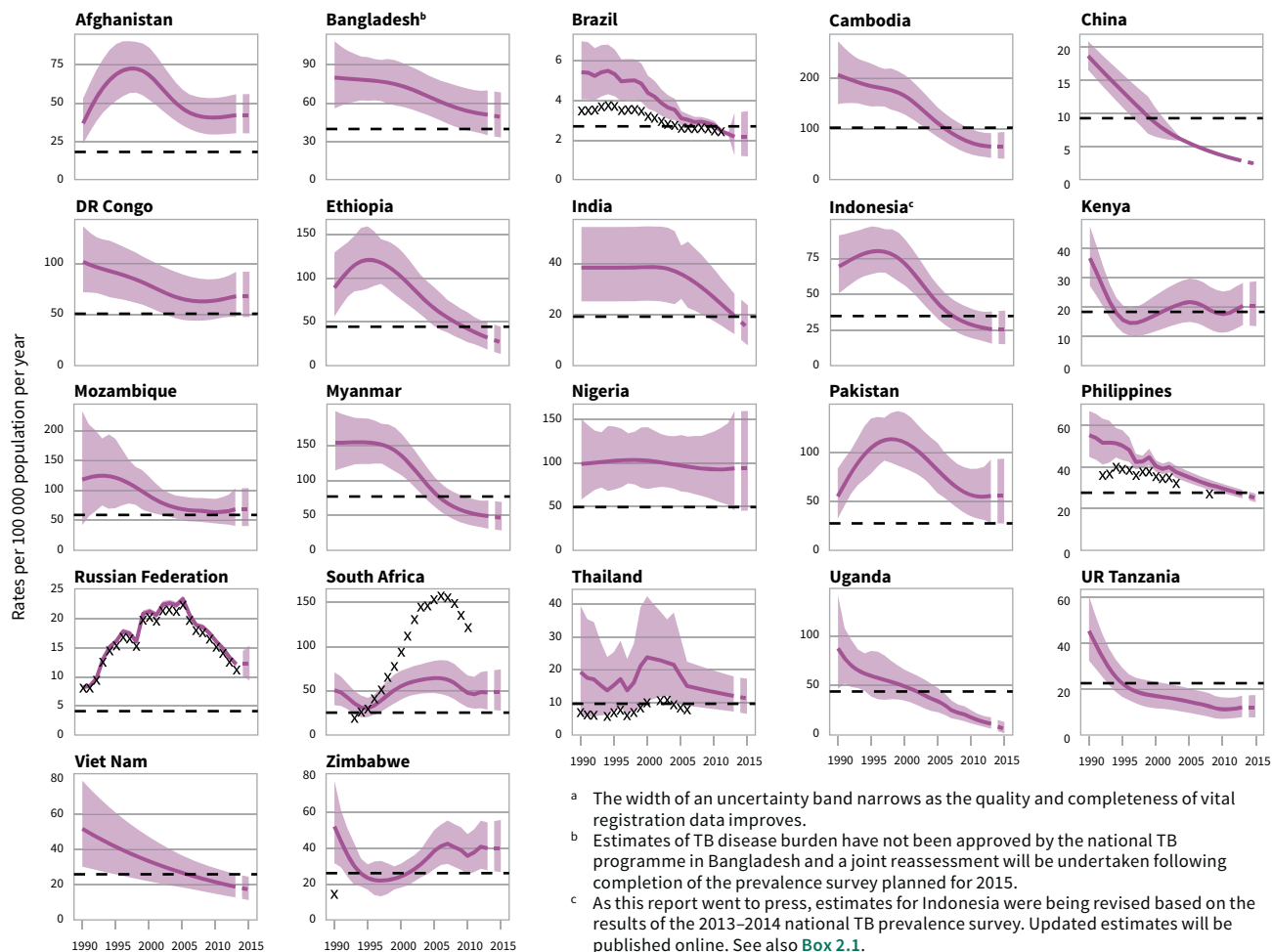
¹ Many countries with a high burden of TB are engaged in the work of the Task Force. Partners that are actively participating in the work of the Task Force include the Centers for Disease Control and Prevention in the USA, the European Centre for Disease Prevention and Control, the Global Fund, Public Health England, the KNCV Tuberculosis Foundation, the London School of Hygiene and Tropical Medicine in the UK, the Research Institute for Tuberculosis in Japan, the Union and the United States Agency for International Development (USAID).

² *TB impact measurement: policy and recommendations for how to assess the epidemiological burden of TB and the impact of TB control.* Geneva, World Health Organization, 2009 (Stop TB policy paper no. 2; WHO/HTM/TB/2009.416). Available at www.who.int/tb/publications/2009/impactmeasurementpolicy/

³ www.who.int/tb/advisory_bodies/impact_measurement_taskforce

FIGURE 2.14

Trends in estimated TB mortality rates 1990–2013 and forecast TB mortality rates 2014–2015, 22 high-burden countries. Estimated TB mortality excludes TB deaths among HIV-positive people. The horizontal dashed lines represent the Stop TB Partnership target of a 50% reduction in the mortality rate by 2015 compared with 1990. The other dashed lines show projections up to 2015.^a Uncertainty is due to adjustments made to the mortality data from vital registration systems that were reported by countries (mortality data from vital registration systems are represented by the “x” symbol).



2.4.1 Strengthening surveillance

Reasons for uncertainty in current estimates of TB incidence include use of expert opinion about both the number of cases that are diagnosed but not reported to national surveillance systems and the number of cases that are not diagnosed at all ([section 2.1](#)). Major challenges in estimating TB mortality include the lack of VR systems of sufficient coverage and quality in many countries, notably in Africa and parts of Asia ([Figure 2.11](#)). The long-term goal of directly measuring the level of and trends in TB disease burden from routine surveillance data, using notification data to measure TB incidence and VR data to measure TB mortality, requires strengthened surveillance in many countries. Countries for which more robust estimates of mortality were available in 2013 are shown in [Figure 2.11](#).

TB surveillance checklist of standards and benchmarks

Strengthening surveillance to move towards the goal of direct measurement of TB incidence and mortality requires a clear understanding of what a ‘model’ surveillance system should look like and a method for assessing the current performance of TB surveillance. Following considerable work in 2011 and 2012, a TB surveillance checklist that defines the standards and associated benchmarks that need to be met for a country’s notification and VR data to be used as a direct measure of TB incidence and mortality was developed. By July 2014, the checklist had been used by 21 countries ([Figure 2.15](#)) as the basis for identifying what standards are already met and the investments required to close remaining gaps ([Box 2.6](#)). These assessments have been undertaken in close collaboration with the Global Fund so that use of the checklist is integrated into the fund’s grant processes and findings can inform investments by the fund as well as national

Comparison of estimates presented in this report with other TB burden estimates published in 2014

Background

Why WHO makes health estimates and general approach

The production and dissemination of health statistics for health action at the country, regional and global levels are core WHO activities mandated by all Member States in the WHO Constitution. WHO works closely with countries, partners and global experts to produce health statistics of the greatest possible accuracy.

For all diseases, periodic updates of global health estimates usually involve statistical modelling to overcome major gaps in country data availability and quality and to obtain comparable global, regional and country health statistics. Given that there are many options in statistical modelling in terms of type of model, assumptions and complexity, an important feature of WHO's global health monitoring is its commitment to transparency and consensus. This is achieved in several ways. Technical advisory groups including independent academic experts provide methodological advice; there is a country consultation process which provides a platform for Member States to understand how estimates are derived; and methods including descriptions of input data sets and software are described so that others can reproduce analyses.

Why estimates produced by different agencies and research groups can differ

Estimates always have uncertainty and the fewer the number of quality data points, the greater the uncertainty. Different researchers can easily produce different estimates for the same country, region or globally and this has happened on many occasions. In recent years, the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, USA has started to publish, mostly in the *Lancet*, estimates for many health indicators globally and for countries. Sometimes these estimates are very different from those published by WHO and UN agencies. WHO reviews and, in cases where scientific rigour can be evaluated, may make use of methods and estimates developed by IHME and other organizations. For instance, the publication of the IHME Global Burden of Disease (GBD) 2010 Study in a special issue of *The Lancet* in 2012^a led to consultations and exchange of data between WHO, UNAIDS, other agencies and their expert groups. Over the past few years, investigation into differences in estimates has led to improvements in data inputs and estimation methods used by IHME and UN agencies. In several areas there is convergence in terms of methods and results of the estimation modelling. In others, more work is needed to discuss data inputs, methods and discrepant results.

TB estimates published in 2014 by IHME and other academic research groups

In 2014, three studies that include estimates of TB disease burden were published. These are:

- Estimates of TB incidence, prevalence and mortality for the period 1990–2013 produced by IHME alongside similar estimates for HIV and malaria, and published in *The Lancet* in July 2014.^b
- An estimate of childhood TB incidence globally in 2010, produced by an academic group based in the USA and published in *The Lancet* in March 2014.^c
- Estimates of childhood TB incidence in the 22 HBCs in 2010, produced by researchers based in the UK, published in *Lancet Global Health* in July 2014.^d

IHME compared with WHO estimates

IHME and WHO global estimates for TB incidence, prevalence and mortality in terms of absolute levels in 2013 and trends since 2000 are summarized in [Table B.2.5.1](#). This shows:

- Estimates of TB prevalence are similar, with vastly overlapping uncertainty intervals. The WHO estimate suggests that rate of decline since 2000 is faster.
- Both IHME and WHO estimate that the TB incidence rate is falling. The WHO estimate suggests that the rate of decline is faster.
- The IHME and WHO estimates of the absolute level of TB incidence are different and uncertainty intervals do not overlap. The WHO estimates are higher.
- Both IHME and WHO estimate that the TB mortality rate is falling. The WHO estimate suggests that the rate of decline is faster.
- The IHME and WHO estimates of the absolute level of TB mortality in 2013 are different and uncertainty intervals have limited overlap. The WHO estimates are lower.

TABLE B.2.5.1

Comparison of IHME and WHO global estimates of TB burden in 2013 and their trend 2000–2013

	IHME	WHO
Incidence rate in 2013 (per 100 000 population)	105 (102–108)	126 (121–131)
Annualized rate of change (2000–2013, %)	-0.69	-1.5
Mortality rate in 2013, excluding HIV (per 100 000 population)	19.2 (17.4 – 20.9)	15.9 (13.9 – 17.9)
Annualized rate of change (2000–2013, %)	-3.7	-4.4
Prevalence rate in 2013 (per 100 000 population)	168 (164–173)	159 (142–176)
Annualized rate of change (2000–2013, %)	-1.4	-3.7

Of note, the most recent IHME estimates have changed considerably from those published as part of the Global Burden of Disease 2010 study,^a suggesting that IHME has made important changes to their model specifications and that outputs are subject to some instability. In addition, IHME's best estimate of global incidence in 2013 (around 7.5 million cases including cases in HIV-positive individuals) is surprisingly close to the number of detected cases reported by countries (nearly 6 million cases in 2013, see [Chapter 4](#)), given strong evidence of large gaps in reporting of detected cases in some countries with a very high burden of TB. For example, unpublished data from a recent prevalence survey in one state in India indicate that more than 30% of detected cases are not reported, which is consistent with result from a previous large-scale household study.^e In Pakistan, the IHME estimate of incidence (225 000 HIV-negative TB cases in 2013) does not reach the number of notified cases (289 000, including an estimated 1 500 HIV-positive cases) in the same year.

Estimates of TB incidence among children published by WHO and three independent academic groups

Between March and July 2014, three independent academic groups published estimates of TB incidence in children, all in the Lancet group of journals. These estimates vary from less than 200 000 new cases in 2013 (Murray et al)^b to a best estimate of 970 000 new cases (uncertainty interval 937 877–1 055 414) in 2010.^c In between these two is an estimate that the median number of children who developed TB disease in the 22 HBCs was 650 977 (range, 424 871–983 118) in 2010.^d The large variation in these estimates illustrates the challenges of estimating the burden of TB in children, a group in which cases are more difficult to diagnose and are rarely bacteriologically confirmed. The WHO estimates presented in this report (Box 2.3) have drawn upon one of these sets of estimates,^d which was commissioned by WHO and used complementary methods (i.e. dynamic modelling as opposed to estimates built up from notification data). WHO is working with multiple partners to improve understanding of the disease burden among children, following a global consultation convened by WHO and the TB Alliance in September 2013.

Conclusion

Differences in estimates of TB disease burden should always be examined in the context of their published uncertainty range and gaps in underlying data. Better quality surveillance data with more complete coverage and global adoption of nationwide vital registration systems with standard cause of death data will result in convergence of estimates of TB burden produced by different institutions. WHO and partners are actively engaged in supporting national TB programmes' efforts to improve the performance of their health information systems, as described in section 2.4 of this chapter.

In early 2015, a thorough review of the current epidemiological and modelling methods used by WHO to estimate TB disease burden will be conducted by an expert group convened by the WHO Global Task Force on TB Impact Measurement (see section 2.4), and updated as appropriate.

- ^a Global Burden of Disease Study 2010. *Lancet* 2012; 380; 9859.
- ^b Murray CJ et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; pii: S0140-6736(14)60844-8. doi: 10.1016/S0140-6736(14)60844-8. [Epub ahead of print]
- ^c Jenkins HE, Tolman AW, Yuen CM, Parr JB, Keshavjee S, Pérez-Vélez CM, Pagano M, Becerra MC, Cohen T. Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. *Lancet* 2014; [http://dx.doi.org/10.1016/S0140-6736\(14\)60195-1](http://dx.doi.org/10.1016/S0140-6736(14)60195-1).
- ^d Dodd PJ, Gardiner E, Coghlan E, Seddon JA. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study. *Lancet Global Health* 2014; [http://dx.doi.org/10.1016/S2214-109X\(14\)70245-1](http://dx.doi.org/10.1016/S2214-109X(14)70245-1).
- ^e Satyanarayana S1, Nair SA, Chadha SS, Shivashankar R, Sharma G, Yadav S, Mohanty S, Kamineni V, Wilson NC, Harries AD, Dewan PK. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. *PLoS One*. 2011;6(9):e24160. doi: 10.1371/journal.pone.0024160. Epub 2011 Sep 2.

governments and other partners. With more than 100 low- and middle-income countries receiving TB grants from the Global Fund, this approach has great potential to make a real difference to TB surveillance worldwide. Assessments of TB surveillance using the checklist of standards and benchmarks is now part of the standard terms of reference for the “epidemiological stage” that is a prerequisite for applications to the Global Fund as part of its new funding model introduced in 2013.

Inventory studies to measure or estimate TB underreporting

One of the standards in the TB surveillance checklist is that all diagnosed cases of TB are reported to the national surveillance system. The two benchmarks that must be satisfied are: 1) that TB reporting is a legal requirement; and 2) that $\geq 90\%$ of TB cases are reported to national health authorities, as determined by a national-level investigation such as an inventory study. To date, few countries have implemented an inventory study but as the number doing so increases, estimates of the level of and trend in TB incidence will improve. Even when underreporting is considerable and notification data are not a good proxy for TB incidence, results from inventory studies can be used to quantify the gap and obtain more precise estimates of disease burden and provide valuable information about where efforts to collaborate with public and private sector providers are needed. In 2012, the Global Task Force on TB Impact Measurement completed a guide on how to design and implement an inventory study, and how to analyse and report results.¹

In the past 10 years, inventory studies combined with capture–recapture analysis have been implemented in the Netherlands, the UK, French Guiana, Egypt, Iraq, Pakistan and Yemen. A workshop to develop protocols for inventory studies in five HBCs (China, Indonesia, the Philippines, Thailand and Viet Nam) was held in Indonesia in September 2014.

Electronic recording and reporting of data

Several of the standards in the TB surveillance checklist are about data quality. In all of the regional and country workshops held between 2008 and 2013, it was evident that it is easier to assess the quality of TB surveillance data in countries with case-based electronic recording and reporting systems. Besides facilitating assessment of data quality, electronic recording and reporting systems have other major advantages compared to systems based solely on paper-based recording and reporting. These include:

- Better programme and resource management, by encouraging staff to use and act upon live data. This

¹ *Assessing tuberculosis underreporting through inventory studies*. Geneva, World Health Organization, 2013 (WHO/HTM/TB/2012.12). Available at: www.who.int/tb/publications/inventory_studies/en/index.html

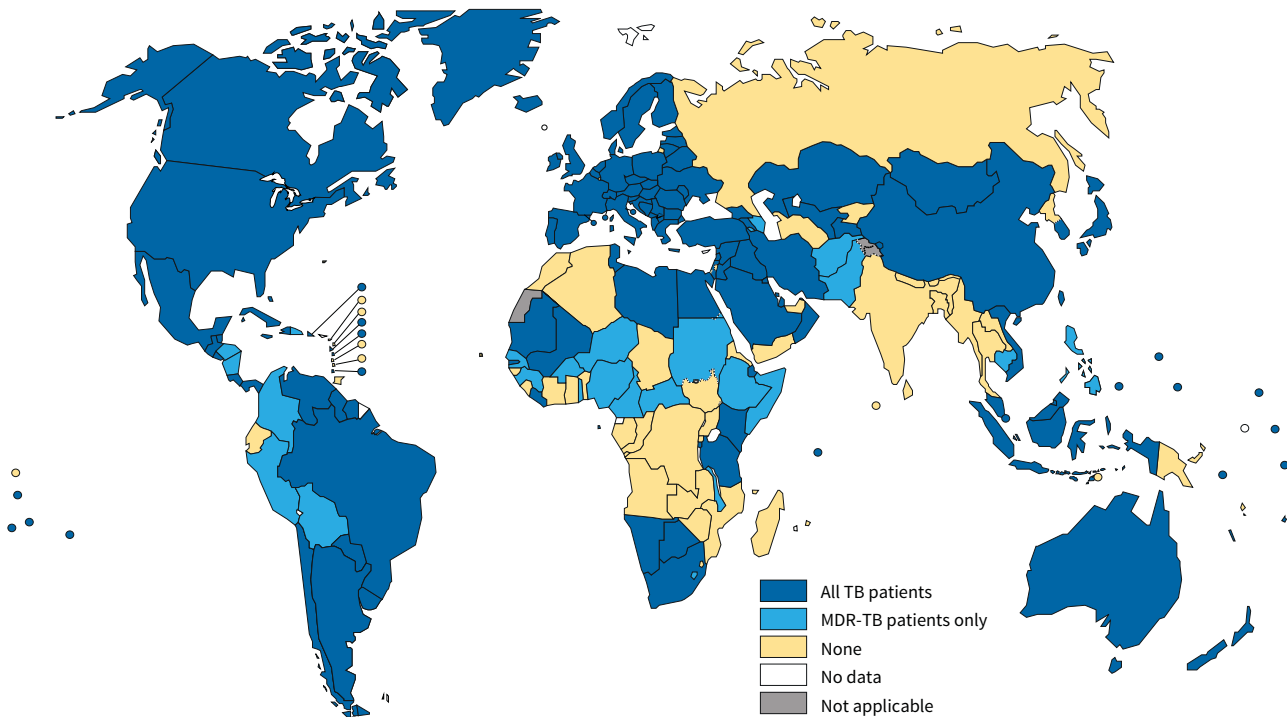
FIGURE 2.15

Countries (in red) where the TB surveillance checklist of standards and benchmarks has been used: status in July 2014



FIGURE 2.16

Availability of national electronic case-based databases of TB patients, 2013



may help to prevent loss to follow up during treatment and assist with management of drug supplies (including avoidance of stock-outs).

- Improved surveillance by making it easier for facilities not traditionally linked to the NTP, such as hospitals, prisons and the private sector, to report TB cases, and by reducing the burden of compiling and submitting data through paper-based quarterly reports.
- Analysis and use of data is facilitated, since data can be readily imported into statistical packages. Results are then available to decision-makers more quickly and it is possible to detect outbreaks promptly.
- Higher quality data, since automated data quality checks can be used and duplicate or misclassified notifications can be identified and removed (which is very difficult or impossible to do nationally with paper-based systems). It is also easier to introduce new data items.
- Identification of clusters of cases in space and time, including clusters of drug-resistant cases, thus allowing early investigation and containment of epidemics.

Countries that have national electronic case-based databases of TB patients are shown in **Figure 2.16**. Recent guidance on electronic recording and reporting for TB care and control, developed by WHO and partners in 2011, is available on the task force's website.¹

2.4.2 National surveys of the prevalence of TB disease

Before 2007, few countries had implemented nationwide prevalence surveys. In the 1990s, national surveys were confined to China, Myanmar, the Philippines and the Republic of Korea. Before 2009 and with the exception of Eritrea in 2005, the last national surveys in the African Region were undertaken between 1957 and 1961. From 2002 to 2008, there was typically one survey per year.

In 2007, WHO's Global Task Force on TB Impact Measurement identified 53 countries that met epidemiological and other criteria for implementing a survey. A set of 22 global focus countries were selected to receive particular support in the years leading up to 2015. The African countries were: Ethiopia, Ghana, Kenya, Malawi, Mali, Mozambique, Nigeria, Rwanda, Sierra Leone, South Africa, Uganda, the United Republic of Tanzania and Zambia. Countries in Asia were: Bangladesh, Cambodia, China, Indonesia, Myanmar, Pakistan, the Philippines, Thailand and Viet Nam. Since early 2008, substantial efforts to support countries to design, implement, analyse and report on surveys have been made. Examples include development of updated guidance,² coordination of technical assistance, expert reviews of protocols, organization of study tours and mid-term survey reviews, and global and regional workshops to support survey design and implementation and to share results and lessons learned among

countries. As part of these efforts, the concept of Asia–Asia, Asia–Africa and Africa–Africa ('AA') collaboration has been strongly promoted.

Following six years of substantial effort at country, regional and global levels, unprecedented progress has been achieved (**Figure 2.17**). If surveys are implemented according to schedule, more than 20 surveys will be implemented between 2011 and 2015. Five national TB prevalence surveys had field operations completed in 2012 (Gambia, Nigeria, Rwanda, Thailand and the United Republic of Tanzania, two in 2013 (Ghana, Sudan) and a further three will be completed in 2014 (Indonesia, Malawi and Zambia). Field operations are systematically followed with lengthy data cleaning and validation before final results are disseminated. These surveys provide an unbiased estimation of disease burden, often for the first time, and contribute to better estimates of disease burden once results are finalized (**Box 2.1**). Surveys are also providing a rich source of data to inform programme policy and strategy. For several recent surveys, country-specific reports and peer-reviewed publications are already available (for example, from China,³ Cambodia,⁴ Ethiopia,⁵ Myanmar,⁶ and Pakistan⁷) and others are in the pipeline.

Although some findings and lessons learned are country-specific, others are common to most surveys:

- Most of the prevalent TB cases in the community were not identified by classical symptom screening (i.e. a cough of more than 2–3 weeks duration and/or blood in the sputum) but rather by chest X-ray screening. This proportion tends to increase over time as programmatic and case management improve.
- In Asia, there is a progressive increase in the prevalence of TB with age. As transmission declines, levels of infection in younger age groups fall and the burden of

¹ *Electronic recording and reporting for TB care and control*. Geneva, World Health Organization, 2012 (WHO/HTM/TB/2011.22). Available at www.who.int/tb/publications/electronic_recording_reporting

² *TB prevalence surveys: a handbook*. Geneva, World Health Organization, 2011 (WHO/HTM/TB/2010.17). Available at www.who.int/tb/advisory_bodies/impact_measurement_taskforce/resources_documents/thelimebook/

³ Wang L, Zhang H, Ruan Y, et al. Tuberculosis prevalence in China, 1990–2010; a longitudinal analysis of national survey data. *Lancet* 2014;383:2057–64

⁴ Mao TE, Okada K, Yamada N et al. Cross-sectional studies of tuberculosis prevalence in Cambodia between 2002 and 2011. *Bull World Health Organ* 2014; 92:573–581. The official report can be downloaded from here: <http://www.cenat.gov.kh/en/content/second-national-tuberculosis-prevalence-survey-cambodia-2011>

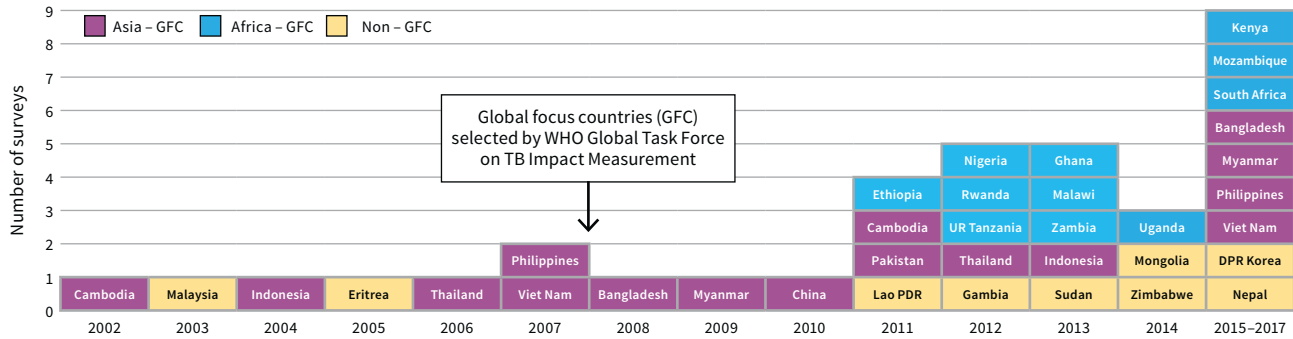
⁵ Kebede AH, Alebachew Z, Tsegaye F et al. The first population-based national tuberculosis prevalence survey in Ethiopia, 2010–2011. *Int J Tuberc Lung Dis*. 2014 Jun;18(6):635–9. The official report can be downloaded from here: <http://www.eph.gov.et/images/downloads/Tuberculosis%20Prevalence%20Survey.pdf>

⁶ The official report can be downloaded from here: http://www.searo.who.int/myanmar/documents/TB_Prevalence_Survey_report.pdf

⁷ The official report can be downloaded from here: <http://www.tbcare1.org/countries/asia/pkn/>

FIGURE 2.17

Global progress in implementing national surveys of the prevalence of TB disease, actual (2002–2014) and expected (2015–2017)



disease shifts to older age groups. This is reinforced by the demographic transition in these countries, which is associated with a general ageing of the population. The age distribution of cases in Africa is more mixed, with some countries (e.g. Gambia, Rwanda) having a pattern similar to that observed in Asia and others (e.g. Ethiopia, Nigeria) having a peak prevalence in younger age groups.

- Prevalence is much higher among men than women. The sex ratio (M:F) is typically between 2:1 and 3:1 in Asia. In Africa, more cases also occur among men.
- Comparison of the number of smear-positive prevalent cases of TB with equivalent notification data (P:N ratio) illustrates the extent to which NTPs are able to promptly detect and treat cases and variation in performance among countries. In countries such as Nigeria and Lao PDR, a relatively high P:N ratio indicates that there is considerable scope for further improvement in case detection using already available approaches to TB diagnosis and treatment and/or by improving reporting of detected cases.
- A smear-positive sputum result does not necessarily mean TB. Recent surveys have identified a considerable proportion of participants with smear-positive specimens who do not have clinical signs consistent with clinical TB, and culture results that are either negative or confirm non-tuberculous mycobacteria. For this reason, in the most recent surveys smear-positive specimens are being retested with GeneXpert MTB/RIF to ensure accurate diagnosis of cases for whom smear results and clinical findings are inconsistent as well as appropriate case management.

- Although most surveys are not designed to estimate prevalence at sub-national level, surveys often show considerable geographical variation in the level of TB prevalence. Therefore specific control activities for areas with a higher prevalence may need to be considered as part of national strategic plans.
- In surveyed countries with a generalized HIV epidemic, implementation of collaborative TB/HIV activities may help to reduce the overall prevalence of HIV among newly diagnosed TB cases. In Rwanda, for example, the prevalence of HIV among prevalent cases detected during the survey was much lower than the prevalence of HIV measured through routine testing of registered TB patients. This suggests that systematic screening of TB in people living with HIV and associated HIV care has had a positive impact.

Given the increasing availability of prevalence survey data, WHO is establishing a global data repository that will allow for the safe storage of summary results and a minimum set of anonymised individual-level data. Standard agreements and survey-specific access controls will be used to define access rights to stored data i.e. NTPs can decide for their own survey dataset whether their data are publicly available or whether researchers need specific permissions from NTPs before a copy of the dataset is provided. Towards the end of 2014, NTPs and survey coordinators will be invited to store their survey data (including anonymised individual-level data) according to a standard set of terms and conditions in this data repository.

Countdown to 2015

KEY FACTS AND MESSAGES

The Millennium Development Goal (MDG) framework includes five indicators: TB incidence, TB mortality, TB prevalence, the case detection rate for new TB cases and the treatment success rate for new TB cases.

The MDG target that the TB incidence rate should be falling by 2015 has been met globally, in all six WHO regions and in most of the 22 high TB burden countries (HBCs). Worldwide, the TB incidence rate has been falling for about a decade.

By 2013, the global TB mortality rate had fallen by 45% compared with a baseline of 1990. An acceleration in the current rate of decline is required to reach the global target of a 50% reduction by 2015. The 50% reduction target has already been met in three WHO regions: the Region of the Americas, the South-East Asia Region and the Western Pacific Region. The other three regions (the African Region, the Eastern Mediterranean Region and the European Region) are unlikely to reach the target. Ten HBCs have met the mortality target or are on track to do so.

By 2013, the global TB prevalence rate had fallen by 41% since 1990. An acceleration in the current rate of decline is required to reach the global target of a 50% reduction by 2015. The 50% reduction target has been met in two WHO regions (the Region of the Americas and the Western Pacific Region) and the South-East Asia Region appears on track to reach it. Ten HBCs have met the target or are on track to do so.

Targets for the treatment success rate among new TB cases and the case detection rate (notifications of new and relapse cases divided by estimated incidence) were not set for 2015. Treatment success rates were above 85% globally in 2012, in three of six WHO regions and in most HBCs. Globally, the case detection rate was 64% in 2013.

There has been encouraging progress towards 2015 targets for TB/HIV interventions that were set in the *Global Plan to Stop TB 2011–2015*. For instance, in the African Region 76% of TB patients knew their HIV status and 69% of HIV-positive TB patients were on antiretroviral treatment in 2013. However, these levels fall short of the 2015 targets of 100%.

Progress towards targets for the response to MDR-TB set out in the *Global Plan to Stop TB 2011–2015* is not on track. The ratio of detected cases to the estimated number of cases among notified TB patients was 45% globally and under 30% in most HBCs, compared with a 2015 target of 100%. Worldwide, the treatment success rate was 48% in the 2011 patient cohort, compared with a target of $\geq 75\%$ by 2015. Substantial efforts to improve the detection and treatment outcomes of people with MDR-TB are required.

As explained in the introduction to this report (**Chapter 1**), the United Nations (UN) established eight Millennium Development Goals (MDGs) at the turn of the 21st century, with targets set for 2015 (www.un.org/millenniumgoals). These goals and targets were designed to drive progress worldwide, and following their endorsement by all countries they have been the focus of international and national development efforts for more than a decade. TB was included as part of MDG 6, with a target that TB incidence should be falling by 2015. In addition, two other global targets for reductions in TB disease burden (prevalence and mortality rates) and two additional indicators fit within the MDG framework (**Box 3.1**).

With two years remaining before the target deadline of 2015, the 2013 edition of the *Global Tuberculosis Report* was accompanied by a special supplement called *Countdown to 2015*. This summarized the status of progress towards targets set within the MDG framework as well as progress towards targets for the response needed to address the specific challenges of multidrug-resistant TB (MDR-TB) and the TB/HIV co-epidemic that were defined in the *Global Plan to Stop TB 2011–2015*.¹ This chapter of the 2014 edition of the *Global Tuberculosis Report* provides an updated summary of progress towards the 2015 targets at global and regional level, and for the 22 high TB burden countries (22 HBCs) that collectively have about 80% of the world's TB cases. Two tables (**Table 3.1** and **Table 3.2**) bring together key findings that are featured in more detail in **Chapter 2**, **Chapter 4**, **Chapter 5** and **Chapter 7**. Both of these tables were completed using data reported by Member States to WHO as well as estimates of the level of and trends in disease burden (incidence, prevalence, mortality) that are produced by WHO in consultation with countries. The data reported by countries and estimates of disease burden appear in the country profiles of the *Global Tuberculosis Report 2014* and were reviewed by countries in advance of publication.

¹ *The Global Plan to Stop TB, 2011–2015*. Geneva, World Health Organization, 2010 (WHO/HTM/STB/2010.2). Available at: http://www.stoptb.org/assets/documents/global/plan/TB_GlobalPlanToStopTB2011-2015.pdf

BOX 3.1

Global targets and indicators that are part of the MDG framework

MDG 6, Target 6c. To halt and reverse the incidence of TB.

Indicators in the MDG framework and associated targets: The indicators in the MDG framework are TB incidence, prevalence and mortality rates; the case detection rate; and the percentage of TB patients successfully treated. The Stop TB Partnership set targets to halve prevalence and mortality rates by 2015 compared with a baseline of 1990. In 1991, the World Health Assembly (WHA) set targets to detect at least 70% of incident cases and to successfully treat at least 85% of TB patients by 2000 (later reset to 2005); these WHA targets were not updated after 2005 but are still used for reference.

In **Table 3.1** “met” means that the target had been reached by 2014; “on track” means that the latest projections suggest that the target will be reached by 2015; and “not on track” means that the target will not be reached in 2015 without a major acceleration in the current rate of progress.

3.1 Targets for reductions in TB disease burden by 2015

3.1.1 Global progress

The MDG target that the TB incidence rate should be falling by 2015 has already been met globally. Worldwide, the TB incidence rate has been falling for about a decade.

Globally, the targets of halving TB prevalence and TB mortality rates by 2015 compared with a baseline of 1990 are not on track to be met. This is in line with previous assessments for TB prevalence, which fell by a best estimate of 41% between 1990 and 2013. However, the latest assessment that the TB mortality target is not on track to be met is more recent. This follows new evidence about the level of TB disease burden in Nigeria from the country's first ever national survey of the prevalence of TB disease, which led to an upward revision of levels of TB incidence, prevalence and mortality. The size of Nigeria's population and share of the regional and global TB burden mean that this change to burden estimates in Nigeria affects both regional and global assessments of progress. Nonetheless, globally the TB mortality rate is estimated to have fallen 45% between 1990 and 2013, demonstrating that major progress has been made.

3.1.2 Regional progress

The target that the TB incidence rate should be falling has been achieved in all six WHO regions. The target of halving the TB mortality rate has already been achieved in three regions: the Region of the Americas, the South-East Asia Region and the Western Pacific Region. The other three regions are not on track to achieve the target. The target of halving the 1990 level of TB prevalence has already been achieved in the Region of the Americas and the Western Pacific Region. The currently available data suggest that the South-East Asia Region is on track to meet the target by the end of 2015; however, a reassessment will be made towards the end of 2014 or early 2015 based on the findings from the 2013/2014 national TB prevalence survey in Indonesia, and again towards the end of 2015 when a national TB prevalence survey is scheduled to be complet-

ed in Bangladesh. The other three regions are not on track to achieve the target, although in the European Region both prevalence and mortality rates have been falling fast for the past decade. In this region (as in the African Region), the upsurge in cases and deaths during the 1990s (see **Figure 2.7** in **Chapter 2**) has made it difficult to halve 1990 levels of prevalence and mortality by 2015.

3.1.3 Progress in the 22 HBCs

The target that the TB incidence rate should be falling has been achieved in 15 out of 22 HBCs. The six countries where TB incidence is assessed as stable are Afghanistan, Bangladesh, the Democratic Republic of the Congo, Mozambique, Nigeria and Pakistan. Updated estimates will shortly be available for Indonesia (see also **Box 2.1**, **Chapter 2**); it is anticipated that the incidence rate will be assessed to be falling.

The target of halving the TB mortality rate has already been achieved in nine HBCs, including all four HBCs in the Western Pacific Region (Cambodia, China, the Philippines, Viet Nam) as well as Brazil, Ethiopia, Myanmar, Uganda and the United Republic of Tanzania. India appears on track to reach the target. A reassessment of the trend in TB mortality in Indonesia is underway; the remaining 11 HBCs appear unlikely to meet the target.

The target of halving the 1990 level of TB prevalence has already been achieved in nine HBCs, including all four HBCs in the Western Pacific Region as well as Brazil, Ethiopia, India, Uganda and the United Republic of Tanzania. Myanmar appears on track to achieve the target. A reassessment of the trend in TB prevalence in Indonesia is underway; the remaining 11 HBCs appear unlikely to meet the target.

Eight of the 22 HBCs are assessed to have met all of the 2015 targets for reductions in TB cases and deaths: these are Brazil, Cambodia, China, Ethiopia, the Philippines, Uganda, the United Republic of Tanzania and Viet Nam. A further two HBCs are on track to do so by 2015: India and Myanmar. Combined, these 10 countries had 46% of the world's population and 47% of estimated incident cases in 2013.

TABLE 3.1

Progress towards 2015 targets set within the MDG framework.

Assessment is for 2013 unless specified

MDG FRAMEWORK: INDICATORS AND TARGETS						
INDICATOR	TB INCIDENCE RATE	TB PREVALENCE RATE	TB MORTALITY RATE	TB CASE DETECTION RATE (%) ^a	TB TREATMENT SUCCESS RATE: NEW AND RELAPSE CASES, 2012 (%) ^a	
TARGET	INCIDENCE RATE FALLING	50% REDUCTION IN PREVALENCE RATE BY 2015 COMPARED WITH 1990	50% REDUCTION IN MORTALITY RATE BY 2015 COMPARED WITH 1990			
GLOBAL						
Global	Met	Not on track	Not on track	64 (61–66)	86	
WHO REGION						
African (AFR)	Met	Not on track	Not on track	52 (46–57)	81	
Americas (AMR)	Met	Met	Met	77 (73–80)	76	
Eastern Mediterranean (EMR)	Met	Not on track	Not on track	58 (49–71)	87	
European (EUR)	Met	Not on track	Not on track	80 (77–84)	75	
South-East Asia (SEAR)	Met	On track	Met	62 (59–65)	88	
Western Pacific (WPR)	Met	Met	Met	83 (79–88)	92	
22 HIGH-BURDEN COUNTRIES						
AFR	DR Congo	Not on track	Not on track	Not on track	51 (47–56)	88 ^b
	Ethiopia	Met	Met	Met	62 (51–74)	91 ^b
	Kenya	Met	Not on track	Not on track	75 (74–77)	86
	Mozambique	Not on track	Not on track	Not on track	37 (30–47)	87 ^b
	Nigeria	Not on track	Not on track	Not on track	16 (11–28)	86 ^b
	South Africa	Met	Not on track	Not on track	69 (60–76)	77
	Uganda	Met	Met	Met	73 (63–81)	77
	UR Tanzania	Met	Met	Met	79 (77–83)	90
	Zimbabwe	Met	Not on track	Not on track	42 (36–49)	81 ^b
AMR	Brazil	Met	Met	Met	82 (72–92)	72
EMR	Afghanistan	Not on track	Not on track	Not on track	53 (47–60)	88
	Pakistan	Not on track	Not on track	Not on track	58 (44–78)	91 ^b
EUR	Russian Federation	Met	Not on track	Not on track	83 (74–91)	69
SEAR	Bangladesh	Not on track	Not on track	Not on track	53 (47–59)	92
	India	Met	Met	On track	58 (54–61)	88
	Indonesia ^d	Reassessment in process as this report went to press			71 (63–80)	86
	Myanmar	Met	On track	Met	68 (61–74)	89 ^b
	Thailand	Met	Not on track	Not on track	80 (71–89)	81
WPR	Cambodia	Met	Met	Met	62 (56–68)	94
	China	Met	Met	Met	87 (79–93)	95
	Philippines	Met	Met	Met	80 (71–90)	88 ^b
	Viet Nam	Met	Met	Met	76 (63–91)	91
CLASSIFICATION ^c						
	Met	Met	Met	≥70%	≥85%	
	On track	On track	On track	55–69%	70–84%	
	Not on track	Not on track	Not on track	<55%	<70%	

^a The bands are defined according to the targets that existed when the MDGs were established.^b Treatment success rates refer to all new cases only.^c *On track* means that the indicator will likely be achieved by 2015 based on the current predicted trend.^d As this report went to press, estimates of the TB disease burden in Indonesia were being revised based on the results of the 2013–2014 national TB prevalence survey. Updated estimates will be published online. See also **Box 2.1** in **Chapter 2**.

TABLE 3.2

Progress towards 2015 targets for the response to TB/HIV and MDR-TB set in the Global Plan to Stop TB 2011–2015. Assessment is for 2013 unless specified

INDICATOR		TB/HIV: 2015 GLOBAL PLAN TARGETS			MDR-TB: 2015 GLOBAL PLAN TARGETS	
		TB PATIENTS WITH KNOWN HIV STATUS (%)	NOTIFIED HIV-POSITIVE TB PATIENTS STARTED ON ART (%)	PEOPLE LIVING WITH HIV NEWLY ENROLLED IN HIV CARE WHO WERE STARTED ON IPT	ESTIMATED MDR-TB CASES THAT WERE DETECTED AND NOTIFIED (%) ^a	TREATMENT SUCCESS RATE: CONFIRMED MDR-TB CASES, 2011 COHORT (%)
TARGET		100%	100%	50% ^b	100%	≥75%
GLOBAL						
Global		48	70		45	48
WHO REGION						
African (AFR)		76	69		74	47
Americas (AMR)		69	65		47	56
Eastern Mediterranean (EMR)		11	38		22	64
European (EUR)		59	54		61	46
South-East Asia (SEAR)		43	81		45	54
Western Pacific (WPR)		35	60		16	52
22 HIGH-BURDEN COUNTRIES						
AFR	DR Congo	44	48		9	59
	Ethiopia	71	68		40	72
	Kenya	94	84		6	70
	Mozambique	91	72	17	19	31
	Nigeria	88	67	3.5	18	63
	South Africa	90	66	>100 ^c	>100 ^d	45
	Uganda	91	65		12	77
	UR Tanzania	83	73	0.4	10	75
	Zimbabwe	92	77	3.5	53	81
AMR	Brazil	65			39	56
EMR	Afghanistan	26		23	6	29
	Pakistan	2.8			20	70
EUR	Russian Federation	e			33	37
SEAR	Bangladesh	1.1	100	0	22	68
	India	63	88		57	50
	Indonesia	2.3	21		13	60
	Myanmar	12	74	19	22	71
	Thailand	83	59		12	
WPR	Cambodia	82	89	55	24	86
	China	39	67		8	50
	Philippines	2.1			47	41
	Viet Nam	70	61		24	72
CLASSIFICATION						
		≥80% tested	≥80%	≥50%	≥80% detected and notified	≥75%
		50–79% tested	50–79%	25–49%	50–79% detected and notified	50–74%
		<50% tested			<50% detected and notified	
		Yellow hatching indicates the overall burden of TB/HIV is low ^f	<50%	<25%	Yellow hatching indicates the overall burden of MDR-TB is low ^g	<50%

A blank white cell indicates that no data are available.

^a The numerator is the number of notified rifampicin-resistant and MDR-TB cases. The denominator is the estimated number of MDR-TB cases among notified cases of pulmonary TB.

^b Approximately 50% of patients newly enrolled in HIV care are expected to be eligible for IPT.

^c The denominator (i.e. number newly enrolled in HIV care) for South Africa may be too low or the numerator may be too high.

^d The denominator (i.e. estimated number of MDR-TB cases) for South Africa may be too low. A national drug resistance survey is underway and will be completed in 2014.

^e The exact percentage could not be calculated for all cases, but more than 90% of new TB cases in the civilian sector were tested for HIV.

^f ≤5% TB cases are HIV positive.

^g ≤3% MDR-TB prevalence in new TB cases and <1000 estimated MDR-TB cases among notified pulmonary TB cases.

The 11 HBCs that are not on track to reach one or more of the three targets for reductions in incidence, prevalence and mortality are the Democratic Republic of the Congo, Kenya, Mozambique, Nigeria, South Africa and Zimbabwe in the African Region; Afghanistan and Pakistan in the Eastern Mediterranean Region; Bangladesh and Thailand in the South-East Asia Region; and the Russian Federation in the European Region. Most of these countries have faced one or more severe challenges including resource constraints, conflict and instability, and generalized HIV epidemics. Of the 11 countries, six are not on track to reach any of the three targets of reductions in burden; these are Afghanistan, Bangladesh, Democratic Republic of the Congo, Mozambique, Nigeria and Pakistan.

3.2 Treatment success and case detection

The treatment success rate among new cases and the case detection rate (calculated as notifications of new and relapse cases divided by estimated incidence) are indicators within the MDG framework (Box 3.1). Targets were not set for these indicators, but previous targets of an 85% treatment success rate and a 70% CDR that were set for 2005 offer a useful reference point.

3.2.1 Global progress

Globally in 2012, the treatment success rate among new cases was 86%, similar to the level reached since 2007. This demonstrates that high quality care for TB patients is being provided in most countries.

Of the 9.0 million (range, 8.7–9.4 million) incident

TABLE 3.3

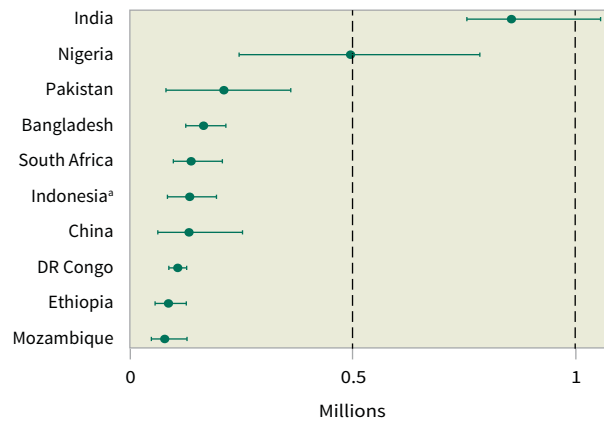
Ten countries that account for 74% (2.4 million) of the estimated “missed” cases globally, 2013. The number of missed cases is defined as the difference between the estimated number of incident cases and notified (new and relapse) cases in 2013

COUNTRY	SHARE OF TOTAL MISSED CASES (%)	CUMULATIVE SHARE OF TOTAL MISSED CASES (%)
India	27	27
Nigeria	15	42
Pakistan	7	49
Bangladesh	5	54
South Africa	4	58
Indonesia ^a	4	62
China	4	66
Democratic Republic of the Congo	3	69
Ethiopia	3	72
Mozambique	2	74

^a As this report went to press, estimates of TB disease burden in Indonesia were being revised based on the results of the 2013–2014 national TB prevalence survey. Estimates of the number of missed cases will also be produced. Updated estimates will be published online.

FIGURE 3.1

Estimated number of missed cases in top-ten countries, 2013. The range shows the lower and upper bounds of the 95% uncertainty interval. The bullet marks the best estimate.



^a As this report went to press, estimates of TB disease burden in Indonesia were being revised based on the results of the 2013–2014 national TB prevalence survey. Estimates of the number of missed cases will also be produced. Updated estimates will be published online.

cases of TB estimated to have occurred in 2013 (Chapter 2), only 5.7 million were both detected and notified to national TB programmes (NTPs) or national surveillance systems (Chapter 4), giving a case detection rate of 64% (range, 61–66%). This leaves a gap of approximately 3.3 million people with TB who were “missed”, either because they were not diagnosed or because they were diagnosed but not reported.

About 74% of the “missed cases” exist in 10 countries (Table 3.3 and Figure 3.1). Major efforts to ensure that all detected cases are reported to NTPs and to improve access to care to reduce levels of under-diagnosis are needed, especially in these countries. Top priority actions to reduce levels of underreporting include intensified collaboration with public hospitals and the private sector; mandatory notification of cases; and specific efforts to compile data on diagnosed cases from facilities that are not routinely reporting to national surveillance systems. In many countries, improving access to basic TB diagnostic and treatment services is essential to reduce levels of under-diagnosis.

Improvements in case detection in India and Nigeria would have a global impact, given the size of the TB burden in these countries and the sizeable gap between notified cases and estimated incidence. A recent study in India suggests that about 50% of detected cases are not reported to the NTP,¹ a finding confirmed in a recent prevalence survey in Gujarat state (unpublished data). The first-ever national TB prevalence survey in Nigeria showed that

¹ Satyanarayana SI et al. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. *PLoS One*. 2011; 6(9):e24160. doi: 10.1371/journal.pone.0024160. Epub 2011 Sep 2.

there were many people with undiagnosed TB and typical TB symptoms in the community, and that access to basic diagnostic and treatment services needs to be substantially improved to ensure that people with TB are promptly identified and treated (for further details see [Box 2.5](#) in [Chapter 2](#)).

3.2.2 Regional progress

The treatment success rate has been sustained at above 85% for several years in three regions: the Eastern Mediterranean, South-East Asia and Western Pacific regions. It was 81% in the African Region in 2012, representing improvement from 79% in 2011. In the European Region and the Region of the Americas, treatment outcomes (at 75% and 76% respectively in 2012) require improvement. In the latter, reducing the proportion of cases for whom the treatment outcome is not documented would help.

In 2013, the case detection rate was relatively high (best estimates of 77–83%) in three regions: the European and Western Pacific regions, and the Region of the Americas. It was much lower in the other three regions, and especially the African Region (best estimate 52%). The estimate for the African Region is strongly influenced by the case detection rate in Nigeria, which was revised downwards (to a best estimate of 16% in 2013) in the latest series of estimates following the findings of the 2012 national TB prevalence survey.

3.2.3 Progress in the 22 HBCs

The treatment success rate in most of the 22 HBCs has been sustained at high levels for several years. In 2012, 16 of the 22 HBCs achieved a treatment success rate of $\geq 85\%$. Improvements are still required in Brazil, the Russian Federation, South Africa, Thailand, Uganda and Zimbabwe.

The case detection rate was relatively high in 2013 in most of the HBCs in the South-East Asia and Western Pacific regions, as well as Brazil and the Russian Federation. It was lowest in Afghanistan, Bangladesh, the Democratic Republic of the Congo, Mozambique, Nigeria and Zimbabwe.

3.3 Targets for the response to the epidemics of TB/HIV and MDR-TB

Several targets for the response to the co-epidemics of TB and HIV and the epidemic of MDR-TB were set in the *Global Plan to Stop TB 2011–2015*. Key TB/HIV targets for 2015 ([Table 3.2](#)) were that 100% of TB patients should know their HIV status, 100% of HIV-positive TB patients should be enrolled on antiretroviral treatment (ART) and that all those newly enrolled in HIV care and eligible for treatment for latent TB infection should be provided with isoniazid preventive therapy (IPT). Reaching these targets is of particular importance in the African Region, since this region accounts for almost 80% of the world's HIV-

positive TB cases ([Chapter 2](#)). For the response to MDR-TB, the main targets for 2015 were that all TB patients with MDR-TB should be detected and enrolled on second-line treatment, and that the treatment success rate should be $\geq 75\%$.

3.3.1 Global progress

Globally, progress in 2013 fell considerably short of targets. Less than half (48%) of TB patients knew their HIV status, 70% of HIV-positive TB patients reported by NTPs were on ART, 45% of the estimated 300 000 reported TB patients with MDR-TB were detected and the treatment success rate (for the 2011 cohort) was 48%. An accurate assessment of IPT coverage among people with HIV who were newly enrolled in care in 2013 was not possible due to data quality issues (see also [Chapter 7, Box 7.1](#)).

A total of 136 000 people with MDR-TB or rifampicin-resistant TB (RR-TB) who are eligible for MDR-TB treatment were notified globally in 2013. This was a large increase (23%) compared with 2012, when 111 000 cases were detected. Nonetheless, a major diagnostic gap remains: the 136 000 represented 45% of the estimated 300 000 notified TB patients with MDR-TB in 2013. There were also diagnosis:treatment gaps, which are growing in some countries: only 97 000 people were started on MDR-TB treatment in 2013.

3.3.2 Regional progress

The African Region bears the highest TB/HIV burden (almost 80% of HIV-positive TB cases in 2013), and has made considerable progress in the implementation of TB/HIV interventions. In 2013, 76% of TB patients knew their HIV status and 69% of HIV-positive TB patients were on ART. Coverage of HIV testing was relatively high in the European Region (59%) and the Region of the Americas (69%), but below 50% in the other three regions. For TB patients detected as being co-infected with HIV, coverage of ART was highest in the South-East Asia Region in 2013 (81%) and lowest in the Eastern Mediterranean Region (38%), and in the range 54–69% elsewhere. Accurate assessments of IPT coverage among people with HIV who were newly enrolled in care in 2013 are not yet available for any region.

Of the 27 high MDR-TB burden countries, 15 are in the European Region. A regional MDR-TB action plan has already been developed under the leadership of the WHO Regional Office for Europe and approved by all Member States. Compared with the other regions, the ratio of detected cases to the estimated number among notified TB patients was relatively high in 2013 (61%, 45 000/74 000). In the South-East Asia Region, where there were an estimated 89 000 cases of MDR-TB among notified TB patients (almost one-third of the global total), the ratio was 45% (40 000/89 000). This was an improvement compared with 2012, mostly due to progress in detection

of cases in India. In the Western Pacific Region, where there were an estimated 71 000 cases of MDR-TB among notified TB patients in 2013 (mostly in China), the ratio was much lower (16%, 11 000/71 000); given success in achieving other global TB targets, a top regional priority is the rapid expansion of MDR-TB diagnosis and treatment services. Other regions have relatively small numbers of cases, and the ratio of detected to estimated cases was relatively high in the African Region (74%). Treatment outcomes for patients treated on second-line regimens were about 50% or less in most regions; the exception is the Eastern Mediterranean Region (64% for the 2011 cohort).

3.3.3 Progress in the 22 HBCs

In almost all of the African HBCs with the highest TB/HIV burden, a very high proportion of TB patients knew their HIV status in 2013. Coverage of ART among HIV-positive TB patients also reached 65–77% in seven African countries. Levels of testing and ART coverage were

especially high in Kenya (94% and 84%, respectively), demonstrating that more could also be achieved in other countries. In HBCs outside Africa, the proportion of TB patients with documented HIV status was generally lower in 2013; Cambodia and Thailand were exceptions. Coverage of ART among those known to be HIV-positive ranged from 21% in Indonesia to 100% in Bangladesh.

In most of the 22 HBCs, less than 30% of the notified TB patients estimated to have MDR-TB remained were detected in 2013. Exceptions were South Africa (where the burden of MDR-TB may be revised upwards when results from the 2013/2014 survey of drug resistance become available), India and Zimbabwe. Compared with the global average and regional figures, 12 of the 22 HBCs are achieving relatively good treatment outcomes for MDR-TB patients ($\geq 60\%$), and eight (Cambodia, Ethiopia, Myanmar, Pakistan, Uganda, the United Republic of Tanzania, Viet Nam and Zimbabwe) have achieved levels of 70% or higher.

TB case notifications and treatment outcomes

KEY FACTS AND MESSAGES

In 2013, 6.1 million cases of TB were notified by NTPs and reported to WHO: 5.7 million were individuals newly diagnosed in 2013 and 0.4 million were previously diagnosed TB patients whose treatment regimen was changed. India and China accounted for 37% of notified cases of TB worldwide in 2013; African countries for 23%; and the 22 HBCs for 81%.

Among pulmonary TB cases, 58% were bacteriologically confirmed (as opposed to clinically diagnosed) in 2013.

Globally in 2012, the treatment success rate was 86% among all new TB cases. Improvement in treatment outcomes is needed in the European Region, where the treatment success rate in 2012 was 75%.

Notifications of TB cases have stabilized in recent years, and in 2013 represented 64% (range, 61–66%) of estimated incident cases. The gap between notifications and incident cases – an estimated total of 3.3 million cases – can be explained by a mixture of underreporting of diagnosed TB cases (for example, failure to notify cases diagnosed in the private sector) and under-diagnosis due to poor access to health care and/or failure to detect cases when people visit health care facilities. Major efforts are needed to ensure that all cases are detected, notified to national surveillance systems, and treated according to international standards.

In 2013, most notified TB cases were adults. Children (aged <15 years) accounted for 6% of notified cases. The male:female ratio of notified cases across all age groups was 1.6 globally, ranging from 1.0 in the Eastern Mediterranean Region to 2.2 in the Western Pacific Region.

Routine recording and reporting of the numbers of TB cases diagnosed and treated by NTPs and monitoring of treatment outcomes was one of the five components of the global TB strategy (DOTS) launched by WHO in the mid-1990s; this remains a core element of its successor, the *Stop TB Strategy* (**Chapter 1**). With the standard definitions of cases and treatment outcomes recommended by WHO and associated recording and reporting framework as a foundation, global monitoring of trends in case notifications and treatment outcomes has been possible since 1995. The number of people diagnosed and treated for TB and associated treatment outcomes is routinely monitored by NTPs in almost all countries, which in turn report these data to WHO in annual rounds of global TB data collection (**Chapter 1**).

This chapter has four parts. **Section 4.1** summarizes the total number of people diagnosed with TB and notified by NTPs in 2013; these numbers are also disaggregated by case type, age and sex. **Section 4.2** presents and discusses the contribution to total case notifications of public–public and public–private mix (PPM) initiatives in 24 countries and of community-based care in 22 countries. **Section 4.3** presents trends in notification between 1990 and 2013 and compares these with trends in estimated TB incidence. The ratios of notified: estimated incident cases (an indicator known as the case detection rate or CDR) are provided for selected years. **Section 4.4** describes the latest data on treatment outcomes (for cases registered for treatment in 2012) as well as treatment outcomes achieved in selected years since 1995.

4.1 Case notifications in 2013 by type of disease, age and sex

The definitions of TB cases recommended by WHO as part of an updated recording and reporting framework issued in March 2013,¹ and used in the 2014 round of global TB data collection, are shown in **Box 4.1**. These updated definitions were necessary to accommodate diagnosis using Xpert MTB/RIF and other WHO-endorsed molecular tests (**Chapter 6**), as well as offering an opportunity to improve aspects of the previous (2006) framework, such as inclusion of more comprehensive reporting of TB cases among children.

¹ *Definitions and reporting framework for tuberculosis – 2013 revision*. Geneva, World Health Organization, 2013 (WHO/HTM/TB/2013.2). Available at www.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf.

BOX 4.1

WHO definitions of TB cases recommended for use since March 2013 and that were used in the 2014 round of global TB data collection^a

Bacteriologically confirmed case of TB A patient from whom a biological specimen is positive by smear microscopy, culture or WHO-approved rapid diagnostic test (such as Xpert MTB/RIF). All such cases should be notified, regardless of whether TB treatment is started.

Clinically diagnosed case of TB A patient who does not fulfil the criteria for bacteriologically confirmed TB but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This definition includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and extrapulmonary cases without laboratory confirmation. Clinically diagnosed cases subsequently found to be bacteriologically positive (before or after starting treatment) should be reclassified as bacteriologically confirmed.

Case of pulmonary TB Any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Miliary TB is classified as pulmonary TB because there are lesions in the lungs. Tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitute a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB.

Case of extrapulmonary TB Any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges.

New case of TB A patient who has never been treated for TB or has taken anti-TB drugs for less than one month.

Previously treated case of TB A patient who has been treated for one month or more with anti-TB drugs in the past. Re-

treatment cases are further classified by the outcome of their most recent course of treatment into four categories.

1. *Relapse* patients have previously been treated for TB, were declared cured or treatment completed at the end of their most recent course of treatment, and are now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).
2. *Treatment after failure* patients have previously been treated for TB and their most recent course of treatment failed i.e. they had a positive sputum smear or culture result at month 5 or later during treatment.
3. *Treatment after loss to follow-up* patients have previously been treated for TB and were declared 'lost to follow-up' at the end of their most recent course of treatment.
4. *Other previously treated* patients are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

Case of multidrug-resistant TB (MDR-TB) TB that is resistant to two first-line drugs: isoniazid and rifampicin. For most patients diagnosed with MDR-TB, WHO recommends treatment for 20 months with a regimen that includes second-line anti-TB drugs.

Case of rifampicin-resistant TB (RR-TB) A patient with TB that is resistant to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether mono-resistance, multidrug resistance, polydrug resistance or extensive drug resistance.

^a *Definitions and reporting framework for tuberculosis – 2013 revision*. Geneva, World Health Organization, 2013 (WHO/HTM/TB/2013.2). Available at <http://www.who.int/tb/publications/definitions/en/>.

In 2013, 6.1 million people with TB were notified to NTPs and reported to WHO. Of these, 5.7 million had a new episode of TB (shown as the total of new and relapse cases in **Table 4.1**) and 0.4 million had already been diagnosed with TB but treatment was changed to a retreatment regimen. Of the 5.7 million new and relapse cases, 5.4 million had TB for the first time and 0.3 million experienced a recurrent episode of TB after being previously cured of the disease. Among the 5.4 million new cases, 2.6 million had bacteriologically confirmed pulmonary TB, 2.0 million had clinically diagnosed pulmonary TB and 0.8 million had extrapulmonary TB.

India and China accounted for 37% of the 5.7 million new and relapse cases of TB that were notified in 2013 (22% and 15%, respectively); the South-East Asia and Western Pacific Regions (which include India and China, respectively) together accounted for 61% of such cases globally. African countries accounted for 23% of new and relapse TB cases globally, with almost one-quarter of these cas-

es from one country – South Africa. The WHO Eastern Mediterranean and European Regions and the Region of the Americas accounted for 16% of new and relapse TB cases notified in 2013 (7.6%, 4.6% and 3.8%, respectively); combined, the 22 HBCs accounted for 81% of such cases.

Among the 22 HBCs, the percentage of new pulmonary cases that were bacteriologically confirmed was relatively high in the Democratic Republic of the Congo (83%) and relatively low in China (37%), Myanmar (38%), the Philippines (45%), the Russian Federation (47%), South Africa (43%) and Zimbabwe (45%).

Most cases were adults (**Table 4.2**); children (aged <15 years) accounted for only 6% of notifications. In WHO's Western Pacific Region, TB represents a markedly aging epidemic, with a progressive increase in the notification rate with age and a peak among those aged ≥65 years old (**Figure 4.1**). A similar pattern is evident in the Eastern Mediterranean Region and, to a lesser extent, in the South-East Asia Region. Elsewhere, notification rates in

TABLE 4.1

Case notifications, 2013

	TOTAL NOTIFIED	NEW AND RELAPSE ^a	RETREATMENT EXCLUDING RELAPSE	NEW OR PREVIOUS TREATMENT HISTORY UNKNOWN			RELAPSE			PERCENTAGE OF PULMONARY CASES BACTERIOLOGICALLY CONFIRMED
				PULMONARY BACTERIOLOGICALLY CONFIRMED	PULMONARY CLINICALLY DIAGNOSED	EXTRA-PULMONARY	PULMONARY BACTERIOLOGICALLY CONFIRMED	PULMONARY CLINICALLY DIAGNOSED	EXTRA-PULMONARY	
Afghanistan	31 622	30 507	1 115	14 277	8 020	7 056	1 154			66
Bangladesh	190 891	184 506	6 385	105 539	42 394	33 704	2 869	0	0	72
Brazil	83 310	76 020	7 290	41 885	18 303	10 148	3 613	1 604	467	70
Cambodia	39 055	37 743	1 312	14 082	9 069	14 203	389	0	0	61
China	855 241	847 176	8 065	275 915	512 469	30 767	28 025			37
DR Congo	113 603	112 439	1 164	71 526	13 887	20 297	3 981	1 943	805	83
Ethiopia	131 677	131 677		43 860	45 464	42 353				49
India	1 415 617	1 243 905	171 712	621 762	292 926	226 557	102 660			71
Indonesia	327 103	325 582	1 521	196 310	103 888	17 420	6 406	1 558		66
Kenya	89 796	89 796		34 686	32 153	14 478	4 632	3 847	0	52
Mozambique	56 220	53 272	2 948	23 115	20 131	5 523	2 081	2 422		53
Myanmar	142 162	134 855	7 307	42 595	70 519	16 887	4 854			40
Nigeria	100 401	94 825	5 576	52 811	33 873	5 313	2 828			62
Pakistan	298 446	288 910	9 536	111 682	118 279	52 646	6 303	0	0	50
Philippines	244 392	229 918	14 474	97 353	123 510	4 386	4 669	0	0	45
Russian Federation	142 533	106 053	36 480	37 779	43 859	8 789	7 866	7 194	566	47
South Africa	328 896	312 380	16 516	109 630	148 658	37 709	7 751	8 627	5	43
Thailand	66 415	63 541	2 874	32 887	19 559	9 293	1 802	0	0	64
Uganda	47 650	45 549	2 101	25 442	12 852	5 328	1 312	615		67
UR Tanzania	65 732	64 053	1 679	24 565	23 371	15 016	1 101			52
Viet Nam	102 196	100 395	1 801	50 607	24 403	18 326	7 059			70
Zimbabwe	35 278	32 899	2 379	11 404	15 807	4 413	1 275			45
High-burden countries	4 908 236	4 606 001	302 235	2 039 712	1 733 394	600 612	202 630	27 810	1 843	56
AFR	1 414 085	1 338 203	75 882	591 519	457 249	224 742	45 232	18 093	1 368	57
AMR	231 330	218 875	12 455	129 469	42 365	33 777	10 004	2 416	844	76
EMR	448 597	434 433	14 164	173 949	148 748	99 897	11 251	112	476	55
EUR	349 745	287 015	62 730	116 082	87 583	41 245	27 162	12 726	2 217	59
SEAR	2 297 033	2 098 170	198 863	1 054 316	580 374	333 666	128 256	1 558	0	67
WPR	1 375 746	1 343 057	32 689	496 303	700 129	96 838	46 025	2 440	1 322	44
Global	6 116 536	5 719 753	396 783	2 561 638	2 016 448	830 165	267 930	37 345	6 227	58

Blank cells indicate data not reported.

^a New and relapse includes cases for which the treatment history is unknown.

2013 peaked in younger adults. The male:female sex ratio was 1.6 globally, but among HBCs this ratio varied from 0.7 in Afghanistan to 2.9 in Viet Nam. Variation among countries may reflect real differences in epidemiology as well as differential access to or use of health care services linked to the NTP.

Not all HBCs reported notification data disaggregated by age and sex. Further efforts are needed in these and some other countries to ensure that all cases reported globally can be disaggregated by age and sex.

4.2 Contribution of public–public and public–private mix initiatives and community-based TB activities to TB case notifications and treatment support in 2013

4.2.1 Public–public and public–private mix (PPM)

Ensuring proper diagnosis, standardized treatment and prompt notification of all TB cases to NTPs requires collaboration with the full range of health care providers. Engaging all care providers in TB care and control is component 4 of the *Stop TB Strategy* (Chapter 1). Its two subcomponents are:

TABLE 4.2

Notifications of new and relapse TB cases by age and sex, 2013

	0-14 YEARS	≥15 YEARS	AGE UNKNOWN	% AGED <15 YEARS	MALE/FEMALE RATIO
Afghanistan	3 454	18 843	8 210	15	0.7
Bangladesh*	5 051	176 586	0	2.8	1.5
Brazil	2 647	73 349	24	3.5	2.0
Cambodia*	64	14 019	0	0.5	1.2
China	4 830	842 346	0	0.6	2.2
DR Congo*	3 086	68 134	306	4.3	1.3
Ethiopia*	21 317	98 644	11 716	18	1.2
India	64 726	1 179 179		5.2	—
Indonesia	26 054	299 528		8.0	1.4
Kenya*	4 383	69 952		5.9	1.4
Mozambique				—	—
Myanmar				—	—
Nigeria	5 776	94 625	0	5.8	1.5
Pakistan*	28 113	254 494		9.9	1.0
Philippines*	2 065	95 156		2.1	2.3
Russian Federation*	3 298	87 129	0	3.6	2.2
South Africa	36 671	275 709	0	12	1.2
Thailand				—	—
Uganda*	649	24 759		2.6	1.9
UR Tanzania*	6 658	56 294		11	1.4
Viet Nam*	143	50 464		0.3	2.9
Zimbabwe	2 567	30 332		7.8	1.3
High-burden countries	221 552	3 809 542	20 256	5.5	1.6
AFR	95 764	954 843	14 005	9.1	1.4
AMR	11 271	200 870	1 864	5.3	1.7
EMR	39 697	369 337	9 923	9.7	1.0
EUR	10 902	251 619	2 458	4.2	2.0
SEAR	102 196	1 766 628	0	5.5	1.5
WPR	15 170	1 121 200	91	1.3	2.2
Global	275 000	4 664 497	28 341	5.6	1.6

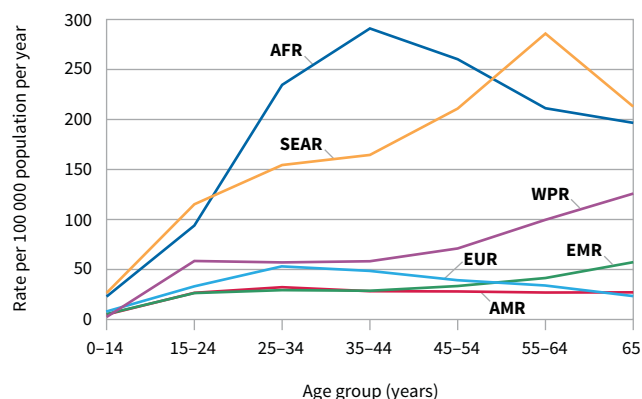
Blank cells indicate data that could not be reported for the age categories shown.

— indicates values that cannot be calculated.

* New cases only.

FIGURE 4.1

Regional TB notification rates by age, 2013^a



^a Countries not reporting cases in these categories are excluded. Cases included make up 55% of reported cases and exclude the following high-burden countries: Afghanistan, Ethiopia, India, Mozambique, Myanmar, Pakistan, Thailand and UR Tanzania.

- involving all public, voluntary, corporate and private providers through PPM approaches; and
- promoting the *International Standards for Tuberculosis Care*.¹

Many countries have scaled up PPM initiatives. Demonstrating progress in terms of the contribution of non-NTP providers to total case notifications requires systematic recording of the source of referral and place of TB treatment locally, and reporting and analysis of aggregated data nationally.² In 2014, 74 countries reported summary data to WHO, and data for 24 of these countries (including 14 HBCs) are shown in Table 4.3. In most of these countries, PPM initiatives contributed about 10% to 40% of total notifications.

Considering that the private medical sector in Africa is smaller than that in Asia, the contribution of private-for-profit and not-for-profit providers in Ethiopia, Kenya, Nigeria and the United Republic of Tanzania is noteworthy. Progress in parts of Asia is also noticeable – almost every third or fourth case in India, Indonesia and Myanmar was notified by non-NTP care providers in 2013. Large public sector hospitals have contributed sizeable proportions of cases in China (over 50% of notified cases), Indonesia and the Philippines. In India, a large proportion of the cases notified by non-NTP providers were from medical colleges: 87% of notifications from public non-NTP providers, 51% of notifications from private providers, and 76% of total (public and private) notifications from non-NTP providers (data not shown). Engagement of large hospitals that were not previously working with or reporting cases to NTPs is one of the major strategies required to improve notification of TB cases. In the

¹ http://www.istcweb.org/ISTC_Documents.html

² WHO recommends that the source of referral and the place of treatment be routinely recorded and reported.

TABLE 4.3

Contribution of public-private and public-public mix (PPM) to notifications of TB cases in 24 countries, 2013

COUNTRY	MAIN TYPES OF CARE PROVIDERS ENGAGED	NUMBER OF TB CASES NOTIFIED BY PUBLIC NON-NTP CARE PROVIDERS ^a	NUMBER OF TB CASES NOTIFIED BY PRIVATE CARE PROVIDERS ^b	PPM CONTRIBUTION TO TOTAL NOTIFICATIONS OF TB CASES IN 2013 (%)
African Region				
Ethiopia	Diverse private care providers	—	18 455	14
Ghana	Diverse non-NTP public and private care providers	1 475	987	16
Kenya	Private hospitals and care providers	—	18 881	21
Nigeria	Public, private and corporate care providers	10 334	13 846	24
Swaziland	Diverse non-NTP public and private care providers	1 882	632	36
UR Tanzania	Private facilities and faith-based organizations	—	10 040	15
Region of the Americas				
Dominican Republic	Diverse private care providers	—	581	13
El Salvador	Diverse non-NTP public and private care providers	833	30	39
Peru	Social security organizations	6 852	—	22
Eastern Mediterranean Region				
Afghanistan	Private clinics, hospitals, laboratories and pharmacies	2 753	2 972	18
Egypt	Health insurance organizations, NGOs and other public non-NTP care providers	2 000	213	27
Pakistan	Private clinics and hospitals	11 759	41 690	18
Sudan	Diverse non-NTP public and private care providers	789	776	7.8
Yemen	Public hospitals including university, military and police hospitals, prisons and private hospitals	3 773	—	37
European Region				
Georgia	Diverse non-NTP public and private care providers, and prisons	228	1558	41
Ukraine	Prisons	3 423	—	7.1
South-East Asia Region				
Bangladesh	Diverse private, non-NTP public and NGO care providers	2 427	20 719	12
India	Diverse private, non-NTP public and NGO care providers	199 564	85 439	20
Indonesia	Public and private hospitals	67 168	26 345	29
Myanmar	Diverse private, non-NTP public and NGO care providers	4 608	29 858	23
Thailand	Diverse non-NTP public and private care providers	1 532	1 267	4.2
Western Pacific Region				
China	General public hospitals	478 431	—	56
Philippines	Private clinics and hospitals	8 253	19 946	12
Viet Nam	Diverse non-NTP public and private care providers	3 684	5 262	8.8

^a Includes all contributions from non-NTP providers, including public hospitals, public medical colleges, prisons/detention centres, military facilities, railways and public health insurance organizations.

^b Private sector providers include private individual and institutional providers, corporate/business sector providers, mission hospitals, nongovernmental organizations and faith-based organizations.

BOX 4.2

PPM in the post-2015 global TB strategy and recent efforts to strengthen PPM in high-burden countries

As a part of implementing the Stop TB Strategy (Chapter 1), many countries have rolled out PPM programmes to help “engage all care providers” in TB care and control. While progress is encouraging in many countries (Table 4.3), much more work remains to be done. The capacity of NTPs and the financial and other investments required to scale up PPM often prove insufficient. For example, there are many countries in which public and private hospitals attract a large number of people with symptoms of TB, but these hospitals are still not contributing optimally to the detection and reporting of TB cases or ensuring quality of treatment that meets international standards. Often, the contribution of private providers to total case notifications is accounted for by a relatively small number of private clinics and other facilities that have engaged with the NTP. Evidence shows that a large proportion of private providers are not yet collaborating with or have any links to NTPs. Workplace TB programmes operated by small and large businesses in collaboration with NTPs are few and far between. The magnitude of the TB caseload managed outside the network of NTPs is reflected in the large quantities of TB medicines of questionable quality that are purchased in private pharmacies, especially in Asia; these quantities sometimes exceed the quantities of quality-assured medicines that are procured by NTPs.^a Against this backdrop of persistent gaps in reporting of detected cases, questionable standards of treatment and the ambitious targets set in WHO’s post-2015 global TB strategy (Chapter 1), the engagement of all public, private, voluntary and corporate care providers in TB prevention, diagnosis and treatment needs to be substantially increased.

The experiences of countries and partners in implementing PPM for over a decade mean that lessons have been learned about how to improve and scale-up PPM strategies, which have been reflected in the post-2015 global TB strategy. The current PPM strategies implemented by NTPs are largely based on collaborative approaches. The second pillar of the post-2015 global TB strategy envisages strengthened collaboration that is backed up by a strong regulatory framework (including mandatory notification of cases) to support sustainable engagement of all public and private care providers. Priority attention to a context-specific combination of six strategic areas of work is suggested:

1. Enhancing investments to ensure that they are commensurate with the magnitude of the problem of engaging all care providers and the capacity needed within NTPs and ministries of health;
2. Optimizing and expanding engagement of large hospitals, academic institutions and nongovernmental organizations;
3. Sharing the burden of engaging numerous solo private practitioners with “intermediary organizations” such as social franchising and social enterprise institutions, non-governmental organizations with the capacity and skills to work with private practitioners, and professional societies and associations;
4. Mobilizing and supporting the corporate sector to initiate and expand workplace TB programmes;
5. Implementing regulatory approaches such as mandatory case notification, rational use of TB medicines, and certification and accreditation systems to identify and support collaborating providers; and
6. Engaging communities and civil society to create demand for quality TB care from all public and private care providers.

Between May and September 2014, three meetings were held to support the development and incorporation of these strategies into the national TB strategic plans of six HBCs (Bangladesh, India, Indonesia, Myanmar, Pakistan and the Philippines) that have an especially high burden of TB in the private sector. In brief:

- In May 2014, USAID and the World Bank co-convened a meeting on sustainable financing for PPM in which participants examined insurance-based, domestic and results-based financing, and innovative service delivery models for utilizing such funding. The report is available at www.usaid.gov/sites/default/files/documents/1864/ppm_tb_report.pdf.
- In June 2014, WHO and the Global Fund co-organized a workshop to identify barriers to PPM expansion and to facilitate the sharing and improvement of the PPM components of national strategic plans. It is expected that the ambitious plans and associated targets will be used by the six HBCs when preparing the concept notes required to apply for funding in the Global Fund’s new funding model. The meeting report is available at www.who.int/tb/careproviders/ppm/meetings/WHO_GF_PPMreport.pdf.
- In September 2014, the American Thoracic Society held a meeting on the role of medical societies in reaching private providers.

^a Wells WA et al. Size and usage patterns of private TB drug markets in the high burden countries. *PLoS One*, 2011, 6(5):e18964.

European Region and the Region of the Americas, contributions to case notifications from public sector providers outside the purview of the Ministry of Health, such as social security organizations and prison health services, are relatively large.

Approaches to engage non-NTP care providers vary according to the local context, but there are some important cross-cutting elements. One is provision of standardized care by non-NTP providers according to national guidelines, in return for provision of free anti-TB drugs and financial or non-financial incentives. A second is the use of the *International Standards for TB Care*, which facilitates the use of best practices in TB diagnosis and treatment among all care providers, especially those in the private sector. Looking forwards, the post-2015 global TB strategy (**Chapter 1**) includes engagement of all care providers as an underlying principle, and the second of the strategy's three pillars emphasises both more traditional elements of PPM as well as new elements such as policies on mandatory notification of cases. Recent work to support PPM expansion in the context of the new global strategy is highlighted in **Box 4.2**.

4.2.2 Community contributions to TB notifications and treatment support

The role of community engagement in contributing to TB prevention, diagnosis and treatment, especially where people with TB have poor access to formal health services, is well-recognized. Fostering such community participation is an explicit component of the *Stop TB Strategy* and a “strong coalition with civil society organizations and communities” is one of the four principles underpinning the post-2015 global TB strategy (**Chapter 1**).

Community-based TB activities can be defined as activities that are conducted outside the premises of formal health facilities, within community-based structures (for example, schools and places of worship) and households. Such activities can be implemented by community health workers¹ and community volunteers,² regardless of whether they are employed and supervised by a government department or by a nongovernmental organization (NGO). Community engagement can increase TB case detection and notifications and also help to improve treatment outcomes.

Accurate monitoring of the contributions of communities to TB notifications and treatment support requires

¹ Community health workers can be defined as people with some formal education who have been given training to contribute to community-based health services, including TB prevention and patient care and support. Their profile, roles and responsibilities vary greatly among countries, and their time is often compensated by incentives in kind or in cash.

² Community volunteers can be defined as community members who have been systematically sensitized about TB prevention and care, either through a short, specific training scheme or through repeated, regular contact sessions with professional health workers.

BOX 4.3

Definitions of standard indicators used to monitor community engagement

Monitoring of community engagement covers the collection and analysis of data about the extent to which community health workers and community volunteers are involved in TB prevention, diagnosis and treatment, including those supervised by the government and those supervised by nongovernmental, community-based, faith-based or patient-based organisations. In 2013, a consultative process organized by WHO resulted in agreement on a minimum set of three standardized indicators, defined below.

Percentage of TB notifications from community referrals: This indicator measures the proportion of notified TB patients (all forms) who were referred by a community health worker or community volunteer.

Percentage of registered TB patients who received treatment support in the community: This indicator measures the proportion of TB patients who were supported during treatment by a community health worker or community volunteer.

Percentage of registered TB patients who received treatment support in the community who were successfully treated: This indicator measures the proportion of TB patients who received treatment support from a community health worker or community volunteer during their TB treatment and who were successfully treated (see **Box 4.5** for definition). *Data for this indicator are not presented in this report because only a few countries reported data, and because there were concerns about the quality of the data received.*

standard indicators and standardized systems for recording and reporting data. In 2013, WHO and partners agreed on a minimum set of standardized indicators (**Box 4.3**) and these were used to collect data from 13 countries in which data were known to be routinely recorded and reported in at least some geographical areas. In 2014, data for the indicators shown in **Box 4.3** were requested from 32 countries as an integral part of the 2014 round of global TB data collection (i.e. data entry screens related to community engagement were part of the online data collection form for these 32 countries). The 32 countries were selected because they had participated in regional workshops on community engagement that were held in the African and South-East Asian Regions in 2013.

Among the 32 countries, 22 reported data for at least one indicator: 17 in the African Region and five in the South-East Asia Region (**Table 4.4**). The percentage of TB notifications from community referrals was reported by 19 countries, and 15 countries reported on the percentage of TB patients who received treatment support in the community. Countries also reported on the overall coverage of monitoring of these two indicators (measured as

TABLE 4.4

Community contributions to TB case notifications and treatment adherence support for TB patients (all forms) in 22 countries,^a 2012–2013

COUNTRIES	CONTRIBUTION TO TB NOTIFICATIONS, 2013		CONTRIBUTION TO TREATMENT ADHERENCE SUPPORT, 2012 COHORT	
	PROPORTION OF TOTAL TB NOTIFICATIONS (ALL FORMS) FROM COMMUNITY REFERRALS IN 2013, IN BASIC MANAGEMENT UNITS (BMUS) THAT REPORTED DATA (%)	GEOGRAPHIC COVERAGE OF DATA REPORTING BY BASIC MANAGEMENT UNITS (BMUS)	PROPORTION OF TB PATIENTS (ALL FORMS) WHO RECEIVED TREATMENT ADHERENCE SUPPORT IN THE COMMUNITY IN 2012, IN BASIC MANAGEMENT UNITS (BMUS) THAT REPORTED DATA (%)	GEOGRAPHIC COVERAGE OF DATA REPORTING BY BASIC MANAGEMENT UNITS (BMUS)
Bangladesh	44% (71784/163106)	476/850 BMUs	Not available	
Botswana	49% (3439/6958)	All BMUs (28)	51% (3900/7576)	All BMUs (28)
Burkina Faso ^b	9% (484/5326)	64/86 BMUs	19% (935/5023)	30/86 BMUs
Côte d'Ivoire ^b	11% (2123/19895)	61/82 BMUs	7% (1656/22822)	22/82 BMUs
DR Congo	30% (3527/11636)	104/515 BMUs	Not available	
Ethiopia ^b	11% (5443/51296)	278/921 BMUs	16% (7097/45449)	54/921 BMUs
Ghana	2% (336/15606)	All BMUs (216)	Not available	
Guinea ^b	12% (1307/11313)	All BMUs	25% (1667/6566)	20/55 BMUs
India ^b	5% (22422/423824)	1200/3000 BMUs	57% (735822/1288141)	2732/3000 BMUs
Indonesia ^b	42% (33170/78960)	43/497 BMUs	1% (4244/328824)	43/497 BMUs
Kenya	4% (3263/89796)	All BMUs (225)	1% (885/98443)	All BMUs (225)
Malawi	5% (438/9690)	84/167 BMUs	Not available	
Mozambique ^c	11% (5656/53272)	All BMUs (641)	26% (5510/20951)	Not available
Myanmar	1% (1613/142162)	All BMUs (347)	Not available	
Nigeria	Not available		34% (30484/90305)	All BMUs (774)
Rwanda	19% (1154/5980)	All BMUs (199)	42% (2460/5888)	All BMUs (199)
Senegal	9% (1162/13464)	All BMUs (76)	5% (671/12339)	All BMUs (76)
Sierra Leone	25% (3038/12334)	All BMUs (170)	6% (486/8230)	All BMUs (170)
South Africa	6% (495/7943)	2/52 BMUs	Not available	
Sri Lanka	Not available		10% (835/8752)	All BMUs (26)
Swaziland	Not available		100% (7162/7162)	All BMUs (82)
UR Tanzania ^b	15% (3700/25463)	47/168 BMUs	35% (21579/62477)	47/168 BMUs

^a Ten countries did not submit data for both indicators: Angola, Bhutan, Lesotho, Liberia, Nepal, Thailand, Timor-Leste, Uganda, Zambia and Zimbabwe. Data reported in the 2014 round of global TB data collection could not be compared with data reported in 2013, since the unit of reporting in 2013 was the lowest administrative unit rather than the BMU.

^b The proportion of patients receiving treatment support in the community was calculated using the total cohort (all BMUs) of TB patients starting treatment in 2012 as the denominator. Data disaggregated by BMU were not reported.

^c The denominator includes new and relapse TB cases only.

the number of TB management units that reported data for these indicators divided by the total number of TB management units, expressed as a percentage). The percentage of notified TB patients accounted for by community referrals ranged from 1% in Myanmar to 49% in Botswana, in the areas in which community-based activities were in place. The proportion of TB patients receiving community-based treatment support ranged from 1% in Kenya to 100% in Swaziland. Among the 22 countries, 10 reported nationwide coverage of community engagement in referrals of cases and nine reported nationwide coverage of community-based support for treatment adherence.

Although a standard system and indicators for reporting data are in place in these countries, the completeness and quality of data remain a challenge. Only a few countries reported data on the treatment outcomes of TB patients who received treatment support from community volunteers or community health workers. Even in these

countries, data were incomplete and difficult to interpret and for this reason are not presented in **Table 4.4**.

It should also be highlighted that there are several countries in which community-based TB activities are a routine component of NTP services, but where it is not yet possible to quantify this contribution. A good example is Lesotho, where a national network of more than 3 000 government-funded community health workers contribute to TB case finding and treatment adherence support, but their contribution is not being documented within the current recording and reporting system (efforts are underway to rectify this). Other countries where there is active engagement of communities and steps are being taken to implement recording and reporting systems that will capture their contribution include Indonesia, Nepal, Senegal, South Africa, Sri Lanka and Zimbabwe.

In addition to improving the documentation and reporting of community-based TB activities, efforts to

engage NGOs that have previously not been involved in TB prevention, diagnosis and treatment have continued. One example, which was featured in the 2013 global TB report, is known as the ENGAGE-TB approach.¹ This focuses on NGOs working on maternal and child health, HIV/AIDS, primary health care, livelihood development, water and sanitation, agriculture and education. Pilot projects have been implemented with support from the Bristol Meyers Squibb Foundation in five countries: the Democratic Republic of Congo, Ethiopia, Kenya, South Africa and the United Republic of Tanzania. Progress made to date in three of these countries is described in **Box 4.4**.

4.3 Trends in case notifications since 1990 and estimates of the case detection rate

Globally, the number of TB cases diagnosed and notified per 100 000 population remained relatively stable between 1990 and 2000, rose sharply between 2000 and 2008, and subsequently slowly started to fall (**Figure 4.2**). Globally and in all WHO regions, a clear gap exists between the numbers of notified cases and the estimated numbers of incident cases. However, this gap has narrowed in the past decade, globally and in all six WHO regions (**Figure 4.3**). Trends in the 22 HBCs are shown in **Figure 4.4**; for other countries these trends are illustrated in country profiles that are available online.²

The case detection rate (CDR)³ for TB is an indicator that is included within the MDG framework (**Chapter 1, Chapter 3**). For a given country and year, the CDR is calculated as the number of new and relapse TB cases (see **Box 4.1** for definitions) that were notified by NTPs (**Table 4.1**), divided by the estimated number of incident cases of TB that year. The CDR is expressed as a percentage; it gives an approximate⁴ indication of the proportion of all incident TB cases that are actually diagnosed, reported to NTPs or national surveillance systems and started on treatment.

The best estimate of the CDR for all forms of TB globally in 2013 was 64% (range, 61–66%), up from 53–55% in 2005 and 38–41% in 1995 – the year in which the DOTS strategy began to be introduced and expanded (**Table 4.5**). The highest CDRs in 2013 were estimated to be in the Region of the Americas (best estimate 77%; range, 73–80%), the Western Pacific Region (best estimate 83%; range, 79–88%) and the European Region (best estimate 80%; range, 77–84%). The other regions had estimated

¹ http://www.who.int/tb/people_and_communities/en/

² www.who.int/tb/data

³ The CDR is actually a ratio rather than a rate, but the term ‘rate’ has become standard terminology in the context of this indicator.

⁴ It is approximate because of uncertainty in the underlying incidence of TB and because notified cases are not necessarily a subset of incident cases that occurred in the same year; see Chapter 2 for further discussion.

BOX 4.4

The ENGAGE-TB approach: progress to date in three countries

The ENGAGE-TB approach^a describes the need for non-governmental organizations (NGOs) and other civil society organizations to integrate community-based TB activities into their existing work. Pilot projects have been implemented with support from the Bristol Meyers Squibb Foundation, including in Ethiopia, the Democratic Republic of the Congo and Kenya.

In Ethiopia, the NGO *Save the Children* has integrated community TB and TB/HIV services into its existing community Maternal, Newborn and Child Health (MNCH) programme, which is implemented in pastoralist communities in the Dollo Abo and Dollo Bay woredas of the remote Somali Region. In the pilot period, there was an eight-fold increase in the number of TB patients placed on treatment, from just 52 in 2012 (before the pilot was initiated) to 427 in 2013.

In the Democratic Republic of the Congo, the NGO *Femme Plus* has integrated TB services into its existing community-based HIV activities in two locations: Kinshasa and Kikwit. The ENGAGE-TB approach is being used to strengthen collaboration among public TB facilities, NGOs and communities, and to improve data quality at the local level. Public TB officers and NGO focal points meet on a quarterly basis to review community-based TB referral and treatment support activities and validate community engagement data, which is then reported in TB registers.

In Kenya, the NGO *Grassroots Poverty Alleviation Programme*, which works primarily with fishing communities, has mainstreamed community-based TB activities into its livelihood programmes, following the provision of basic training to staff.

^a http://www.who.int/tb/people_and_communities/en/

FIGURE 4.2

Global trends in case notification (black) and estimated TB incidence (green) rates, 1990–2013. Case notifications include new and relapse cases (all forms).

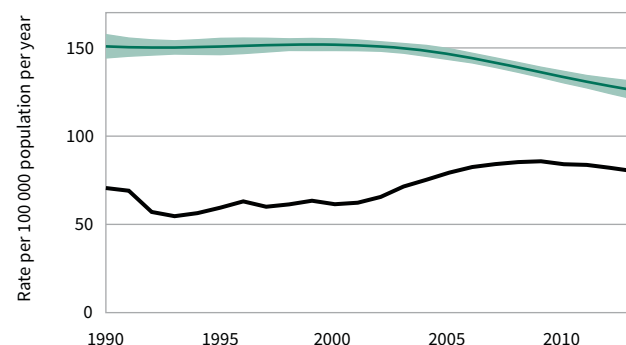
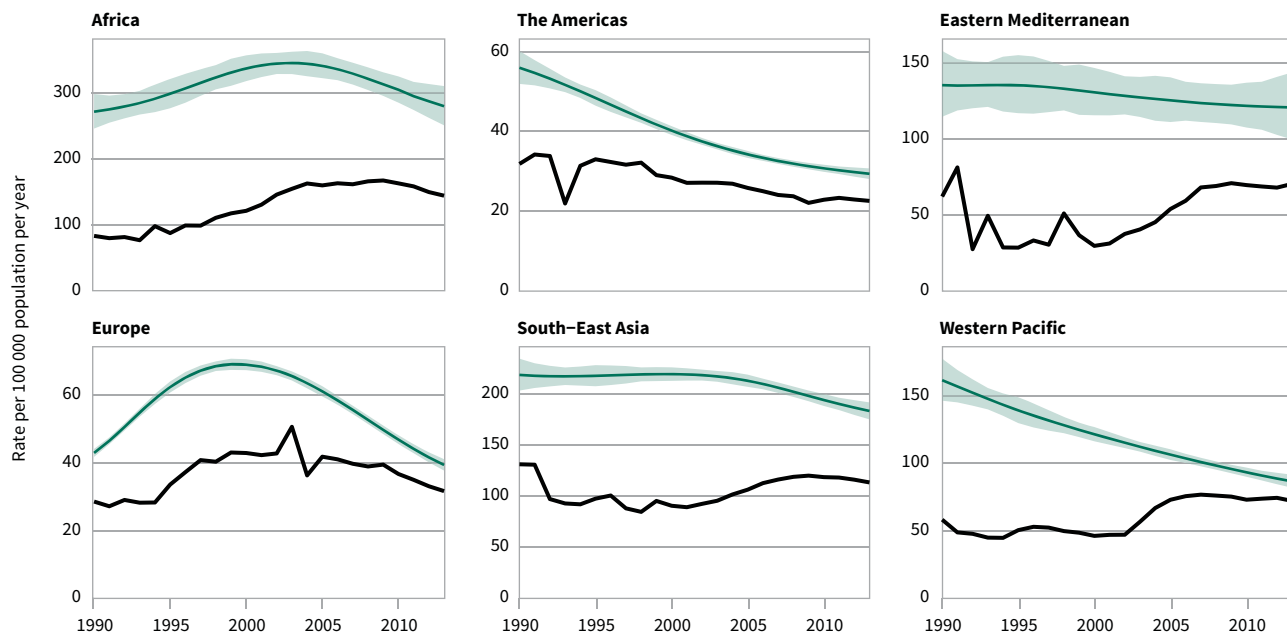


FIGURE 4.3

Case notification and estimated TB incidence rates by WHO region, 1990–2013. Regional trends in case notification rates (new and relapse cases, all forms) (black) and estimated TB incidence rates (green). Shaded areas represent uncertainty bands.



CDRs in the range of around 46–71%, with best estimates in the range 52–62%. The lowest estimated CDR in 2013 was in the African Region; this follows a downward revision compared with previous estimates following the results of the national TB prevalence survey in Nigeria (see also [Chapter 2](#)). Given the size of the population and TB burden in Nigeria, revisions to estimates for this country have had a major impact on estimates for the entire African Region.

All regions have improved their estimated CDRs since the mid-1990s, with improvements particularly evident since 2000. Among the 22 HBCs, the highest rates of case detection in 2013 (>75%) were estimated to be in Brazil, China, Kenya, the Philippines, the Russian Federation, Thailand, the United Republic of Tanzania and Viet Nam. The lowest rates, with best estimates of around 50% or less, were in Afghanistan, Bangladesh, the Democratic Republic of the Congo, Mozambique, Nigeria and Zimbabwe.

The gap between notifications to national surveillance systems and the true number of incident cases can be explained by two factors. The first is underreporting of diagnosed TB cases, for example because private sector providers fail to notify cases. The second is under-diagnosis of people with TB for reasons such as poor access to health care and failure to recognize TB signs and symptoms and test for TB when people do present to health care facilities. Achieving the goal of universal health coverage, implementing PPM initiatives such as those described in [section 4.2](#), and ensuring that there is an effective regula-

tory framework that includes mandatory notification of cases are essential to reduce underreporting and under-diagnosis, and are part of WHO’s post-2015 global TB strategy recently endorsed by all Member States at the World Health Assembly ([Chapter 1](#)).

4.4 Treatment outcomes

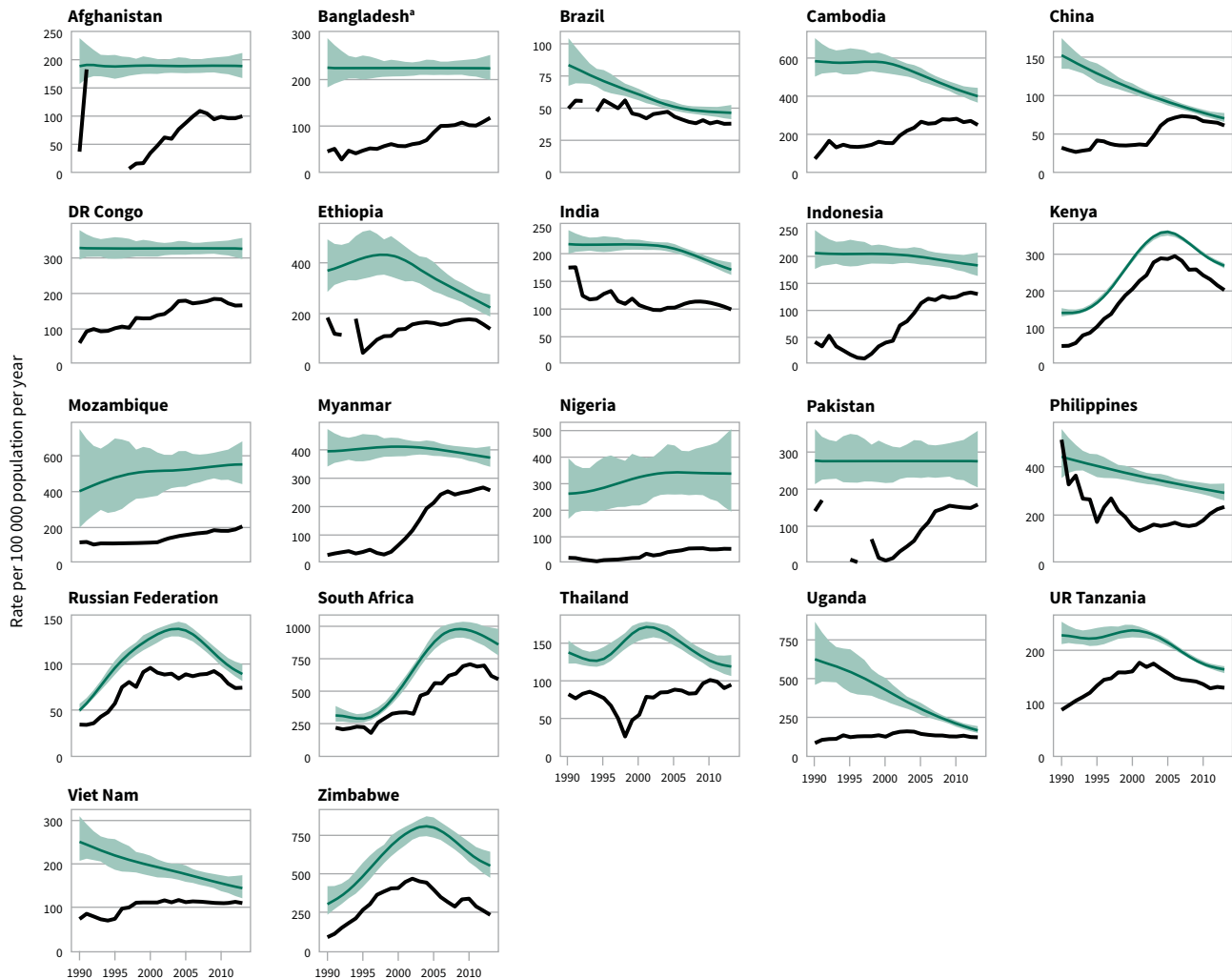
The definitions of TB treatment outcomes for drug-susceptible TB that are recommended by WHO as part of an updated recording and reporting framework issued in March 2013, and used in the 2014 round of global TB data collection, are shown in [Box 4.5](#).

Data on treatment outcomes for new cases of TB are shown in [Table 4.6](#) and [Figure 4.5](#). Globally, the treatment success rate for the 5.3 million new cases that were treated in the 2012 cohort was 86%. It is impressive that as the size of the global treatment cohort grew from 1.0 million in 1995 to 4.2 million in 2005 and 5.3 million in 2012, the treatment success rate progressively improved.

Among the six WHO regions, the highest treatment success rates were in the Western Pacific Region (92%), the South-East Asia Region (88%) and the Eastern Mediterranean Region (87%). The treatment success rate was 81% in the African Region, a sizeable improvement from 73% in 2010. In the Region of the Americas and the European Region, the success rate was 76% and 75%, respectively. In the Region of the Americas, treatment outcomes would probably be considerably improved if the number of patients in the “not evaluated” category could be reduced.

FIGURE 4.4

Case notification and estimated TB incidence rates, 22 high-burden countries, 1990–2013. Trends in case notification rates (new and relapse cases, all forms) (black) and estimated TB incidence rates (green). Shaded areas represent uncertainty bands.



^a Estimates of TB disease burden have not been approved by the national TB programme in Bangladesh and a joint reassessment will be undertaken following completion of the prevalence survey planned for 2015

In the European Region, there were similar proportions of patients in the failed, died, lost to follow-up and not evaluated categories.

Of the 22 HBCs, 15 reached or exceeded a treatment success rate of 85% among all new cases in 2012. The six countries that reported lower treatment success rates were Brazil (72%), the Russian Federation (69%, up from 65% in 2011), South Africa (77%), Thailand (81%), Uganda (77%, up from 73% in 2011) and Zimbabwe (81%). In the Russian Federation, improvement of treatment outcomes has been recognized as a high priority by the Ministry of Health and actions to improve it have been defined. These include earlier detection of MDR-TB, earlier enrolment of patients with MDR-TB on second-line treatment, strengthening patient support to improve adherence to treatment

(especially among the most socially and economically disadvantaged), and the introduction of a patient-based monitoring system for those with M/XDR-TB and HIV co-infection. The increase in the percentage of patients successfully treated between 2011 and 2012 suggests that these measures may have had a positive effect.

Treatment outcomes in 2012 were worse among HIV-positive TB patients compared with HIV-negative TB patients (Box 4.6). Further efforts are needed to narrow this gap.

TABLE 4.5

Estimates of the case detection rate for new and relapse cases (%), 1995–2013.^a Best estimates are followed by the lower and upper bounds of the 95% uncertainty interval.

	1995		2000		2005		2010		2013	
Afghanistan	—	—	18	17–20	47	43–50	52	48–56	53	47–60
Bangladesh	21	19–24	25	24–28	38	36–41	45	42–49	53	47–59
Brazil	79	71–89	74	69–80	85	79–91	81	75–87	82	72–92
Cambodia	24	21–26	27	25–30	52	49–56	65	61–69	62	56–68
China	32	29–36	33	31–35	74	70–78	86	82–91	87	79–93
DR Congo	31	28–34	40	37–43	55	52–58	56	53–59	51	47–56
Ethiopia	11	8.7–14	33	28–41	48	40–57	66	58–77	62	51–74
India	59	55–63	49	48–52	49	47–51	60	57–63	58	54–61
Indonesia	9	7.9–10	20	18–22	57	53–61	66	61–72	71	63–80
Kenya	61	58–63	72	70–74	80	78–82	81	79–82	75	74–77
Mozambique	23	16–39	23	18–31	30	25–37	33	29–39	37	30–47
Myanmar	9.9	8.8–11	15	14–17	53	50–56	66	62–70	68	61–74
Nigeria	4.3	3.1–6.2	6.5	5.2–9.6	13	10–18	16	12–22	16	11–28
Pakistan	3.8	3.0–4.8	2.8	2.4–3.5	33	27–39	55	46–68	58	44–78
Philippines	42	38–48	42	39–45	47	44–51	58	53–63	80	71–90
Russian Federation	60	55–65	75	71–81	65	62–69	83	77–89	83	74–91
South Africa	59	51–64	58	54–63	60	56–65	73	68–79	69	60–76
Thailand	60	53–64	32	31–36	56	53–60	80	74–86	80	71–89
Uganda	22	18–30	29	25–35	47	42–54	60	55–67	73	63–81
UR Tanzania	60	55–64	67	64–71	73	71–76	78	75–80	79	77–83
Viet Nam	33	29–39	56	51–64	63	57–70	71	63–80	76	63–91
Zimbabwe	55	46–64	56	52–62	50	46–54	53	48–59	42	36–49
High-burden countries	37	36–39	38	37–39	52	51–54	62	60–64	62	59–65
AFR	29	27–32	36	34–38	47	44–50	53	50–57	52	46–57
AMR	68	66–71	71	69–73	75	74–77	74	72–77	77	73–80
EMR	21	18–24	23	20–26	43	38–48	57	51–65	58	49–71
EUR	54	52–55	62	61–64	68	67–70	78	76–81	80	77–84
SEAR	45	43–47	41	40–43	50	49–51	61	59–63	62	59–65
WPR	36	34–39	38	36–40	69	66–71	78	75–81	83	79–88
Global	39	38–41	40	40–41	54	53–55	63	62–65	64	61–66

— indicates values that cannot be calculated.

^a Estimates for all years are recalculated as new information becomes available and techniques are refined, so they may differ from those published previously. The lower and upper bounds are defined as the 2.5th and 97.5th centiles of outcome distributions produced in simulations.

TABLE 4.6

Treatment success for all new cases (%) and cohort size (thousands), 1995–2012

a. Treatment success (%)							b. Cohort size (thousands)						
	1995	2000	2005	2010	2011	2012 ^a		1995	2000	2005	2010	2011	2012 ^a
Afghanistan	—	85	90	86	88	88	Afghanistan		3.1	10	26	26	29
Bangladesh	71	81	90	91	91	92	Bangladesh	11	38	119	150	148	165
Brazil	17	71	72	72	73	72	Brazil	46	34	78	78	71	75
Cambodia	91	91	91	89	94	94	Cambodia	4.4	15	34	40	37	38
China	93	93	92	95	95	95	China	131	214	788	877	856	885
DR Congo	74	78	85	89	87	88	DR Congo	16	36	65	109	92	105
Ethiopia	61	80	78	77	89	91	Ethiopia	5.1	30	39	152	91	45
India	25	34	87	89	89	88	India	265	349	1 071	1 229	1 209	1 288
Indonesia	91	87	89	89	88	86	Indonesia	3	52	244	296	314	329
Kenya	75	80	81	86	87	86	Kenya	6.5	28	98	90	82	98
Mozambique	39	75	79	85	—	87	Mozambique	11	13	18	20		21
Myanmar	67	82	83	88	88	89	Myanmar	7.9	17	73	127	135	137
Nigeria	49	79	75	81	85	86	Nigeria	9.5	16	35	78	84	90
Pakistan	70	74	82	90	92	91	Pakistan	0.8	4.1	117	256	255	111
Philippines	60	88	89	90	87	88	Philippines	90	50	81	162	190	214
Russian Federation	65	68	67	66	65	69	Russian Federation	0.05	3.6	74	94	89	90
South Africa	58	63	69	53	77	77	South Africa	28	86	259	338	292	328
Thailand	64	69	71	83	82	81	Thailand	20	23	49	48	49	58
Uganda	44	63	73	68	73	77	Uganda	15	14	21	40	43	26
UR Tanzania	73	78	83	89	88	90	UR Tanzania	20	24	59	59	59	62
Viet Nam	89	92	92	92	93	91	Viet Nam	38	53	55	88	89	104
Zimbabwe	53	69	66	76	80	81	Zimbabwe	9.7	14	43	46	40	38
High-burden countries	53	67	85	86	88	88	High-burden countries	739	1 119	3 430	4 403	4 252	4 337
AFR	60	71	74	73	79	81	AFR	178	365	886	1 220	1 103	1 142
AMR	50	76	75	73	75	76	AMR	129	111	187	200	189	196
EMR	79	81	82	88	89	87	EMR	46	64	226	386	391	242
EUR	67	75	77	74	73	75	EUR	34	42	221	255	244	245
SEAR	33	50	87	89	89	88	SEAR	318	512	1 639	1 980	1 986	2 114
WPR	80	90	90	92	93	92	WPR	296	360	1 030	1 240	1 233	1 344
Global	57	69	84	84	87	86	Global	1 001	1 453	4 188	5 280	5 145	5 283

Blank cells indicate data not reported.

— indicates values that cannot be calculated.

^a Data for Afghanistan, Bangladesh, Brazil, Cambodia, China, India, Indonesia, Kenya, Russian Federation, South Africa, Thailand, Uganda, UR Tanzania and Viet Nam include relapse cases.

BOX 4.5

Definitions of treatment outcomes recommended for use since March 2013 and that were used in the 2014 round of global TB data collection^a

Cured A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.

Completed treatment A TB patient who completed treatment without evidence of failure but with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.

Died A TB patient who died from any cause during treatment.

Failed A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.

Lost to follow-up A TB patient who did not start treatment or whose treatment was interrupted for two consecutive months or more.

Not evaluated A TB patient for whom no treatment outcome is assigned. This includes cases 'transferred out' to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.

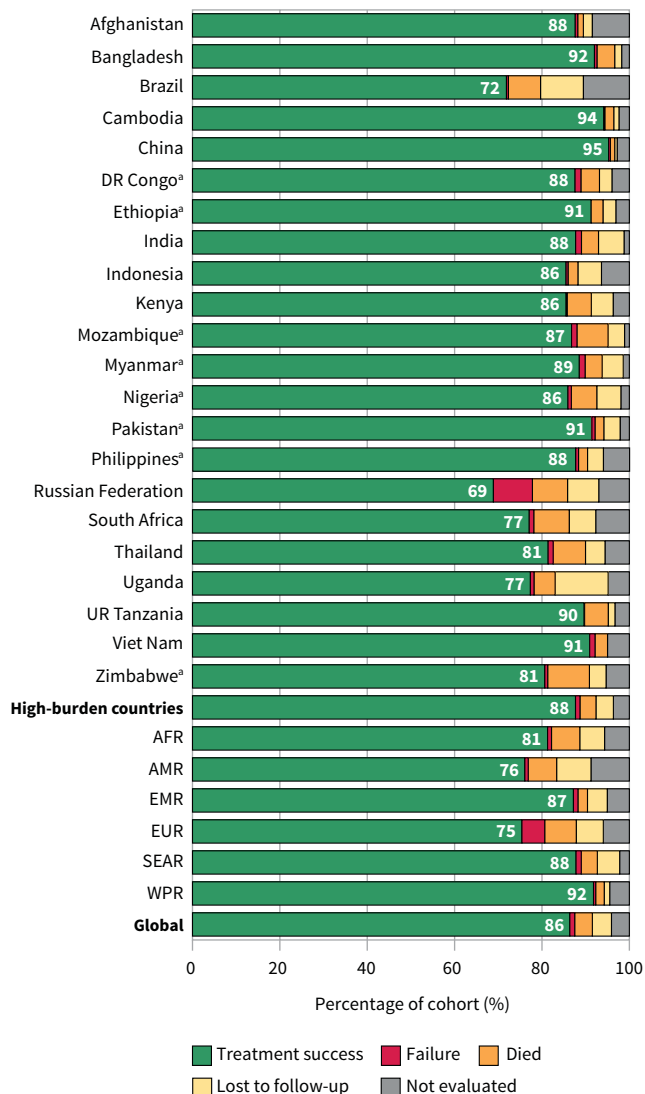
Successfully treated A patient who was cured or who completed treatment.

Cohort A group of patients in whom TB has been diagnosed, and who were registered for treatment during a specified time period (e.g. the cohort of new cases registered in the calendar year 2012). This group forms the denominator for calculating treatment outcomes. The sum of the patients included in the above treatment outcome categories should equal the number of cases registered. It should be highlighted that in the new definitions recommended since March 2013 *any patient found to have drug-resistant TB and placed on second-line treatment should be removed from the drug-susceptible TB outcome cohort*. This means that management of the standard TB register and of the second-line TB treatment register needs to be coordinated to ensure proper accounting of the outcomes of treatment (see also [Chapter 5](#)).

^a *Definitions and reporting framework for tuberculosis – 2013 revision*. Geneva, World Health Organization, 2013 (WHO/HTM/TB/2013.2). Available at www.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf.

FIGURE 4.5

Treatment outcomes for new and relapse cases, 2012, globally, for the six WHO regions and 22 high-burden countries



^a Treatment outcomes for new cases only.

BOX 4.6

Outcomes of TB treatment by HIV status

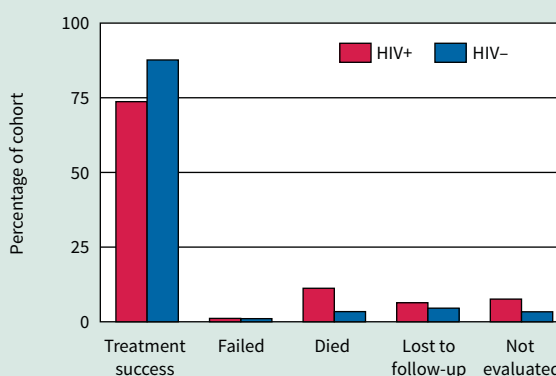
In the 2014 round of global TB data collection, 132 countries reported treatment outcomes for 2012 that were disaggregated by HIV status, up from 96 countries that reported disaggregated data for 2011. These 132 countries included 23 of the 41 high TB/HIV burden countries (listed in [Table 7.1](#) of [Chapter 7](#)) and collectively accounted for 70% (n=397 332) of the HIV-positive TB patients reported by NTPs in 2012, up from 58% of HIV-positive TB patients reported by NTPs in 2011.

Overall, treatment outcomes in 2012 continued to be worse for HIV-positive TB patients (74%) compared with HIV-negative TB patients (88%). The difference was smaller in the African region (75% and 83%, respectively). There were large differences in the Western Pacific and Eastern Mediterranean Regions, where the treatment success rates among HIV-positive TB patients were only 55% and 53% respectively, compared with 94% and 82% among HIV-negative patients.

Globally, the proportion of TB patients that died during treatment was more than three times higher among HIV-positive TB patients (11% versus 3.4%). In the African Region, HIV-positive TB patients were twice as likely to die as HIV-negative TB patients (10% compared with 5%). In both the European region and the Region of the Americas, 19% of HIV-positive TB patients died during treatment, compared with just over 5% of HIV-negative TB patients. The proportion of patients categorized as lost to follow-up, who may also have died of TB, was also higher for those who were HIV-positive. In the Western Pacific Region, the treatment outcome was not evaluated for 30% of HIV-positive TB patients cases compared with just 3% of HIV-negative TB patients. This large difference was largely driven by data reported by China, where the treatment outcome was not evaluated for 47% of HIV-positive TB patients.

FIGURE B4.6.1

Outcomes of TB treatment by HIV status, 2012



Drug-resistant TB

KEY FACTS AND MESSAGES

Drug-resistant TB (DR-TB) poses a major threat to control of TB worldwide. By the end of 2013, data on anti-TB drug resistance were available for 144 countries, accounting for 95% of the world's population and estimated TB cases. Half of these (72 countries) have continuous surveillance systems, while the other half relies on special surveys.

In 2013, six of the 36 countries with a high TB and/or high MDR-TB burden completed drug resistance surveys: Azerbaijan, Myanmar, Pakistan, Philippines, Thailand and Viet Nam. In mid-2014, surveys were ongoing in a further five of these countries: China, India, Kenya, South Africa and Ukraine.

Globally, an estimated 3.5% (95% CI: 2.2–4.7%) of new cases and 20.5% (95% CI: 13.6–27.5%) of previously treated cases have MDR-TB. In 2013, there were an estimated 480 000 (range: 350 000–610 000) new cases of MDR-TB worldwide, and approximately 210 000 (range: 130 000–290 000) deaths from MDR-TB. Among patients with pulmonary TB who were notified in 2013, an estimated 300 000 (range: 230 000–380 000) had MDR-TB. More than half of these patients were in India, China and the Russian Federation.

A new analysis of trends focusing on the years 2008–2013 shows that, at the global level, the proportion of new cases with MDR-TB remains unchanged. However, serious MDR-TB epidemics in some countries jeopardise progress.

Extensively drug-resistant TB (XDR-TB) has been reported by 100 countries. On average, an estimated 9.0% (95% CI: 6.5–11.5%) of people with MDR-TB have XDR-TB.

A total of 136 412 people with MDR-TB or rifampicin-resistant TB (RR-TB) who were eligible for MDR-TB treatment were notified globally in 2013, mostly by countries in the European

Region, India and South Africa. Overall, an increase in the number of notified cases of MDR-TB has been evident since 2009, and the increase between 2012 (when 110 000 cases were detected) and 2013 was particularly large, at 23%. The biggest increases between 2012 and 2013 were in India, Ukraine and Uzbekistan.

Despite progress in the detection of MDR/RR-TB cases, a major diagnostic gap remains: 55% of reported TB patients estimated to have MDR-TB were not detected in 2013. The detection figures were lowest in the Eastern Mediterranean Region (22%) and the Western Pacific Region (16%).

Almost 97 000 patients were started on MDR-TB treatment in 2013. Gaps between numbers diagnosed and numbers started on treatment widened between 2012 and 2013 in several countries. The ratio of enrolled to diagnosed cases was lower than 60% in 10 high MDR-TB burden countries in 2013 and lowest in Myanmar (34%), South Africa (41%), and Tajikistan (30%).

Five high MDR-TB burden countries (Ethiopia, Kazakhstan, Myanmar, Pakistan and Viet Nam) achieved treatment success rates of $\geq 70\%$. However, overall only 48% of patients with MDR-TB were successfully treated, largely as a result of high mortality and loss to follow-up. Of 1 269 XDR-TB patients reported in 40 countries in the 2011 cohort overall, only 284 (22%) completed their treatment successfully and 438 (35%) patients died.

Innovative approaches and more funding to increase the uptake of programmatic management of DR-TB globally are urgently required to detect and enrol more patients on MDR-TB treatment, and to improve outcomes.

Drug-resistant TB (DR-TB) threatens global TB control and is a major public health concern in several countries. The first part of this chapter ([section 5.1](#)) summarizes the progress made in the global coverage of surveillance of anti-TB drug resistance and the key findings from the data that have been collected, with a focus on resistance to multidrug-resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB). Emerging work based on molecular technologies and the first steps towards global surveillance of resistance to drugs that may be part of new TB treatment regimens is highlighted. The second part of this chapter presents an assessment of global and national progress in diagnosing and treating MDR-TB ([section 5.2](#)).

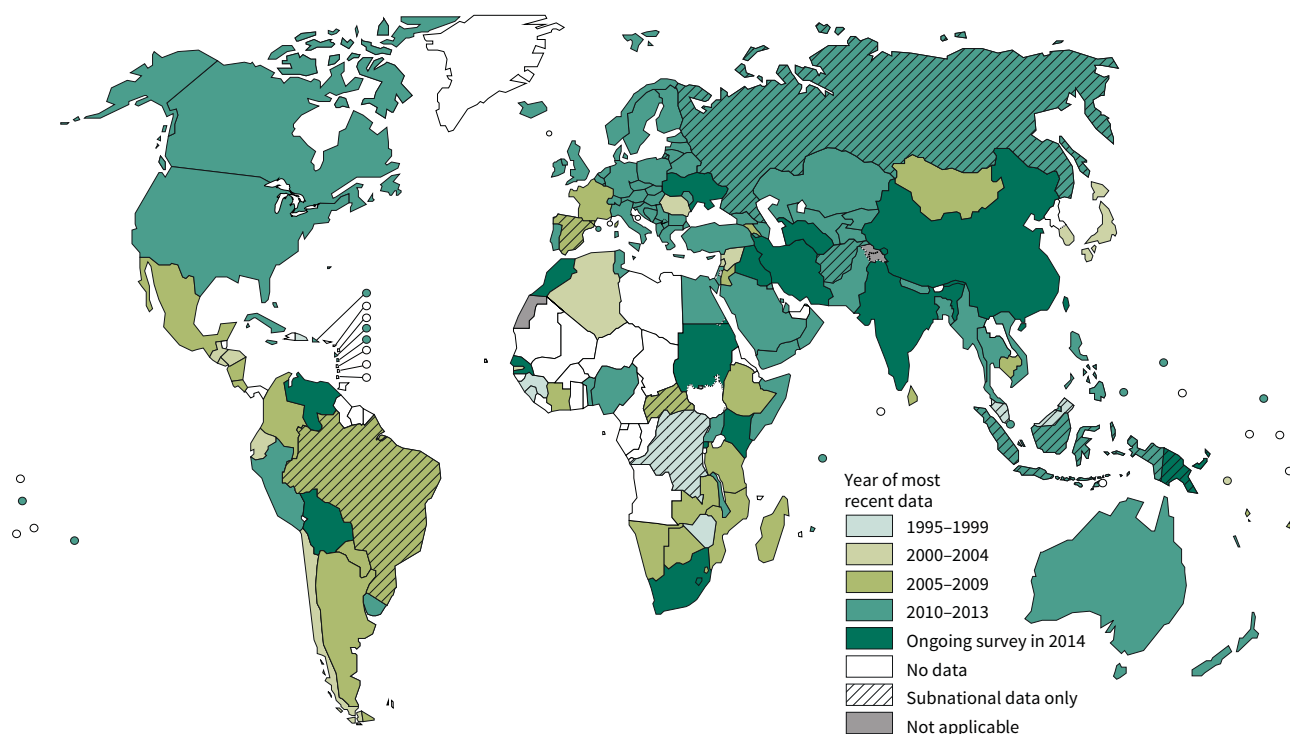
5.1 Surveillance of drug-resistant TB

5.1.1 Progress in the coverage of drug resistance surveillance

Since the launch of the Global Project on Anti-tuberculosis Drug Resistance Surveillance in 1994, data on drug resistance have been systematically collected and analysed from 144 countries worldwide (74% of 194 WHO Member States). Exactly half of them (72 countries) have continuous surveillance systems based on routine diagnostic drug susceptibility testing (DST) of all TB patients and the remaining 72 countries rely on special epidemiological surveys of representative samples of patients. Over the past two decades, all 22 high TB and/or 27 high MDR-TB

FIGURE 5.1

Progress in global coverage of surveillance data on drug resistance, 1994–2014



burden countries (for a total of 36 countries) have either established a continuous surveillance system or conducted at least one survey to monitor drug resistance. Progress towards achieving global coverage of drug resistance surveillance data is shown in **Figure 5.1**.

Continuous surveillance for MDR-TB, based on routine DST of TB patients and systematic collection and analysis of data, is the most effective approach to monitor trends in drug resistance. Among the 36 high TB and/or MDR-TB burden countries, ten (Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Latvia, Lithuania, Republic of Moldova, the Russian Federation and Ukraine) have established high quality surveillance systems to monitor drug resistance. All of these belong to the eastern European and central Asian regions where the MDR-TB burden is highest.

Special surveys conducted every 3–5 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 due to lack of laboratory capacity or resources. Of the 36 high TB and/or MDR-TB burden countries, 26 have generated drug resistance data through special surveys. Half of them (13 countries) have conducted surveys recently, between 2010 and 2013. These are Afghanistan (Central region), Azerbaijan, Bangladesh, Kyrgyzstan, Myanmar, Nigeria, Pakistan, the Philippines, Tajikistan, Thailand, Uganda, Uzbekistan and Viet Nam. Three countries have not completed a survey since the mid-1990s: the Democratic Republic of the

Congo, Kenya and Zimbabwe. However, a national survey is currently being implemented in Kenya and surveys are planned in the Democratic Republic of the Congo and Zimbabwe in 2014–2015.

Six high TB and/or MDR-TB burden countries (Afghanistan, Brazil, the Democratic Republic of the Congo, India, Indonesia and the Russian Federation) still rely on drug resistance surveillance data gathered from sub-national areas only. In 2014, Brazil launched a large nationwide sentinel system to monitor drug resistance and the first-ever nationwide drug resistance survey was started in India. The remaining countries should consider conducting nationwide drug resistance surveys in the short term to better understand the burden of MDR-TB and to guide the planning of diagnostic and treatment services.

In mid-2014, drug resistance surveys were ongoing in 16 countries. These include: the first nationwide surveys in India, Iraq, Sudan, Turkmenistan and Ukraine; the first survey in Papua New Guinea (four provinces); and repeat surveys in Bolivia, China, Iran (Islamic Republic of), Kenya, Lesotho, Morocco, Rwanda, Senegal, Venezuela and South Africa.

Central and Francophone Africa remain the parts of the world where drug resistance surveillance data are most lacking, largely as a result of weak laboratory infrastructure.

BOX 5.1

Recent trends in MDR-TB: a new analysis

By 2013, data on trends in drug resistance were available for 96 countries. Collectively, they accounted for 53% of the estimated global burden of MDR-TB, and included 16 of the 36 high TB and/or MDR-TB burden countries: Belarus, China, Estonia, Georgia, Kazakhstan, Latvia, Lithuania, Mozambique, Myanmar, Pakistan, the Philippines, Republic of Moldova, the Russian Federation, Thailand and Viet Nam.

There was a total of 1098 country-year data points (874 national and 224 subnational areas); the number of national data points on levels of drug resistance per country is shown in [Figure B5.1.1](#). Where possible, subnational area data points were pooled to generate national data points. Trends were assessed between 2008 and 2013 wherever possible, or otherwise between the last two available data points, using log-linear regression. For countries without trend data, missing values were estimated using multiple imputation methods. This was done after exclusion of outlier points (i.e.

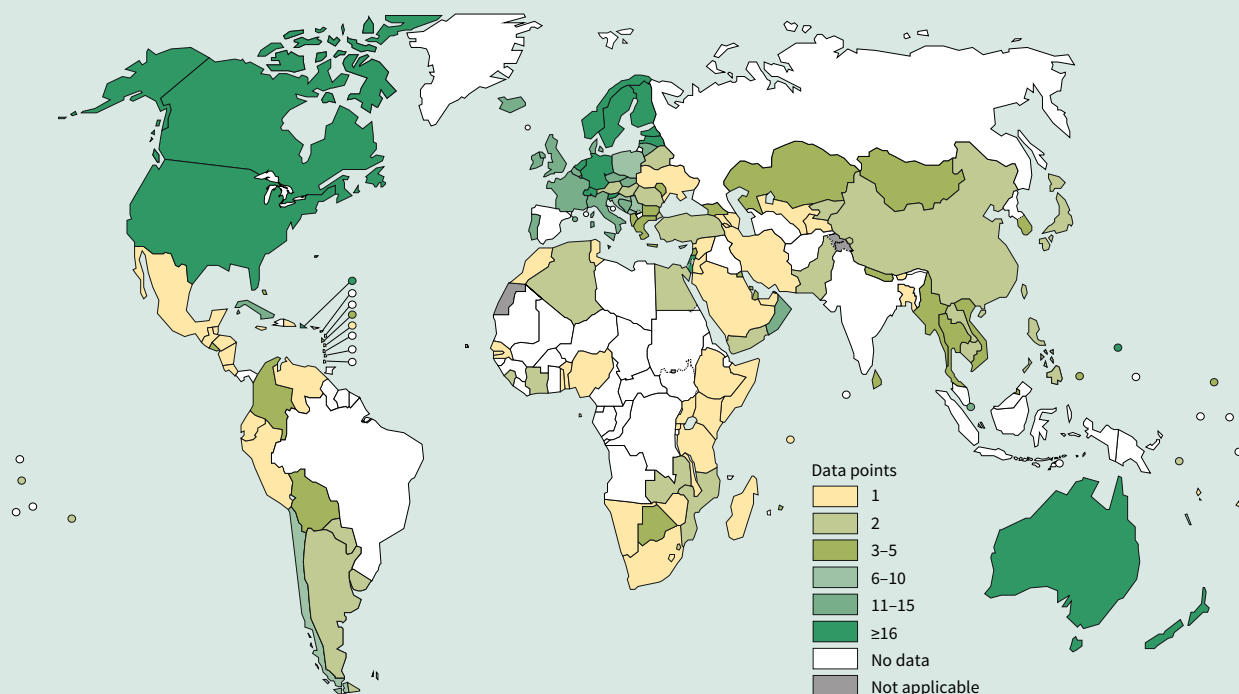
extreme trends mostly due to small numbers). Estimates of the percentage of new TB cases with MDR-TB were then combined with estimates of overall TB prevalence ([Chapter 2](#)) to generate estimates of trends in the population prevalence of MDR-TB.

Globally, the percentage of new TB cases that have MDR-TB was 3.5% in 2013 and has not changed compared with recent years.

To improve the robustness of estimates of trends in MDR-TB, more countries need to build capacity for continuous surveillance or in the interim undertake repeat surveys (in both cases, covering all care providers). Ultimately, the combination of universal health coverage and universal DST called for in the post-2015 global TB strategy ([Chapter 1](#)) are required for reliable measurement of trends in drug resistance in all countries.

FIGURE B5.1.1

Number of national drug resistance surveillance country-year data points, 1994–2013^a



^a The data points for China, Lao People's Democratic Republic and Pakistan include data from national prevalence surveys.

5.1.2 Recent trends in levels of drug resistance: a new analysis

Of the 144 countries with surveillance data on drug resistance, 35% (51 countries) have only one data point. Countries relying on special surveys to measure levels of drug resistance should plan to repeat surveys regularly, approximately every three to five years, until capacity for continuous surveillance is established. A new analysis of trends in MDR-TB focused on the years 2008–2013 is presented in **Box 5.1**. At the global level, the proportion of new cases with MDR-TB was 3.5% in 2013 and has not changed compared with recent years. However, some countries (especially in eastern Europe and the Russian Federation) are experiencing serious MDR-TB epidemics.

5.1.3 Percentage of new and previously treated TB cases that have MDR-TB

Globally, 3.5% (95% CI: 2.2–4.7%) of new TB cases and 20.5% (95%CI: 13.6–27.5%) of previously treated cases are estimated to have MDR-TB (**Table 5.1**). These estimates are essentially unchanged from those published in recent global TB reports.

The proportions of new and previously treated TB cases with MDR-TB at the country level are shown in **Figure 5.2** and **Figure 5.3**, and for the 27 high MDR-TB burden countries also in **Table 5.1**. Eastern European and central Asian countries continue to have the highest levels of MDR-TB. Among new cases, the proportions with MDR-TB were highest in Belarus (35.2% in 2013), Kazakhstan (25.2% in 2013), Kyrgyzstan (26.4% in 2011), the Republic of Moldova (23.7% in 2012), the Russian Federation (average: 19.3% in 2012) and Uzbekistan (23.2% in 2011). Among previously treated TB cases, the proportions with MDR-TB were highest in Belarus (54.5% in 2013), Kazakhstan (55.0% in 2012), Kyrgyzstan (55.1% in 2013), the Republic of Moldova (62.3% in 2012), Tajikistan (56.0% in 2012) and Uzbekistan (62.0% in 2011). In the Russian Federation, even though the average proportion of previously treated cases with MDR-TB does not exceed 50%, the proportion is well above 50% in several Federal Subjects.

Levels of drug resistance among new cases remain low (<3%) in many parts of the world, including in almost all countries in the Region of the Americas; most African countries where drug resistance surveys have been conducted; most of the South-East Asia Region; most of western Europe; and several countries in the Western Pacific Region.

The burden of resistance to isoniazid without concurrent resistance to rifampicin is presented in **Box 5.2**.

TABLE 5.1

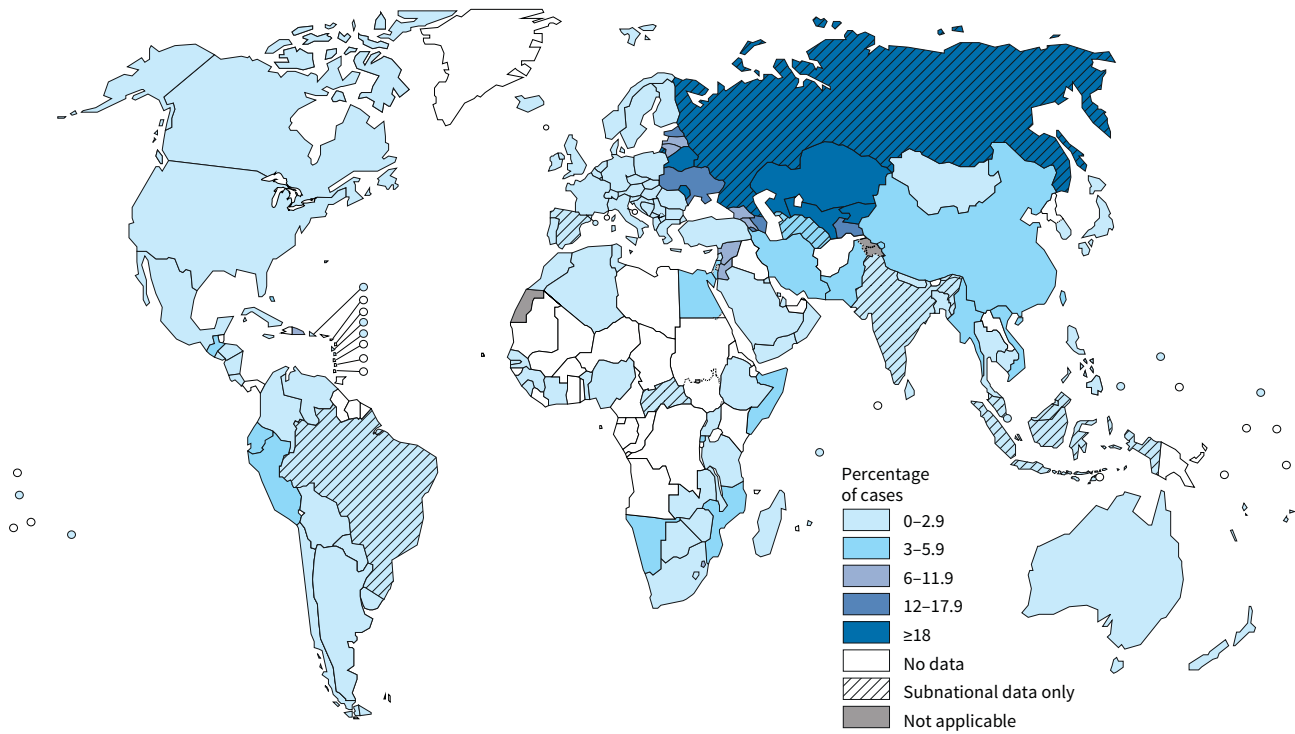
Estimated proportion of TB cases that have MDR-TB, globally and for 27 high MDR-TB burden countries and WHO regions

	ESTIMATED % OF NEW TB CASES WITH MDR-TB ^a	CONFIDENCE INTERVAL	ESTIMATED % OF RETREATMENT TB CASES WITH MDR-TB ^a	CONFIDENCE INTERVAL
Armenia	9.4	7.0–12	43	38–49
Azerbaijan	13	10–16	28	22–34
Bangladesh	1.4	0.7–2.5	29	24–34
Belarus	35	33–37	55	51–57
Bulgaria	2.3	1.3–3.8	23	17–31
China	5.7	4.5–7.0	26	22–30
DR Congo	2.6	0.01–5.5	13	0.2–28
Estonia	17	12–24	48	32–63
Ethiopia	1.6	0.9–2.8	12	5.6–21
Georgia	11.0	9.7–13	38	34–42
India	2.2	1.9–2.6	15	11–19
Indonesia	1.9	1.4–2.5	12	8.1–17
Kazakhstan	25	24–26	55	54–56
Kyrgyzstan	26	23–31	55	52–58
Latvia	8.8	6.6–12	26	18–35
Lithuania	11	9.5–14	44	39–49
Myanmar	5.0	3.1–6.8	27	15–39
Nigeria	2.9	2.1–4.0	14	10–19
Pakistan	4.3	2.8–5.7	19	14–25
Philippines	2.0	1.4–2.7	21	16–29
Republic of Moldova	24	21–26	62	59–65
Russian Federation	19	14–25	49	40–59
South Africa	1.8	1.4–2.3	6.7	5.4–8.2
Tajikistan	13	9.8–16	56	52–60
Ukraine	14	14–15	32	31–33
Uzbekistan	23	18–30	62	53–71
Viet Nam	4.0	2.5–5.4	23	17–30
High MDR-TB burden countries	4.0	2.3–5.7	22	13–31
AFR	2.4	0.2–5.0	13	0.02–27
AMR	2.2	1.3–3.0	13	4.9–22
EMR	3.6	2.3–5.0	22	12–32
EUR	14	9.7–19	44	36–52
SEAR	2.2	1.8–2.7	16	12–20
WPR	4.4	2.6–6.3	22	18–26
Global	3.5	2.2–4.7	21	14–28

^a Best estimates are for the latest available year. Estimates in italics are based on data from countries from the same epidemiological region.

FIGURE 5.2

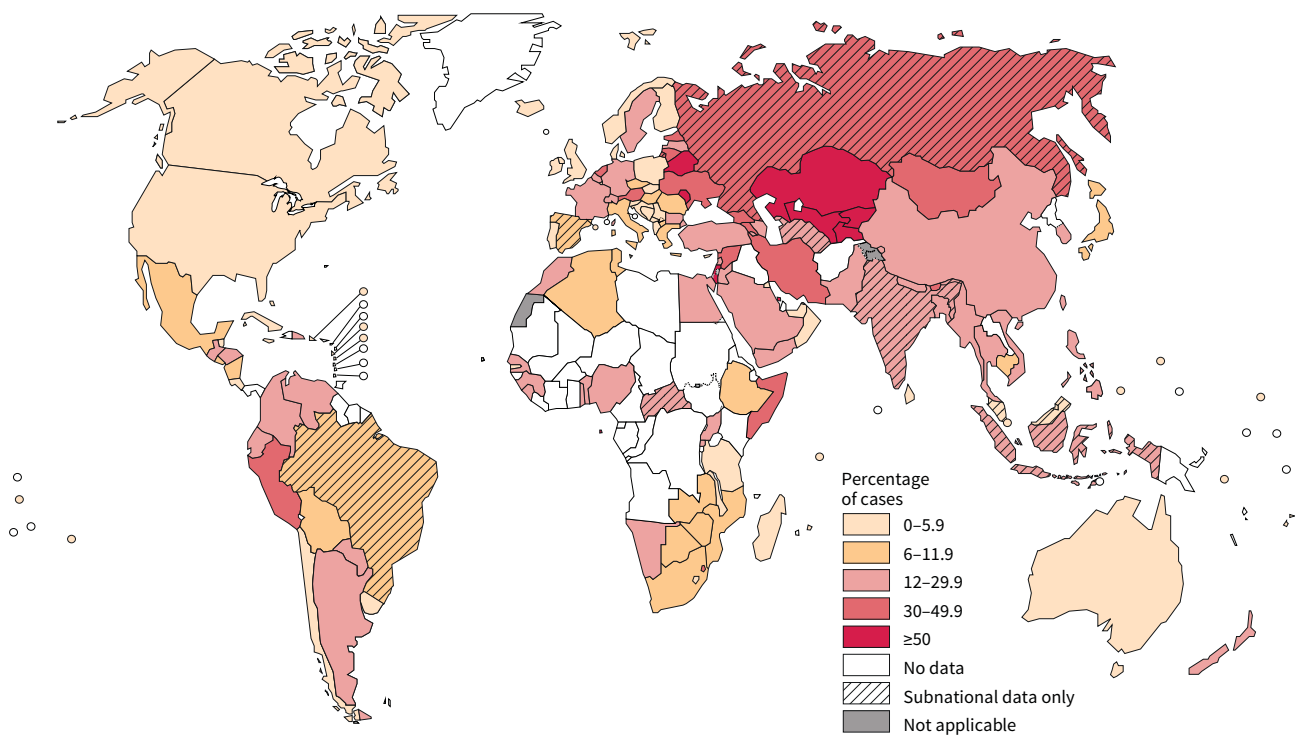
Percentage of new TB cases with MDR-TB^a



^a Figures are based on the most recent year for which data have been reported, which varies among countries.

FIGURE 5.3

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



^a Figures are based on the most recent year for which data have been reported, which varies among countries. The high percentages of previously treated TB cases with MDR-TB in Bahrain, Bonaire, Israel, Saint Eustatius and Saba, and Sao Tomé and Príncipe refer to only a small number of notified cases (range: 1-8 notified previously treated TB cases).

5.1.4 Estimated global incidence and mortality of MDR-TB and estimated number of MDR-TB cases among notified TB patients in 2013

Data compiled from surveys and continuous surveillance of drug resistance among TB patients allow estimation of the total number of incident cases of MDR-TB worldwide in 2013. The number of incident cases includes not only cases among notified TB patients, but also cases among people diagnosed with TB that were not notified to NTPs (and in whom MDR-TB may not have been detected) and cases among people not yet diagnosed with TB. Globally in 2013, there were an estimated 480 000 (range: 350 000–610 000) new cases of MDR-TB. There were approximately 210 000 (range: 130 000–290 000) deaths from MDR-TB in 2013. Methods used to produce these estimates are described in an [online technical appendix](#) (available at www.who.int/tb/data).

Data compiled from surveys and continuous surveillance of drug resistance among TB patients also allow production of global as well as country-specific estimates of the number of MDR-TB cases among notified TB patients with pulmonary TB. These are the MDR-TB cases that could be found by national TB programmes (NTPs) if all notified patients were tested for drug resistance to rifampicin and isoniazid using WHO-recommended diagnostic tests. As agreed at a global MDR-TB stakeholders meeting in October 2013 and subsequently endorsed by WHO's Strategic and Technical Advisory Group for TB (STAG-TB), this is a very useful indicator for assessing country performance in detecting cases of MDR-TB and enrolling them on treatment, especially when levels of detection of MDR-TB fall far short of 100% ([Box 5.3](#)).^{1,2} Globally in 2013, there were an estimated 300 000 (range: 230 000–380 000) MDR-TB cases among notified TB patients. Country-specific estimates are discussed in [section 5.2](#).

5.1.5 Resistance to second-line drugs

Extensively drug-resistant TB (XDR-TB) had been reported by 100 countries globally by the end of 2013. A total of 75 countries and five territories reported representative data from continuous surveillance or special surveys regarding the proportion of MDR-TB cases that had XDR-TB. Combining their data, the average proportion of MDR-TB cases with XDR-TB was 9.0% (95% CI: 6.5–11.5%), similar to the 2012 estimate (9.6%). Fifteen of these countries reported 10 or more XDR-TB cases in the most recent year for which data were available. Among those countries, the proportion of MDR-TB cases with XDR-TB was

¹ *MDR-TB stakeholders' meeting, 27–28 October 2013. Meeting report.* Geneva, World Health Organization, 2013. Available at: <http://www.stoptb.org/wg/mdrtb/meetings.asp>

² *Strategic and Technical Advisory Group for Tuberculosis (STAG-TB). Report of the 14th meeting 16–18 June 2014.* Geneva, World Health Organization, 2014. (WHO/HTM/TB/2014.16).

BOX 5.2

Burden of resistance to isoniazid without concurrent resistance to rifampicin

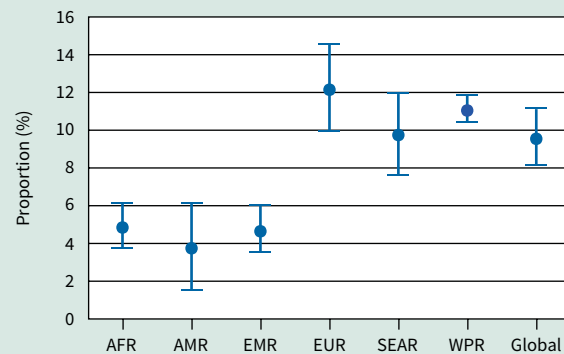
Isoniazid is a powerful anti-TB drug forming the basis of first-line therapy. Isoniazid resistance is usually investigated in parallel with rifampicin resistance, with resistance to both drugs defining a case of MDR-TB.

Levels of resistance to isoniazid without concurrent rifampicin resistance were analysed among those countries meeting pre-defined data quality benchmarks for the proportion of TB patients with results available for culture and DST (for details, see the [online technical appendix](#) available at www.who.int/tb/data). Using the most recent data for each country, DST results were available for 173 391 patients from 154 countries for the period 1995–2013. The proportions of TB patients with strains that were resistant to isoniazid but susceptible to rifampicin were weighted by the number of new TB cases that were notified in the country to generate regional and global averages.

Among all TB cases, the global average of isoniazid resistance without concurrent rifampicin resistance was 9.5% (95%CI: 8.0–11.0%). In new and previously treated TB cases respectively, the global averages were 8.1% (95%CI: 6.5–9.7%) and 14.0% (95%CI: 11.6–16.3%). The distribution of isoniazid resistance without concurrent rifampicin resistance among all TB cases by WHO region is shown in [Figure B.5.2.1](#).

FIGURE B5.2.1

Proportion of all TB cases with resistance to isoniazid but without resistance to rifampicin by WHO region, 1994–2013



Given the rapid expansion of Xpert MTB/RIF testing in many countries, it is important to remember that on average around one in 10 TB patients determined to be sensitive to rifampicin will have isoniazid resistance that cannot be detected by Xpert MTB/RIF. Patients with poor treatment outcomes should always be investigated for resistance to both rifampicin and isoniazid.

BOX 5.3

Framework for estimating MDR-TB burden and monitoring the response

Indicators are important to monitor the global MDR-TB burden and the programmatic response. Accordingly, it is important to identify which indicators are best suited to describe the burden in different contexts. WHO convened a consultation with NTP staff, donors, and all other major stakeholders during an MDR-TB global stakeholders meeting held in Paris in October 2013, with the aim of reaching agreement on which indicator(s) to use and for what purpose. The recommendations from these discussions were subsequently discussed and endorsed by WHO's Strategic and Technical Advisory Group for TB (STAG-TB) in June 2014. Consensus was reached on the following five indicators and their application:

- **Estimated number of MDR-TB cases among notified cases of pulmonary TB.** This should be used for assessing programmatic performance in diagnostic and treatment coverage, at country and global levels. It is also appropriate for planning and budgeting purposes.
- **MDR-TB incidence.** A global estimate is useful for global advocacy. Country-specific numbers become increasingly relevant as a) overall detection of TB cases approaches 100% and b) treatment coverage among notified TB cases approaches 100%.

- **MDR-TB prevalence.** A global estimate is useful for advocacy. Since incidence and prevalence can be confused, global publications should highlight only one of these two indicators. Prevalence numbers are not appropriate at the country level unless prevalence has been directly measured in a TB prevalence survey.
- **MDR-TB mortality.** A global estimate is useful for global advocacy. Country-specific estimates are only appropriate for countries in which there is a vital registration system of high quality and coverage.
- **Proportion of new and previously treated TB cases with MDR-TB.** This is useful for monitoring trends in levels of drug resistance at global and country levels.

In different parts of this *Global Tuberculosis Report*, all of the recommended estimates of burden are provided in the appropriate place ([Chapter 2](#), [Chapter 5](#)). To simplify communication messages, the Executive Summary refers only to one measure of the burden of cases (incidence). In future, WHO will explore the feasibility of estimating the burden of all rifampicin-resistant TB cases other than MDR-TB, and stratifying disease burden by, for instance, age group and HIV status.

highest in Georgia (20.0%), Kazakhstan (22.7%), Latvia (21.7%), Lithuania (24.8%) and Tajikistan (Dushanbe city and Rudaki district: 21.0%). Among the 36 countries with high TB and/or MDR-TB burden, 23 have surveillance data on second-line drug resistance but only eight have established a national surveillance system for second-line drug resistance among patients with MDR-TB. Efforts should be made to ensure that all patients diagnosed with MDR-TB undergo susceptibility testing to fluoroquinolones and injectable agents and that the results are recorded and reported.

The proportion of MDR-TB cases with resistance to any fluoroquinolones for which testing was done, including ofloxacin, levofloxacin and moxifloxacin, was 17.0% (95% CI: 12.0–22.0%). A total of 29.8% (24.3–35.3%) of patients with MDR-TB have resistance to a fluoroquinolone, a second-line injectable agent, or both. These patients would be eligible to receive regimens containing new TB drugs (for further details, see [section 5.2.7](#)), when options to treat with existing drugs have been exhausted.

5.1.6 The increasing role of molecular technologies

Increasingly, molecular technologies are being incorporated into drug resistance surveys to simplify logistics. GenoType® MTBDRplus (Hain Lifescience, Germany) was used in the national survey completed in 2012 in Nigeria and is currently being used in the national survey in Sudan. In Pakistan, Xpert® MTB/RIF (Cepheid,

USA) identified additional cases missed by culture in the national survey completed in 2014. In ongoing surveys in Papua New Guinea and Senegal, Xpert MTB/RIF is being used to screen specimens for rifampicin resistance and identify those requiring further testing at national or supranational TB reference laboratories. Surveys planned in 2014–2015 in Côte d'Ivoire, the Democratic Republic of the Congo, Indonesia and Zimbabwe will adopt the same testing algorithm. This approach greatly reduces the workload for laboratories and decreases the cost of national surveys. It may also result in the detection of cases that would otherwise have been missed by culture and conventional DST, particularly in settings with delays in transporting sputum samples to laboratories for testing. Although not a complete surrogate for MDR-TB, particularly in settings where levels of drug resistance are low, rifampicin resistance is the most important indicator of MDR-TB and has serious clinical implications for affected patients.

5.1.7 Introducing global surveillance of resistance to drugs that may be part of new TB drug regimens

Novel anti-TB drugs and new TB drug regimens are in clinical trials ([Chapter 9](#)). Both fluoroquinolones and pyrazinamide are key drugs being tested as part of new regimens for drug-susceptible TB. In this context, understanding the background prevalence of resistance to fluoroquinolones and pyrazinamide at the population level is

critical for assessing the feasibility of the introduction of new drugs and shorter regimens for TB treatment.

In 2013, a new project to assess levels of resistance to fluoroquinolones and pyrazinamide among TB patients using both phenotypic and genotypic testing methods was funded by the Bill & Melinda Gates Foundation with additional support from USAID and the TB Alliance. It covers five countries: Azerbaijan, Belarus, Bangladesh, Pakistan and South Africa. The project is managed by WHO in close collaboration with the NTPs of participating countries and the members of the supranational reference laboratory network that support them (see also [Chapter 6](#)). By July 2014, a collection of around 5 000 strains gathered from population-representative surveys had been investigated. Preliminary results show that levels of resistance to pyrazinamide among all TB patients are lower than those of rifampicin (range: 3–41%), and that pyrazinamide resistance is significantly associated with rifampicin resistance in all sites. Levels of resistance to ofloxacin are lower than those of rifampicin in all countries (range: 1–17%, with the exception of Asian countries where fluoroquinolones are extensively used for TB treatment in the private health sector). Levels of resistance to moxifloxacin are negligible in all sites.

Two additional countries (the Philippines and Ukraine) will join this project in 2014–2015. In late 2014 and early 2015, collection and analysis of clinical outcome data will be used to assess the clinical relevance of phenotypic and genotypic testing results. The correlation between phenotypic testing and gene mutations and levels of cross-resistance between fluoroquinolones will also be assessed. Final outcomes of this surveillance project will be available in 2015. These will inform both laboratory practices for surveillance and diagnosis of drug resistance, and provide guidance to the development of diagnostic algorithms and the introduction of new treatment regimens.

5.2 Management of drug-resistant TB

5.2.1 Coverage of drug susceptibility testing (DST)

The diagnosis of DR-TB requires TB patients to be tested for susceptibility to anti-TB drugs, either by conventional DST or rapid molecular diagnostics. Notification data combined with data from drug resistance surveillance suggest that if all patients notified with pulmonary TB had been tested in 2013, around 300 000 cases of MDR-TB would have been found ([section 5.1.4](#) and [Box 5.3](#)).

Targets included in the *Global Plan to Stop TB 2011–2015* call for 20% of all new bacteriologically confirmed TB cases (i.e. considered to be at high risk for MDR-TB) as well as all previously treated cases to undergo DST to first-line TB drugs. According to WHO recommendations all patients with MDR-TB should undergo DST to fluoroquinolones and second-line injectable agents to determine if they have XDR-TB.

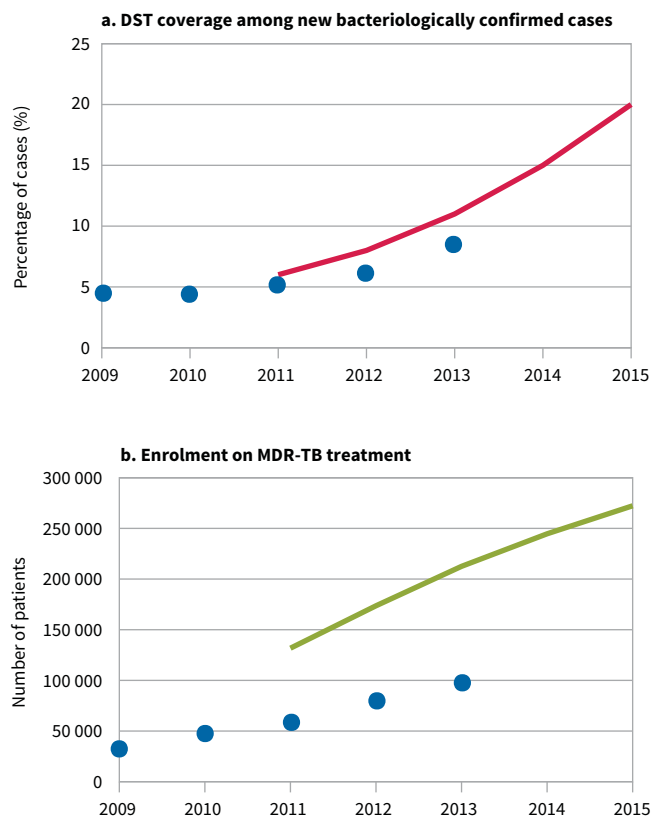
For the first time this year, in this section of the Report

([section 5.2](#)) the DST coverage figures for all years refer to TB cases tested at any time during their treatment for rifampicin resistance – with or without isoniazid – using conventional or molecular diagnostics ([Table 5.2](#) and [Figure 5.5](#)). In addition, in this section, the number of detected MDR-TB cases plus other rifampicin-resistant TB cases (as opposed to MDR-TB cases only) are presented for all years in [Figure 5.7](#) and in [Table 5.3](#). The reason for this change (compared with previous global reports) is that all of these cases are considered eligible for MDR-TB treatment in the latest WHO guidance on the programmatic management of drug-resistant TB issued in 2014 ([Box 5.4](#)).¹

In 2013, DST results for rifampicin (with or without isoniazid) were reported by 154 (71%) countries and territories for new TB cases and by 138 (64%) countries and territories for previously treated cases. Globally, 8.5% of new bacteriologically confirmed TB cases and 17% of those previously treated for TB were tested for drug resistance in 2013.

FIGURE 5.4

DST coverage among new cases and enrolment on MDR-TB treatment, compared with the targets in the Global Plan to Stop TB, 2011–2015. Lines indicate the planned targets, blue circles show the actual situation in 2009–2013.



¹ *Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis*. Geneva, World Health Organization. 2014. (WHO/HTM/TB/2014.11).

TABLE 5.2

DST coverage among TB and MDR-TB cases, globally and for 27 high MDR-TB burden countries and WHO regions, 2013

	NEW BACTERIOLOGICALLY CONFIRMED CASES		RETREATMENT CASES		CONFIRMED MDR-TB CASES	
	NUMBER WITH DST ^a RESULTS	% OF CASES WITH DST RESULT	NUMBER WITH DST ^a RESULTS	% OF CASES WITH DST RESULT	NUMBER WITH DST ^b RESULTS	% OF CASES WITH DST RESULT
Armenia	394	100	73	20	66	63
Azerbaijan	1 605	76	2 221	55		—
Bangladesh	446	0.4	4 611	50	205	38
Belarus	2 145	95	1 097	86	1 353	100
Bulgaria	619	73	109	43	26	96
China	30 156	11	11 656	32		—
DR Congo	344	0.5	1 070	14	26	48
Estonia	180	>100	44	72	49	98
Ethiopia	212	0.5	1 095	—	0	0.0
Georgia	1 750	96	538	45	369	92
India		—		—	2 239	8.9
Indonesia	53	0.03	3 740	39	441	88
Kazakhstan	7 589	96	7 297	99		—
Kyrgyzstan	2 157	>100	993	74		—
Latvia	572	100	109	85	69	87
Lithuania	1 039	—	312	—		—
Myanmar	5 527	13	8 551	70	71	4.4
Nigeria		—		—	13	11
Pakistan	5 161	4.6	3 510	22	2 213	94
Philippines	3 137	3.2	13 419	70	927	75
Republic of Moldova	1 423	76	915	63	782	84
Russian Federation	31 677	84	12 066	23		—
South Africa		—		—	8 763	88
Tajikistan	864	39	947	80	11	1.2
Ukraine	13 056	81	8 619	52		—
Uzbekistan	5 472	99	3 844	45	528	17
Viet Nam	353	0.7	3 955	45	199	96
High MDR-TB burden countries	115 931	6.2	90 791	17	18 350	22
AFR	5 083	0.9	9 925	7.1	9 045	64
AMR	27 922	22	6 252	24	1 364	46
EMR	13 584	7.8	5 452	21	2 299	79
EUR	95 161	82	43 027	41	3 758	9.5
SEAR	12 333	1.2	19 018	5.8	3 088	11
WPR	63 512	13	38 593	47	2 326	39
Global	217 595	8.5	122 267	17	21 880	23

Blank cells indicate data not reported.

— indicates values that cannot be calculated.

^a DST is for rifampicin resistance only or for both rifampicin and isoniazid resistance.

^b DST is for a fluoroquinolone and a second-line injectable drug.

FIGURE 5.5

DST coverage in previously treated TB cases, globally and for WHO regions, 2009–2013.^a Numbers of cases tested are shown for each bar.

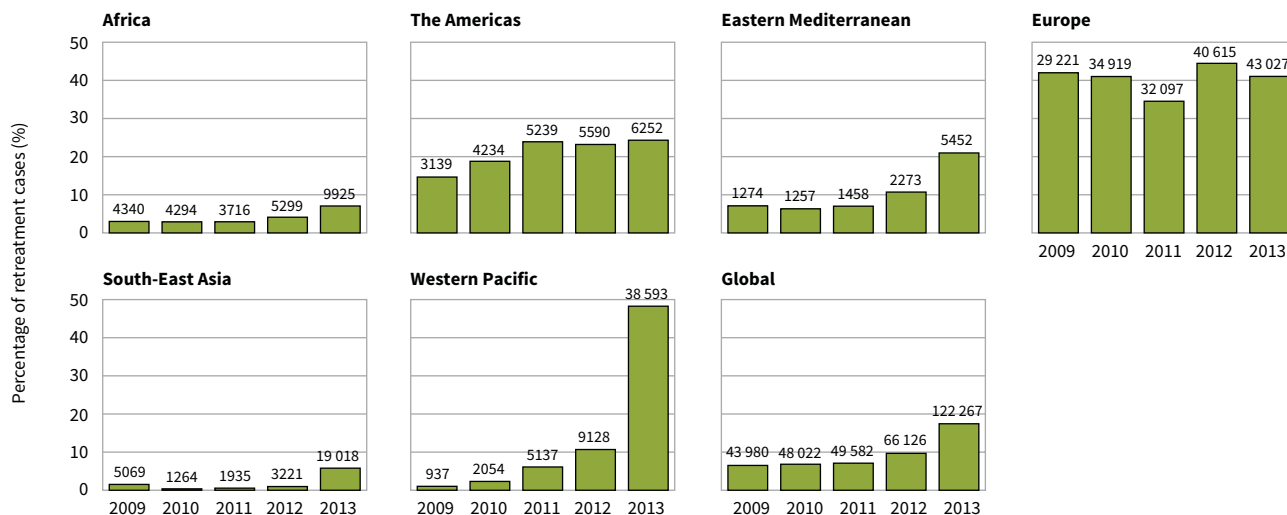


FIGURE 5.6

Number of MDR-TB cases estimated to occur among notified pulmonary TB cases, 2013

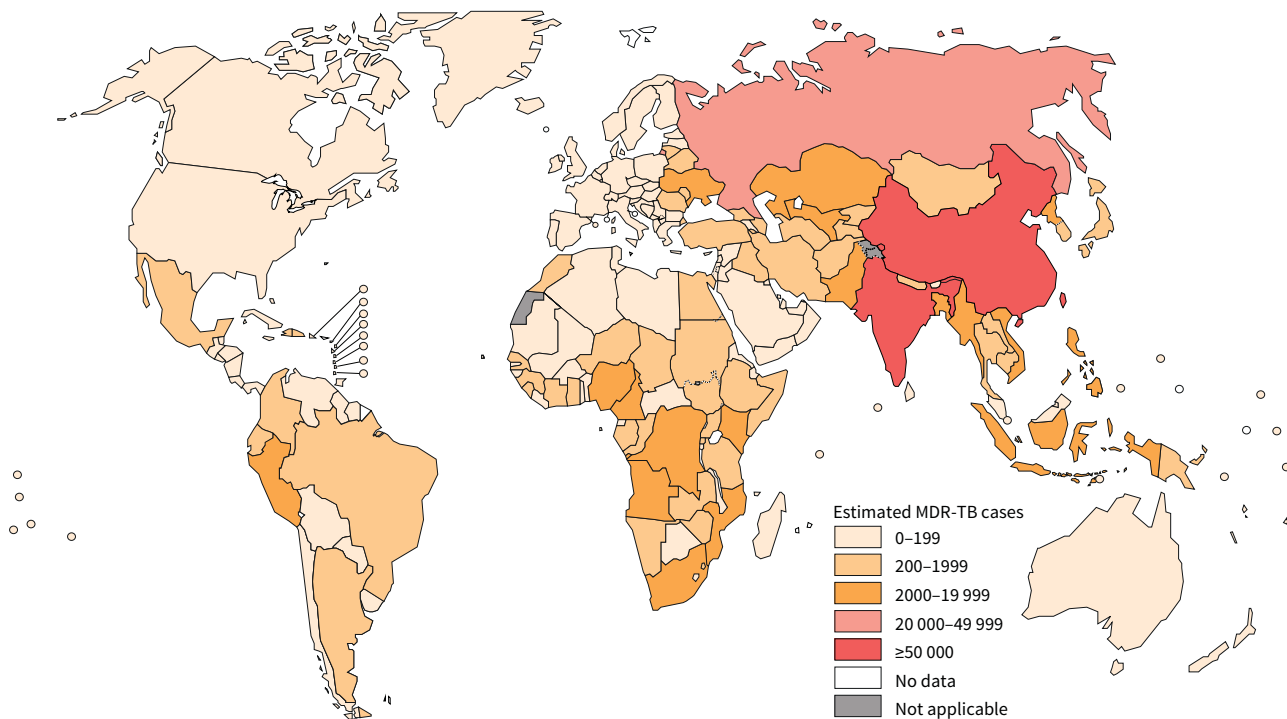


FIGURE 5.7

MDR-TB cases and additional rifampicin-resistant TB cases detected (red) compared with TB cases enrolled on MDR-TB treatment (blue), global trend and trend in 27 high MDR-TB burden countries, 2009–2013

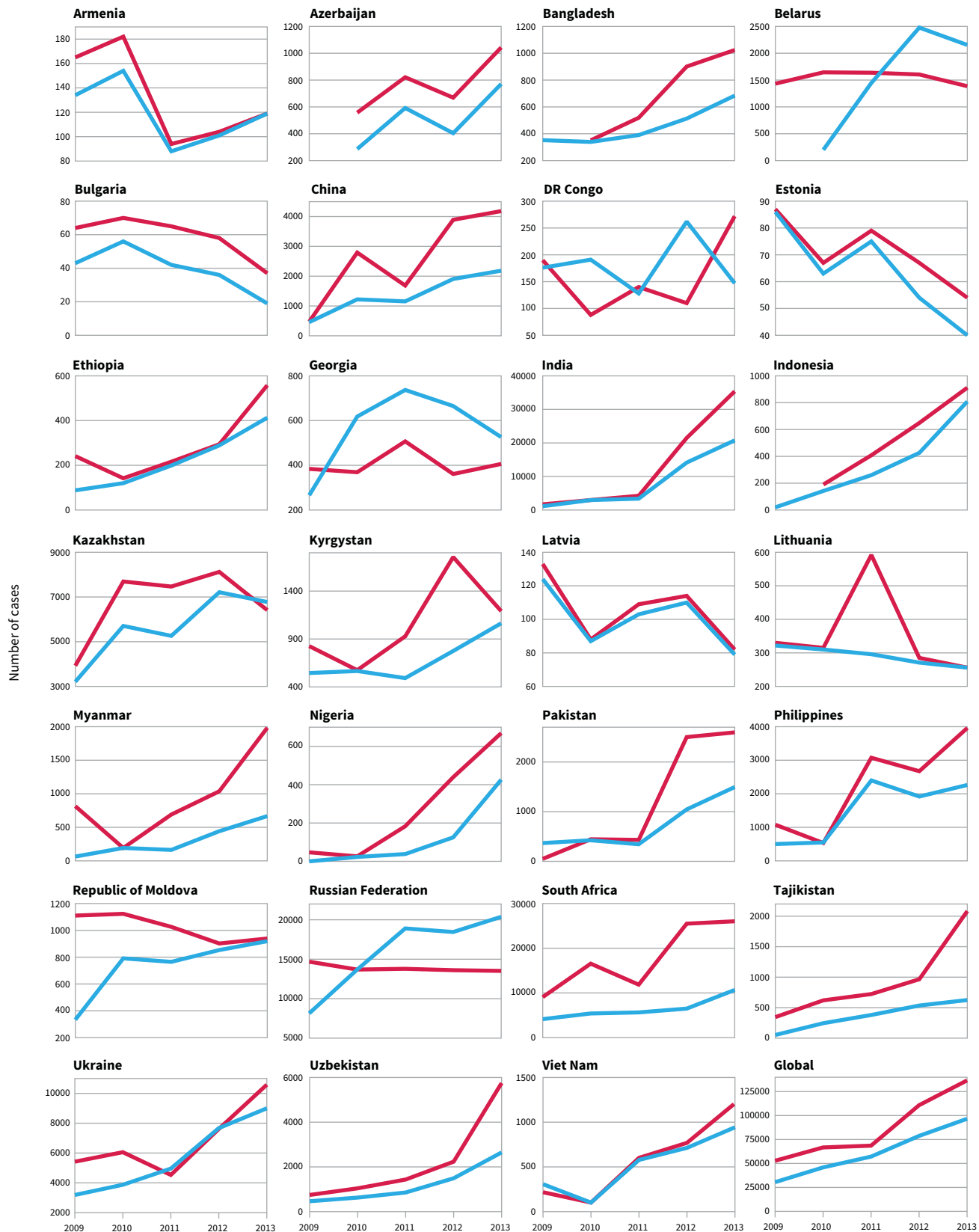


TABLE 5.3

Estimated MDR-TB cases in 2013, notified cases of rifampicin-resistant TB and MDR-TB and enrolments on MDR-TB treatment in 2013, and treatment outcome reporting for 2011 cohort, globally and for 27 high MDR-TB burden countries and WHO regions

	ESTIMATED MDR-TB AMONG NOTIFIED PULMONARY TB CASES, 2013		NOTIFIED MDR/RR-TB CASES, 2013		CASES ENROLLED ON MDR-TB TREATMENT, 2013		MDR-TB CASES REPORTED WITH TREATMENT OUTCOME DATA, 2011 COHORT	
	BEST ESTIMATE	UNCERTAINTY INTERVAL	NUMBER	NOTIFIED/ ESTIMATED MDR-TB (%) ^a	NUMBER	ENROLLED/ NOTIFIED MDR/ RR-TB (%)	NUMBER	% ^b
Armenia	190	170–220	119	63	119	100	121	>100
Azerbaijan	1 600	1 300–1 800	1 043	65	771	74	565	70
Bangladesh	4 700	3 500–5 900	1 024	22	684	67	240	47
Belarus	1 800	1 800–1 900	1 386	77	2 154	>100	1 600	100
Bulgaria	78	58–99	37	47	19	51	55	100
China	54 000	48 000–61 000	4 183	7.7	2 184	52	1 070	67
DR Congo	3 100	400–5 800	272	8.8	147	54	138	>100
Estonia	64	49–78	54	84	40	74	64	82
Ethiopia	1 400	800–2 500	558	40	413	74	116	55
Georgia	720	650–780	406	56	526	>100	611	>100
India	62 000	50 000–74 000	35 385	57	20 763	59	3 378	80
Indonesia	6 800	5 200–8 500	912	13	809	89	260	68
Kazakhstan	6 600	6 400–6 700	6 411	97	6 776	>100	5 261	71
Kyrgyzstan	1 800	1 600–1 900	1 191	66	1 064	89	492	61
Latvia	91	72–110	82	90	79	96	83	79
Lithuania	—	—	256	—	256	100	—	—
Myanmar	9 000	6 900–11 000	1 984	22	667	34	163	24
Nigeria	3 700	2 800–4 600	669	18	426	64	38	40
Pakistan	13 000	10 000–16 000	2 596	20	1 495	58	427	>100
Philippines	8 500	6 900–10 000	3 962	47	2 262	57	1 312	>100
Republic of Moldova	1 700	1 600–1 700	939	55	919	98	761	76
Russian Federation	41 000	35 000–48 000	13 521	33	20 372	>100	15 896	>100
South Africa	6 900	5 700–8 000	26 023	>100	10 663	41	6 523	65
Tajikistan	1 100	1 000–1 300	2 084	>100	625	30	380	63
Ukraine	9 400	9 200–9 700	10 585	>100	9 000	85	3 810	89
Uzbekistan	7 900	7 400–8 500	5 751	73	2 647	46	855	62
Viet Nam	5 100	4 100–6 100	1 204	24	948	79	579	96
High MDR-TB burden countries	250 000	180 000–330 000	122 637	49	86 828	71	44 798	85
AFR	44 000	11 000–76 000	32 480	74	14 418	44	8 260	67
AMR	7 100	4 600–9 600	3 362	47	2 977	89	2 895	83
EMR	17 000	12 000–22 000	3 687	22	2 013	55	874	>100
EUR	74 000	62 000–86 000	45 136	61	46 517	>100	31 634	93
SEAR	89 000	75 000–100 000	40 335	45	23 766	61	4 305	65
WPR	71 000	47 000–94 000	11 412	16	6 926	59	4 238	96
Global	300 000	230 000–380 000	136 412	45	96 617	71	52 206	84

Blank cells indicate data not reported.

— indicates data not available.

^a Notified cases of MDR/RR-TB in 2013 as a percentage of the best estimate of MDR-TB cases among all cases of pulmonary TB in the same year. The percentage may exceed 100% if estimates of the number of MDR-TB are too conservative and if linkage between the clinical and laboratory registers is inadequate.

^b The percentage of MDR-TB cases originally notified in 2011 with outcomes reported. The percentage may exceed 100% as a result of updated information about MDR-TB cases in 2011, inadequate linkages between notification systems for TB and MDR-TB, and the inclusion in the treatment cohort of cases of MDR-TB from a year prior to 2011.

BOX 5.4

Companion Handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis (PMDT)

WHO published the *Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis* in 2014. The Companion Handbook is an implementation document for NTP managers, clinicians, nurses, public health decision-makers, and technical and implementing partners committed to the prevention, diagnosis, treatment and care of drug-resistant TB.

The Handbook covers all of the key policy areas in MDR-TB care and control issued by WHO in recent years, inclusive of the *WHO Guidelines for programmatic management of drug-resistant tuberculosis 2011*, and subsequent WHO policy guidance on diagnostics and new anti-TB drugs.

In the section on diagnostics, the Handbook takes account of the revolutionary changes in diagnosis of TB and drug-resistant TB resulting from the introduction and scale-up of rapid molecular technologies, particularly the Xpert MTB/RIF assay, since early 2011 (see also [Chapter 6, Box 6.1](#)). The treatment section also takes into account the most recent WHO interim policy recommendations for the use of bedaquiline and delamanid, the first drugs since the introduction of rifampicin in the late 1960s to be released specifically for the treatment of MDR-TB. The Handbook contains examples to enable the user to weigh and decide on optimal treatment options as well as the composition of appropriate drug regimens.

The Handbook also highlights other innovations that have been added to the comprehensive response to MDR-TB care delivery. These include active pharmacovigilance, a discipline that is becoming crucially important when introducing new TB drugs and novel regimens and when using drugs “off-label”. There are chapters devoted specifically to access to drugs under development for compassionate use, and the ethics of diagnosis, treatment and care, which are fundamental to the management of MDR-TB. The methods and options to deliver palliative/end-of-life care and issues related to stigma and discrimination are also addressed as essential components of a comprehensive response to MDR-TB. The role of electronic health (eHealth) tools to enhance specific aspects of patient care, surveillance and programme management are described, taking advantage of rapid innovations in electronic communications. In the near future, the contents of the Companion Handbook will be adapted to make it more easily accessible via mobile devices and tablet computers.

The proportion of new and previously treated cases with DST results has increased by 41% and 78% respectively compared with 2012, but still remains below the targets set in the Global Plan ([Figure 5.4](#) and [Figure 5.5](#)). Coverage was highest in the European Region, where 82% of new cases were tested in 2013, and in the Western Pacific Region where 47% of previously treated cases underwent testing, reflecting relatively better access to DST in these regions. Levels of testing were particularly low in the African and South-East Asia Regions (0.9% and 1.2% of new bacteriologically confirmed cases and 7.1% and 5.8% of previously treated cases, respectively).

Among the 27 high MDR-TB burden countries – which account for >80% of estimated MDR-TB cases in the world – the proportion of TB patients who were tested for drug susceptibility in 2013 varied markedly ([Table 5.2](#)). In the 14 European countries that reported data, it ranged from 39% to 100% among new cases, and exceeded 70% among previously treated cases in six of these countries. Among the non-European high MDR-TB burden countries, testing among new cases was highest in Myanmar (13%) and China (11%). In previously treated cases, the coverage of testing was higher and reached 70% in Myanmar and the Philippines. In South Africa, India and Nigeria, 79%, 18% and 10% of TB cases overall respectively were tested although DST data were not available separately for new and previously treated cases.

Among patients who were notified and confirmed to have MDR-TB in 2013, 23% were reported to have had DST performed for both fluoroquinolones and second-line injectable drugs. Second-line DST coverage exceeded 90% in Belarus, Bulgaria, Estonia, Georgia, Pakistan and Viet Nam. South Africa alone accounted for 40% of the MDR-TB cases worldwide for which second-line DST results were reported. Second-line DST reports were available for 79% of MDR-TB cases in the Eastern Mediterranean Region and 64% in the African Region (up from 2% and 62% in 2012), and only 9.5–11% in the European and South-East Asian Regions. The increase in second-line DST coverage in the Eastern Mediterranean Region was mainly due to progress in Pakistan, which accounts for 80% of notified MDR-TB cases in the region.

Evidence of progress in DST coverage notwithstanding, the low coverage of DST in many countries remains one of the main constraints limiting the detection of MDR-TB and XDR-TB among people diagnosed with TB. Increased coverage of diagnostic DST is urgently needed to improve the detection of MDR-TB and XDR-TB. This requires accelerated strengthening of laboratory capacity and uptake of new rapid diagnostics (see [Chapter 6](#)), as well as improved reporting from diagnostic centres.

5.2.2 Notification of RR-TB and MDR-TB cases

Globally, 136 412 cases of MDR-TB or RR-TB were notified to WHO in 2013, with India, the Russian Federation,

South Africa and Ukraine reporting almost two thirds of the total (Table 5.3).

Of the MDR/RR-TB cases reported globally in 2013, almost 80% were from the European Region (45 136), India (35 385) and South Africa (26 023). The 136 412 reported cases eligible for MDR-TB treatment represented 45% (up from 36% in 2012) of the estimated 300 000 (range, 230 000–380 000) MDR-TB cases among pulmonary TB patients that were notified in 2013 (Table 5.3), and 28% of the estimated 480 000 (range: 350 000–610 000) incident MDR-TB cases in the world in 2013. Much of the increase between 2012 and 2013 was accounted for by India (21 498 to 35 385), Uzbekistan (2 233 to 5 751) and Ukraine (7 615 to 10 585). In the Democratic Republic of Congo, Myanmar, Tajikistan, and Uzbekistan, MDR/RR-TB notifications increased by more than 90% in 2013 compared with 2012. In contrast, in Belarus, Bulgaria, Estonia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, and the Russian Federation, MDR/RR-TB notifications decreased between 2012 and 2013.

In the African and European Regions in 2013, the numbers of notified MDR/RR-TB cases were equivalent to 74% and 61% respectively of the estimated MDR-TB cases among notified pulmonary TB patients. The ratio was lower in the Region of Americas (47%), and South East Asia (45%). The lowest regional figures were in the Eastern Mediterranean (22%) and the Western Pacific (16%) regions. In 2013, China, the country estimated to have the largest number of TB patients with MDR-TB in the Western Pacific Region (54 000), only reported 4 183 MDR/RR-TB cases (7.7% of the estimated number if all TB patients had been tested for MDR-TB). The Russian Federation detected and reported 13 521 MDR/RR-TB cases (33% of the estimated number). The number of notified MDR/RR-TB cases exceeded the number estimated using notification and drug resistance surveillance data in South Africa, Tajikistan and Ukraine (Table 5.3), indicating either reporting of laboratory results without linkage to patient registers and/or that estimates of MDR-TB are too conservative (for example, because drug resistance surveillance data have become outdated).

5.2.3 Enrolment of notified RR-TB and MDR-TB cases on treatment

The number of patients enrolled globally on MDR-TB treatment increased from 30 500 in 2009 to 96 617 in 2013 (a three-fold increase). There was a 25% increase in enrolments between 2012 and 2013 in the 27 high MDR-TB burden countries, which reflected progress in 19 of these countries, with the largest absolute increments in India, South Africa, the Russian Federation, Ukraine and Uzbekistan.

Globally, the ratio of the number of patients starting second-line MDR-TB treatment to those notified with MDR/RR-TB in 2013 was 71% (Table 5.3). This ratio was

over 70% in 14 high MDR-TB burden countries, and was highest in the European Region (>100%) and in the Region of Americas (89%). The ratio was lowest in the African (44%) and Eastern Mediterranean (55%) Regions. In Belarus, Georgia, Kazakhstan and the Russian Federation, enrolments outstripped notifications of MDR/RR-TB (Figure 5.7). This may be caused by empirical treatment of TB patients considered at risk of having MDR-TB but for whom a laboratory-confirmed diagnosis is missing, incomplete reporting of laboratory data, or enrolment of 'backlogs' of MDR-TB patients who were detected before 2013. The ratio of enrolled to diagnosed cases was lower than 60% in 10 high MDR-TB burden countries in 2013 and lowest in Myanmar (34%), South Africa (41%), and Tajikistan (30%). This ratio has decreased in recent years in several countries. The ratio of diagnosed cases to cases enrolled on treatment increased on average by more than 25% annually between 2009 and 2013 in China, the Democratic Republic of the Congo, Myanmar, Nigeria and Pakistan, indicating that progress in detection is outstripping capacity to provide treatment. In many countries, waiting lists of people requiring treatment for MDR-TB are persisting or growing, reflecting inadequate programme capacity to match treatment to diagnosis, particularly in settings where the use of rapid molecular diagnostics such as Xpert MTB/RIF (Figure 5.7) has expanded.

Despite increases in the number of patients enrolled on MDR-TB treatment between 2012 and 2013, the overall number remains well below Global Plan targets (Figure 5.4b and Table 5.3). The slow rates of increase in two countries with high burdens of MDR-TB, China and the Russian Federation, are a major reason why progress falls short of these targets. To reach the Global Plan targets and advance towards universal access to treatment, bold and concerted actions are required, especially in these two countries.

5.2.4 Enrolment of notified XDR-TB cases on treatment

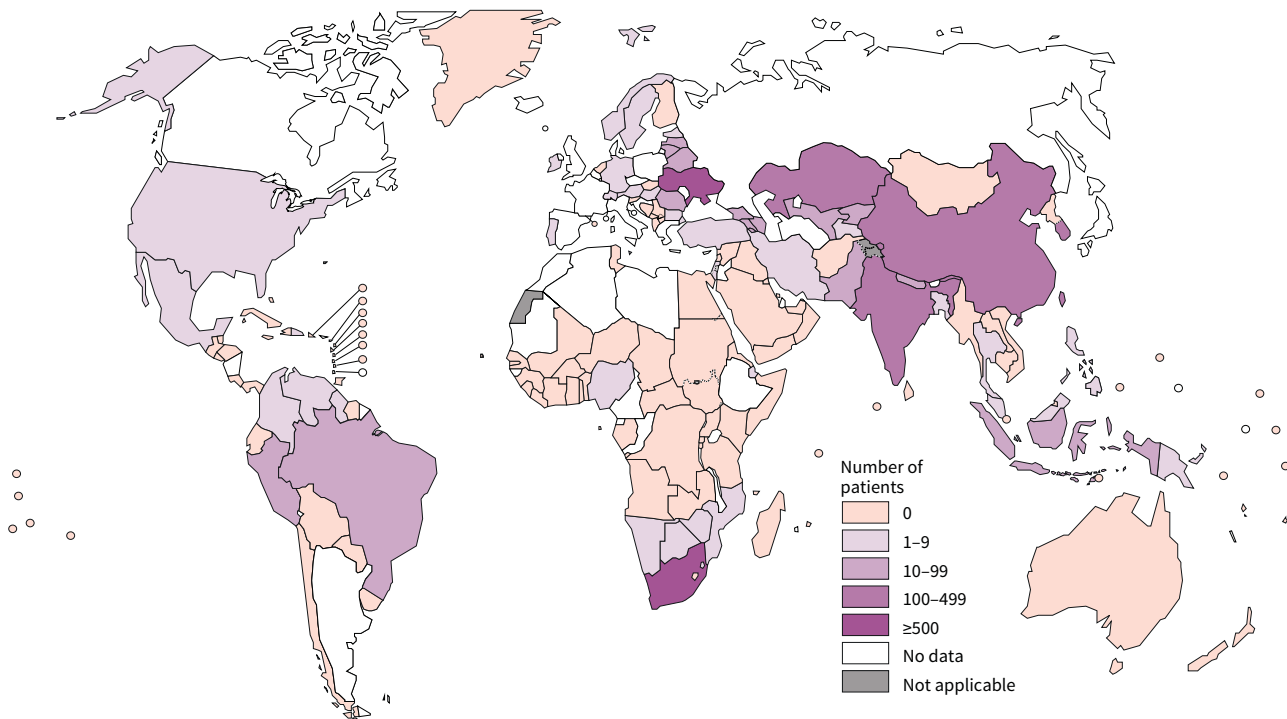
In 2013, 54 countries and territories reported treating XDR-TB cases. Globally, 3 232 XDR-TB cases were enrolled on treatment, up from 1 852 cases in 2012 and reflecting increases in enrolments in 17 high MDR-TB burden countries. Most of the cases in 2013 were notified from Ukraine (1 006), South Africa (612), India (364) and Kazakhstan (305).

5.2.5 Treatment outcomes for patients with MDR-TB and XDR-TB

The Global Plan included a target that all countries would report outcomes for all notified MDR-TB cases by 2015. In 2011, 126 countries, including all of the 27 high MDR-TB burden countries, reported treatment outcomes for cases started on MDR-TB treatment in 2011 (the country cohort size ranged from 1 to 15 896 cases). The number of

FIGURE 5.8

Number of patients with laboratory-confirmed XDR-TB started on treatment in 2013



cases reported in annual cohorts has increased progressively in all six WHO regions over time, reaching 52 206 cases globally in 2011, an increase of 47% compared with 2010 (Table 5.3 and Figure 5.9). This is equivalent to 84% of MDR-TB cases detected and notified by countries in the same year. The shortfall reflects incomplete reporting of outcomes for all MDR-TB cases due to weaknesses in reporting systems as well as, in some instances, adjustments to statistics between the time of notification and reporting of final treatment outcomes.

Overall, the proportion of MDR-TB patients in the 2011 cohort who successfully completed treatment (i.e. cured or treatment completed) was 48% (median: 59.5%), while 25% of cases were reported as lost to follow-up or had no outcome information (Figure 5.9). Reported treatment success was highest in the Eastern Mediterranean Region (64%), and lowest (under 50%) in the African and European regions. In the Region of the Americas, the proportion of MDR-TB cases with a successful outcome has increased since 2007 alongside a reduction in the proportion of patients without treatment outcomes. In the 2011 cohort, treatment failure was highest in the European Region (15% respectively) and the death rate was highest in South East Asia (21%). The Global Plan target of achieving at least 75% treatment success in MDR-TB patients by 2015 was only reached by 29 of the 126 countries reporting outcomes for the 2011 cohort. Only five high MDR-TB burden countries (Ethiopia, Kazakhstan, Myanmar, Pakistan and Viet Nam) achieved at least 70% treatment success in the 2011 cohort.

High treatment success was maintained alongside the scale-up of PMDT in several countries. Among the 27 high MDR-TB burden countries, the cohorts in Pakistan and Viet Nam expanded considerably between 2010 and 2011 (a two-fold and six-fold increase in patient enrolments, respectively) while maintaining treatment success at ≥70%. Azerbaijan, Ethiopia, Indonesia, Nigeria, Tajikistan and Uzbekistan also expanded their MDR-TB treatment cohorts between 2010 and 2011 while maintaining treatment success of >50%.

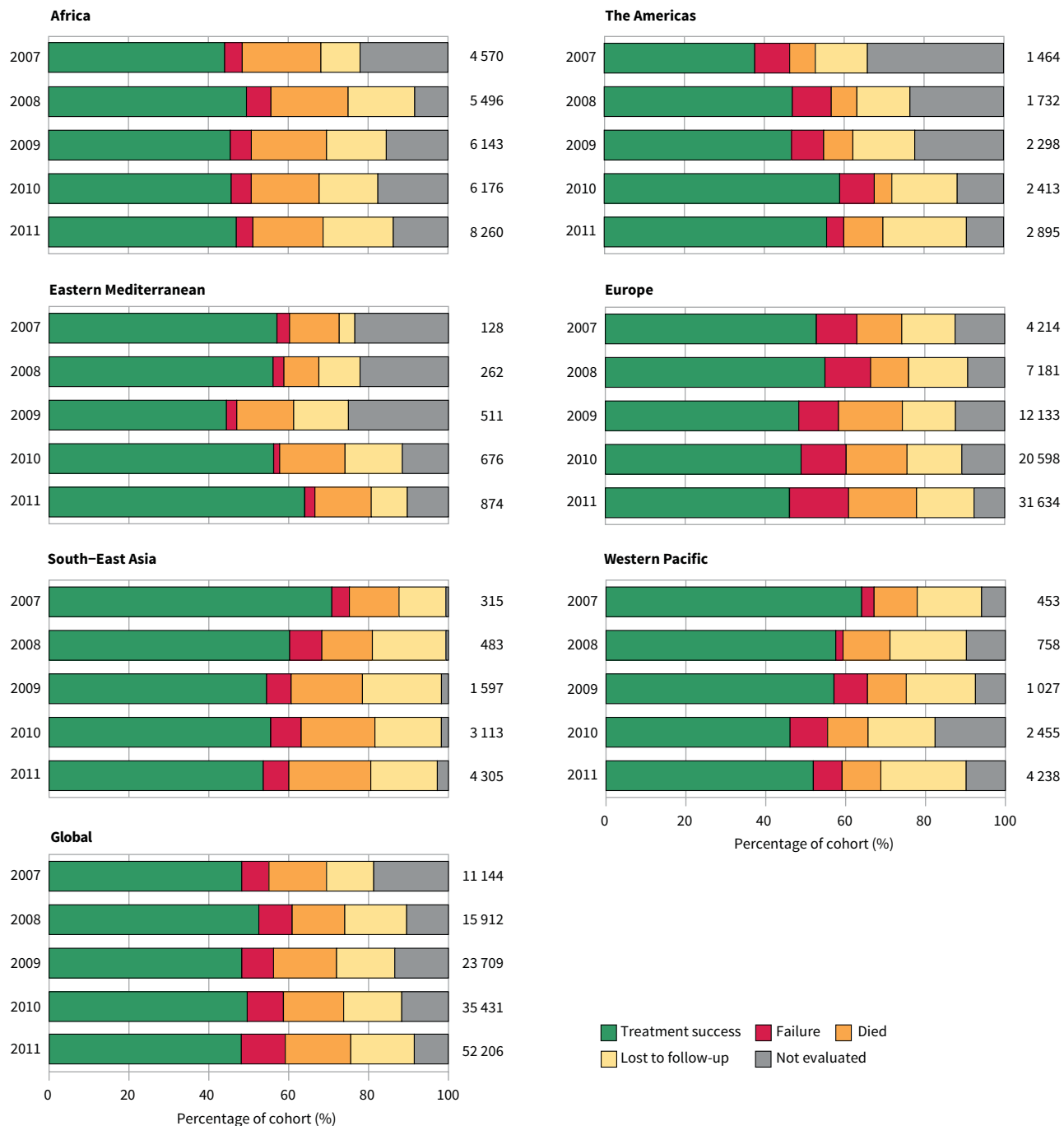
Among 1 269 XDR-TB patients in 40 countries for whom outcomes were reported, overall 284 (22%) completed treatment successfully and 438 (35%) died; 126 (10%) failed treatment and 421 (33%) were lost to follow up or their treatment outcome was not evaluated. In South Africa, which accounted for 59% of XDR-TB patients with outcomes reported in 2011, treatment success was only 15% and 40% of patients died; 36% of patients were lost to follow up or not evaluated. The high mortality of XDR-TB patients in South Africa is likely to be associated with a high level of HIV co-infection in TB patients (see Chapter 7). New drugs and more effective regimens are urgently needed to improve the outcomes for patients with XDR-TB.

5.2.6 Accelerating the scale-up of detection and enrolment on treatment for DR-TB

Common constraints to treatment scale-up include a critical shortage of trained staff, the limited market and high price of second-line medications (Box 5.5), inade-

FIGURE 5.9

Treatment outcomes for patients diagnosed with MDR-TB by WHO Region, 2007–2011 cohorts. The total number of cases with outcome data is shown beside each bar.



quate numbers of facilities for treatment and monitoring, incomplete diagnosis of patients, and other health service weaknesses required for effective programmatic management of DR-TB (PMDT).

Building in-country capacity to plan, manage and evaluate PMDT is one of the measures to address these weaknesses. In 2014, WHO released an implementation guide containing its latest recommendations to help countries address these challenges (Box 5.4). TB control services, including PMDT, are provided within the framework of

national health systems and shortages of health workers have been observed in many countries. This shortage results, among other things, in an inability of health systems to deliver the diagnostic and treatment services necessary to provide M/XDR-TB care of high quality. The low proportion of estimated MDR-TB cases that are detected and then enrolled on treatment is inextricably linked to this shortage of adequately trained, motivated and remunerated health workers, including laboratory staff.

In many countries, one of the reasons for inadequate

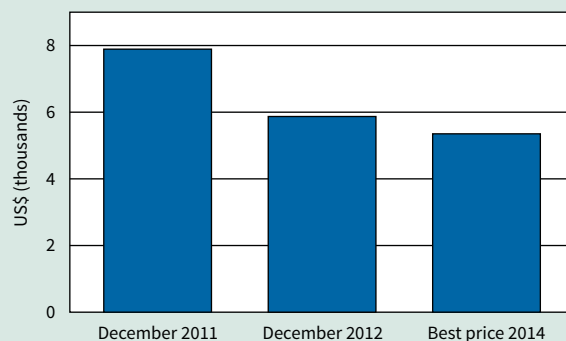
BOX 5.5

Improving access to second-line drugs

Many of the drugs used to treat MDR-TB have a narrow indication and thus the market is small. This hampers their manufacture and registration and keeps prices high. To address this challenge, the Global Drug Facility (GDF; www.stoptb.org/gdf), a major procurer of TB drugs for the public health sector of many countries worldwide, has diversified its supplier base in recent years (from 10 to 19 since 2009) and increased the supply of second-line drugs (from 12 to 23 since 2009). The GDF price for the high-end regimen for M/XDR-TB has dropped progressively (Figure 5.5.1) and a much more affordable generic formulation of linezolid, a Group 5 drug used to treat XDR-TB patients, has been introduced.

FIGURE 5.5.1

Price for a high-end MDR-TB regimen,^a 2011, 2012 and 2014 (GDF prices in US\$, ex-works)



^a Regimen: 12 Cm-Mfx-Pto-Cs-PAS / 12 Mfx-Pto-Cs-PAS.

access to DR-TB treatment is that the PMDT network is too centralized. Hospital-based models of care, which are still dominant in many countries (Box 5.6), present a barrier for the expansion of PMDT because of their dependence on hospitals or referral centres for DR-TB services. The expansion of ambulatory care in decentralized PMDT services is necessary to expand access.

The involvement of all relevant non-NTP health care providers is also important to scale up PMDT and improve access to DR-TB services (Box 5.7). Unfortunately, reliable data on these activities is often not collected by NTPs. In 2013, only seven high MDR-TB burden countries provided information on the numbers of patients started on MDR-TB treatment by non-NTP health care providers. The Philippines and Viet Nam reported that 27% and 17% respectively of MDR-TB cases were treated by non-NTP providers, while figures of 6–9% were reported to be treated in the private sector in Myanmar and four Eastern European countries: Kyrgyzstan, Tajikistan, Ukraine and Uzbekistan.

Intensified global guidance and support including direct technical assistance in recent years has helped to

BOX 5.6

Models of care for MDR-TB: from centralized hospital-based services to decentralized ambulatory care

WHO recommends that, where possible, patients with MDR-TB should be treated in ambulatory or community-based settings rather than relying upon hospital-based models of care.^{a,b} However, national policies and practices vary and hospitalization is still the predominant model of care in many countries.

Among the 27 high MDR-TB burden countries, the Philippines reports the lowest level of hospitalization (5% of MDR-TB patients), followed by Myanmar (10%). In contrast, hospitalization for 100% of MDR-TB patients in 2013 (at least for part of their treatment) was reported by all three of the highest MDR-TB burden countries: India, China and the Russian Federation. The average duration of hospitalisation was relatively short in India, at 7 days. In China, the average length of stay was 60 days and approximately 8 months (240 days) in the Russian Federation. The percentage of MDR-TB patients who were hospitalized for any duration of stay in Eastern European countries ranged between 75% and 100%, with the lowest figures in Central Asia (30–40% in Kazakhstan, Tajikistan and Uzbekistan). In high MDR-TB burden countries in the African Region, there is wide variation in the extent to which patients with MDR-TB are hospitalized, from a low of 21% of patients in the Democratic Republic of the Congo to a high of 100% in Nigeria.

Overall in high MDR-TB burden countries, the average duration of hospital stay ranged from 7 to 240 days, with a median of 90 days. The number of visits to a health facility after diagnosis of MDR-TB also varied markedly, from less than 30 (Bangladesh, the Democratic Republic of the Congo, Estonia, Myanmar, South Africa, Viet Nam) to over 700 (Georgia and Russian Federation).

There is evidence that reliance on inpatient care decreased in some high MDR-TB burden countries between 2010 and 2013. These include Estonia, South Africa, Tajikistan, Uzbekistan and Viet Nam.

^a Fitzpatrick C, Floyd K. A systematic review of the cost and cost effectiveness of treatment for multidrug-resistant tuberculosis. *Pharmacoeconomics* 2012;30(1):63–80.

^b Bassili A, Fitzpatrick C, Qadeer E, Fatima R, Floyd K, Jaramillo E. A systematic review of the effectiveness of hospital- and ambulatory-based management of multidrug-resistant tuberculosis. *Am J Trop Med Hyg* 2013;89(2):271–80.

support the scale-up of detection and treatment of DR-TB and this was boosted in late 2013 by the establishment of the Global Drug-resistant TB Initiative (Box 5.8).

5.2.7 Improving treatment outcomes

With limited treatment options for MDR- and XDR-TB patients, reaching the global target for treatment success will require urgent attention to health service weaknesses

BOX 5.7

Involvement of all health care providers in MDR-TB diagnosis and treatment: four country examples

Engagement of all relevant health care providers in the management of DR-TB cases is one intervention among several that are required to achieve universal access to care for people with MDR-TB. Although limited progress has been made to date in engaging non-NTP health care providers in the management of DR-TB, good practices have been demonstrated in several settings. Assessments conducted by WHO in four countries in 2013–2014 documented a range of different approaches and models that work. These are summarized below.

Pakistan operates a successful public-private mix (PPM) model for management of DR-TB in which PMDT sites had been established in 15 public and 3 private tertiary hospitals by the end of 2013. These hospitals offer diagnosis, treatment and management of DR-TB. Linkages between the PMDT sites and relevant TB basic management units and community health workers have been established to cater for patients receiving ambulatory care. Community health workers supervise the daily treatment and provide health education for DR-TB patients. DR-TB patients also receive food packages and other financial support (e.g. for transport, accommodation) if this is needed during treatment. In addition, general practitioners have been trained to identify TB patients at risk of DR-TB and to refer them for diagnostic testing. Under a collaborative agreement with the NTP, all involved laboratories participate in a quality assurance mechanism for DST organized by the national TB reference laboratory.

In **Myanmar**, Médecins Sans Frontières (MSF) is supporting a model of care which includes a comprehensive package of diagnosis, treatment, case management and other patient support (e.g. food packages, transport, accommodation) for DR-TB patients. By the end of 2013, the model covered 38 out of 330 townships in the country, which are in the catchment area of MSF clinics. Clinic personnel, together with their network of “DOT” (directly observed treatment) workers, provide food packages and health education to DR-TB patients during their treatment. MSF clinics receive second-line TB drugs free of charge from the NTP. In another collaborative activity with the Myanmar Medical Association (MMA) and four other NGOs,

a community-based treatment supporter network has been established to provide DOT and patient support including food packages, financial support for transport or accommodation and health education on infection control to patients on MDR-TB treatment. In addition, private practitioners are aware of the national algorithms for the diagnosis of DR-TB and the locations of the designated PMDT centres for patient referral.

In **Nigeria**, PPM efforts to diagnose and treat DR-TB have mainly focused on hospital-based models of care. However, in the private sector specifically, providers have managed to reduce the duration of hospitalization to three months. By the end of 2013, one of the 10 PMDT centres and one out of the four DR-TB diagnostic centres in the country had been established outside NTP facilities. Even so, the existing TB provider network, as well as the medical association and private practitioners’ association, needs to be better engaged in the referral of patients suspected of having DR-TB for diagnosis. In addition, a greater emphasis on ambulatory care and the inclusion of TB and MDR-TB in the National Health Insurance Scheme are important elements being considered for future PMDT scale-up in the country.

In **Turkey**, TB reporting from both public and private sectors is high as a result of the effective enforcement of compulsory notification and free-of-charge diagnosis and treatment services. These measures also enable close monitoring of the use of TB drugs outside the NTP. All patients under investigation for DR-TB are referred to one of four chest diseases training and research hospitals for diagnosis and initiation of second-line treatment. After discharge from hospital, DOT and patient support are provided by TB dispensaries or family physicians. Anti-TB associations also provide financial support for transport, accommodation and other special needs to DR-TB patients when they are on treatment.

A technical consultation was convened by WHO in Geneva from 23–24 June 2014 to discuss the development of a framework for PPM for DR-TB. The framework document will be published before the end of 2014.

that contribute to patient losses to follow-up, non-adherence to treatment and incomplete reporting of treatment outcomes. In particular, countries need to analyse the reasons for the poor treatment outcomes of patients with MDR-TB and intensify measures to improve adherence and monitoring. The high losses to follow-up and missing data are of great concern and need immediate corrective action. TB programmes need to apply a package of services for MDR-TB patients that include free TB and ancillary medications, free laboratory testing, enablers and social support, and the use of innovative, patient-centred models for care delivery. Monitoring and collection of data need to be improved. The extremely poor outcomes of treat-

ment of XDR-TB patients are worrying and prevention of drug resistance and acquisition of further drug resistance during treatment for MDR-TB are of utmost importance.

Introduction of new drugs and novel regimens could potentially improve the treatment outcomes of patients with MDR- and XDR-TB. At the end of 2012, the US Food and Drug Administration approved bedaquiline for the treatment of MDR-TB and WHO issued an interim policy on its use in 2013 and interim WHO policy guidance on its use was issued in October 2014. In April 2014, delamanid was also granted a marketing authorization by the European Commission for use MDR-TB treatment. These two drugs are the first new compounds to be approved for

BOX 5.8

The Global Drug-resistant TB Initiative (GDI): supporting the scale-up of PMDT

A landmark resolution endorsed by all Member States at the 2009 World Health Assembly demonstrated strong national and international commitment to scale-up efforts to address the challenge of DR-TB through achieving universal access to MDR-TB diagnosis and care.^a To support these efforts, the previous Green Light Committee Initiative was substantially reformed and today regional Green Light Committees (rGLCs) in all six WHO regions, with secretariats hosted by WHO regional offices, have been established. A new Global Framework was launched in 2011, with a focus on increased technical support to countries through decentralized structures. Since then, this structure has been reinforced. At a global MDR-TB stakeholders meeting held in October 2013, the Global Drug-resistant TB Initiative (GDI) was established to coordinate global MDR-TB activities. The GDI Core Group was formed in February 2014, and held its first meeting the following May. The GDI has the following strategic areas of work:

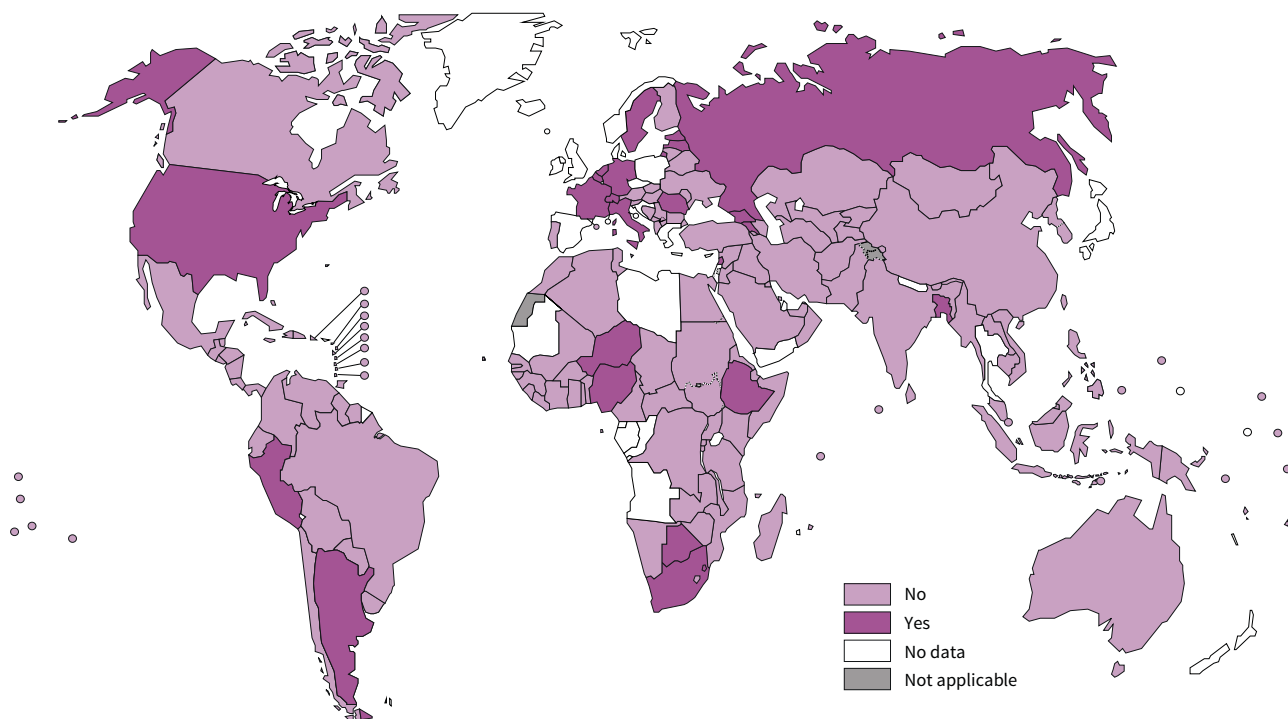
1. **Develop targeted advocacy strategies and resource mobilization** for DR-TB management scale-up.
2. **Facilitate integration and coordination of efforts** to align diagnostic services for patients with access to high-quality care.
3. **Build global consensus** on the management of DR-TB for patient-centred care delivery (“care for cure”).
4. **Promote strategies to facilitate patient access** to high-quality DR-TB care, through a long-term, in-country capacity building approach targeting both the public and private sector.
5. **Support prioritization of research** to generate evidence for PMDT scale-up.

The procedures of the GDI will be aligned to those of the Global Laboratory Initiative, an analogous structure which has provided global guidance to and coordination of TB diagnostic activities since its creation in 2008 (GLI; see also Chapter 6). Further information about the GDI and the GLI is available online.

^a Resolution WHA62.15. *Prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis*. Geneva, World Health Organization, 2009 (WHA62/2009/REC/1):25–29.

FIGURE 5.10

Countries that had used bedaquiline for the treatment of M/XDR-TB as part of expanded access, compassionate use or under normal programmatic conditions by the end of 2013



use in TB treatment for over 40 years, and the only ones ever to be released specifically for the treatment of MDR-TB.¹ By the end of 2013, at least 24 countries reported having used bedaquiline to treat a total of 186 patients (5 countries did not specify the number of cases treated) as part of efforts to expand access to treatment for MDR-TB, either for compassionate use or under normal programmatic conditions in the public or private sectors (Figure 5.10). Three quarters of these patients were reported by three countries: Armenia, South Africa and Swaziland. Through donor support, several countries in Africa, Asia and Europe have introduced shorter regimens in observational studies under operational research conditions or started including repurposed drugs in treatment regimens to improve treatment outcomes of MDR-TB and XDR-TB patients.

The use of electronic systems to manage MDR-TB patient data could also help to improve the completeness of reporting on treatment outcomes. Guidance on the design and implementation of electronic systems for recording and reporting data was produced by WHO and technical partners in 2011.² The definitions for monitoring of RR-TB and MDR-TB and treatment outcomes were revised in 2013,³ to enhance the monitoring of patients. One of the Global Plan targets is for all 27 high MDR-TB countries to manage their data on treatment of MDR-TB patients electronically by 2015. By 2013, 16 of these coun-

tries reported that national electronic databases were in place for TB patients and another five had systems for MDR-TB patients only (see Figure 2.16 in Chapter 2).

Palliative and end-of-life care delivered through home-based or institutional services is fundamental to alleviate the suffering associated with MDR-TB and XDR-TB, particularly in patients with advanced disease when standard treatment options have failed. In 2013, only 42 countries (including 16 of the 27 high MDR-TB burden countries) reported that palliative and end-of-life care was provided within the scope of their NTPs. When considered in the context of the poor outcomes reported in patients with MDR-TB and especially XDR-TB, this finding attests to the persistent and huge unmet need for palliative care services in countries with the largest burdens of DR-TB.

Alongside all the measures to ensure better detection and treatment outcomes for patients with M/XDR-TB, preventing the emergence DR-TB remains of paramount importance. This can only be achieved if patients with drug-susceptible disease – who still represent the vast majority of TB cases in most countries – are provided with the appropriate treatment and support to complete their regimens fully (see also the *Supplement* to this Report). This position has been reiterated by the post-2015 global TB strategy (see Chapter 1) endorsed by the World Health Assembly in 2014.

¹ *Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis.* (WHO/HTM/TB/2014.11). Geneva, World Health Organization, 2014.

² *Electronic recording and reporting for TB care and control.* Geneva, World Health Organization, 2012 (WHO/HTM/TB/2011.22).

³ *Definitions and reporting framework for tuberculosis – 2013 revision.* Geneva, World Health Organization, 2013. (WHO/HTM/TB/2013.2)

Diagnosics and laboratory strengthening

KEY FACTS AND MESSAGES

Laboratory confirmation of TB and drug resistance is key to ensuring that individuals with TB signs and symptoms are correctly diagnosed and have access to the correct treatment as soon as possible. Of the 4.9 million incident (new and relapse) pulmonary TB patients notified globally in 2013, 2.8 million (58%) were bacteriologically confirmed, i.e., were smear- or culture-positive or positive according to a WHO-recommended rapid diagnostic such as Xpert® MTB/RIF.

In October 2013, WHO released a Policy Update on Xpert MTB/RIF which expands the recommended use of Xpert MTB/RIF to include the diagnosis of TB in children and some forms of extrapulmonary TB. The guidance also includes an additional recommendation about the use of Xpert MTB/RIF as the initial diagnostic test in all individuals suspected of having pulmonary TB.

In line with strong WHO recommendations on its use, 60% of countries reported that national policy in 2013 indicated the use of Xpert MTB/RIF as the initial diagnostic test for people at risk of drug-resistant TB, and 56% reported that national policy indicated its use as the initial diagnostic test for people living with HIV.

By the end of June 2014, a total of 3 269 GeneXpert machines comprising 15 846 modules had been procured in the public sector in 108 of the 145 countries eligible for concessional pricing. More than 1 million cartridges are being procured each quarter.

Of the 133 countries and territories that reported data on the number of smear microscopy centres undergoing external quality assessment in 2013, only 41% indicated the existence

of a scheme that covered all centres in the country. Strengthening the quality of microscopy networks can be facilitated with the new Global Laboratory Initiative (GLI) *TB Microscopy Network Accreditation Assessment Tool* launched in October 2013.

In 2009, WHO recommended that fluorescent light-emitting diode (LED) microscopy be phased in as an alternative to Ziehl-Neelsen (ZN) microscopy. However, LED microscopes were reported to be present in only 6% of microscopy centres in 2013. Within one year, the percentage of microscopy centres in China using LED microscopes increased from 2% in 2012 to 33% in 2013, with Global Fund support.

Detection of TB without investigation for drug resistance can lead to ineffective treatment, further development and spread of drug-resistant strains and additional suffering and costs for patients. The new post-2015 global TB strategy calls for drug susceptibility testing (DST) as a universal standard of care.

Between 2009 and the end of June 2014, nearly 90 000 people with MDR-TB were detected through the EXPAND-TB project, which has established capacity to detect drug-resistant TB using line probe assays, liquid culture and Xpert MTB/RIF in 27 low- and middle-income countries.

2014 marks the 20th anniversary of the WHO/Global Laboratory Initiative (GLI) TB Supranational Reference Laboratory (SRL) Network. Recent additions to the network are the Aga Khan University of Pakistan and the Statens Serum Institut of Denmark. The National Institute of TB and Respiratory Diseases in New Delhi, India became an SRL-National Centre of Excellence (SRL-CE).

The bacteriological confirmation of TB and the determination of drug resistance are critical to ensuring that a patient is correctly diagnosed with TB and started on the most effective treatment regimen. New rapid diagnostics integrated into tiered quality-assured laboratory networks, together with efficient referral systems, constitute fundamental components of any modern and effective national TB programme. As part of the post-2015 global TB strategy's first pillar on integrated, patient-centred care and prevention ([Chapter 1](#)), the early diagnosis of TB is emphasized and inclusion of drug susceptibility testing (DST) is now targeted as a universal standard for patient care, including for both new and previously treated patients.

Sputum smear microscopy has been the primary meth-

od for detecting TB and monitoring treatment response in most resource-constrained countries for decades. While inexpensive and requiring minimal biosafety standards, microscopy is not a sensitive test, particularly in people living with HIV and in children: it provides no information on the viability and drug susceptibility of the bacilli, and it cannot distinguish between *Mycobacterium tuberculosis* complex and non-tuberculosis mycobacteria. Though diagnosis based on culture is considered the reference standard, results take weeks to obtain and testing requires a well-equipped laboratory, highly trained staff, and an efficient transport system to ensure viable specimens. Culture is also critical for monitoring patients' response to treatment for drug-resistant TB (DR-TB). Phenotypic DST on cultured specimens is the conventional

method used to detect resistance to first- and second-line TB drugs.

Following significant investments in TB diagnostics research and development in the past decade (**Chapter 9**), rapid and more sensitive tests are now available to replace or complement existing conventional tests. Nevertheless, of the 4.9 million incident pulmonary TB patients notified globally in 2013, only 2.8 million (58%) were bacteriologically confirmed, i.e., were smear- or culture-positive or positive according to a WHO-recommended rapid diagnostic such as Xpert® MTB/RIF (Cepheid, Sunnyvale USA). The remaining 42% of patients who were not bacteriologically confirmed were diagnosed clinically, i.e. based on symptoms, chest X-ray abnormalities or suggestive histology. The common symptoms of TB combined with the poor specificity of X-ray screening may result in false diagnoses and people without TB being enrolled on TB treatment when it is not needed. Furthermore, a low rate of laboratory confirmation reflects an under-diagnosis of true TB cases and contributes in part to the continuing global gap between notified and estimated incident TB cases (5.7 and 9.0 million in 2013, respectively).

Detection of TB without investigating for drug resistance can lead to ineffective treatment, further development and spread of drug-resistant strains and additional suffering and costs for patients. As described in **Chapter 5**, the proportion of new and previously treated cases receiving DST has steadily increased but remains below global targets. Globally, 8.5% of new bacteriologically confirmed TB cases and 17% of those previously treated for TB were tested for drug resistance in 2013. Given the large burden of undiagnosed DR-TB, strengthening DST capacity is a high priority for national TB programmes (NTPs).

Section 6.1 of this chapter summarizes the key developments in WHO guidance on TB diagnostics and laboratory strengthening during 2013–2014. **Section 6.2** provides the status of laboratory capacity globally, regionally and nationally based on data reported to WHO by countries in 2014. The focus is on the 36 countries in the combined list of 22 high burden countries (HBCs) and 27 high MDR-TB burden countries, and on the achievements of the EXPAND-TB Project in building capacity in reference laboratories in 27 countries. **Section 6.3** describes recent activities to strengthen TB laboratories, including quality assurance of reference and peripheral laboratories and the WHO/Global Laboratory Initiative (GLI) Supranational Reference Laboratory (SRL) Network.

6.1 Developments in WHO policy guidance on TB diagnostics and laboratory strengthening, 2013–2014

The landscape of TB diagnostics continues to evolve, with new technologies at various stages in the product development pipeline (details are provided in **Chapter 9**). Once adequate data on the performance of new diagnostics

are available, WHO follows a systematic process for policy development, involving synthesis of the available evidence through systematic reviews, meta-analyses where possible, assessment of the evidence by an external Expert Group using the GRADE approach,¹ and development of policy guidance² for dissemination to Member States and other stakeholders. Policy documents are reviewed every 3–5 years, and revised as necessary when new evidence becomes available.

The first WHO policy guidance on the use of Xpert MTB/RIF was issued in December 2010. The recommendations were that Xpert MTB/RIF should be used as the initial diagnostic test in individuals at risk of having MDR-TB or HIV-associated TB (strong recommendation), and that Xpert MTB/RIF could be used as a follow-on test to microscopy in other populations, especially in smear-negative specimens (conditional recommendation, recognizing major resource implications). The 2010 recommendations applied to the use of Xpert MTB/RIF in sputum specimens only, as data on its performance for testing of extrapulmonary specimens at that time were limited. The recommendations were extrapolated to children from data for adults.

Following rapid uptake of Xpert MTB/RIF (**Box 6.1**), a substantial body of new evidence had been generated by early 2013. This included additional data about the test's performance in detection of extrapulmonary TB and TB in children, and more evidence about affordability and cost-effectiveness from early implementers in a variety of settings. WHO therefore embarked on a review of its policy guidance. Three systematic reviews were commissioned on the sensitivity and specificity of Xpert MTB/RIF for the diagnosis of pulmonary and extrapulmonary TB and rifampicin-resistant TB (RR-TB), in adults and children. A review of published studies on the affordability and cost-effectiveness of Xpert MTB/RIF was also conducted.

An Expert Group convened by WHO in May 2013 reviewed the expanded body of evidence, according to GRADE procedures. Based on the outcomes of the review and the recommendations of the Expert Group, supported by WHO's Strategy and Technical Advisory Group for TB (STAG-TB), updated WHO policy guidance was released in October 2013.³ The new policy guidance widens the recommended use of Xpert MTB/RIF, including for the diagnosis of TB in children and – on selected specimens – for the diagnosis of extrapulmonary TB. The guidance also includes an additional recommendation about the use of Xpert MTB/RIF as the initial diagnostic test in all individuals suspected of having pulmonary TB. The lat-

¹ www.gradeworkinggroup.org

² *WHO handbook for guideline development*. Geneva, World Health Organization, 2012. Available at: http://apps.who.int/iris/bitstream/10665/75146/1/9789241548441_eng.pdf.

³ www.who.int/tb/laboratory/xpert_policyupdate

Global roll-out of Xpert MTB/RIF

Following initial WHO recommendations issued in December 2010, Xpert MTB/RIF has been quickly adopted by countries as an effective tool for the rapid detection of TB and rifampicin resistance at lower levels of the health system. By the end of June 2014, 3 269 GeneXpert machines comprising 15 846 modules^a had been procured in the public sector in 108 of the 145 countries eligible for concessional pricing (Figure B6.1.1). In the period July 2013–June 2014, more than 1 million cartridges were procured each quarter (Figure B6.1.2). South Africa accounted for 56% of the cartridges (4.2 million out of 7.5 million) and 26% of the modules procured globally between December 2010 and the end of June 2014, although other countries are scaling up their use. Other major procurers of cartridges include India, Brazil and China, which have procured 380 000, 290 000 and 240 000 cartridges, respectively. Substantial funding and technical support from sources including the Global Fund, PEPFAR, USAID, UNITAID, TB REACH and Médecins Sans Frontières have enabled ministries of health to rapidly establish capacity to use Xpert MTB/RIF.

In 2010, WHO policy guidance included a strong recommendation that Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB. Many countries have incorporated this guidance into their national policies, and are at various stages of implementation to reach country-specific goals for roll-out. Globally, 61% of all countries and 24 of the 27 high MDR-TB burden countries (89%) reported that national policy in 2013 stated that Xpert MTB/RIF should be used as the initial diagnostic test in people at risk of drug-resistant TB (see Table B6.1.1). Given its improved sensitivity over microscopy for detection of TB among people living with HIV, 56% of countries globally reported that national policy states that Xpert MTB/RIF should be used as the initial diagnostic test in people living with HIV. Countries of the WHO African region have led in the adoption of this recommendation, with 71% reporting having done so.

The wide scale-up of Xpert MTB/RIF in many countries has led to a growing need for electronic recording and reporting systems that can centrally monitor machine use and performance and efficiently manage the data that are being generated. Open-source software including GXAlert (Abt Associates, Cambridge USA) and XpertSMS (Interactive Health Solutions, Karachi Pakistan) has been developed as solutions with the following capabilities:

- Central collection of data to provide a real-time dashboard that displays error rates by machine, as well as cartridge supply by site to help prevent stockouts or expiry;

FIGURE B6.1.1

Global capacity for Xpert MTB/RIF testing, by June 2014

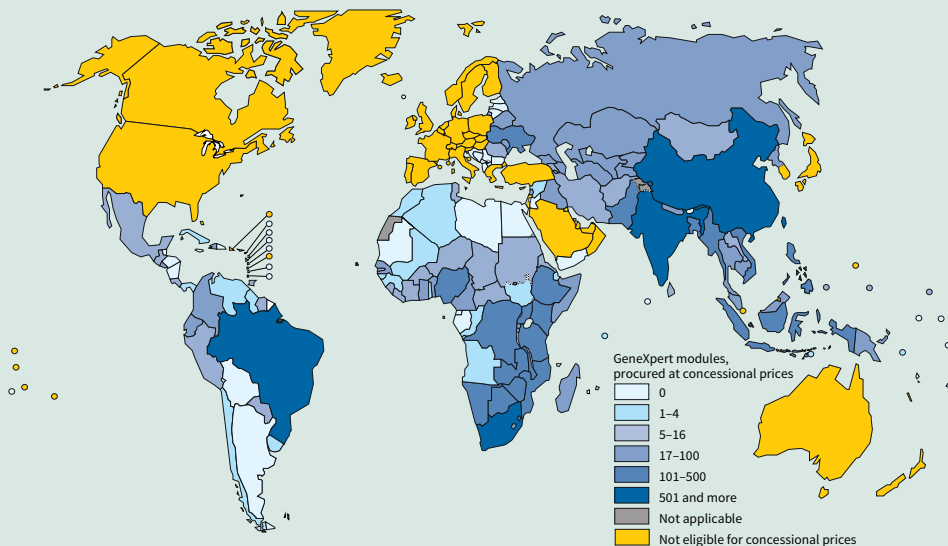
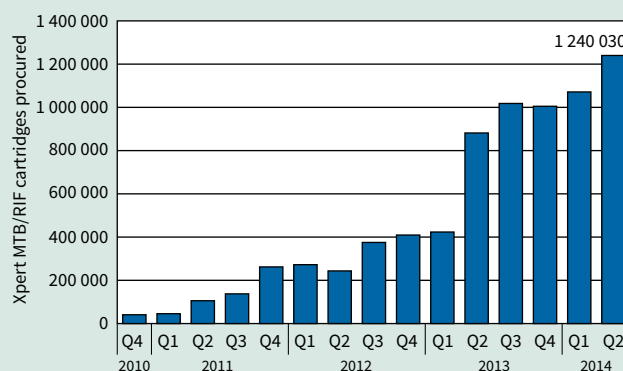


FIGURE B6.1.2

Quarterly number of Xpert MTB/RIF cartridges procured at concessional prices, October 2010 – end June 2014



- Automatic generation and sending of messages via text or email (including by USB modem) to clinicians to inform them of test results and/or to patients to inform them about the availability of results;
- Provision of real-time test results, stratified by many variables including age, sex, and the reason for testing (patient group) if indicated in the comments field; and
- Storage of data either in external servers (such as GXAlert or XpertSMS servers) or on a national-based server, depending on the preference of the ministry of health.
- Costs for electronic recording and reporting systems vary and can include modems, connectivity, installation and data hosting costs.

^a The range of GeneXpert instruments includes systems with 1, 2, 4, 16, 48 or 80 modules.

TABLE B6.1.1

Incorporation of WHO policy guidance on Xpert MTB/RIF, 2013^a

YES <input checked="" type="checkbox"/> NO <input type="checkbox"/>	HIGH TB BURDEN	HIGH MDR-TB BURDEN	XPRT MTB/RIF AS THE INITIAL DIAGNOSTIC TEST FOR TB IN PEOPLE LIVING WITH HIV	XPRT MTB/RIF AS THE INITIAL DIAGNOSTIC TEST IN PEOPLE AT RISK OF DRUG-RESISTANT TB
Afghanistan	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Armenia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Azerbaijan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Bangladesh	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Belarus	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Brazil	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Bulgaria	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Cambodia	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
China	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
DR Congo	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Estonia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ethiopia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Georgia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
India	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Indonesia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Kazakhstan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Kenya	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Kyrgyzstan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Latvia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Lithuania	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Mozambique	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Myanmar	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Nigeria	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Pakistan	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Philippines	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Republic of Moldova	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Russian Federation	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
South Africa	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Tajikistan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Thailand	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Uganda	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ukraine	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
UR Tanzania	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Uzbekistan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Viet Nam	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Zimbabwe	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
High-burden countries			82%	86%
High MDR-TB burden countries			89%	89%
AFR			71%	73%
AMR			52%	50%
EMR			53%	53%
EUR			48%	55%
SEAR			55%	73%
WPR			50%	56%
Global			56%	61%

^a The regional and global figures are aggregates of data reported by low- and middle-income countries and territories. Data for the variables shown in the table are not requested from high-income countries in the WHO data collection form.

est recommendations are summarized in **Box 6.2**.

An Implementation Manual accompanying the WHO Policy Update on Xpert MTB/RIF was released in April 2014.¹ The manual provides updated guidance on the selection of target patient groups; the positioning of machines; interpretation of test results; how to improve budget data; updated checklists of the essential elements that must be in place before Xpert MTB/RIF implementation begins; and key actions necessary for implementation. The manual also includes an annex of standard operating procedures for processing extrapulmonary specimens.

A comprehensive list of existing WHO policy documents, including those on the use of microscopy, culture, DST and non-commercial and molecular methods, can be found at: www.who.int/tb/laboratory/policy_statements.

6.2 Status of laboratory capacity globally, regionally and nationally

In most low- and middle-income countries, smear microscopy remains the mainstay of TB diagnosis, despite its relatively low sensitivity and inability to distinguish between drug-resistant and drug-susceptible strains. Microscopy remains essential to monitor treatment in drug-susceptible TB patients and a microscopy network with adequate population coverage and high quality performance is therefore critical. The *Global Plan to Stop TB 2011–2015* includes the target that countries maintain at least one smear microscopy centre per 100 000 population.² Globally the target has been met (1.1 centres per 100 000 population in 2013), but significant disparities remain at regional and country levels (**Table 6.1**). For example, the Western Pacific and Eastern Mediterranean regions had less than one centre per 100 000 population in 2013. After 2015, this target will need to be revised given the increased use of Xpert MTB/RIF as an initial diagnosis-

¹ www.who.int/tb/publications/xpert_implem_manual

² *The Global Plan to Stop TB, 2011–2015*. Geneva, World Health Organization, 2010 (WHO/HTM/STB/2010.2).

BOX 6.2

WHO recommendations on Xpert MTB/RIF (October 2013)

The 2013 WHO Policy Update on Xpert MTB/RIF recommends the following:

- **Xpert MTB/RIF should be used** rather than conventional microscopy, culture and DST as the initial diagnostic test in adults and children suspected of having MDR-TB or HIV-associated TB (strong recommendation).
- **Xpert MTB/RIF may be used** rather than conventional microscopy and culture as the initial diagnostic test in all adults and children suspected of having TB (conditional recommendation acknowledging resource implications).
- **Xpert MTB/RIF may be used** as a follow-on test to microscopy in adults suspected of having TB who are not at risk of MDR-TB or HIV-associated TB, especially when further testing of smear-negative specimens is necessary (conditional recommendation acknowledging resource implications).
- **Xpert MTB/RIF should be used** in preference to conventional microscopy and culture as the initial diagnostic test in testing cerebrospinal fluid (CSF) specimens from patients suspected of having TB meningitis (strong recommendation given the urgency of rapid diagnosis).
- **Xpert MTB/RIF may be used** as a replacement test for usual practice (including conventional microscopy, culture, or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having extrapulmonary TB (conditional recommendation).



Recommendations should be read in conjunction with associated remarks described in the Policy update.^a

^a www.who.int/tb/laboratory/xpert_policyupdate

tic test, especially in settings with high burdens of HIV and MDR-TB. Furthermore, geographic variations in the TB epidemic within a country and differences in access between urban and rural settings require that the number and placement of microscopy centres be strategically considered within countries.

Quality assurance of microscopy remains a critical activity of all laboratory networks, and a comprehensive external quality assessment (EQA) programme should be implemented that includes on-site evaluation, random blinded rechecking, and panel testing. Of the 133 countries and territories that reported data on the number of smear microscopy centres undergoing EQA in 2013, only 41% indicated the existence of a scheme that covered all centres in the country, with a further 7% covering at least 95% of centres. Among the 22 HBCs, only two reported such a scheme that encompassed all centres in 2013 (Bangladesh and India) and four more reported a programme that included at least 95% of centres (Cambodia, Myanmar, Pakistan and Viet Nam). **Section 6.3** further describes efforts to implement quality management systems and strengthen microscopy networks.

Fluorescent light-emitting diode (LED) microscopy is more sensitive than conventional Ziehl–Neelsen (ZN) light microscopy and has further qualitative, operational and cost advantages. In 2009, WHO recommended that LED microscopy be phased in as an alternative for ZN microscopy. Globally, the switch to LED microscopes has been gradual; it was reported to have occurred in only 6% of microscopy centres in 2013. Nonetheless, major progress is evident in certain countries. The percentage of microscopy centres in China using LED microscopes increased from 2% in 2012 to 33% in 2013, with Global Fund support. Among HBCs, other adopters of LED microscopy include South Africa (100% of microscopy sites in 2013), Mozambique (19%), the United Republic of Tanzania (17%), Bangladesh (17%), Nigeria (14%), Myanmar (13%), Ethiopia (13%) and Cambodia (13%). Adoption of LED microscopy remains particularly low in Afghanistan (0%), Indonesia (0%), Brazil (<1%), Zimbabwe (<1%), the Democratic Republic of the Congo (1%), India (2%), Pakistan (2%) and Viet Nam (2%).

The current target in the *Global Plan to Stop TB 2011–2015* for both culture and DST (to at least rifampicin and isoniazid) capacity is one laboratory per 5 million population. In 2013, 12 of the 27 high MDR-TB burden countries did not reach the target (**Table 6.1**), and several countries with large TB caseloads continue to completely lack in-country capacity for phenotypic DST. The following 11 countries reported more than 1000 notified TB cases in 2013 but no capacity to perform phenotypic DST: Afghanistan, Burkina Faso, Chad, Congo, Gabon, Guinea-Bissau, Papua New Guinea, Sierra Leone, Somalia, South Sudan and Timor Leste. Eritrea and Liberia both reported that they gained initial capacity in 2013.

TABLE 6.1

Laboratory capacity, 2013^a

YES <input checked="" type="checkbox"/> NO <input type="checkbox"/>	HIGH TB BURDEN	HIGH MDR-TB BURDEN	SMEAR MICROSCOPY			CULTURE		DRUG SUSCEPTIBILITY TESTING		LINE PROBE ASSAY		XPRT MTB/RIF
			NUMBER OF LABORATORIES	LABORATORIES PER 100 000 POPULATION	PERCENTAGE OF LABORATORIES USING LED MICROSCOPES	NUMBER OF LABORATORIES	LABORATORIES PER 5 MILLION POPULATION	NUMBER OF LABORATORIES	LABORATORIES PER 5 MILLION POPULATION	NUMBER OF LABORATORIES	LABORATORIES PER 5 MILLION POPULATION	NUMBER OF SITES
Afghanistan	<input checked="" type="checkbox"/>	<input type="checkbox"/>	667	2.2	0	3	0.5	0	0	0	0	1
Armenia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	29	1.0	3	1	1.7	1	1.7	1	1.7	2
Azerbaijan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	64	0.7	5	7	3.7	2	1.1	3	1.6	11
Bangladesh	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	1 085	0.7	17	3	<0.1	3	<0.1	1	<0.1	26
Belarus	<input type="checkbox"/>	<input checked="" type="checkbox"/>	154	1.6	2	29	15	8	4.3	8	4.3	8
Brazil	<input checked="" type="checkbox"/>	<input type="checkbox"/>	3 026	1.5	<1	345	8.6	39	1.0	0	0	0
Bulgaria	<input type="checkbox"/>	<input checked="" type="checkbox"/>	34	0.5	38	30	21	12	8.3	4	2.8	0
Cambodia	<input checked="" type="checkbox"/>	<input type="checkbox"/>	215	1.4	13	4	1.3	1	0.3	0	0	10
China	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	3 328	0.2	33	1 284	4.6	249	0.9	133	0.5	160
DR Congo	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	1 522	2.3	1	2	0.1	1	<0.1	1	<0.1	26
Estonia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	6	0.5	33	2	7.8	2	7.8	2	7.8	2
Ethiopia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	2 107	2.2	13	7	0.4	7	0.4	7	0.4	23
Georgia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	11	0.3	9	2	2.3	1	1.2	2	2.3	1
India	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	13 048	1.0	2	53	0.2	45	0.2	41	0.2	54
Indonesia	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	5 566	2.2	0	18	0.4	10	0.2	2	<0.1	23
Kazakhstan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	466	2.8	0	126	38	22	6.7	12	3.6	19
Kenya	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1 860	4.2	9	7	0.8	6	0.7	2	0.2	21
Kyrgyzstan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	122	2.2	23	8	7.2	2	1.8	2	1.8	8
Latvia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	16	0.8	0	4	9.8	1	2.4	1	2.4	2
Lithuania	<input type="checkbox"/>	<input checked="" type="checkbox"/>	13	0.4	8	6	9.9	6	9.9	2	3.3	8
Mozambique	<input checked="" type="checkbox"/>	<input type="checkbox"/>	325	1.3	19	3	0.6	2	0.4	1	0.2	14
Myanmar	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	486	0.9	13	3	0.3	2	0.2	2	0.2	24
Nigeria	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	1 515	0.9	14	5	0.1	3	<0.1	4	0.1	49
Pakistan	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	1 396	0.8	2	11	0.3	8	0.2	4	0.1	32
Philippines	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	2 561	2.6	0	18	0.9	3	0.2	0	0	16
Republic of Moldova	<input type="checkbox"/>	<input checked="" type="checkbox"/>	57	1.6	0	4	5.7	4	5.7	4	5.7	28
Russian Federation	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	5 296	3.7	5	330	12	218	7.6	6	0.2	72
South Africa	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	207	0.4	100	15	1.4	15	1.4	15	1.4	207
Tajikistan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	87	1.1	5	4	2.4	1	0.6	2	1.2	11
Thailand	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1 081	1.6	6	65	4.8	18	1.3	12	0.9	14
Uganda	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1 333	3.5	5	4	0.5	4	0.5	2	0.3	37
Ukraine	<input type="checkbox"/>	<input checked="" type="checkbox"/>	808	1.8	—	81	9.0	32	3.5	3	0.3	15
UR Tanzania	<input checked="" type="checkbox"/>	<input type="checkbox"/>	945	1.9	17	5	0.5	1	0.1	3	0.3	35
Uzbekistan	<input type="checkbox"/>	<input checked="" type="checkbox"/>	305	1.1	<1	7	1.2	2	0.3	3	0.5	11
Viet Nam	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	975	1.1	2	24	1.3	2	0.1	2	0.1	27
Zimbabwe	<input checked="" type="checkbox"/>	<input type="checkbox"/>	211	1.5	<1	2	0.7	2	0.7	1	0.4	58
High-burden countries			—	1.1	6	—	2.5	—	0.7	—	0.3	—
High MDR-TB burden countries			—	1.0	6	—	2.5	—	0.8	—	0.3	—
AFR			—	1.5	11	—	0.5	—	0.4	—	0.3	—
AMR			—	2.0	1	—	16	—	0.9	—	0.2	—
EMR			—	0.7	4	—	1.5	—	0.4	—	<0.1	—
EUR			—	1.3	4	—	12	—	4.9	—	1.2	—
SEAR			—	1.2	2	—	0.4	—	0.2	—	0.2	—
WPR			—	0.5	14	—	4.4	—	0.8	—	0.5	—
Global			—	1.1	6	—	4.3	—	1.0	—	0.4	—

— indicates values that cannot be calculated.

^a The regional and global figures are aggregates of data reported by low- and middle-income countries and territories. Data for the variables shown in the table are not requested from high-income countries in the WHO data collection form.

BOX 6.3

Impact of the EXPAND-TB project

The EXPAND-TB project is a multi-donor, multi-country project that was established in 2009. To date it is the biggest collaborative effort on TB laboratory strengthening globally, with unique features that show the impact of multiple partners working towards a common goal. The EXPAND-TB project benefits from complementary contributions to the provision of diagnostics commodities, laboratory infrastructure, technical assistance and country capacity development from many technical partners and donors, including UNITAID, FIND, GLI, the Global Drug Facility, the Global Fund, the United States government, the World Bank and others, with project management and oversight provided by WHO.

The overall goal of EXPAND-TB is to establish modern, rapid diagnostics in state-of-the-art TB reference laboratories. It is being implemented in 27 low- and middle-income countries that together carry 40% of the estimated global burden of MDR-TB among notified TB patients. Data on the number of MDR-TB cases detected since 2009 illustrate the contribution of the project to the three pillars required for successful management of drug-resistant TB: addressing barriers to diagnosis of MDR-TB; aligning access to diagnostics with capacity for treatment delivery; and provision of quality-assured second-line medicines.

Since 2009, when building or refurbishment of laboratories began in the 27 countries participating in the project, 97 laboratories have been equipped with new technologies (liquid culture and line probe assay) and with the required biosafety infrastructure. By the end of June 2014, almost 90 000 MDR-TB cases were diagnosed in and notified by these laboratories. In 2013 alone, more than 65 000 cases eligible for MDR-TB treatment were notified in the 27 project countries, representing about one half of the global total in that year.

The EXPAND-TB Project works on the principle of prolonged and dedicated technical support embedded in or closely associated with NTPs and ministries of health. The overarching aim is local laboratory capacity strengthening through country capacity building and mentoring. Since the start of the project, almost 2300 laboratory staff, managers and other medical personnel have been trained by the EXPAND-TB implementation team, supported by manufacturers (Hain LifeScience, Becton Dickinson, Cepheid) in over 240 training sessions focused on liquid culture and DST, LPA, Xpert MTB/RIF, rapid speciation, laboratory biosafety and quality management, and sample collection and transportation.

Improved diagnostic capacity has enabled countries to better plan their procurement of quality-assured second-line drugs. In turn, this has positively influenced the market for second-line anti-TB medicines. The price of the most expensive MDR-TB regimen fell 30% between 2011 and 2014.^a In addition, the laboratory capacity established under EXPAND-TB have created a new pathway for the rapid introduction of future technologies, providing a blueprint for the scale-up of both TB and MDR-TB diagnosis.

^a www.who.int/tb/tbteam/GDF.pdf

Patients with MDR-TB require DST for second-line drugs to refine and optimize their treatment regimen. Some countries with small caseloads of MDR-TB patients have reasonably opted to rely on partner laboratories (including WHO/GLI Supranational Reference Laboratories) for such testing, instead of building in-country capacity. However, 22 countries with reported MDR-TB cases indicated that they had neither in-country capacity nor a linkage with a partner laboratory for second-line DST: Albania, Burkina Faso, Cambodia, Central African Republic, Cote D'Ivoire, Eritrea, Ghana, Jordan, Kenya, Kuwait, Lesotho, Liberia, Madagascar, Malawi, Mali, Sao Tomé and Príncipe, South Sudan, Sudan, Swaziland, Syria, Togo and Yemen. Countries with sizeable TB and MDR-TB caseloads should aim as a priority to build sustainable DST capacity in-country to allow the timely diagnosis of drug-resistant strains.

As a high-throughput molecular tool for use at central and regional levels, line probe assays (LPAs) have been adopted by many countries for rapid first-line DST (to rifampicin and isoniazid) on smear-positive specimens. 84 countries and territories reported at least one facility with capacity to perform LPA tests in 2013. Of the 27 high MDR-TB burden countries, 13 reported more than one laboratory per five million population using LPAs. This represents an increase from the eight high MDR-TB countries that reported such coverage in 2011, partly due to the establishment of the technology in the EXPAND-TB project. As the largest collaborative effort to strengthen TB reference laboratories to date, the EXPAND-TB project has established capacity for rapid DST in 27 low- and middle-income countries and has significantly contributed to the increase in MDR-TB cases detected globally (Box 6.3).

In future, the increasing number of drug-resistant cases being detected by Xpert MTB/RIF and LPAs will require adjustment of country culture and phenotypic DST capacities. The introduction of Xpert MTB/RIF and LPAs reduces the need for culture as the initial diagnostic test; yet the growing number of drug-resistant TB cases will require culture capacity for monitoring of treatment and DST of other anti-TB drugs to guide treatment adjustments. It is also imperative that the increasing capacity of countries to diagnose drug-resistant TB is matched by increased capacity to provide appropriate treatment to all diagnosed cases (see also Chapter 5).

Quality-assured DST is critical to ensure accurate detection of drug resistance for subsequent treatment decisions and to avoid false diagnoses. Of the high TB and MDR-TB burden countries that reported on EQA coverage of DST laboratories in 2013 (33 of 36), 27 (82%) reported having a scheme that encompassed all DST laboratories. Of the 112 reporting countries globally, 81 (72%) indicated a scheme that encompassed all laboratories, and 79% reported that (among laboratories tested) at least 95% of them demonstrated acceptable performance. Ensuring

quality continues to be a critical need at all levels of laboratory networks, and as described in the following section, tools have recently been developed that guide NTPs in their efforts to strengthen quality at both reference and peripheral laboratories.

6.3 Strengthening TB laboratories globally, regionally and nationally

Strengthening TB laboratories requires not only the introduction of modern diagnostics at various levels of the network (Section 6.2), but also ensuring the quality of every step in the diagnostic process, including sample collection, receipt and registration of samples at the laboratory, testing of samples and recording and reporting of test results. Implementing a system of quality management in every laboratory is therefore needed, and the Global Plan includes a target that more than half of all national TB reference laboratories should have a quality management system in place by 2015.

In 2011, the GLI *Stepwise Process toward TB Laboratory Accreditation tool* was launched,¹ led by the Royal Tropical Institute (KIT), The Union, the United States Centers for Disease Control and Prevention and WHO, with funding from the United States Agency for International Development (USAID). The tool is primarily recommended for National TB Reference Laboratories to guide them in the implementation of a quality management system that meets international accreditation standards. As a complementary tool, the WHO-AFRO *Guidelines for the Stepwise Laboratory Improvement Process Towards Accreditation in the African Region* (SLIPTA) provides a checklist to assess the implementation of a quality system at all levels of laboratory services. In 2013, 104 of 159 responding countries and territories (65%) indicated that a formal quality management system towards achieving laboratory accreditation was at least partially implemented at the NRL.

Evaluation of national microscopy networks using a structured assessment tool allows, at a minimum, the

validation of the TB microscopy laboratory components of the network where integrated supervision systems exist, and provides a working model that can lay the foundation for integration across disease-specific programmes. To help countries to adequately manage their microscopy networks, the *TB Microscopy Network Accreditation: An Assessment Tool*

was launched by the GLI in October 2013. Development of the tool was led by The Union, the United States Cent-

ers for Disease Control and Prevention, KNCV Tuberculosis Foundation, KIT, the Pakistan NTP and WHO, with funding from USAID. The tool provides guidance on the implementation of WHO recommendations related to the support and monitoring of microscopy networks, and how to validate whether or not quality standards are applied in all microscopy laboratories.

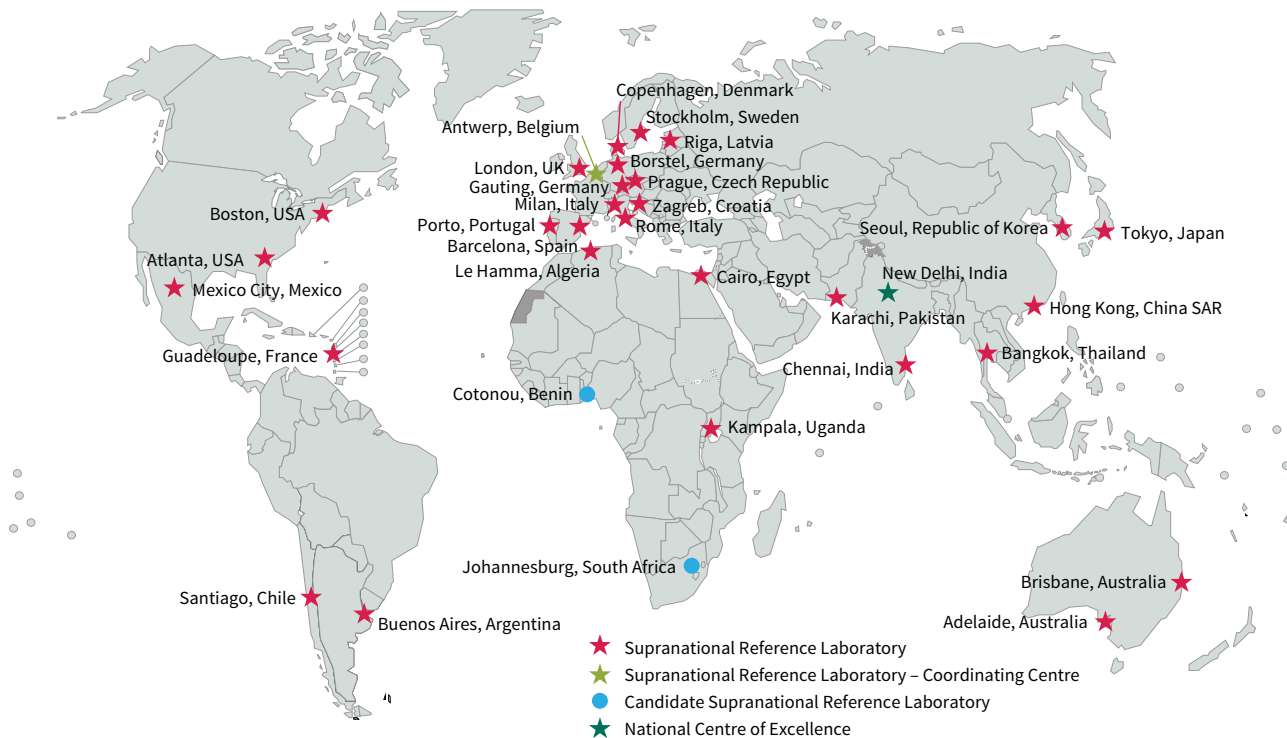
The WHO/GLI SRL Network comprises 33 laboratories that provide long-term technical assistance to countries under the framework of collaborative agreements. The network was developed in 1994, initially to ensure the quality of drug resistance surveys; 2014 marks the 20-year anniversary of the SRL Network (see also the special supplement that accompanies this global TB report). In keeping with increasing demand, SRLs currently provide a wide range of technical assistance services to strengthen national and central level laboratories globally. 152 countries and territories reported having a formal link with a partner SRL in 2013.

In the past year, the Aga Khan University of Pakistan and the Statens Serum Institut of Denmark have been designated as SRLs, and links have been formed with countries that previously did not benefit from SRL support. In addition, a new category of the SRL Network has been specifically designed to recognize well-performing national and regional TB reference laboratories in large, middle-income countries. These 'National Centres of Excellence' of the SRL Network (SRL-CE) have similar terms of reference (and national status) to that of an SRL but with an in-country focus for its laboratory strengthening and capacity building activities. The SRL-CEs will be of particular value for establishing and maintaining high-quality services to support NTPs and partners in scaling up the programmatic management of drug-resistant TB, including through the coordination of technical assistance, provision of monitoring and supervision and provision of training to laboratory staff involved in diagnostic testing for drug resistance and monitoring of treatment for patients with MDR-TB. To meet its objectives, a SRL-CE commits to provide minimum service requirements such as establishing formal links with at least two intermediate level laboratories within the country and undertaking at least one annual technical assistance visit to each laboratory. A SRL-CE needs to be nominated by their NTP to the WHO country office, establish a collaborative agreement with an existing SRL, undergo a laboratory assessment by WHO, and actively implement a quality management system towards accreditation. The National Institute of TB and Respiratory Diseases in New Delhi, India, became the first SRL-CE in April 2014. The SRL network in July 2014 is shown in Figure 6.1.

¹ www.gliquality.org

FIGURE 6.1

The Supranational Reference Laboratory Network



Addressing the co-epidemics of TB and HIV

KEY FACTS AND MESSAGES

In 2013, an estimated 1.1 million (13%) of the 9.0 million people who developed TB worldwide were HIV-positive. The African Region accounted for 78% of the estimated number of HIV-positive incident TB cases.

The number of people dying from HIV-associated TB has been falling since 2004. However, globally there were still 360 000 deaths from HIV-associated TB in 2013, equivalent to 25% of all TB deaths (among HIV-negative and HIV-positive people) in 2013 and around 25% of the estimated 1.5 million deaths from HIV/AIDS.

The prevalence of HIV co-infection among TB patients is highest in the African Region. Of the 1.1 million TB patients with an HIV test result in 44 countries, 41% tested positive in 2013. Among the high TB/HIV burden countries, this ranged from 7% in Mali to 74% in Lesotho and Swaziland.

Globally, 48% of notified TB patients had a documented HIV test result in 2013, and higher in the African Region (76%). Among the 41 countries with the highest TB/HIV burden, 16 achieved levels of $\geq 90\%$. Progress in increasing coverage of HIV testing among TB patients slowed between 2012 and 2013.

Coverage of co-trimoxazole preventive therapy (CPT) among HIV-positive TB patients remains high, and this increased slightly to 85% globally and 87% in the African Region in 2013.

Between 2012 and 2013, there was an encouraging increase in the global coverage of antiretroviral therapy (ART) for notified TB patients who were known to be co-infected with HIV, from 60% to 70%. However, considerably more progress is needed to reach the target of 100%. Moreover in 2013, the number of HIV-positive TB patients started on ART represented only 32% of the estimated number of HIV-positive people who developed TB in 2013.

As in previous years, most of the HIV-positive people who were initiated on isoniazid preventive therapy (IPT) were in South Africa. Although provision of IPT is increasing in some other countries in Africa, only 21% of countries globally and 14 of the 41 high burden TB/HIV countries reported provision of IPT to people living with HIV in 2013.

Preventing TB deaths among people living with HIV requires intensified scale-up of TB prevention, diagnosis and treatment interventions and earlier initiation of ART among people living with HIV and those with HIV-associated TB. Further scale-up of collaborative TB/HIV activities could be facilitated by joint TB and HIV programming, which would help to overcome constraints, promote synergies and achieve efficiency gains, especially between TB and HIV programmes.

Globally, people living with HIV are 29 times more likely to develop TB disease than those who are HIV-negative.¹ Beginning in the 1980s, the HIV epidemic led to a major upsurge in TB cases and TB mortality in many countries, especially in southern and eastern Africa (**Chapter 2, Chapter 4**).

In 2013, 1.1 million (13%) of the 9.0 million people who developed TB worldwide were HIV-positive (**Chapter 2, Table 2.1**); 78% of these HIV-positive TB cases were in the African Region. The number of people dying from HIV-associated TB has continued to fall globally, from a best estimate (and peak) of 540 000 in 2004 to 360 000 in 2013 (with approximately equal numbers of deaths among men and women).² This reflects progress in most regions, including the African Region. However, it represents an enormous burden of preventable suffering and the target set by WHO, UNAIDS and the Stop TB Partnership to halve the number of HIV-associated TB deaths by 2015 (compared with 2004) is unlikely to be met globally.

WHO recommendations on the interventions needed to prevent TB in HIV-positive people and to reduce the impact of HIV co-infection among HIV-positive TB patients have been available since 2004,^{3,4} and are collectively known as collaborative TB/HIV activities. They include establishing and strengthening coordination mechanisms for delivering integrated TB and HIV services, HIV testing for all patients with presumptive and diagnosed TB, providing antiretroviral therapy (ART)

¹ The probability of developing TB among people living with HIV divided by the probability of developing TB among HIV-negative people is the incidence rate ratio (IRR). The mean estimated global IRR (all ages) in 2013 was 29 (range 26–31). However, there is considerable variation among countries: in 2013, the median IRR was 22 (interquartile range 13–32). Further details are provided in an **online technical appendix**.

² Estimates of the total burden of TB disease and of the number of TB cases and deaths among HIV-positive people are updated annually by WHO. The main updates and the reasons for them are explained in more detail in **Chapter 2** (see especially **Box 2.1**) and in an online technical appendix (www.who.int/data).

³ *Interim policy on collaborative TB/HIV activities*. Geneva, World Health Organization, 2004 (WHO/HTM/TB/2004.330; WHO/HTM/HIV/2004.1). Available at http://whqlibdoc.who.int/hq/2004/who_htm_tb_2004.330_eng.pdf

⁴ *WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders*. Geneva, World Health Organization, 2012 (WHO/HTM/TB/2012.1). Available at http://whqlibdoc.who.int/publications/2012/9789241503006_eng.pdf

and co-trimoxazole preventive therapy (CPT) to all HIV-positive TB patients, providing HIV prevention services for TB patients, intensifying TB case-finding among people living with HIV, offering isoniazid preventive therapy (IPT) to people living with HIV who do not have active TB, and preventing the transmission of TB infection in health care and congregate settings. The latter three activities are referred to as the *Three 'Is' for HIV/TB* and, together with earlier ART, are the principal interventions for preventing TB among people living with HIV. Since 2010, the rapid molecular test Xpert MTB/RIF has been recommended as the primary diagnostic test for TB among people living with HIV who have TB signs and symptoms. WHO has recommended ART for all HIV-positive TB patients within the first 8 weeks of initiation of TB treatment, irrespective of their CD4 cell count, since 2012. Earlier initiation of ART (within 2 weeks of TB treatment) is also an important intervention, particularly for those TB patients with profound immunosuppression (e.g. CD4 cell count less than 50) among whom it has been shown to improve survival.

WHO began monitoring the implementation of collaborative TB/HIV activities in 2004. This chapter presents the latest status of progress, using data for each year 2004–2013.

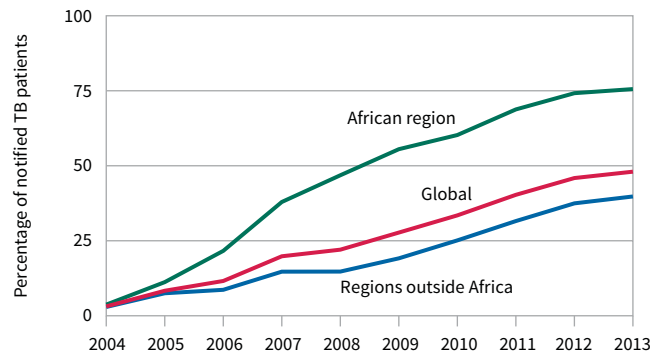
7.1 HIV testing and documentation of HIV status among TB patients

WHO recommends that routine HIV testing should be offered to all patients with presumptive and diagnosed TB as well as to partners of known HIV-positive TB patients.¹ In 2013, 2.9 million notified TB patients had a documented HIV test result, equivalent to 48% of notified TB cases (Table 7.1, Figure 7.1). This represented an increase from 2.8 million and 46% respectively in 2012, and more than 15 times the coverage reported in 2004 (Figure 7.1). Globally, 83 countries reported that $\geq 75\%$ of TB patients had a documented HIV test result, down slightly from the 87 countries that reported such levels of coverage in 2012 (Figure 7.2). The countries that moved from the $\geq 75\%$ to $< 75\%$ categories between 2012 and 2013 included two high TB/HIV burden countries: Cameroon and Ghana. Despite this progressive increase in the percentage of TB patients with known HIV status, global progress in coverage slowed between 2012 and 2013 (Figure 7.1). Both TB and HIV programmes need to routinize HIV testing of people with diagnosed and presumptive TB as well as TB screening among HIV-positive people to ensure early access to life-saving interventions.

The percentage of TB patients with known HIV status

FIGURE 7.1

Percentage of notified TB patients with known HIV status, 2004–2013



remains highest in the African Region, where it continues to increase. In 2013, 76% of TB patients had a documented HIV test result, up from 74% in 2012 (Table 7.1 and Figure 7.1). Of the 47 African countries, there were 30 in which $\geq 75\%$ of TB patients had a documented HIV test result in 2013 (Figure 7.2); this is similar to 2012 levels.

Overall, among the 41 countries identified as priorities for the global TB/HIV response (listed in Table 7.1), 57% of notified TB patients had a documented HIV test result in 2013, representing a steady increase since 2007 and up from 53% in 2012. Levels of coverage ranged from 2% in Indonesia to 98% in Rwanda. Sixteen countries reported that more than 90% of TB patients knew their HIV status in 2013, of which five (Kenya, Mozambique, Rwanda, Swaziland and Zimbabwe) have consistently sustained testing levels of $\geq 90\%$ since 2011. A further eight countries (Burkina Faso, Lesotho, Malawi, Namibia, South Africa, Togo, Uganda, and Zambia) have consistently reported that $\geq 80\%$ TB patients know their HIV status. However, 10 high TB/HIV burden countries reported that less than 50% of their TB patients knew their HIV status. This included seven countries with generalized HIV epidemics: Angola, Cameroon, Central African Republic, Chad, Congo, the Democratic Republic of Congo and Sudan.

The percentage of TB patients with a documented HIV test result in the Region of the Americas was 69% in 2013 (Table 7.1), up from 62% in 2012. This reflected progress in several countries, although in Brazil, which accounted for over a third of all cases tested in the region, the situation was relatively stable (65% in 2013, similar to 2012). In Peru, a new policy on HIV testing for all TB patients was introduced in 2013 alongside strengthened collaboration between the TB and HIV programmes and improvements to recording and reporting; here, the percentage of TB patients with documented HIV status increased from 18% in 2012 to 66% in 2013. Other notable increases between 2012 and 2013 occurred in Haiti (81% to 86%) and Mexico (71% to 74%).

In the European Region the percentage of TB patients

¹ WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders. Geneva, World Health Organization, 2012 (WHO/HTM/TB/2012.1). Available at http://whqlibdoc.who.int/publications/2012/9789241503006_eng.pdf

TABLE 7.1

HIV testing for TB patients, treatment for HIV-positive TB patients and prevention of TB among people living with HIV, 41 high TB/HIV burden countries and WHO regions, 2013. Numbers in thousands except where indicated.

	ESTIMATED HIV-POSITIVE INCIDENT TB CASES ^a		NUMBER OF NOTIFIED TB PATIENTS WITH KNOWN HIV STATUS	% OF NOTIFIED TB PATIENTS WITH KNOWN HIV STATUS	% OF TB PATIENTS WITH AN HIV TEST RESULT WHO WERE HIV-POSITIVE	% OF NOTIFIED HIV-POSITIVE TB PATIENTS STARTED ON CPT	% OF NOTIFIED HIV-POSITIVE TB PATIENTS STARTED ON ART	NUMBER OF HIV-POSITIVE TB PATIENTS ON ART AS % OF ESTIMATED HIV-POSITIVE INCIDENT TB CASES ^b	NUMBER OF HIV-POSITIVE PEOPLE PROVIDED WITH IPT
Angola	7.5	6.7–8.3	24	40	11	100	—	—	
Botswana	5.0	4.8–5.5	6.3	91	61	92	72	55	
Brazil	13	13–13	54	65	17	—	—	—	
Burkina Faso	1.1	1.0–1.3	5.3	96	13	98	98	60	
Burundi	1.9	1.8–2.1	6.6	87	15	95	64	33	
Cambodia	2.3	2.1–2.6	32	82	3.9	89	89	48	1.3
Cameroon	19	18–23	21	41	38	91	64	28	
Central African Republic	6.9	4.0–7.9	4	45	40	—	—	—	
Chad	4.6	2.9–6.6	4.6	40	23	—	—	—	
China	4.5	4.3–9.9	329	39	1.4	—	67	69	
Congo	5.3	3.4–8.2	3.2	30	41	9	100	25	
Côte d'Ivoire	8.0	7.3–8.9	23	89	24	77	55	38	
Djibouti	0.39	0.33–0.44	1.6	51	7.5	78	30	9.2	
DR Congo	16	9.8–75	50	44	14	70	48	21	
Ethiopia	22	19–32	93	71	11	—	68	32	15
Ghana	3.6	3.4–4.0	11	73	21	74	42	28	
Haiti	4.4	4.0–5.1	15	86	20	73	57	38	19
India	120	100–140	888	63	5.0	95	88	32	
Indonesia	15	8.7–20	7.6	2.3	21	30	21	2.2	
Kenya	48	47–50	84	94	38	99	84	55	
Lesotho	15	10–20	9.8	91	74	98	70	34	
Malawi	15	9.5–20	18	92	56	90	88	59	100
Mali	0.63	0.61–0.65	6	97	6.9	100	100	66	
Mozambique	81	64–100	51	91	56	97	72	25	48
Myanmar	17	16–18	17	12	32	89	74	23	0.5
Namibia	7.7	5.4–9.9	9.7	92	45	99	80	45	16
Nigeria	140	81–220	88	88	22	87	67	9.2	8
Russian Federation	7.9	6.9–9.1	70 ^c	—	—	—	—	—	
Rwanda	2.5	2.2–2.9	5.9	98	25	96	79	46	
Sierra Leone	2.2	1.7–2.8	11	91	13	51	64	41	0.7
South Africa	270	240–310	295	90	62	81	66	45	340
Sudan	2.6	2.2–2.9	5.4	27	6.1	—	39	4.9	
Swaziland	13	11–14	6.4	91	74	99	80	29	0.4
Thailand	12	10–13	55	83	15	63	59	41	
Togo	1.1	0.96–1.2	2.6	97	20	89	72	34	
Uganda	32	29–38	43	91	48	96	65	42	
Ukraine	7.2	7.1–7.2	42	88	20	49	48	55	16
UR Tanzania	30	29–31	55	83	37	98	73	50	0.2
Viet Nam	9.4	8.0–12	71	70	6.2	72	61	29	
Zambia	37	35–40	41	90	62	93	67	46	
Zimbabwe	56	48–66	32	92	69	77	77	31	11
High TB/HIV burden countries	1 100	990–1 200	2 600	57	20	86	70	32	576
AFR	870	790–960	1 068	76	41	87	69	34	539
AMR	32	31–33	160	69	14	51	65	21	24
EMR	5.1	4.0–6.4	51	11	2.4	57	38	7.1	0.3
EUR	21	20–22	206	59	8.0	56	54	29	19
SEAR	170	150–190	981	43	6.1	88	81	28	1.1
WPR	23	19–26	480	35	2.7	58	60	34	2.6
Global	1 100	1 000–1 200	2 946	48	18	85	70	33	586

Blank cells indicate data not reported.

— indicates values that cannot be calculated.

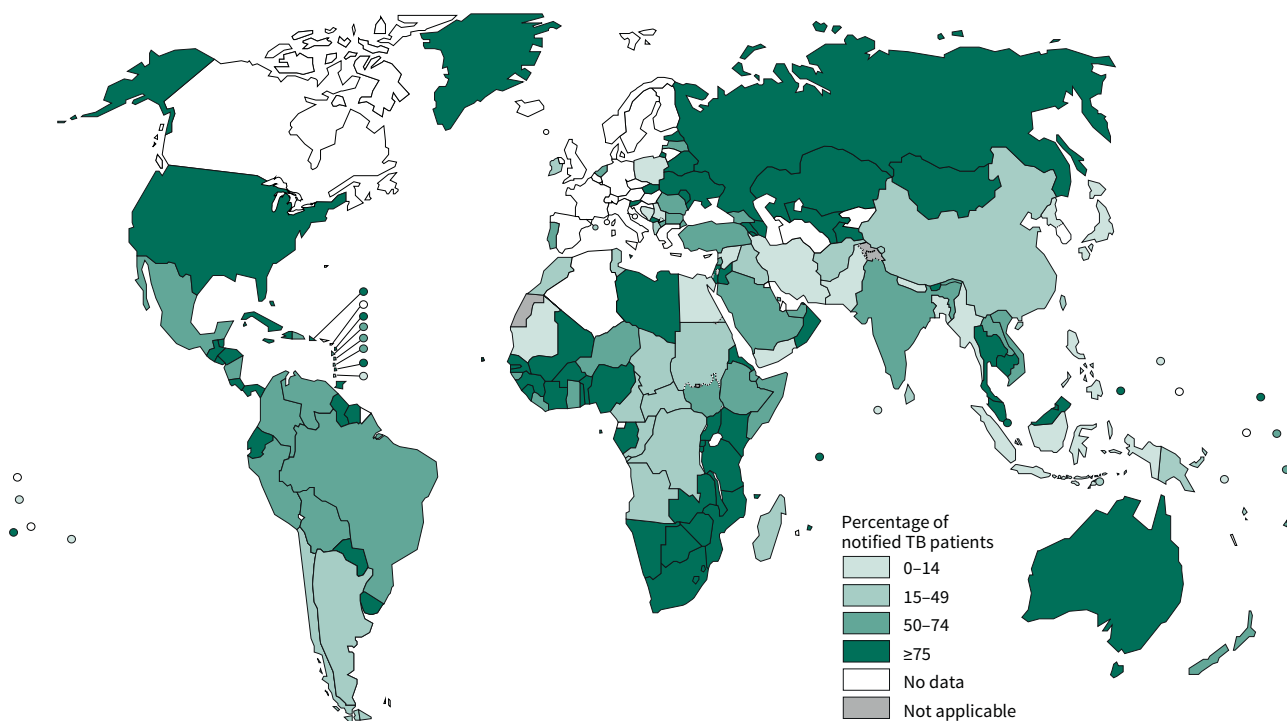
^a Best estimates are followed by the lower and upper bounds of the 95% uncertainty interval.

^b The numerator (i.e. all notified HIV-positive TB cases on ART) includes all notified new, relapse and non-relapse retreatment cases. The denominator (i.e. estimated HIV-positive incident TB cases) includes new and relapse cases only.

^c Data for the Russian Federation are for new TB patients in the civilian sector only.

FIGURE 7.2

Percentage of notified TB patients with known HIV status by country, 2013^a



^a Data for the Russian Federation are for new TB patients in the civilian sector only.

who had a documented HIV test result was 59% in 2013, similar to levels of coverage achieved in 2012. In the Russian Federation, which accounts for more than half of the regional TB/HIV burden, there was a small decrease (49% in 2013 compared with 51% in 2012). As in previous years, however, HIV testing is likely to have been done for a much higher percentage of TB patients than both of these figures suggest. This is because the national data on TB patients with known HIV status reported to WHO are for new TB cases in the civilian sector only (i.e. excluding cases from the prisons and retreatment cases), while the denominator reported to WHO and available for use in calculations of coverage is all notified TB cases. Other sources of data indicate that more than 90% of new TB patients in the civilian sector had a documented HIV test result. Ukraine, which has the second largest TB/HIV burden in the European region, reported that the HIV status of 88% of TB patients was known, up from 75% in 2012.

In the other three WHO regions in which concentrated HIV epidemics are the norm, the percentage of TB patients with known HIV status has remained consistently low. The Eastern Mediterranean Region had the lowest coverage of HIV testing in 2013 (11%), representing a decline from 13% in 2012. In the South-East Asia region, there was a modest improvement from 39% in 2012 to 43% in 2013, mostly explained by an increase from 56% to 63% in India. This improvement in India was facilitated by the

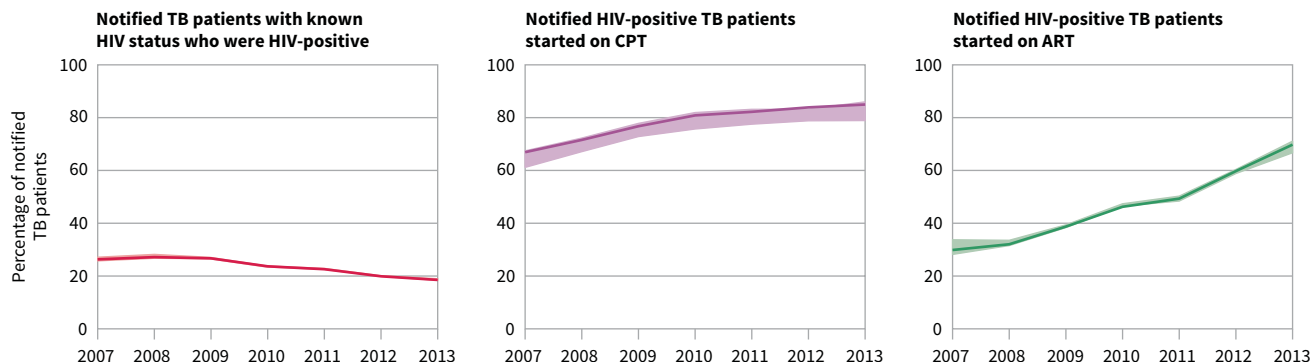
decentralization and integration of HIV testing services into both general health care and TB-specific services. In the Western Pacific Region, 35% of TB patients knew their HIV status overall in 2013, a small increase from 32% in 2012. This increase was mainly due to China, where national coverage increased from 34% to 39% between 2012 and 2013. Although data for 2013 were not available when this report went to press, coverage in the high TB/HIV burden counties of China was much higher, at 88%, in 2012. In Cambodia, another priority TB/HIV country with a concentrated HIV epidemic in the Western Pacific Region, 82% TB patients knew their HIV status in 2013, similar to the level achieved since 2011.

7.2 Levels of HIV infection among TB patients with HIV test results

The highest rates of HIV co-infection were reported for TB patients in the African Region (Table 7.1), where 41% of those with an HIV test result were positive (compared with 43% in 2012). The percentage of TB patients found to be HIV-positive in the 28 African countries in the list of 41 priority countries ranged from <12% in Angola, Ethiopia and Mali to 74% in Lesotho and Swaziland. In the Region of the Americas, the percentage of TB patients with a documented HIV test result who were HIV-positive was 14%. In the European and South-East Asia regions, the percentage of TB patients with an HIV positive test result averaged 8% and 6% respectively. In the Eastern

FIGURE 7.3

Percentage of notified TB patients with known HIV status who were HIV positive, and percentage of notified HIV-positive TB patients enrolled on cotrimoxazole preventive therapy (CPT) and antiretroviral therapy (ART), 2007–2013^a



^a The solid lines show values for countries that reported data. The shaded areas show upper and lower limits when countries that did not report data are considered.

Mediterranean and Western Pacific Regions, less than 3% of TB patients with a documented HIV test result were HIV-positive. The global average across all regions was 18%, and 20% among the 41 high TB/HIV burden countries that accounted for more than 95% of estimated HIV-positive incident TB cases in 2013. Overall, the percentage of TB patients testing HIV-positive has been falling globally (Figure 7.3).

Globally, the number of HIV-positive TB patients reported by NTPs (545 000) in 2013 represented about 50% of the 1.1 million HIV-positive people estimated to have developed TB in the same year (Figure 7.4). There was considerable variation among regions (data not shown): the reported proportion was highest in the European Region (80%), and relatively high in the Region of the Americas (67%) and the Western Pacific Region (57%); the African Region (50%) was the same as the global average; and the proportion was lowest in the South-East Asia Region (35%) and the Eastern Mediterranean Region (24%).

7.3 Antiretroviral therapy and co-trimoxazole preventive therapy for HIV-positive TB patients

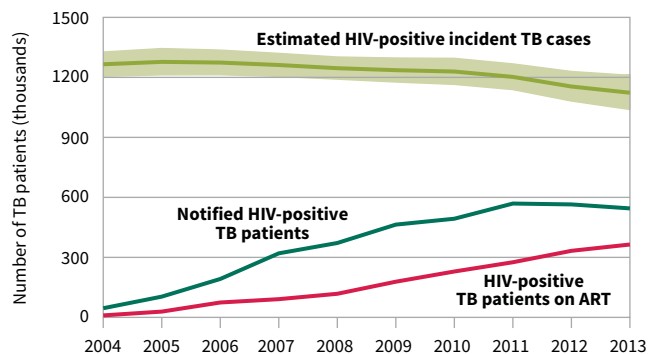
ART is the intervention that can have the biggest impact on TB morbidity and mortality among HIV-positive TB patients. The number of notified HIV-positive TB patients on ART has grown from a very low level in 2004 (Figure 7.4) to reach 364 000 in 2013. Among HIV-positive TB patients notified by NTPs in 2013,¹ 70% were on ART globally (Table 7.1, Figure 7.3). This is a considerable improvement from 60% in 2012.

In the African Region, 69% of HIV-positive TB patients

¹ In the annual WHO TB data collection form, countries are asked to report the number of TB patients notified in the most recent calendar year who were living with HIV and who “started or continued on ART”.

FIGURE 7.4

ART enrolment among HIV-positive TB patients compared with the reported number of HIV-positive TB patients and the estimated number of HIV-positive people who developed TB,^a 2004–2013



^a Notified HIV-positive TB patients on ART includes new and relapse TB cases plus prevalent TB cases re-registered for treatment change (e.g. after treatment failure). Estimated HIV-positive incident TB cases includes only new and relapse TB cases.

reported by NTPs in 2013 were started on ART (up from 59% in 2012). Among the top 10 highest TB/HIV burden countries, there were five in which coverage improved by more than 30% in relative terms between 2012 and 2013: India, Mozambique, South Africa, Uganda and the United Republic of Tanzania. These five countries accounted for more than 50% of the global burden of HIV-associated TB in 2013. In India, a combination of decentralized ART services and improved recording and reporting facilitated a particularly large relative increase of 50%, from 59% in 2012 to 88% in 2013. Among other priority TB/HIV countries, however, less than 50% of the HIV-positive TB patients reported by NTPs were enrolled on ART in 2013 (Table 7.1).

Despite overall progress in ART coverage, there remains

a substantial gap between the number of HIV-positive TB patients started on ART and the estimated total number of HIV-positive people with TB in need of both TB treatment and ART. For example, the global number of HIV-positive TB patients started on ART in 2013 is equivalent to only 32% of the estimated 1.1 million HIV-positive people who developed TB in 2013 (Table 7.1, Figure 7.4). The ratio of HIV-positive TB patients on ART to the estimated number of HIV-positive people who developed TB in 2013 was above 50% in only 8 of the 41 high TB/HIV burden countries: Botswana, Burkina Faso, China, Kenya, Malawi, Mali, Ukraine and the United Republic of Tanzania (Figure 7.5). Detection of TB among HIV-positive people, coverage of HIV testing among TB patients, and enrolment of HIV-positive TB patients on ART all need to be improved.

Globally, 431 000 HIV-positive TB patients were enrolled on CPT in 2013, representing 85% of all notified HIV-positive TB patients, slightly higher than levels achieved in 2011 and 2012 (Table 7.1, Figure 7.3). The African and South-East Asia Regions maintained their particularly high levels of enrolment on CPT from 2012, at 87% and 88% respectively (Table 7.1). Of the 35 high TB/HIV burden countries (out of a total of 41) that reported data, only three reported that less than 50% of HIV-positive TB patients were enrolled on CPT in 2013: Congo (9%), Indonesia (30%) and Ukraine (49%).

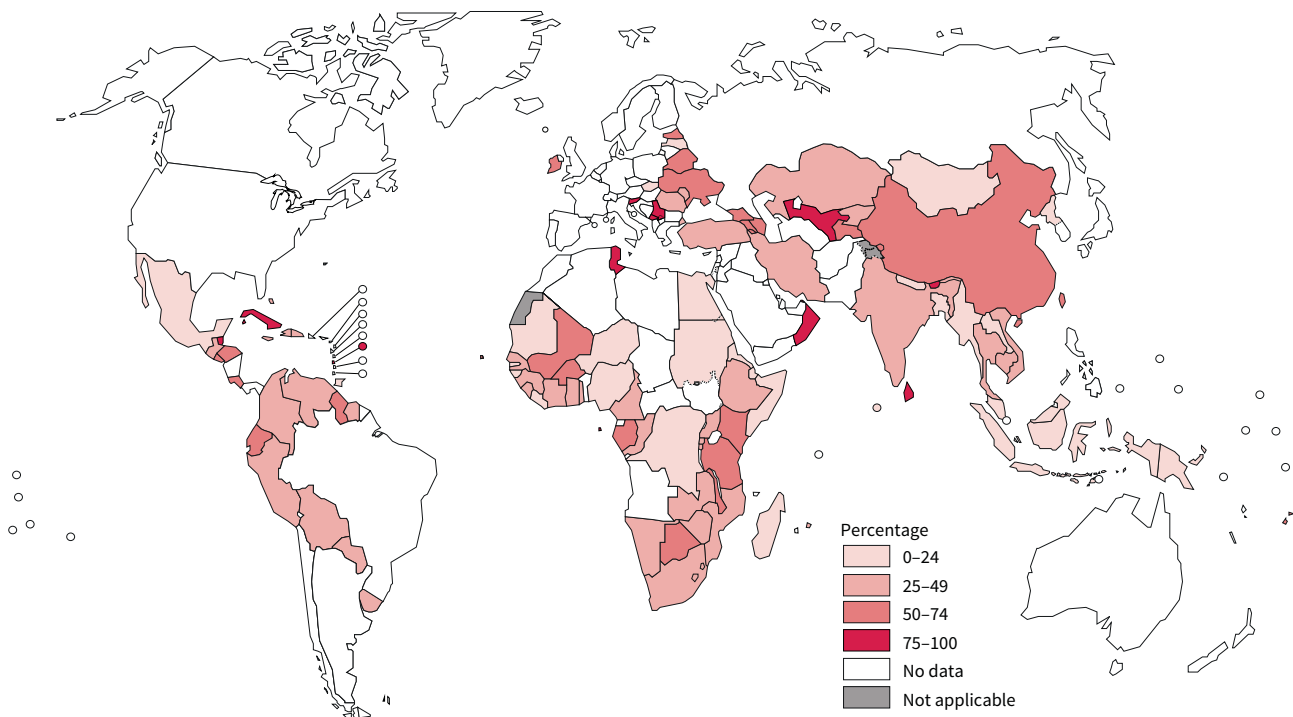
7.4 Intensified TB case-finding and initiation of isoniazid preventive therapy and ART among people living with HIV

Systematic screening for TB among people living with HIV is recommended by WHO as an essential component of the HIV package of care, along with ART, IPT and infection control. It is the first essential step before both IPT initiation and TB diagnosis. In 2013, 64 countries reported a total of 5.5 million people enrolled in HIV care who were screened for TB, up from 4.1 million in 62 countries in 2012. Data on TB screening is patchy and, while countries may be routinely screening people in HIV care for TB, capturing the data to demonstrate this remains challenging. As part of efforts to increase emphasis on global impact monitoring and data quality, new WHO guidelines on monitoring and evaluation of collaborative TB/HIV activities are due to be issued in 2014 (Box 7.1). These recommend that TB screening continues to be reported as a core national indicator, but that data are no longer collected and reported at the global level.

In 2013, WHO strengthened its recommendation that Xpert MTB/RIF should be used rather than conventional microscopy, culture and DST as the initial diagnostic test for adults and children suspected of having HIV-associated TB. However, discussions in global meetings indicate that a major motivation for the roll-out of Xpert MTB/

FIGURE 7.5

Number of HIV-positive TB patients on ART as a percentage of estimated HIV-positive incident TB cases, 2013^a



^a The numerator (i.e. all notified HIV-positive TB cases on ART) includes all notified new, relapse and non-relapse retreatment cases. The denominator (i.e. estimated HIV-positive incident TB cases) includes new and relapse cases only.

BOX 7.1

Improving data quality and updated WHO guidance on global and country monitoring of collaborative TB/HIV activities

Each year during the development of global reports on TB and HIV produced by WHO and UNAIDS, data provided by NTPs and national HIV programmes are analysed for their consistency and coherence. Queries about any discrepancies are sent to countries as part of an overall process of data validation and follow-up. Among the most frequent discrepancies between reports from HIV and TB programmes are reported numbers of HIV-positive TB patients started on ART. Internal inconsistencies in the data reported by national HIV programmes include different figures for the number of people newly enrolled in HIV care in different parts of the online reporting system used by UNAIDS, and inconsistencies in the number of people reported to be newly enrolled in care and those reported to be ever enrolled in HIV care (numbers are often the same, which is implausible). The number of people newly enrolled in care is the denominator required for calculation of IPT coverage, so these data inconsistencies create major problems for monitoring of IPT coverage. Persistent inconsistencies in data suggest weaknesses not only in reporting and recording systems, but also in the level of communication and collaboration between programmes and associated services at all or some levels.

Of the 96 countries for which data on ART initiation were reported by both the NTP and national HIV programme in 2013, there were three countries that reported discrepant data that could not be reconciled even after follow-up: Indonesia, South Sudan and Uganda (the differences in numbers were 4 270, 8 994 and 4 527, respectively). Use of common unique identifiers, regular coordination meetings at all levels and joint monitoring and supervision visits should help to reduce these differences as well as resulting gaps in service provision.

In 2013, 53 countries reported data on the total number of people (including 0) who were newly enrolled in HIV care and initiated on IPT, and 59 countries reported the total number of people who were newly enrolled in HIV care and had TB. In the UNAIDS Global AIDS response progress reporting (GARPR) tool, the number of people newly enrolled in HIV care (requested in two parts of the online system) was not consistently reported and ten countries reported very different figures. A total of 24 (45%) countries had discrepancies that meant it was not possible to reliably calculate levels of IPT coverage.

Renewed efforts are required to improve data quality. The updated WHO *Guide to monitoring and evaluation for collaborative TB/HIV activities* and the *Consolidated strategic information guide for the health sector* (both to be issued in 2014) have taken these well-known challenges into consideration, and prompt implementation of these guidelines by countries should help to reduce issues with data quality experienced to date. Important updates include a reduction in the number of core indicators required for global and national reporting; new optional indicators for use at national and local level that focus on the quality of collaborative TB/HIV activities; and a recommendation to use the estimated number of incident TB cases (new and relapse) as the denominator for calculating coverage levels for HIV testing and other related indicators. To enhance infection control interventions, an indicator to monitor TB among health care workers will be added. The number of HIV-positive people screened for TB will no longer be an indicator used for monitoring at the global level, but remains a recommended indicator at the national level.

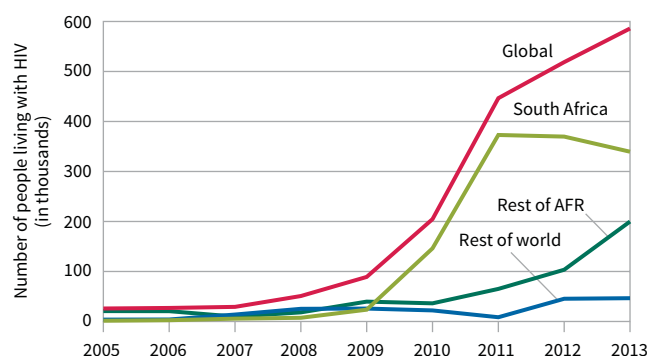
RIF has often been the national response to multidrug-resistant TB (MDR-TB).¹ To maximize the detection of TB cases among HIV-positive people, Xpert MTB/RIF needs to be widely implemented in settings where HIV care is provided, using all available funding sources. Early detection of TB in HIV care settings can in turn expedite timely initiation of ART.

In 2013, 59 countries reported data about the number of notified TB cases among those newly enrolled in HIV care. For 14 of these countries, there were problems with the data reported for the numbers enrolled in HIV care (for example, numbers newly enrolled in care exceeded the number ever enrolled in care). Among the 43 countries with more reliable data, 19 674/185 133 (11%) of those newly enrolled in HIV care were reported to have been notified with TB in the same year.

Among the 45 countries that reported any initiation of IPT (representing approximately 60% of the estimat-

FIGURE 7.6

Provision of isoniazid preventive therapy (IPT) to people living with HIV, 2005–2013



ed global burden of HIV-associated TB), almost 600 000 HIV-positive people were reported to have received preventive therapy in 2013. This was an increase from just over 500 000 people in 2012 (Figure 7.6). As in previous years, South Africa continued to account for the highest proportion (58%) of the global total in 2013; a total of 340 000 HIV-positive people were reported to have

¹ Meeting Report of the Xpert MTB/RIF Implementers Global Forum, 1–2 May 2014. Geneva, World Health Organization, 2014. Available at: <http://www.stoptb.org/wg/gli/assets/documents/Xpert%20Implementers%20Global%20Forum%20meeting%20report.pdf>.

been started on IPT in 2013. There is also evidence of IPT scale-up over the past four years in other countries in the African Region. Countries achieving higher levels in 2013 included Malawi (100 000), Mozambique (48 000), Namibia (16 000), Ethiopia (15 000) and Zimbabwe (11 000). Haiti (19 000) and Ukraine (16 000) also achieved higher levels of IPT coverage in 2013. However, as with TB screening, countries continue to find it challenging to implement IPT and capture the related data. Currently 79% of countries worldwide are not reporting the initiation of IPT as part of HIV care, including 28 high TB/HIV burden countries.

ART is a powerful intervention for TB prevention and reduces the individual risk of TB disease among people living with HIV by 65%,¹ irrespective of CD4 cell count. The impact is further enhanced by combined provision of ART and IPT. Since 2013, WHO has recommended initiation of ART among people living with HIV who have a CD4 count of ≤ 500 cells/mm³ (a higher threshold than previously recommended). There has been impressive uptake by countries, with close to half of the WHO HIV focus countries adopting the new recommendation by June 2014.² However, to avert preventable TB morbidity and mortality among people living with HIV, further scale-up of the policy is needed, including through the expansion of HIV testing and counselling and through task shifting and decentralization of ART services. Globally, nearly 13 million people were receiving ART in 2013, equivalent to 37% of the estimated number of people living with HIV.³

7.5 Joint TB and HIV programming

Addressing the co-epidemics of TB and HIV through the implementation and scale-up of collaborative TB/HIV activities requires intense coordination, collaboration and regular communication between TB and HIV programmes and other stakeholders. It is important to overcome programmatic constraints and promote synergies and efficiency gains, especially between TB and HIV programmes. Joint TB and HIV programming allows for a broader approach that not only covers the full scope of TB and HIV interventions but also provides timely opportunities for alignment of plans, optimization of support systems and the integration of services where this is appropriate. Harmonizing monitoring and evaluation systems is important (**Box 7.1**), and efforts are being made to provide clearer guidance on use of standard indicators across TB and HIV programmes. Data on people newly initiated on ART are increasingly consistent across countries. Despite progress, separate programmes in many countries still have difficulties in synchronizing and integrating their monitoring and measurement efforts.

The recent decision of the Board of the Global Fund to require the 41 TB/HIV priority countries to submit a single proposal (concept note) provides an opportunity to promote joint TB and HIV programming and the delivery of integrated and more patient-centred TB and HIV services. Early experience of the process of concept note development has showed that allocating enough time for gap analysis and harmonization of national strategic plans, as well as joint country dialogue with adequate and equal representation of TB and HIV stakeholders at all levels, are key ingredients for success. The identification of components of the health system critical for joint programming as well as intense communication and harmonization among technical assistance providers are also essential.

¹ Suther AB et al. Antiretroviral therapy for prevention of tuberculosis in adults with HIV: a systematic review and meta-analysis. *PLoS Med* 2012, 9(7): e1001270. doi:10.1371/journal.pmed.1001270).

² *Executive Summary of the Global Update on the Health Sector Response to HIV, 2014*, Geneva, World Health Organization. Available at: http://apps.who.int/iris/bitstream/10665/128196/1/WHO_HIV_2014.15_eng.pdf

³ *The Gap Report*. UNAIDS, Geneva, 2014 Available at: http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2014/UNAIDS_Gap_report_en.pdf

Financing

KEY FACTS AND MESSAGES

The funding required for a full response to the global TB epidemic in low- and middle-income countries is estimated at about US\$ 8 billion per year in 2014 and 2015 (excluding research and development for new TB diagnostics, drugs and vaccines).

Of the US\$ 8 billion required each year, about two thirds is for the detection and treatment of drug-susceptible TB; 20% for treatment of MDR-TB; 10% for rapid diagnostic tests and associated laboratory strengthening; and 5% for collaborative TB/HIV activities. Recent projections indicate that in 2015, about US\$ 6 billion could be mobilized from domestic sources and that US\$ 2 billion will be needed from international donors.

Based on reports to WHO from 122 countries that account for 95% of reported TB cases, funding for TB prevention, diagnosis and treatment reached US\$ 6.3 billion in 2014, almost double the level of 2006. Compared with the latest global estimates of resource requirements for a full response to the TB epidemic, this leaves a gap of around US\$ 2 billion per year. Countries themselves reported funding gaps amounting to US\$ 0.9 billion in 2014.

Of the US\$ 6.3 billion available in 2014, most (US\$ 3.8 billion) is for diagnosis and treatment of drug-susceptible TB. Funding for MDR-TB is growing, especially since 2009, reaching US\$ 1.8 billion in 2014. Countries reported funding gaps amounting to US\$ 0.77 billion for drug-susceptible TB and US\$ 0.15 billion for MDR-TB in 2014.

Overall, about 89% (US\$ 5.5 billion) of the reported funding of US\$ 6.3 billion in 2014 is from domestic sources. International donor funding has increased since 2006, reaching about US\$ 0.7 billion in 2014. However, the global average for the share of funding provided from domestic sources conceals enormous variation among individual countries as well as country groups.

Domestic funding dominates in three (not mutually exclusive) groups: Brazil, the Russian Federation, India, China and South Africa (BRICS); upper middle-income countries; and regions outside Africa and Asia. International donor funding dominates in the group of 17 HBCs outside BRICS and in low-income countries. At the individual country level, international donor funding remains absolutely critical in most of the 22 HBCs. Only Brazil, China, India, Kenya, the Russian Federation, South Africa and Thailand report levels of domestic funding that exceed contributions from international donor funding. In several countries, more than 90% of available funding in 2014 is from international donor sources.

The cost per patient treated for drug-susceptible TB in 2013 fell into the range of US\$ 100–US\$ 500 in most countries with a high burden of TB. The cost per patient treated for MDR-TB was most often in the range US\$ 5000–10 000, but the average varied from US\$ 9 235 in low-income countries to US\$ 48 553 in upper middle-income countries.

Progress in TB prevention, diagnosis and treatment requires adequate funding sustained over many years. WHO began annual monitoring of funding for TB in 2002, with findings published in global TB reports and peer-reviewed publications.¹ Particular attention has always been given to the 22 high-burden countries (HBCs) that account for about 80% of estimated incident cases (**Chapter 2**) and about 80% of TB cases reported by national TB programmes (NTPs) to WHO (**Chapter 4**).

This chapter covers four main topics. It starts with a summary of the most up-to-date estimates of financial resources required for a full response to the TB epidemic in 2014 and 2015. This is followed by presentation and discussion of trends in funding for TB prevention, diagnosis and treatment by category of expenditure and source of funding for the period 2006 (when the *Stop TB Strategy* and *Global Plan to Stop TB 2006–2015* were both launched),^{2,3} to 2014, for 122 countries (accounting for 95% of reported TB cases in 2013) for which data were available. The third part of the chapter analyses funding gaps reported by NTPs to WHO, with breakdowns by category of expenditure and country group. The final part of the chapter contains a new analysis of the unit costs of treatment for drug-susceptible and multidrug resistant TB (MDR-TB). Further country-specific data can be found in finance profiles that are available online.⁴

8.1 Estimates of funding required in 2014 and 2015 for a full response to the global TB epidemic

An updated version of the *Global Plan to Stop TB 2006–2015*, covering the last five years of the plan, was issued in 2010.⁵ This set out the actions and

¹ The most recent publication is: Floyd K, Fitzpatrick C, Pantoja A and Raviglione M. Domestic and donor financing for tuberculosis care and control in low-income and middle-income countries: an analysis of trends, 2002–11, and requirements to meet 2015 targets. *The Lancet Global Health*, 2013; 1: e105–15.

² Raviglione M, Uplekar M. WHO's new Stop TB strategy. *Lancet* 2006; 367: 952–5.

³ *The Global Plan to Stop TB, 2006–2015*. Geneva, World Health Organization, 2006 (WHO/HTM/STB/2006.35).

⁴ www.who.int/tb/data

⁵ *The Global Plan to Stop TB, 2011–2015*. Geneva, World Health Organization, 2010 (WHO/HTM/STB/2010.2).

estimated funding requirements for a full response to the TB epidemic for the five-year period 2011–2015, based on the *Stop TB Strategy*, with the overall goal of achieving the 2015 global targets for reductions in cases of and deaths from TB i.e. that incidence should be falling and that prevalence and mortality rates should be halved compared with their levels in 1990 (Chapter 1). Key components of the plan included increasing the number of patients detected and treated according to WHO’s recommended strategy from 5.8 million in 2011 to 6.9 million by 2015 (which would be equivalent to more than 80% of projected incident cases in that year); ensuring that all previously treated patients and all new patients with known risk factors for MDR-TB are tested for drug resistance by 2015 (including with recently endorsed rapid tests such as Xpert MTB/RIF that are discussed in Chapter 6); enrolment of all reported TB patients with MDR-TB (projected to number around 300 000 in 2015) on second-line treatment; HIV testing of all patients with TB; and prompt initiation of ART in all HIV-positive TB patients.

From January to March 2013, the Global Plan datasets were used in combination with new country-specific planning and budgeting work with nine high TB or high MDR-TB burden countries to produce updated estimates of funding needs for TB prevention, diagnosis and treatment in low- and middle-income countries.¹ The nine countries were Ethiopia, India, Indonesia, Kazakhstan, Kenya, Nigeria, Pakistan, South Africa and Ukraine. Analyses were conducted in the context of estimates of funding needs and funding gaps required for the Global Fund’s replenishment efforts in 2013.² WHO subsequently extended these analyses to cover all low- and middle-income countries and not only the countries eligible to apply to the fund.³ Notable countries (in terms of TB burden and funding requirements) that are not eligible to apply to the Global Fund include Brazil, China and the Russian Federation.

During the course of the work done for the first replenishment meeting held in April 2013, it should be highlighted that the Global Fund, WHO, UNAIDS, and other partners agreed that funding needs for ART for HIV-positive TB patients should be included in estimates of HIV resource needs to avoid double-counting. For this reason, the estimates of resource requirements for TB/HIV interventions included in the updated estimates of

resource needs for TB are lower than those contained in the Global Plan.

The total funding required in all low- and middle-income countries was estimated at about US\$ 8 billion in 2014 and 2015. Of this total, about two-thirds was for the detection and treatment of drug-susceptible TB; 20% for treatment of MDR-TB; 10% for rapid diagnostic tests and associated laboratory strengthening; and 5% for collaborative TB/HIV activities (excluding ART). It was also estimated that of the total required in 2015, about US\$ 6 billion could be mobilized from domestic sources and around US\$ 2 billion would be needed from international donor sources. The capacities of Brazil, the Russian Federation, India, China and South Africa (BRICS, which collectively account for almost 50% of reported TB cases worldwide) to mobilize most of their funding needs from domestic sources, in contrast with other country groups including the 17 other HBCs and low-income countries (mostly in Africa) where large amounts of international funding would be needed, were highlighted.

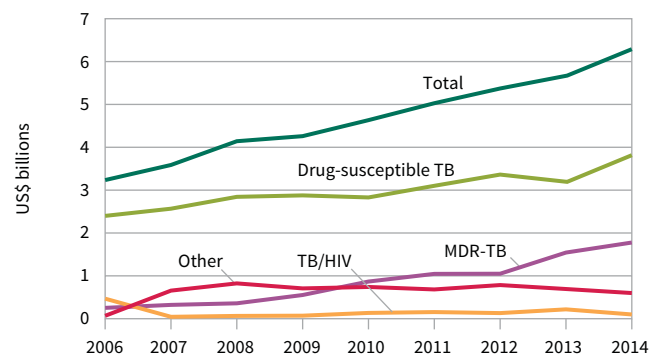
8.2 TB funding, overall and by category of expenditure and source of funding, 2006–2014

Data reported by NTPs to WHO since 2006 allowed analysis of funding trends 2006–2014 in 122 countries (Table 8.1). These countries accounted for 95% of the global number of TB cases reported in 2013, and included 119 low and middle-income countries plus three high TB and/or MDR-TB burden countries that have reached high-income status (Estonia, Latvia and the Russian Federation). The methods used to collect, review and analyse financial data are summarized in Box 8.1.

In these 122 countries, funding for TB care and control reached US\$ 6.3 billion in 2014, almost double the US\$ 3.3 billion that was available in 2006 (Figure 8.1). Most of this funding was for the diagnosis and treatment of drug-susceptible TB but there has been a marked increase in funding for MDR-TB, especially since 2009

FIGURE 8.1

Funding for TB prevention, diagnosis and treatment by intervention area, 2006–2014 (constant 2014 US\$ billions)



¹ Funding required for research and development for new TB diagnostics, drugs and vaccines was not considered. In the Global Plan, it is estimated that about US\$ 2 billion per year is needed for research and development.

² *The Global Fund to Fight AIDS, Tuberculosis and Malaria fourth replenishment (2014–2016): needs assessment*. Geneva, Global Fund to Fight AIDS, Tuberculosis and Malaria, 2013.

³ Floyd K, Fitzpatrick C, Pantoja A and Ravigliione M. Domestic and donor financing for tuberculosis care and control in low-income and middle-income countries: an analysis of trends, 2002–11, and requirements to meet 2015 targets. *The Lancet Global Health*, 2013; 1: e105–15.

TABLE 8.1

122 countries included in analyses of TB financing, by income group and WHO region, 2014^{a,b}

	LOW-INCOME (21% OF NOTIFIED CASES GLOBALLY IN 2013)	LOWER-MIDDLE-INCOME (48% OF NOTIFIED CASES GLOBALLY IN 2013)	UPPER-MIDDLE-INCOME (26% OF NOTIFIED CASES GLOBALLY IN 2013)	BRICS (46% OF NOTIFIED CASES GLOBALLY IN 2013)	17 HIGH-BURDEN COUNTRIES EXCLUDING BRICS (34% OF NOTIFIED CASES GLOBALLY IN 2013)	14 HIGH MDR-TB BURDEN COUNTRIES (NOT IN THE LIST OF 22 HIGH-BURDEN COUNTRIES) (2% OF NOTIFIED CASES GLOBALLY IN 2013)
African	Benin, Burkina Faso, Burundi, Central African Republic, Chad, DR Congo, Eritrea, Ethiopia, Gambia, Guinea , Guinea-Bissau, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, Rwanda, Sierra Leone, Togo, Uganda, UR Tanzania, Zimbabwe	Cabo Verde, Cameroon, Congo, Côte d'Ivoire, Ghana, Lesotho, Mauritania, Nigeria, Sao Tomé and Príncipe, Senegal, Swaziland, Zambia	Angola , Botswana, Gabon, Namibia, South Africa	South Africa	DR Congo, Ethiopia, Kenya, Mozambique, Nigeria, Uganda, UR Tanzania, Zimbabwe	
Americas	Haiti	Bolivia, El Salvador, Guatemala, Guyana, Honduras, Nicaragua, Paraguay	Argentina, Brazil, Colombia, Dominican Republic, Ecuador, Jamaica, Mexico , Panama, Suriname, Venezuela (Bolivarian Republic of)	Brazil		
Eastern Mediterranean	Afghanistan, Somalia, South Sudan	Djibouti, Egypt, Morocco, Pakistan, Sudan, Syria, West Bank and Gaza Strip , Yemen	Iran (Islamic Republic of), Iraq , Jordan, Lebanon, Tunisia		Afghanistan, Pakistan	
European	Tajikistan	Armenia, Georgia, Kyrgyzstan , Republic of Moldova, Ukraine , Uzbekistan	Belarus , ^c Bosnia and Herzegovina , Bulgaria, Kazakhstan , Montenegro, Romania, Serbia, The Former Yugoslav Republic of Macedonia , Turkey	Russian Federation		Armenia, Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Republic of Moldova, Tajikistan, Ukraine, Uzbekistan
South-East Asia	Bangladesh, Democratic People's Republic of Korea , Myanmar, Nepal	Bhutan, India, Indonesia, Sri Lanka, Timor-Leste	Maldives, Thailand	India	Bangladesh, Indonesia, Myanmar, Thailand	
Western Pacific	Cambodia	Kiribati, Lao People's Democratic Republic, Micronesia (Federal States of), Mongolia, Papua New Guinea, Philippines, Solomon Islands, Vanuatu, Viet Nam	China, Fiji, Malaysia, Marshall Islands , Palau , Tonga, Tuvalu	China	Cambodia, Philippines, Viet Nam	
Excluded due to insufficient data	Comoros	Samoa	Albania, Algeria, American Samoa, Azerbaijan, Belize, Costa Rica, Cuba, Dominica, Grenada, Libya, Palau, Peru, Saint Lucia, Saint Vincent and the Grenadines, Turkmenistan			Azerbaijan, Lithuania

^a Analyses focus primarily on low and middle-income countries. Three high-income countries (Estonia, Latvia and the Russian Federation) were included because they are in the list of 22 high-burden countries or the list of 27 high MDR-TB burden countries.

^b Countries included for the first time in trend analysis are shown in bold.

^c Belarus is not included in trend analyses as data were reported for the first time in 2013.

Methods use to compile, validate and analyze financial data reported to WHO

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

Each year, WHO requests all low and middle-income countries (and the Russian Federation, the only HBC that is a high-income country) to report the funding required for TB prevention, diagnosis and treatment in their current fiscal year, by category of expenditure and source of funding; and expenditures for the most recently completed fiscal year, also by category of expenditure and source of funding. In the 2014 round of global TB data collection, the fiscal years were 2014 and 2013, respectively. Categories of expenditure for diagnosis and treatment of drug-susceptible TB used since 2006 are: first-line drugs; NTP staff; programme management and supervision activities; laboratory supplies and equipment; advocacy, communication and social mobilization; community-based care; public-private mix approaches; the Practical Approach to Lung Health; and operational research including surveys. Categories of expenditure for MDR-TB used since 2006 are second-line drugs and programmatic management of MDR-TB. Budgets and expenditures for collaborative TB/HIV activities are requested as one consolidated category of expenditure. Funding available from all sources for these categories of expenditure is requested as well as a breakdown into four categories: domestic funding excluding loans; external loans, also considered domestic funding; the Global Fund; and grant financing from sources other than the Global Fund.

All high-income countries (except the Russian Federation) are requested to report funding requirements and expenditures in total, without any breakdown by category of expenditure or source of funding.

All countries are asked to report on the utilization of inpatient and outpatient care required for treatment of people with drug-susceptible and MDR-TB, on a per patient basis (i.e. the average number of days spent in hospital, and the average number of outpatient visits to a health facility). These are used in combination with other data to estimate the financial resources used for TB care and control that are not reflected in TB-specific reports of funding requirements, available funding and expenditures (further details are provided below).

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

- **Routine checks for plausibility and consistency, including validation checks that are built into the online reporting system.** Examples of validation checks are checks for implausibly large year-to-year changes (for example in total reported funding by source and by category of expenditure), or implausibly high or low values of funding for drugs relative to the number of TB patients (that differ substantially from prices quoted by the Global TB Drug Facility).

- **Discussions with country respondents to resolve queries.**

- **Triangulation with other data sources.** One example is the detailed budgets prepared by NTPs that are peer-reviewed by WHO as part of efforts to strengthen the budgeting of national strategic plans for TB care and control. Comprehensive and robust budgets for national strategic plans are now an essential requirement for funding applications to the Global Fund, as part of this agency's new funding model introduced in 2013. Two tools promoted by WHO (the WHO TB planning

and budgeting tool and OneHealth)^{c,d} for estimating funding requirements allow mapping of detailed budgets to the line items used in the WHO TB data collection form, and comparisons with data reported online. Triangulation is also undertaken with data available from the Global Fund,^e USAID,^f and the Organization for Economic Cooperation and Development's Creditor Reporting System.

In 2014, additional efforts to improve the quality of financial data reported to WHO included presentations and discussions with NTP staff during workshops on the development of national strategic plans, establishment of new links with in-country health economists providing support to NTPs and participation in a recently-established working group on financing for countries in the European Region (called the Wolfheze financing group). An extra question about the average cost of drugs per patient treated was also introduced to the data collection form in 2014, to allow reviewers to better assess the validity of budgets reported for first and second-line drugs and to identify whether these budgets include funding for buffer stocks.

In reviewing and validation data, particular attention has always been given to the 22 HBCs. A summary of data validation methods used for HBCs is provided in [Table B8.1](#).

TB funding reported by NTPs usually does not include the financial costs associated with the inpatient and outpatient care required during TB treatment (among HBCs, the notable exceptions are China and the Russian Federation, since treatment is provided in TB-specific clinics or hospitals for which earmarked budgets and funding exist). Since many detailed costing studies in a wide range of countries show that these costs account for a large share of the cost of treating someone with TB, analyses of TB financing undertaken by WHO have always included estimates of the funding used for both inpatient and outpatient care.

As in past reports, WHO estimates the funding used for inpatient and outpatient care of TB patients by multiplying the number of outpatient visits and days of inpatient care per patient (reported by NTPs each year) by the cost per bed-day and clinic visits available from the WHO-CHOICE database and then by the reported number of TB patients notified or projected to be notified. This is done separately for drug-susceptible TB and MDR-TB. Three exceptions were Sierra Leone, South Sudan and Cape Verde, for which data on the total number of TB beds were used in combination with the cost per bed day to estimate the funding used for inpatient care. This approach was used because data on the actual utilization of inpatient care – the average number of days of inpatient care per patient – were not reported. However, it is not ideal because WHO-CHOICE unit costs per bed day do not apply to the longer-term (and typically less resource-intensive) care that is provided on TB-specific wards or in TB hospitals. For a further three countries (Belarus, Burkina Faso and the Democratic Republic of the Congo), data from recent National Health Account (NHA) data were used. It is hoped that in the near future, such data from NHAs will be routinely available for many more countries, including a breakdown by source of funding (domestic vs international) that is currently not available for any country.

^a Floyd K, Pantoja A, Dye C. Financing tuberculosis monitoring system. *Bulletin of the World Health Organization*; 2007; 85:334–40

^b Floyd K, Fitzpatrick C., Pantoja A and Raviglione M. Domestic and donor funding for tuberculosis care and control in low-income and middle-income countries: an analysis of trends 2002–11, and requirements to meet 2015 targets. *The Lancet Global Health*; 1: e105–15

TABLE B8.1

Methods used to review and validate financing data reported by NTPs, high TB and MDR-TB burden countries

COUNTRY	ROUTINE REAL-TIME CHECKS FOR PLAUSIBILITY AND INTERNAL CONSISTENCY (TRENDS OVER TIME), REVIEW AND FOLLOW-UP CHECKS BY WHO FINANCE DATA REVIEWERS	REVIEW BY IN-COUNTRY WHO TB MEDICAL OFFICER	INVOLVEMENT WITH WHO STAFF IN NATIONAL TB STRATEGIC PLANNING AND BUDGETING WORKSHOPS AND ASSOCIATED ASSESSMENT OF SOURCES OF FUNDING USING WHO RECOMMENDED COSTING TOOLS ^{c-d}	RESULTS FROM INDEPENDENT ECONOMIC EVALUATION
22 HIGH TB BURDEN COUNTRIES				
Afghanistan	yes	yes	yes (2013)	no
Bangladesh	yes	yes	yes (2014)	yes
Brazil	yes	yes	no	no
Cambodia	yes	yes	yes (2009)	yes
China	yes	yes	no	yes
Democratic Republic of the Congo	yes	yes	yes (2014)	no
Ethiopia	yes	sometimes	yes (2014)	yes
India	yes	yes	yes (2013)	yes
Indonesia	yes	yes	yes (2013)	no
Kenya	yes	yes	yes (2013)	yes
Mozambique	yes	mostly	yes (2013)	no
Myanmar	yes	yes	yes (2011)	no
Nigeria	yes	yes	yes (2013)	yes
Pakistan	yes	yes	no (2013)	yes
Philippines	yes	yes	yes (2011)	yes
Russian Federation	yes	yes	no	yes
South Africa	yes	yes	yes (2013)	yes
United Republic of Tanzania	yes	yes	no	yes
Thailand	yes	yes	yes (2013)	no
Uganda	yes	yes	yes (2013)	yes
Viet Nam	yes	yes	no	no
Zimbabwe	yes	yes	yes (2013)	no

REMAINING HIGH MDR-TB BURDEN COUNTRIES

Armenia	yes	Wolfheze Working group on financing	yes (2010)	no
Azerbaijan ^a	no	no	no	no
Belarus	yes	Wolfheze Working group on financing	no	no
Bulgaria	yes	no	no	no
Georgia	yes	no	no	no
Kazakhstan	yes	no	yes (2013)	no
Kyrgyzstan	yes	yes	yes (2013)	no
Latvia	yes	no	no	no
Lithuania ^a	no	no	no	no
Republic of Moldova	yes	no	no	no
Tajikistan	yes	no	no	no
Ukraine	yes	no	yes (2013)	no
Uzbekistan	yes	no	yes (2011)	no

^a Data for Azerbaijan and Lithuania have never been reported to WHO.

^c *Planning and budgeting for TB control activities*. Geneva, World Health Organization, 2014 http://www.who.int/tb/dots/planning_budgeting_tool/en/

^d *Planning and budgeting for TB control activities as part of sector wide national strategic health plans and policies*. Geneva, Inter-Agency working group, 2014 <http://www.who.int/choice/onehealthtool/en/>

^e Global Fund Data and the Open Data Protocol <http://web-api.theglobalfund.org/odata/>, accessed May 2014

^f FY 2013 Congressional Budget Justification for Foreign Operations. Released March and April 2012, USAID <http://www.state.gov/f/releases/iab/fy2013cbj/pdf/>

^g Choosing interventions that are cost effective (WHO-CHOICE). Geneva, World Health, 2008 http://www.who.int/choice/cost-effectiveness/inputs/health_service/en/

^h National Health Accounts <http://www.who.int/health-accounts/en/>

TABLE 8.2

Reported NTP budget by intervention area and estimated cost of inpatient and outpatient care for drug-susceptible (DS-TB) and MDR-TB, 36 high TB or MDR burden countries, 2014 (current US\$ millions)

	NTP BUDGET				RESOURCES REQUIRED FOR INPATIENT AND OUTPATIENT CARE		ESTIMATED TOTAL RESOURCES REQUIRED FOR TB CARE
	TOTAL	DS-TB	MDR-TB	TB/HIV	DS-TB ^a	MDR-TB ^a	
22 HIGH-BURDEN COUNTRIES							
Afghanistan	9.5	8.6	0.9	<0.1	6.5	0.1	16
Bangladesh	57	45	11	0.4	4.8	0.5	62
Brazil	79	68	8.6	2.3	32	1.3	112
Cambodia	31	29	1.5	0.6	5.6	<0.1	36
China ^a	347	314	29	4.4			347
Democratic Republic of the Congo	66	61	2.1	3.0	5.1	<0.1	71
Ethiopia	94	84	9.8	0.5	8.3	0.2	102
India	252	167	85	0	167	52	471
Indonesia	127	115	9.6	3.0	24	2.7	154
Kenya	57	51	4.5	2.1	2.8	0.4	60
Mozambique	19	8.7	6.7	4.0	4.3	0.1	24
Myanmar	36	24	7.5	4.2	2.3	0.1	38
Nigeria	139	123	7.9	8.0	5.8	1.8	147
Pakistan	114	80	33	0.6	95	2.7	212
Philippines	117	91	25	0.6	159	4.6	280
Russian Federation ^{a,b}	1 827	1 060	708	60			1 827
South Africa ^c	162	107	55	0	103	336	601
Thailand ^d	16	10	5.9	0.1	3.1	<0.1	19
Uganda ^e	24	21	2.5		0.8	0.2	25
United Republic of Tanzania	61	43	2.8	15	1.9	<0.1	63
Viet Nam	73	67	5.1	1.1	38	2.0	113
Zimbabwe	31	26	1.4	4.0	0.6	<0.1	32
22 high-burden countries total	3 739	2 603	1 022	114	669	405	4 813
REMAINING HIGH MDR-TB BURDEN COUNTRIES							
Armenia	6.2	5.7	0.5	0	3.6	2.1	12
Azerbaijan							—
Belarus	19	4.4	15	<0.1	15	22	57
Bulgaria	13	10	2.1	0	9.7	0.5	23
Estonia	0.9	0.4	0.4	<0.1	1.3	0.9	3.1
Georgia	13	11	2.4	<0.1	4.4	2.1	19
Kazakhstan	200	166	33	1.0	161	112	473
Kyrgyzstan					6.3	1.6	8.0
Latvia	2.3	1.0	1.2	<0.1	6.7	2.5	11
Lithuania							—
Republic of Moldova	33	27	3.7	2.5	5.9	4.5	43
Tajikistan	29	25	4.5	0.1	5.1	1.3	36
Ukraine	110	32	77	2.2	116	106	332
Uzbekistan	89	77	12	0.2	35	8.1	132
27 high MDR-TB burden countries	3 927	2 697	1 139	91	981	666	5 574
36 high-TB or high MDR-TB burden countries	4 255	2 961	1 173	120	1 038	669	5 962

Blank cells indicate data not reported.

— indicates values that cannot be calculated.

^a No amount is shown for China and the Russian Federation because the NTP budgets reported by those countries include all budgets for inpatient and outpatient care.

^b In the Russian Federation, the staff and infrastructure reported for TB care and control were allocated to DS-TB (60%) and MDR-TB (40%) by WHO based on the proportion of beddays used by DS-TB and MDR-TB patients.

^c South Africa reported no TB/HIV budget in 2014 because it is included in the HIV programme budget.

^d Data reported are only national level budgets for the Bureau of TB and the National Health Security Office, and do not include provincial and local, private sector, etc. It was not possible for Thailand to report funding for other levels in 2014.

^e Uganda reported an additional US\$ 15.2 million for TB/HIV activities funded through the HIV programme budget. Only budgets financed through the TB programme are shown in the table.

FIGURE 8.2

Funding for drug-susceptible TB and MDR-TB, 2006–2014, by country group (constant 2014 US\$ millions)

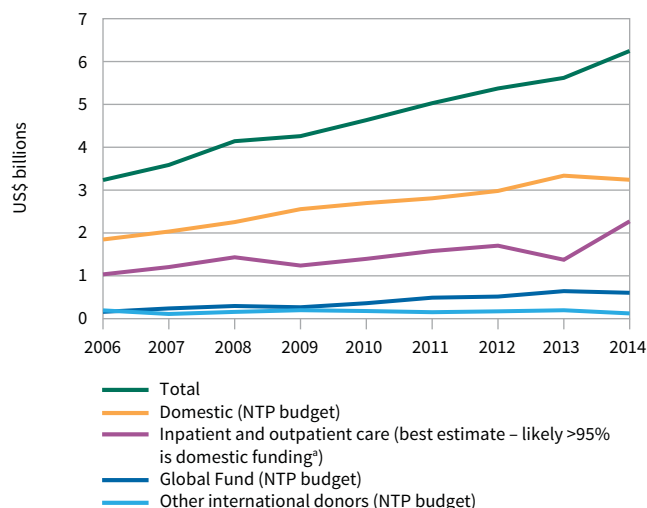


(Figure 8.2). The increase in funding for MDR-TB was most pronounced in BRICS, but was also evident in other HBCs. A detailed breakdown of the funding estimated to be required for drug-susceptible TB, MDR-TB and collaborative TB/HIV activities, based on NTPs assessments of their needs, is shown for the 36 high TB and MDR-TB burden countries in 2014 in Table 8.2. Inpatient care accounts for a variable proportion of the total estimated cost of outpatient and inpatient care in these 36 countries (data not shown). For drug-susceptible TB, the share in 2014 ranged from 1% in the Philippines to 97% in Estonia. In most of the 22 HBCs, the share was in the range 30–60%, with durations of stay ranging from 5–56 days. For MDR-TB, the share in 2014 ranged from 1% in the Philippines to >95% in Bangladesh, Estonia, Georgia, South Africa and the United Republic of Tanzania (the duration of inpatient care is 60–180 days in these countries). In other HBCs, hospitalization accounted for about 60% of the cost of MDR-TB treatment, with durations of stay of 5–240 days.

Domestic funding for the TB-specific budgets of NTPs accounts for the largest single share of funding, followed by funding for inpatient and outpatient care (Figure 8.3). Since almost all (96%) of the funding estimated to be used for inpatient and outpatient care is accounted for by middle- or high-income countries, it can be assumed that virtually all of this funding is from domestic sources (international donor funding for inpatient and outpatient care is only likely to occur in low-income countries, via general budget support to the health sector). Thus, overall, about 89% of the estimated funding of US\$ 6.3 billion in 2014 is from domestic sources. International donor funding for the TB-specific budgets of NTPs has increased since 2006, reaching about US\$ 0.7 billion in 2014. It is important to highlight that the funding reported by NTPs does not capture all of the international donor funding for TB, since donor funding is also provided to entities other than NTPs, including international and national gov-

FIGURE 8.3

Funding for TB prevention, diagnosis and treatment by funding source, 2006–2014 (constant 2014 US\$ billions)



^a 96% of funding for inpatient and outpatient care is accounted for by middle and high-income countries; such countries do not typically receive international donor funding for inpatient and outpatient care services. Data is an estimate based on country-reported utilization.

ernmental and nongovernmental organizations. A more comprehensive analysis of international donor funding, based on donor reports to the Organization for Economic Cooperation and Development (OECD), is provided in Box 8.2. NTP reports also do not include data on out-of-pocket expenditures, which will receive increased attention in future (Box 8.3).

It is also important to emphasize that the global average for the share of funding provided from domestic sources conceals enormous variation among individual countries as well as country groups that can be defined based on TB burden, geography, political/economic profile and income level (Figure 8.4, Table 8.3). Domestic funding dominates in three (not mutually exclusive) groups: BRICS, upper

International donor funding for TB prevention, diagnosis and treatment, based on donor reports to the Organization for Economic Cooperation and Development

Not all of the international donor funding that is provided for TB prevention, diagnosis and treatment is channelled through NTPs. The financial data reported to WHO by NTPs therefore understate the total amount of international donor funding being provided each year. The creditor reporting system (CRS) of the Organization for Economic Cooperation and Development (OECD) is the most comprehensive source of information about international donor funding. Reports are provided by 31 multilateral organizations, the 26 countries that are members of the OECD's Development Assistance Committee and a further 2 non-committee members (Kuwait and the United Arab Emirates). The OECD compiles data on commitments and disbursements from both governments and multilateral organizations. Government contributions to multilateral organizations are not attributed to the government of origin but only to the multilateral organization. Disbursement data include both direct transfers to countries as well as the provision of goods and services, such as in-kind transfers or technical assistance. Data on gross disbursements (as opposed to commitments that may not always be translated into actual funding) were analysed for 2004–2012.

Figure B8.2.1 and Figure B8.2.2 show that most of the international donor funding provided 2004–2012 came from the Global Fund (66%), followed by the government of the United States of America (17%). Remaining funding came from other countries (11%) and other multilateral organizations (6%), among which the largest donors were the governments of Canada (4%) and the United Kingdom (3%). The Global Fund disbursed TB funding (in at least one year between 2004 and 2012) in 105 of the 109 countries that received any TB donor assistance. The government of the United States of America provided funding to 50 of these 109 countries at some point during the years 2004–2012, and supported 50 countries in each of the years 2009–2012. The top recipients of funding, with total amounts of over US\$ 100 million each during the years 2004–2012, were (in descending order of the total disbursements received): China, India, Indonesia, the Philippines, Bangladesh, Nigeria and Pakistan. Collectively, these countries accounted for 56% of the TB cases notified in 2012. Most funding was provided to countries in Africa and Asia (Figure 8.2.3).

FIGURE B8.3.1

Trends in donor funding for TB prevention, diagnosis and treatment by source, 2004–2012

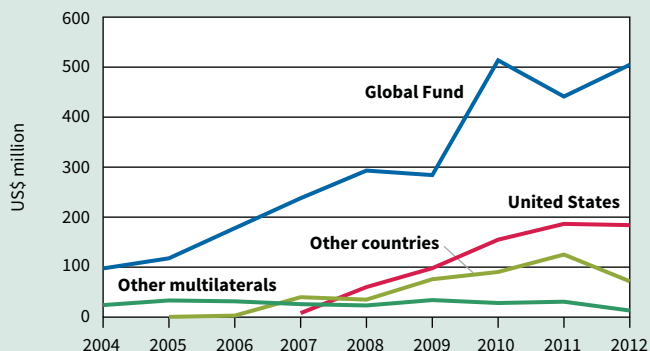
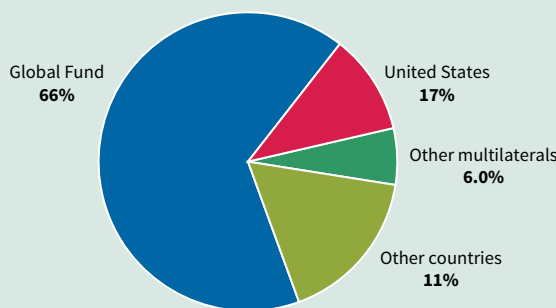


FIGURE B8.3.2

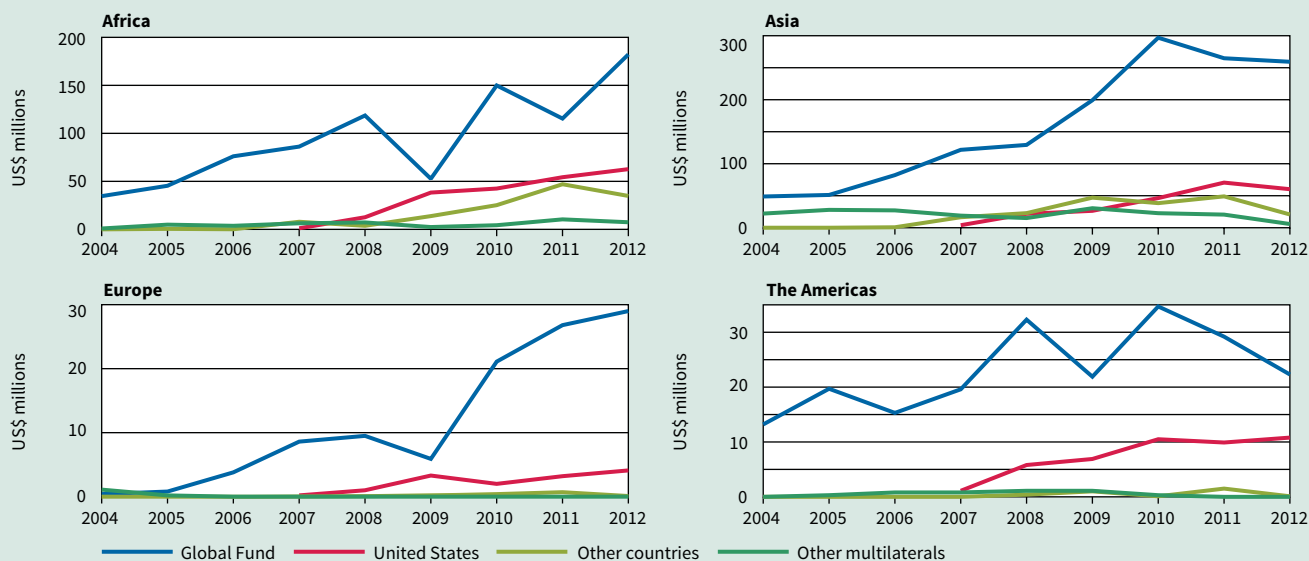
Donor funding for TB prevention, diagnosis and treatment by source, 2004–2012



The Global Fund has consistently been the largest provider of international donor funding, including over US\$ 500 million in 2012. Funding increased steadily from 2004 to 2008 and rose sharply from 2009 to 2010. Disbursements from the government of the United States of America steadily increased from 2007 to 2011, before levelling off in 2012.

FIGURE B8.3.3

Donor funding for TB prevention, diagnosis and treatment by region, 2004–2012



Addressing and monitoring catastrophic costs for TB patients and their households

One of the targets for the post-2015 global TB strategy is that no TB patient or their household should face catastrophic costs due to TB (Chapter 1). A recent systematic review^a showed that, on average, TB patients in low- and middle-income countries face medical expenses, other costs required to seek or stay in care and income losses equivalent to more than 50% of his or her annual income. Half of the costs are incurred before TB treatment starts – in seeking diagnosis. The financial burden varies among countries and according to the model of care used, with the total cost as a proportion of income ranging from 2% to over 300%. The financial burden is on average greater for persons who have MDR-TB and relatively higher for the poorest. On average, income losses represent about 60% of the total costs faced by patients; about 25% of total costs are for direct medical costs such as tests, medicines and hospitalization; and the remainder is for other care-related costs, such as transport and food.

To cover these costs, patients often have to resort to coping mechanisms that may be irreversible. Up to 75% of TB patients must take out a loan; up to 50% sell household items; and up to 66% rely on financial support from relatives.^a Further negative effects include that children of parents ill with TB may drop out of school to seek paying work or care for parents. Some patients stop treatment before cure and may suffer worsening health, transmit disease or die. For others, the prospect of financial loss means delaying help-seeking with similar risks. Moreover, health care related impoverishment increases the future risk of TB for the whole affected family.

Universal Health Coverage (UHC), which is defined as “universal access to needed health services without financial hardship in paying for them”^b is essential to minimize costs. However, UHC as currently defined does not protect against high non-medical costs and income losses. Therefore, social protection (or social transfers), in cash or in kind, are important to enhance food security and nutrition and to provide a minimum level of income security and access to services. Social protection is included as a core element of the post-2015 global TB strategy. The added dimension of financial risk protection through reduced or mitigated income losses and non-medical costs is illustrated in Figure 8.3.1.^d

The target of zero catastrophic costs in the post-2015 global TB strategy refers to income losses as well as direct costs. This is in contrast to the indicator of “catastrophic health care expenditure”, which WHO has defined as direct health care expenditures (not including income losses) of >40% of annual discretionary income.^d

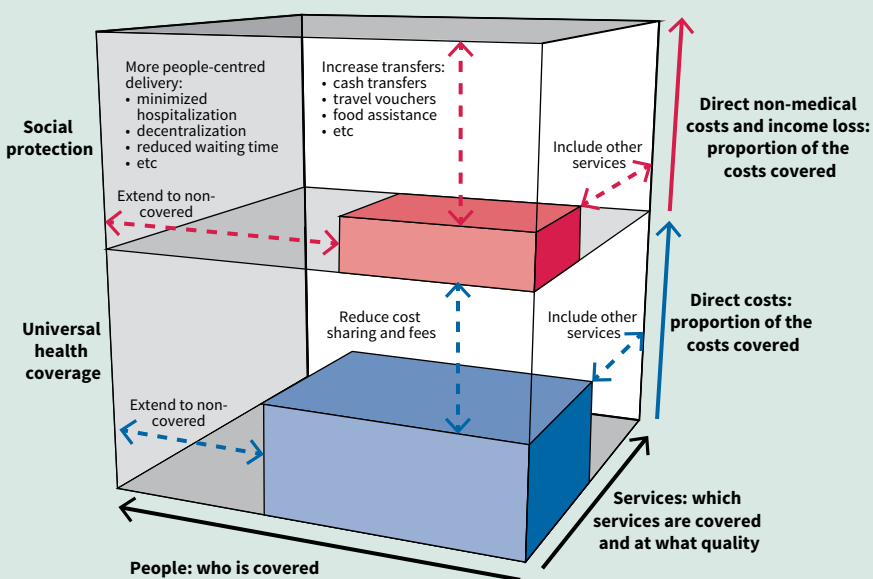
WHO is currently developing a measurement approach to monitor progress towards the catastrophic cost target for TB. Measurement of two indicators is being explored. These are:

- The percentage of TB-affected households facing a total cost (direct and indirect combined) that is above a certain percentage of annual household annual income.
- The percentage of TB-affected households experiencing “dissaving” (such as taking a loan or selling assets), as a proxy for catastrophic costs.

The appropriate cut-off for the first indicator needs to be defined, and the usefulness of different types of “dissaving” as a proxy for high costs needs to be further validated. Both approaches will require data collection in patient and/or household surveys, which may be done as ad-hoc surveys in a random sample of facilities or sentinel sites, or be part of other surveys (e.g. a Demographic and Health Survey).

FIGURE B8.3.1

The three dimensions of UHC, with the added dimension of financial risk protection for non-medical costs. Adapted from World Health Report 2010.^b Elements in red are non-medical costs and additional interventions within health care and beyond to provide financial protection/compensation.



Source: Lönnroth K, Glaziou P, Weil D, Floyd K, Uplekar M, Raviglione M. Monitoring universal health coverage and social protection in the context of tuberculosis care and prevention. *PLoS Med* 11(9): e1001693. doi:10.1371/journal.pmed.1001693

^a Tanimura T, et al. Financial burden for tuberculosis patients in low- and middle-income countries – a systematic review. *ERJ* 2014; 2014; 43: 1763–1775.

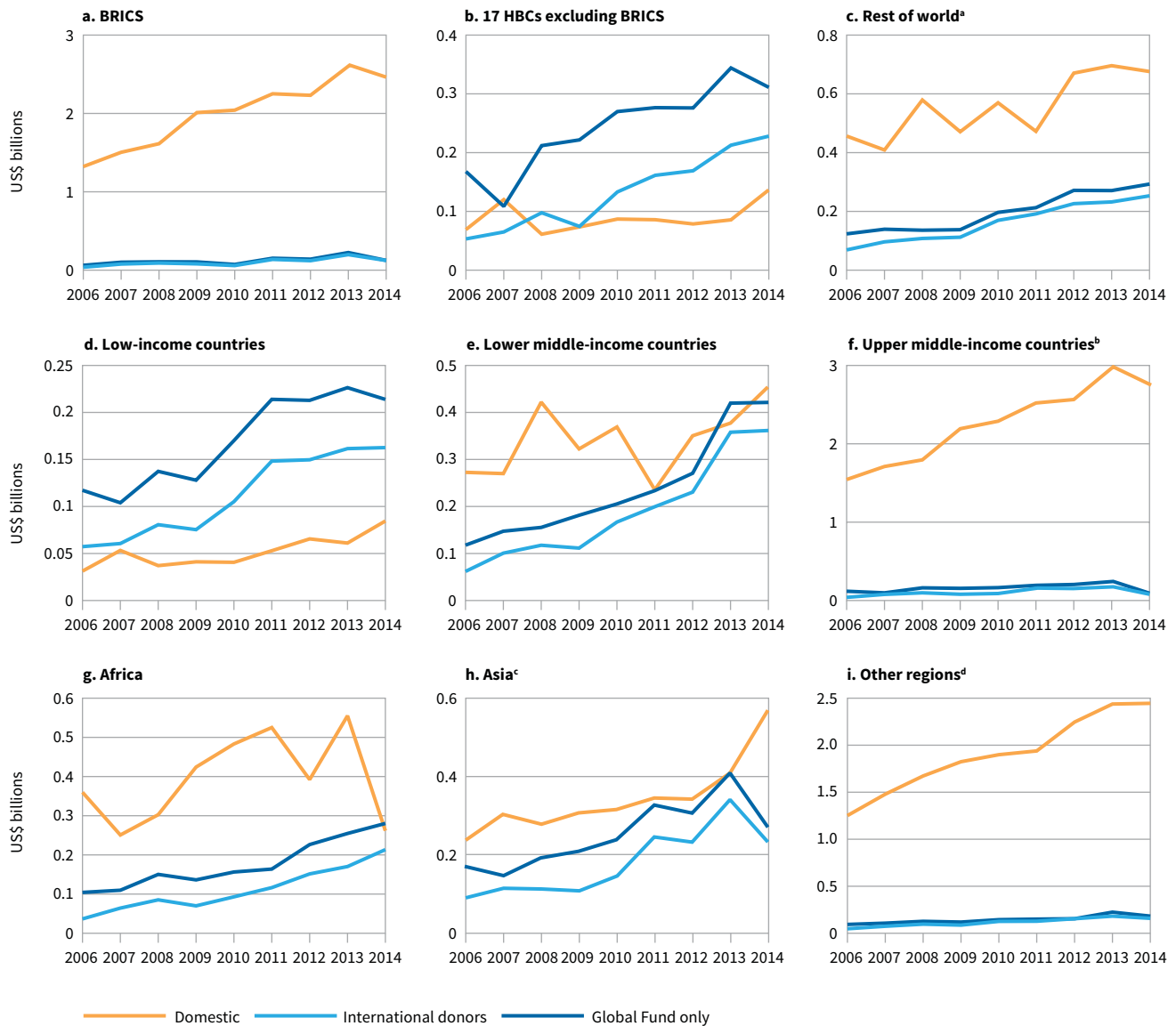
^b *World Health Report 2010: health systems financing – the path to universal coverage*. Geneva: WHO, 2010. <http://www.who.int/whr/2013/report/en/index.html>

^c International Labour Organization, *World of Work Report 2010*. http://www.ilo.org/public/portugue/region/eurpro/lisbon/pdf/worldwork_2010.pdf

^d Lönnroth K, et al. Monitoring universal health coverage and social protection in the context of tuberculosis care and prevention. *PLoS Med* 11(9): e1001693. doi:10.1371/journal.pmed.1001693

FIGURE 8.4

Funding for TB prevention, diagnosis and treatment from domestic sources and international donors, 2006–2014 for 9 country groups: A) BRICS B) 17 Other HBCs C) Rest of World, D) Low-income countries, E) Lower middle-income countries, F) Upper middle-income countries/High-income and high MDR-TB burdened countries, G) Africa, H) Asia and I) Other regions (constant 2014 US\$ billions)



^a Rest of the world includes 99 countries that are not in the list of 22 high TB burden or 27 high MDR-TB burdened countries.
^b This includes three high-income countries: Estonia, Latvia and the Russian Federation.
^c Asia includes the WHO regions of South-East Asia and the Western Pacific.
^d "Other regions" includes three WHO regions: the Eastern Mediterranean Region, the European Region, and the Region of the Americas.

middle-income countries and regions outside Africa and Asia. International donor funding dominates in the group of 17 HBCs outside BRICS and in low-income countries. In lower middle-income countries, domestic funding has risen from US\$ 0.3 in 2006 to almost US\$ 0.5 billion in 2014, and international donor funding has assumed greater and greater importance, almost reaching parity with domestic funding in 2014. Most of the increase in lower middle-income countries has been driven by grants from

the Global Fund. At the individual country level, international donor funding remains absolutely critical to funding for TB prevention, diagnosis and treatment in most of the 22 HBCs. Only Brazil, China, India, Kenya, the Russian Federation, South Africa and Thailand report levels of domestic funding that exceed contributions from international donor funding and in several countries more than 90% of the available funding is from international donor sources.

TABLE 8.3

Reported NTP budget, available funding for NTP budget from domestic and international donor sources, funding gap and share of NTP budget provided by domestic and international donor funding, 36 high TB or MDR burden countries, 2014 (current US\$ millions)

	TOTAL NTP BUDGET	DOMESTIC FUNDING (A)	INTERNATIONAL DONOR FUNDING (B)	SHARE OF AVAILABLE NTP FUNDING (A+B) PROVIDED FROM DOMESTIC SOURCES (%)	SHARE OF AVAILABLE NTP FUNDING (A+B) PROVIDED BY INTERNATIONAL DONORS (%)	FUNDING GAP
22 HIGH-BURDEN COUNTRIES						
Afghanistan	9.5	0.8	5.4	13%	87%	3.3
Bangladesh	57	2.9	19	13%	87%	35
Brazil	79	68	1.2	98%	1.7%	9.3
Cambodia	31	1.2	9.8	11%	89%	20
China ^a	347	271	11	96%	4.1%	65
Democratic Republic of the Congo	66	2.1	14	13%	87%	50
Ethiopia	94	6.5	28	19%	81%	59
India	252	165	86	66%	34%	0
Indonesia	127	17	38	30%	70%	72
Kenya	57	13	9.6	58%	42%	34
Mozambique ^b	19		4.3	—	—	15
Myanmar	36	5.5	18	24%	76%	13
Nigeria	139	12	53	19%	81%	74
Pakistan ^b	114		34	—	—	80
Philippines	117	32	29	52%	48%	56
Russian Federation	1 827	1 827	0	100%	0%	0
South Africa	162	136	26	84%	16%	0
Thailand ^c	16	8.6	5.2	62%	38%	2.1
Uganda	24	2.1	5.5	27%	73%	16
United Republic of Tanzania	61	8.1	11	43%	57%	42
Viet Nam	73	6.6	13	33%	67%	54
Zimbabwe	31	0.7	13	5.0%	95%	17
22 high-burden countries total	3 739	2 586	436	86%	14%	717
REMAINING HIGH MDR-TB BURDEN COUNTRIES						
Armenia	6.2	3.4	2.8	55%	45%	0
Azerbaijan						
Belarus	19	7.6	4.0	66%	34%	7.8
Bulgaria	13	8.5	4.1	68%	32%	0
Estonia	0.9	0.9	< 0.1	97%	2.8%	0
Georgia	13	5.8	7.1	45%	55%	0
Kazakhstan	200	196	4.1	98%	2.1%	0
Kyrgyzstan						
Latvia	2.3	2.2	0	100%	0%	0.1
Lithuania						
Republic of Moldova	33	4.1	6.9	37%	63%	22
Tajikistan	29	20	9.2	69%	31%	0
Ukraine	110	35	27	56%	44%	49
Uzbekistan	89	69	21	77%	23%	0
27 high MDR-TB burden countries	3 927	2 834	457	86%	14%	636
36 high-TB or high MDR-TB burden countries	4 255	2 937	522	85%	15%	796

Blank cells indicate data not reported.

— indicates values that cannot be calculated.

^a The large gap in China is in part due to the withdrawal of financing from the Global Fund for MDR-TB diagnosis and treatment, for which alternative sources of funds have not yet been confirmed.

^b Mozambique and Pakistan were not able to report domestic funding expected in 2014.

^c Data reported are only national level budgets for the Bureau of TB and the National Health Security Office, and do not include provincial and local, private sector, etc. It was not possible for Thailand to report funding for other levels in 2014. However, given the policy of universal health coverage, it is estimated that other resources required for TB prevention, diagnosis and treatment are financed from domestic sources.

8.3 Funding gaps reported by national TB programmes, 2006–2014

Despite growth in funding from domestic and international donor sources, many NTPs continue to be unable to mobilize all the funding that they estimate necessary to fully implement their national strategic plans (Figure 8.5). Funding gaps (i.e. the difference between assessments by NTPs of funding needs for TB prevention, diagnosis and treatment and the actual amount of funds mobilized) have persisted and increased over time, possibly explained by increased ambition (in scale and speed) in plans for the scale-up of recommended interventions. In 2014, reported funding gaps amounted to a total of US\$ 0.9 billion.

Lower-middle income countries account for the largest reported funding gaps (about US\$ 0.5 billion in 2014), of which US\$ 0.3 billion was in five countries (Indonesia, Nigeria, Pakistan, the Philippines and Viet Nam). There may be additional capacity to mobilize more domestic funding in these countries; an interesting contrast is India, where no funding gap was reported for 2014 and where domestic funding increased noticeably between 2013 and 2014 (this increase is the main reason for the upward trajectory of domestic funding shown for Asia in Figure 8.4). Funding gaps have been falling in upper middle income countries (Figure 8.5), mostly explained

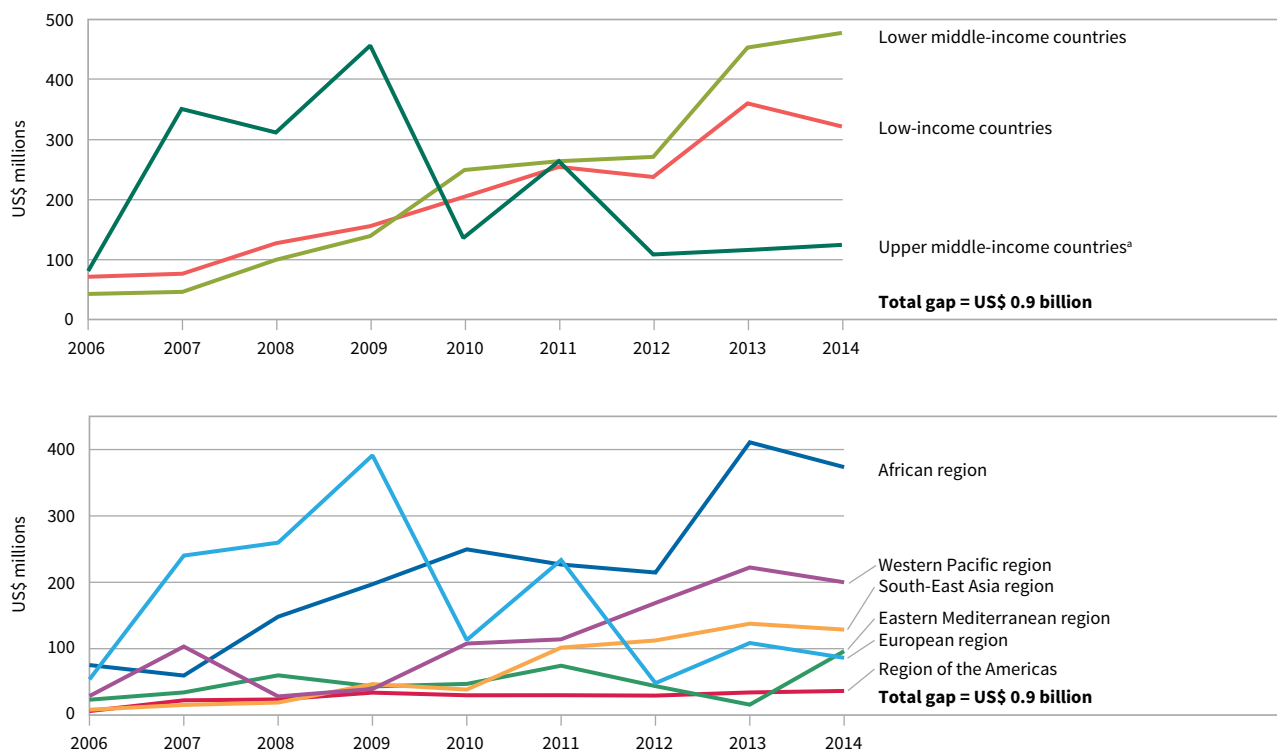
by large reductions in the funding gaps reported by the Russian Federation and Kazakhstan; these two countries reported no funding gaps in 2014. Funding gaps reported by low-income countries have been steadily increasing, reaching US\$ 0.3 billion in 2014. Geographically, the African and Western Pacific Regions account for almost 70% of the total funding gaps reported by NTPs. In the Western Pacific Region, the largest gaps are those reported by China, the Philippines and Viet Nam, which total almost US\$ 0.2 billion in 2014 (Table 8.3).

Of the US\$ 0.9 billion funding gap reported by NTPs in 2014, US\$ 0.77 billion is for drug-susceptible TB and US\$ 0.15 billion is for MDR-TB. Relative to total funding needs, the funding gap is larger for drug-susceptible TB (Figure 8.6). Domestic funding accounts for a larger share of the funding required for MDR-TB compared with drug-susceptible TB, which is not surprising given that most of the high MDR-TB burden countries are middle or high-income countries and 14 of 27 are in the European Region.

The gap between the US\$ 8 billion estimated to be needed for a full response to the TB epidemic in 2014 and 2015 (section 8.1) and the US\$ 6.3 billion available in 2014 (section 8.2) is US\$ 1.7 billion.

FIGURE 8.5

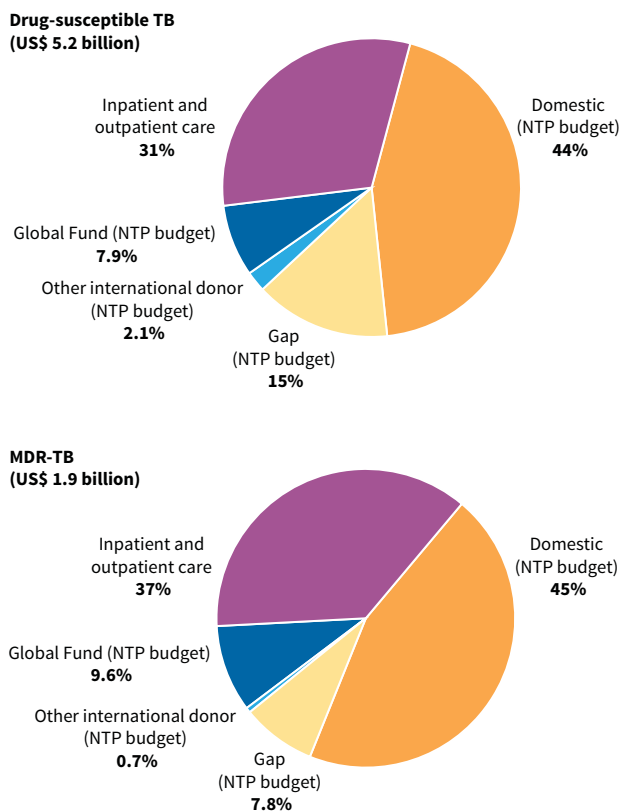
Reported funding gaps by income group and by region, 2006–2014 (constant 2014 US\$ millions)^a



^a Upper middle-income countries includes three high income countries: Estonia, Latvia and the Russian Federation.

FIGURE 8.6

Funding sources and funding gaps for drug-susceptible TB and MDR-TB, 2014^a



^a In the Russian Federation, the staff and infrastructure reported for TB care and control were allocated to drug-susceptible TB (60%) and MDR-TB (40%) by WHO based on the proportion of beddays used by patients with drug-susceptible and MDR-TB.

8.4 Unit costs of treatment for drug-susceptible and MDR-TB, 2013

The cost per patient treated for drug-susceptible and MDR-TB could be estimated for 122 countries (listed in [Table 8.1](#)), including 34 of the 36 countries that are in the list of high TB and/or high MDR-TB burden countries. Following intensified work on financial monitoring in 2014,¹ this is the first global report in which it has been possible to present estimates for such a large number of countries: previous estimates were restricted to the 22 HBCs and did not include estimates for MDR-TB. The methods used for analysis of unit costs are summarized in [Box 8.4](#).

Unit cost estimates for 2013 are shown for drug-susceptible and MDR-TB in [Figure 8.7](#) and [Figure 8.8](#). The cost per patient treated for drug-susceptible TB was generally

in the range US\$ 100–US\$ 1000. Notable exceptions were Bangladesh (US\$ 74) and certain countries of the former Soviet Union that had much higher costs. Low-income countries spent on average US\$ 458 per patient treated, while upper-middle income or high-income countries invested an average of US\$ 5 006. For MDR-TB, the cost per patient treated ranged from an average of US\$ 9 235 in low-income countries to US\$ 48 553 in upper middle-income countries.

In the 22 HBCs, the estimated cost per patient treated for drug-susceptible TB with first-line drugs ranged from US\$ 74 in Bangladesh to US\$ 7 810 in the Russian Federation in 2013. Approximately 80% of this cost was accounted for by reported NTP expenditures, with the remainder accounted for by inpatient and outpatient care. The estimated cost per patient treated for MDR-TB ranged from US\$ 2 571 in Kenya to US\$ 31 962 in the Russian Federation in 2013. The average cost of first-line drugs to treat drug-susceptible TB was US\$ 46, compared to a much higher average cost of US\$ 5 240 for the second-line drugs required to treat a patient with MDR-TB.

In all of the 22 HBCs, the cost per patient treated for drug-susceptible TB was less than gross domestic product (GDP) per capita. Four of these countries – China, India, Indonesia, and Pakistan, which together account for 49% of the global TB burden – all have costs per patient treated that are relatively low compared with their GDP per capita. While the level of GDP per capita clearly influences the cost of TB treatment, the size of the total patient case load is also an important factor (for example, when numbers of patients treated are very large, economies of scale can be realised).

The cost per patient treated is typically higher in countries of the former Soviet Union, ranging from US\$ 1 788–US\$ 13 828 for drug-susceptible TB and US\$ 5 593–US\$ 49 256 MDR-TB. In these countries, lengthy hospitalizations play a more significant role in the total cost of care. These admissions last up to 75 days per patient for drug-susceptible TB and up to 180 days for MDR-TB, and account for approximately 40% and 60% of the total per patient cost, respectively. Nonetheless, there is evidence of falling lengths of stay in some of these countries and a transition to a greater reliance on outpatient care. This trend is most evident in Georgia, Kazakhstan, Ukraine, and Uzbekistan. For example, patients with MDR-TB in Uzbekistan were admitted to hospital for an average of 270 days in 2008 and 95 days in 2014.

¹ This was made possible by a grant to the Global TB Programme for work on unit costs from the Bill & Melinda Gates Foundation.

FIGURE 8.7

Estimated cost per patient treated for drug-susceptible TB, 2013

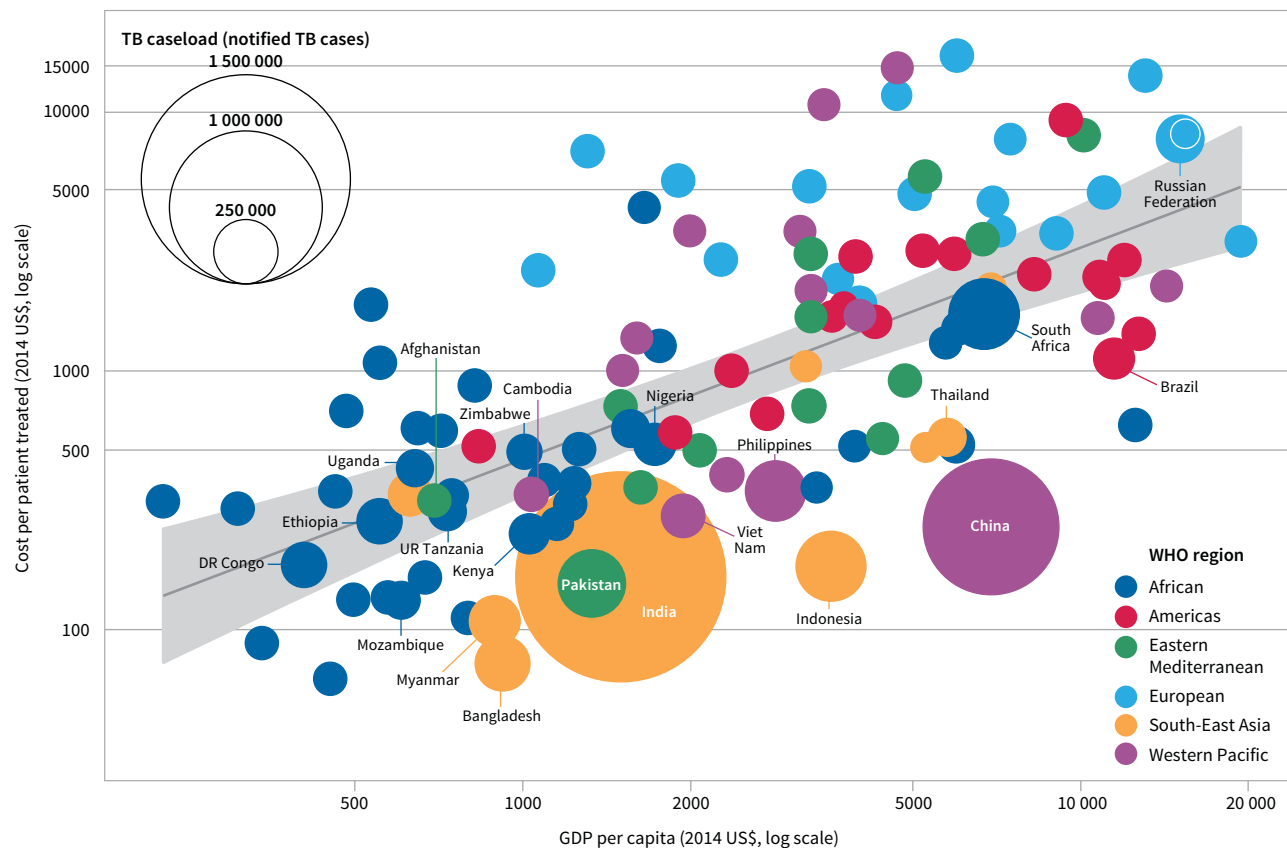
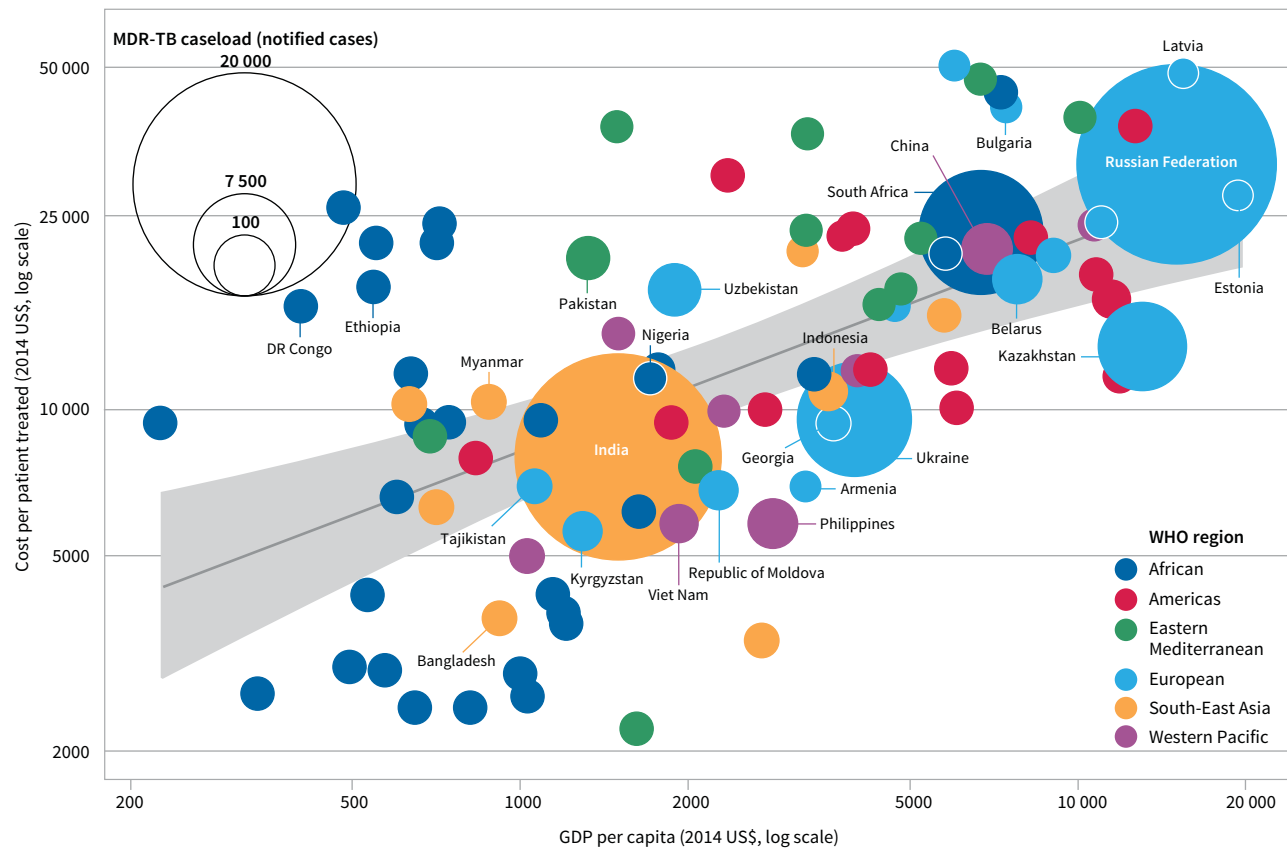


FIGURE 8.8

Estimated cost per patient treated for MDR-TB, 2013



BOX 8.4

Methods used to estimate the cost per patient treated for drug-susceptible and MDR-TB

Two main data sources were used. The first was the validated expenditure data reported by NTPs that are stored in the WHO global TB database. The second was country-specific estimates of the unit costs of bed days and outpatient visits available from WHO's **CHOosing Interventions that are Cost-Effective** (WHO-CHOICE) model and associated database (managed by the Health systems governance and financing department). In a few instances when no expenditure data could be reported, information about the total funding available was used as a proxy for expenditures. For a few countries, WHO-CHOICE estimates were replaced with estimates of unit costs obtained directly from recent studies or discussions with experts.

Costs were calculated separately for drug-susceptible and MDR-TB. In each case, the numerator was the total estimated cost of treatment, which has two main parts: (1) the national expenditures reported by the NTP; and (2) the costs associated with the utilization of health services by TB patients.

As explained in **Box 8.1**, national NTP expenditures are reported annually to WHO using the online WHO global TB data collection system, and then reviewed and validated. Categories of expenditure considered as costs for MDR-TB were second-line drugs, and all other inputs/activities implemented for the programmatic management of MDR-TB. All other categories (with the exception of collaborative TB/HIV activities) were assumed to be for drug-susceptible TB. In addition to the standard data validation process that is part of the annual round of global TB data collection, intensified efforts to improve the

completeness and quality of data required for estimation of unit costs were undertaken between January and May 2014. These included: review and discussion of data and the provisional results of analyses with NTP staff and those providing technical assistance to NTPs during workshops related to the development of national strategic plans; greater analysis and use of data related to orders of first and second-line drugs available from the Global TB Drug Facility; new data about TB expenditures available from National Health Accounts; and discussions with members of a newly established working group on TB financing in the European Region (called the Wolfheze financing working group).

The total costs associated with utilization of inpatient and outpatient care were calculated using information about the typical number of days of inpatient care and outpatient visits required on a per patient basis during treatment (reported separately for drug-susceptible and MDR-TB by NTPs) combined with WHO CHOICE unit cost estimates, multiplied by the number of patients treated in a given year (based on notification data – see **Chapter 4** for drug-susceptible TB and **Chapter 5** for MDR-TB). Multiplying quantities of visits and bed days by their price estimates yields the total cost estimate of inpatient and outpatient services.

Unit costs were then calculated as the sum of NTP expenditures and total costs for utilization of inpatient and outpatient care, divided by the reported number of patients treated. Again, this calculation was done separately for drug-susceptible and MDR-TB.

Research and development

KEY FACTS AND MESSAGES

Efforts to develop new TB diagnostics, drugs, and vaccines have intensified during the past decade. However, considerable progress and investment is still needed.

Increased and sustained investment in new TB diagnostics remains essential for the development of an accurate, easy-to-use, affordable point-of-care assay for the rapid and early diagnosis of TB.

There is significant industry interest in TB diagnostics, with more than 50 companies involved in assay development. However, though many new diagnostic technologies are under development or are available on the market, funding for accelerated field evaluation of diagnostic accuracy and robustness of these assays is insufficient.

To facilitate development of new diagnostic tests, four priority target product profiles have been developed through a consensus-building approach among stakeholders to define optimal and minimal characteristics of the four priority tests and help manufacturers understand their market potential.

There are 10 new or repurposed anti-TB drugs currently in late phases of clinical development.

After 40 years of neglect, two drugs have recently been approved by stringent regulatory authorities for the treatment of MDR-TB under specific conditions. The first, bedaquiline, was approved by the US Food and Drug Administration (FDA) in December 2012; WHO issued interim guidance on its use in the treatment of MDR-TB in June 2013. The second drug, delamanid, was formally approved for use in MDR-TB patients by the European Medicines Agency in April 2014.

Results from two Phase III trials investigating four-month regimens for the treatment of drug-susceptible TB that include fluoroquinolones were released in 2013 and 2014. These shorter regimens did not prove as effective as the six-month standard of care regimen currently recommended by WHO. A series of new combination regimens, including new and/or re-purposed drugs, are being tested in a series of early bactericidal activity or two-month sputum-culture conversion Phase II studies. Some of these show potential for treatment of both drug-susceptible and drug-resistant TB.

There are currently 15 vaccine candidates in clinical trials. Most are designed for prevention of TB, either through the prevention of infection or prevention of progression to disease in infected persons. Several of these vaccines are currently in or will shortly enter Phase II and IIb trials and will be tested in further Phase III trials.

Research and development is one of the three pillars of the WHO post-2015 global TB strategy, and will play a crucial role in accelerating the reductions in TB incidence and mortality required to reach post-2015 global TB targets.

The goal of the post-2015 global TB strategy endorsed by the World Health Assembly (WHA) in May 2014 is to end the global TB epidemic (**Chapter 1**). Despite major progress in TB prevention, diagnosis and treatment since the mid-1990s (**Chapters 2–4**), reaching this goal will require major technological breakthroughs from the research and development pipeline. Critical components include: availability of affordable, short, effective and well-tolerated treatments for all forms of TB (latent TB infection, drug-susceptible and drug-resistant TB disease); a point-of-care diagnostic test with capacity to identify resistance to the most important anti-TB drugs; and an effective vaccine.

2014 is the fourth successive year in which a chapter on research and development has been included in the *Global Tuberculosis Report*. The status of progress in the development of new TB diagnostics, drugs and vaccines as of September 2014 is summarized, drawing on information provided by the secretariats of the relevant Working Groups of the Stop TB Partnership and recent publications.

9.1 New diagnostics for TB

Targets for the post-2015 global TB strategy include a 95% reduction in TB deaths and a 90% reduction in TB incidence by 2035 (**Chapter 1**). To achieve these targets, the implementation of new tools and health system strategies is of critical importance.

There are several diagnostic technologies under development and companies have shown renewed interest in TB products following the WHO policy recommendations and subsequent global roll-out of the Xpert MTB/RIF assay for the rapid detection of pulmonary and extra-pulmonary TB and rifampicin resistance in adults and children (**Chapter 6**). Xpert MTB/RIF has been a game-changer in the TB diagnostic landscape but concerns remain with respect to the single-source manufacturer, implementation challenges for the lower levels of the health system, and cost.

However, major gaps remain in the diagnostic pipeline. There are insufficient tests under development for the diagnosis of TB in children, assessment of susceptibility to drugs that may be part of new treatment regimens, prediction of progression from latent TB infection (LTBI) to active TB disease and alternatives to TB culture for treatment monitoring. The development and implementation of such tests will be essential to

meet targets outlined in the post-2015 global TB strategy.

Despite the robust TB diagnostic pipeline reported in 2013,¹ there has been little progress in conducting rigorous field trials of these new diagnostic technologies in different epidemiological settings to determine their diagnostic accuracy and robustness in the settings of intended use. The Foundation for Innovative New Diagnostics (FIND) remains the lead organization conducting field evaluations of different technologies, but the engagement of other stakeholders and adequate funding are urgently needed. In 2013, no data on the performance characteristics of any new diagnostic technology was submitted to WHO for the systematic evaluation process used in the formulation of policy guidance (Box 9.1).

9.1.1 Diagnostic pipeline

An overview of the diagnostic pipeline is shown in Figure 9.1. The list of technologies is not necessarily complete or exhaustive but reflects those technologies documented in reports published by UNITAID and Treatment Action Group (TAG).² New tools using molecular technologies such as nucleic acid amplification tests (NAATs) are the most advanced. However, most tests are intended for use at reference laboratory level only, requiring dedicated infrastructure and experienced staff. Other technologies under development include tests to detect TB, drug resistance, or TB and drug resistance combined. These include microarray-based multiplexing diagnostic platforms for the simultaneous detection of a large number of resistance-conferring mutations. Clearly, additional funding is urgently needed to expedite the progress of promising new technologies through the pipeline, conduct the necessary evaluation studies, and catalyse innovation towards the development of new tests suitable for use at lower levels of the health system.

9.1.2 TB diagnostic tests that could potentially be reviewed by WHO in 2015

TB LAMP (Eiken, Japan)

In 2012, WHO reviewed the evidence for the use of the loop-mediated isothermal amplification (LAMP) platform as a replacement test for acid-fast bacilli (AFB) microscopy but did not proceed with the development of policy recommendations due to insufficient evidence. FIND has subsequently re-evaluated TB LAMP in multiple country settings in comparison with fluorescent smear

BOX 9.1

Evidence required for WHO review of new diagnostics

Phase 1: Research and Development

- Upstream research and development to define and validate a prototype;
- Laboratory validation under international standards that culminates in a design-locked product;
- WHO interacts with developers if requested to discuss end-user requirements such as biosafety, assay robustness and intended settings of use.

Phase 2: Evaluation and Demonstration

- The performance of the new diagnostic product should be evaluated in controlled trials at 3–5 trial sites in high-burden TB and HIV countries;
- Product registration with global and/or national regulatory authorities;
- Product specifications and performance should subsequently be validated in uncontrolled trials under field conditions in 5–10 trial sites in high-burden TB and HIV countries, and include cost-effectiveness studies.

Phase 3: Evidence Assessment

NEW TECHNOLOGIES

- Submission of a dossier with Phase I and Phase II data to WHO.

FAST-FOLLOWER

- Manufactured under ISO 13:485 standards;
- Equivalent performance demonstrated – Supranational Reference Laboratory comparison;
- Structured evidence assessment using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach;
- WHO does not recommend technologies for individual country use.

Phase 4: Phased uptake and collection of evidence for scale-up

- New diagnostic successfully implemented in routine diagnostic services by early implementers in high-burden countries;
- Systematic assessment of proposed algorithms, laboratory workload, operational constraints and cost-effectiveness;
- Lessons learnt by early implementers used for country adaptation.

Phase 5: Scale-up and Policy refinement

- Scale-up of the new diagnostic, with subsequent data used to inform and refine WHO policy guidance in a dynamic and on-going process.

¹ *Global Tuberculosis Report 2013*. World Health Organization, Geneva. Available at http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf?ua=1

² Daniels C. “The tuberculosis diagnostics pipeline” in *2014 Pipeline Report: HIV, Hepatitis C Virus (HCV) and Tuberculosis Drugs, Diagnostics, Vaccines, Preventive Technologies, Research Toward a Cure, and Immune-Based and Gene Therapies in Development*. New York, Treatment Action Group, 2014. Available at: <http://www.treatmentactiongroup.org/sites/g/files/g450272/f/201407/2014%20Pipeline%20Report%20Full.pdf>

FIGURE 9.1

An overview of progress in the development and evaluation of TB diagnostics, August 2014

TECHNOLOGIES IN DEVELOPMENT ^a
<p>Volatile organic compounds</p> <ul style="list-style-type: none"> ■ BreathLink, Menssana Research, USA ■ Prototype breathalyzer device, Next Dimensions Technology, USA <p>Molecular technologies</p> <ul style="list-style-type: none"> ■ Alere Q, Alere, USA ■ B-SMART, LabCorp, USA ■ Genedrive MTB/RIF ID, Epistem, UK ■ LATE-PCR, Brandeis University, USA ■ GeneXpert XDR cartridge, Cepheid, USA ■ TruArray MDR-TB, Akkoni, USA ■ INFINITIMTB Assay, AutoGenomics, USA ■ FluoroType MTB / FluoroType MTB RNA, Hain Lifesciences, Germany <p>Culture-based technologies</p> <ul style="list-style-type: none"> ■ BNP Middlebrook, NanoLogix, USA ■ TREK Sensititre MYCOTB MIC plate, Trek Diagnostic Systems/ Thermo Fisher Scientific, USA <p>Other technologies</p> <ul style="list-style-type: none"> ■ TB Rapid Screen, Global BioDiagnostics, USA ■ TBDx, Signature Mapping Medical Sciences, USA
TECHNOLOGIES SCHEDULED FOR EVALUATION BY WHO IN 2015
<p>Molecular technologies</p> <ul style="list-style-type: none"> ■ TB LAMP, Eiken, Japan ■ Molecular technologies for genotypic DST (including sequencing technologies) ■ Line probe assays <p>Non-molecular technologies</p> <ul style="list-style-type: none"> ■ Alere Determine TB-LAM, Alere, USA
ON THE MARKET BUT EVIDENCE FOR USE NOT YET SUBMITTED TO WHO FOR EVALUATION
<p>Molecular technologies</p> <ul style="list-style-type: none"> ■ iCubate System, iCubate, USA ■ TB drug resistance array, Capital Bio, China ■ EasyNAT TB Diagnostic kit, Ustar Biotechnologies, China ■ Truelab/Truenat MTB, Molbio/bigtec Diagnostics, India
EVALUATED BY WHO AND NOT RECOMMENDED
<ul style="list-style-type: none"> ■ Commercial serodiagnostics (all manufacturers) ■ Interferon-gamma release assays for the detection of active TB (all settings)
TECHNOLOGIES ENDORSED BY WHO
<p>Molecular technologies</p> <ul style="list-style-type: none"> ■ Xpert MTB/RIF (pulmonary, extrapulmonary and paediatric samples) ■ Line probe assays for the detection of MTB and rifampicin resistance conferring mutations in AFB smear positive sputum or MTB cultures <p>Microscopy</p> <ul style="list-style-type: none"> ■ Light and LED Microscopy ■ Same-day diagnosis <p>Culture-based technologies</p> <ul style="list-style-type: none"> ■ Commercial liquid culture systems and rapid speciation ■ Non-commercial culture and DST (MODS, NRA, CRI)

^a This is not an exhaustive list of technologies in development. Those listed are the ones documented in publications by UNITAID and TAG.

microscopy, Xpert MTB/RIF and culture and plans to submit a dossier of performance characteristics and diagnostic accuracy to WHO for review in 2015.

Urinary LAM (Alere, USA)

The lateral flow test Determine TB LAM (lipoarabinomannan) has been evaluated in several studies for the detection of active TB in people who are severely immunocompromised. A systematic review of the performance characteristics of the assay will be undertaken in 2015 if sufficient data are available.

Molecular DST methods

In 2012, the Hain Lifescience MTBDR sl assay for the detection of resistance conferring mutations for fluoroquinolones and second-line injectable agents was evaluated as a replacement test for conventional drug susceptibility testing (DST). WHO did not proceed with the development of policy guidance for the use of the assay due to sub-optimal sensitivity compared with phenotypic DST in detecting resistance to fluoroquinolones and second-line injectable agents as well as uncertainty related to which mutations confer resistance to specific drugs. Recent improvements have been made to the assay, and, provided that sufficient data are available, a systematic review of line probe assays will be done in 2015 to update the 2008 WHO policy guidance on the use of these tests.

Recent advances in terms of cost and speed have made next generation sequencing more affordable and more accessible. It is anticipated that either or both of these approaches, correlated with phenotypic DST and patient outcome data, will help to clarify the molecular basis of resistance, especially among the second-line anti-TB drugs. WHO is currently overseeing a drug resistance surveillance project with the primary aim of determining the prevalence of resistance to pyrazinamide and fluoroquinolones among new and previously treated TB cases in several countries with a high TB burden (Chapter 5). All strains included in the project are undergoing phenotypic DST testing as well as DNA sequencing using both conventional and next generation sequencing technologies. WHO plans to convene an Expert Group in 2015 to review the evidence for the use of DNA sequencing platforms as a possible alternative to phenotypic DST and to use new knowledge to facilitate and guide the development of future rapid drug resistance detection assays.

9.1.3 Target product profiles (TPPs)

Diagnostic manufacturers are increasingly expressing the need to be informed about the type of TB diagnostics they should invest in, as well as the potential market size for these products. The development of target product profiles (TPPs) is therefore an important step to align the needs of end-users with the specifications and targets that product developers should meet in terms of the per-

formance and operational characteristics of such tests.¹

In April 2014, the WHO Global TB Programme convened a meeting on behalf of the Global Laboratory Initiative (GLI) and New Diagnostics Working Group (NDWG) to develop consensus on the minimal and optimal specifications of four different types of TB diagnostic tests that were identified by multiple stakeholders to be high priority. Extensive work by McGill University, FIND, Médecins Sans Frontières (MSF), the NDWG of the Stop TB Partnership and the GLI informed this process. A brief description of the four priority TPPs on which consensus was reached – all of which are designed for tests that can be implemented at low levels of the health system – and their agreed key performance characteristics is provided below. Detailed descriptions of the TPPs are included in the full meeting report.²

A point of care non-sputum based test capable of detecting all forms of TB

One of the most urgently needed tests is a rapid biomarker-based test that can diagnose pulmonary TB (PTB) and ideally also extrapulmonary TB (EPTB) using non-sputum samples (e.g., urine, blood, oral mucosal transudates, saliva, exhaled air) with the purpose of initiating TB treatment within the same clinical encounter or on the same day. Such a test should perform with a sensitivity at least as good as AFB microscopy in both HIV-positive and HIV-negative people and optimally have a sensitivity and specificity at least equivalent to the Xpert MTB/RIF assay for the detection of AFB smear-negative pulmonary TB, childhood intra-thoracic TB and EPTB.

A point of care triage test

Since most individuals suspected of having TB do not have the disease, a triage test could help to narrow down the population that needs confirmatory testing. A triage test needs to be a simple, low-cost test for use by first-contact providers in the community to rule out TB and direct individuals who require further evaluation to a confirmatory test (e.g. Xpert MTB/RIF or similar molecular test). A triage strategy that reduces testing with expensive tests and potentially enables more patients to be tested could benefit patients and health systems. Such a test would at a minimum need to achieve an overall sensitivity and specificity of 90% and 70% respectively, compared with confirmatory tests for pulmonary TB. Optimally, the performance characteristics would reach sensitivity and specificity values greater than 95% and 80% respectively, compared with confirmatory tests for pulmonary TB.

Rapid sputum-based test for TB detection at the microscopy level

A rapid, sensitive, easy to perform sputum-based test for TB detection that replaces sputum smear microscopy in decentralized settings (i.e. microscopy centres) has the

potential to improve programmes and patient care in two ways. First, it would increase the number of diagnosed and treated TB patients and thus reduce transmission; second, it would reduce morbidity because of earlier diagnosis and treatment. A test at the level of a microscopy centre would leverage existing infrastructure that is based on smear microscopy. Conceivably, NAATs or other technologies could be used. A test that is able to replace smears for both initial diagnosis and treatment monitoring (e.g. through detecting viable bacteria) is likely to be adopted more than a test that would only facilitate initial diagnosis. Optimally, such a test would achieve a diagnostic sensitivity for TB detection greater than 95% in comparison with culture with high specificity (greater than 98%). At a minimum, the test would show a sensitivity of more than 80% compared with culture and a specificity of greater than 98%.

Next generation test for DST at microscopy centres

Currently, there is only one first-line regimen for treating drug-susceptible TB, which includes isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E). Two alternative regimens have been evaluated for first-line therapy in Phase II clinical studies:^{3,4} REMox – R, moxifloxacin (M), Z, and E; and PaMZ – Pa824, M, and Z. If the planned Phase III studies show benefit of either one of these regimens, it is likely that at least one of these regimens will be introduced and implemented, at least initially, in parallel to HRZE. Optimally, a next generation test would allow for the diagnosis of TB disease and detection of drug resistance up-front to inform decision-making concerning the choice of first-line therapy, the presence of additional second-line drug resistance and need for further testing.

As a consequence, DST at the microscopy centre level will be needed. The TPP for this type of test was therefore primarily designed according to the intended use. Consensus was reached that the following anti-TB agents should ideally be included in resistance testing at the microscopy level (they are presented in order of decreasing priority):

1. rifampicin;
2. fluoroquinolones (including moxifloxacin);
3. isoniazid and pyrazinamide; and

¹ Kik SV et al. Tuberculosis diagnostics: which target product profiles should be prioritised? *Eur Respir J* 2014; 44(2):537–40.

² Report: Consensus meeting on high-priority target product profiles, 28–29th April 2014. Geneva, World Health Organization, 2014. Available at: <http://www.who.int/tb/laboratory/resource/en/>

³ Diacon AH et al. 14-day bactericidal activity of PA-824, bedaquiline, pyrazinamide, and moxifloxacin combinations: a randomised trial. *Lancet* 2012; 380(9846): 986–93.

⁴ Dorman SE et al. Substitution of moxifloxacin for isoniazid during intensive phase treatment of pulmonary tuberculosis. *Am J Respir Crit Care Med* 2009; 180(3): 273–80.

4. second-line injectable agents (aminoglycosides and capreomycin).

Optimally, all anti-TB agents would be included, but as a minimum at least rifampicin should be included.

9.1.4 New diagnostic technologies

The portfolio of new diagnostic technologies appears to have stalled and despite several assays being under development and even introduced into the market, no innovative technologies are expected to generate the necessary evidence for WHO evaluation 2015. As a priority, increased and targeted investment is needed to conduct assay evaluations of the most promising products to expedite regulatory approval as well as WHO review.

9.2 New drugs and drug regimens to treat and prevent TB

The anti-TB drugs currently used in first-line treatments are more than 40 years old. The regimen that is currently recommended by WHO for new cases of drug-susceptible TB is highly efficacious, with cure rates of around 90% in HIV-negative patients. Nonetheless, it requires six months of treatment with first-line drugs.¹ The regimens for treatment of MDR-TB currently recommended by WHO are lengthy (at least 20 months of treatment with second-line drugs for most patients), and are associated with multiple and sometimes serious side-effects and compounded by low cure rates (see [Chapter 5](#)). There are also interactions between some anti-TB drugs and antiretroviral therapy (ART) for people living with HIV. New drugs are required to shorten and simplify treatment, to improve the efficacy and tolerability of treatment for MDR-TB and to improve the treatment of TB among people living with HIV.

The status of the pipeline for new anti-TB drugs in August 2014 is shown in [Figure 9.2](#). In total, there are currently 10 new or repurposed drugs in Phase II or Phase III trials; one drug, rifapentine (a rifamycin that has a longer half-life than R) is in both Phase II and Phase III trials, for different indications.

The following sections highlight results published from October 2013 to September 2014 in terms of treatment of drug-susceptible TB, MDR-TB and latent TB infection.

9.2.1 Treatment of drug-susceptible TB

Fluoroquinolone-containing regimens (gatifloxacin and moxifloxacin) for the treatment of drug-susceptible TB

Two Phase III trials evaluating four-month combination regimens for treatment of drug-susceptible TB that include a fluoroquinolone were completed in 2013: the OFLOTUB trial, in which gatifloxacin (G) was substituted for ethambutol (E), and the ReMOX trial, in which moxifloxacin (M) was substituted for either ethambutol or isoniazid.

Results of the OFLOTUB trial were presented at the Union Conference in Paris in October 2013.² A total of

1836 patients were randomised in five African countries to receive either a four-month treatment composed of gatifloxacin 400 mg once daily – irrespective of body weight – combined with rifampicin, isoniazid and pyrazinamide in the intensive phase and maintained for the continuation phase of treatment with rifampicin and isoniazid (2RHGZ/2GRH), or the six-month standard WHO-recommended regimen (2RHEZ/4RH). The primary endpoint was an unfavourable outcome, measured as the total of treatment failure, recurrence and death or dropout during treatment measured 24 months following the end of treatment. The difference in unfavourable outcome [test-control] (modified intent-to-treat population, n=1356) was +3.5% (95% CI: -0.7%, 7.7%), with heterogeneity across countries (*p* for interaction 0.02). The ‘non-inferiority’ of the four-month to the standard regimen was thus not demonstrated for the primary endpoint – i.e. the trial failed to demonstrate that the gatifloxacin-containing four-month treatment regimen was not inferior to the standard six-month regimen.

The ReMOX trial tested the non-inferiority of a) seventeen weeks of isoniazid, rifampicin and moxifloxacin supplemented by pyrazinamide for the first eight weeks (INH-arm), and b) seventeen weeks of rifampicin and moxifloxacin supplemented by pyrazinamide and ethambutol for the first eight weeks (ETH-arm), to twenty-six weeks of isoniazid and rifampicin supplemented by ethambutol and pyrazinamide in the first eight weeks (control-arm). A total of 1931 patients were randomised in 50 sites located in nine countries. The number of patients classified as having a favourable treatment outcome (per protocol population) was 467 (92%) in the control arm, 436 (85%) in the INH-arm, and 419 (80%) in the ETH-arm. The risk differences of favourable outcomes when compared to the control were 6.1% (97.5% CI 1.7–10.5) for the INH-arm and 11.4% (6.7–16.1) for the ETH-arm, respectively, for a margin of non-inferiority set at 6%.³ Neither of the experimental arms met the non-inferiority criteria; modified intention to treat and sensitivity analyses gave consistent results. There was no difference between the incidence of grade 3 and 4 adverse events with 123 patient reports (19%) in the control arm 127 (19%) in the INH-arm and 111 (17%) in the ETH-arm.

These results add to those from the Rifaquin trial that evaluated the safety and efficacy of two treatment regi-

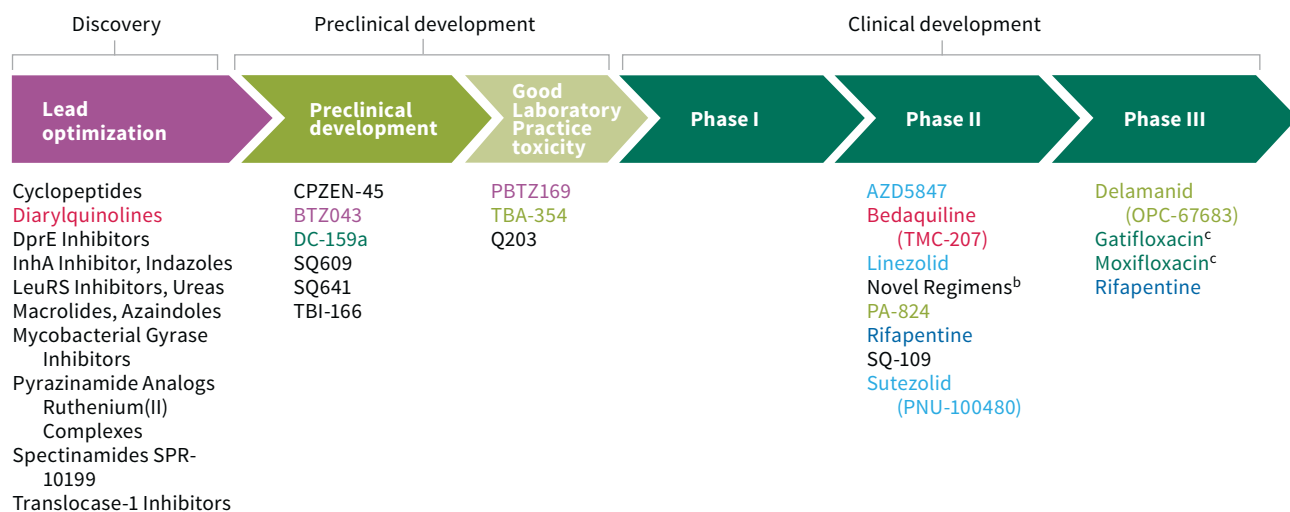
¹ A combination of rifampicin (R), isoniazid (H), ethambutol (E) and pyrazinamide (Z) for two months, followed by a four-month continuation phase of R and H (2RHEZ/4RH).

² Merle C et al. *A randomized controlled trial of a 4-month gatifloxacin-containing regimen for the treatment of drug-susceptible pulmonary tuberculosis: main efficacy and safety results of the Oflotub trial*. 44th Union World Conference on Lung Health, Late-breaker session, Paris, 2013.

³ Gillespie et al. REMoxTB: A Double-Blind Randomized Controlled Non-Inferiority Phase 3 Trial of Two Four-Month Moxifloxacin Regimens for the Treatment of Drug-Sensitive Tuberculosis. ICAAC 2014, Washington, DC, abstract L-1062.

FIGURE 9.2

The development pipeline for new TB drugs, August 2014^a



Chemical classes: fluoroquinolone, rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone

^a Details for projects listed can be found at <http://www.newtbdugs.org/pipeline.php> and ongoing projects without a lead compound series identified can be viewed at <http://www.newtbdugs.org/pipeline-discovery.php>

^b Combination regimens: NC-001-(J-M-Pa-Z), Phase IIa, NCT01215851; NC-002-(M-Pa-Z), Phase IIb, NCT01498419; NC-003-(C-J-Pa-Z), Phase IIa, NCT01691534; PanACEA-MAMS-TB-01-(H-R-Z-E-Q-M), Phase IIb, NCT01785186

^c These trials have been completed and results published. See chapter text for further details.

mens for drug-susceptible TB, in which moxifloxacin was substituted for isoniazid in the intensive phase of treatment and rifapentine was used in the continuation phase of treatment.¹ Both new regimens were well-tolerated. The six-month regimen with a weekly dose of rifapentine (1200 mg) and moxifloxacin in the continuation phase was not inferior to the currently recommended six-month regimen. However, the four-month regimen with twice-weekly doses of rifapentine (900 mg) and moxifloxacin in the continuation phase was clearly inferior to the currently recommended regimen.

From these three trials, it can be inferred that 4-month fluoroquinolone-containing regimens cannot be recommended for the treatment of uncomplicated smear-positive TB, and that the inclusion of a third-generation fluoroquinolone as a substitute for either ethambutol or isoniazid does not allow treatment to be shortened by two months.

Rifapentine

Spurred by murine studies demonstrating that substantial shortening of treatment duration was possible with the daily use of rifapentine (P), the TB Trials Consortium (TBTC) investigated whether high and daily doses of rifapentine could allow treatment for drug-susceptible TB to be shortened. TBTC Study 29 (a Phase II trial) compared two-month culture conversion in smear-positive pulmonary TB patients receiving standard therapy of isoniazid, pyrazinamide, ethambutol and randomized to combined treatment with either rifampin 10mg/kg or rifapentine 10 mg/kg, all given 5 days per week and

with no food instructions.² There was a non-significant increase in sputum conversion of ~3% on both solid and liquid media in the rifapentine arm; the safety and tolerability of the rifapentine regimens was also good. Immediately following this study, TBTC implemented Study 29X, which enrolled 334 sputum smear-positive pulmonary TB patients in 2011 and 2012.³ Patients were randomly assigned to standard therapy with isoniazid, pyrazinamide, and ethambutol supplemented by either rifampin 10 mg/kg or rifapentine in doses of 10, 15 or 20 mg/kg, given seven days a week with food supplements. All regimens were well tolerated and safe. At eight weeks, sputum conversion on solid media was 83% for the rifampin arm and 91–98% in the rifapentine arms; in MGIT liquid medium the rates were 60% and 72–76%. These rates were judged to support further investigation of whether treatment could be shortened using daily doses of rifapentine.

A Phase I study was conducted by the National Institutes of Health (NIH)/AIDS Clinical Trial Group (ACTG)

¹ Jindani A et al. 2013. *A Multicentre Randomized Clinical Trial to Evaluate High-dose Rifapentine with a Quinolone for Treatment of Pulmonary TB: The RIFAQUIN Trial*. Oral abstract and paper 147LB. 20th Conference on Retroviruses and Opportunistic Infections (CROI), March 3–6, 2013, Atlanta.

² Dorman S et al. Substitution of Rifapentine for Rifampin During Intensive Phase Treatment of Pulmonary Tuberculosis: Study 29 of the Tuberculosis Trials Consortium. *J Infect Dis*. 2012, 206 (7): 1030–1040.

³ Dorman S et al. *A dose-ranging study of daily rifapentine-containing regimens for intensive phase treatment of pulmonary TB: Tuberculosis Trials Consortium Study 29x*. Abstract OP-230-02., 44th Union World Conference on Lung Health; Paris, France; Nov 2, 2013.

to investigate novel dosing strategies with high dose daily rifapentine designed to increase drug exposures (A5311). This study enrolled 44 healthy volunteers in two arms: Arm 1 administered 20 mg/kg either once daily or split as 10 mg/kg twice a day, in two periods, and Arm 2 administered 15 mg/kg with an egg or a low fat breakfast, also twice a day. Of the 44 patients, 20 discontinued their treatment early, and six developed rifamycin hypersensitivity syndrome, leading to early termination of treatment. Both dividing the dose and giving an egg increased exposure significantly (38–47%). Exposures obtained were 34–117% higher than those achieved in TBTC Study 29X (described above).¹

Two additional Phase II studies of daily rifapentine in the treatment of active TB were completed in 2013. Both used moderate doses of rifapentine, of 7.5–10 mg/kg.

- The first trial (RioMAR) was conducted in Rio de Janeiro, Brazil. It was originally supported by the National Institute of Allergy and Infectious Diseases (NIAID), and subsequently by TBTC. RioMAR enrolled adults with sputum smear-positive pulmonary TB, randomly assigned to a regimen of rifapentine 7.5 mg/kg/day + moxifloxacin 400 mg/day + isoniazid and pyrazinamide (PMHZ), or a control regimen of rifampin 10 mg/kg/day, ethambutol, isoniazid and pyrazinamide (REHZ). Directly-observed treatment was administered 7 days/week for 8 weeks. The study enrolled only 121 of the approximately 210 patients that were anticipated. The PMHZ regimen was safe and well tolerated. Stable culture conversion at the end of the intensive phase on Lowenstein-Jensen (LJ) medium was 51/60 (85%) in the PMHZ arm versus 44/51 (86%, $p=0.85$) in the REHZ arm; and in MGIT medium was 39/46 (85%) in the PMHZ arm versus 29/42 (69%, $p=0.08$) in the REHZ arm. In the per-protocol group, proportions with stable conversion at the end of the intensive phase in MGIT medium were 34/36 (94%) in the PMHZ arm versus 27/37 (73%, $p=0.01$) in the REHZ arm.²
- The second Phase II trial was conducted in Cape Town, South Africa. This adaptive design, two-stage, randomized clinical trial assessed the activity and safety of intensive phase regimens containing rifapentine 450 mg daily or rifapentine 600 mg daily or rifampin 600 mg daily, in addition to isoniazid, pyrazinamide, and ethambutol for the treatment of drug-susceptible, smear-positive pulmonary TB in adults at a single study centre in Cape Town, South Africa. As demonstrated in other studies, rifapentine at these doses was safe and well-tolerated. There was a trend towards poorer efficacy with the rifapentine 450 mg regimen compared with the 600 mg regimen.³

The planned TBTC Study 31 will compare two four-month daily rifapentine-based regimens for treatment of drug-susceptible TB with standard six-month daily rifampin-

based therapy. The intensive phases in the two regimens are expected to be isoniazid, pyrazinamide, ethambutol combined with rifapentine 20 mg/kg, or isoniazid, pyrazinamide, moxifloxacin combined with rifapentine 20 mg/kg, both dosed seven days a week, with food. Continuation phases will be isoniazid + rifapentine in the first arm, and isoniazid+moxifloxacin+rifapentine in the second arm. The study will enroll approximately 2400 people, and will be conducted in collaboration with the ACTG. Enrollment is expected to begin in the first half of 2015.

9.2.2 Treatment of TB in children

The Global Alliance for TB Drug Development has partnered with the WHO Global TB Programme and the WHO Department of Essential Medicines and Health Products to initiate the project Speeding Treatments to End Pediatric Tuberculosis (STEP-TB), funded by UNICEF. The goal of STEP-TB is to make available and ensure access to correctly dosed, properly formulated, affordable, high-quality pediatric TB medicines that meet the current WHO guidelines for these drugs. The project's main focus is the lowering of market barriers that are key impediments to supplying purchasers, providers, and ultimately patients with appropriate, high-quality TB medicines for children. The project will act as a market catalyst and creator by facilitating the availability, uptake, and use of improved pediatric TB medicines – incentivizing manufacturers to produce medicines to address a major public health issue.

9.2.3 New drugs for the treatment of MDR-TB

For the first time in more than 40 years, two new molecular entities were recently approved by regulatory authorities for the treatment of MDR-TB. In December 2012, the US Food and Drug Administration (FDA) approved bedaquiline “as part of combination therapy to treat adults with multi-drug resistant pulmonary TB when other alternatives are not available”. Following this, WHO produced interim policy guidance on the use of bedaquiline in the treatment of MDR-TB, which was published in June 2013.⁵ In November 2013, the Committee for Medicinal Prod-

¹ Dooley et al. *Rifapentine safety and PK with novel dosing strategies to increase drug exposures for TB: ACTG A5311*. Abstract 816. 21st Conference on Retroviruses and Opportunistic Infections, Boston, Massachusetts, USA, March 3–6, 2014.

² MB Conde et al. *A Phase 2 Trial of a rifapentine plus moxifloxacin-based regimen for pulmonary TB treatment*. 21st Conference on Retroviruses and Opportunistic Infections (CROI 2014). Boston, March 3-6, 2014. Abstract 93.

³ At the time this report went to press, results were scheduled to be presented at the 45th Union World Conference on Lung Health, Barcelona, Spain in October 2014.

⁴ <http://www.tb Alliance.org/children/response/>

⁵ The use of bedaquiline in the treatment of multidrug-resistant tuberculosis: Interim policy guidance. Geneva, World Health Organization, 2013 (WHO/HTM/TB/2013.6). Available at: http://apps.who.int/iris/bitstream/10665/84879/1/9789241505482_eng.pdf?ua=1

ucts for Human Use (CHMP) of the European Medicines Agency (EMA) recommended the granting of a conditional marketing authorisation for delamanid for use as part of an appropriate combination regimen for pulmonary MDR-TB in adult patients “when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability”. In November 2013, the EMA CHMP recommended granting a conditional marketing authorisation for bedaquiline with the same indication, that was formally approved in April 2014.

Further to the Phase II trial carried out to investigate the safety and efficacy of bedaquiline in the treatment of MDR-TB, a Phase III trial to investigate the safety and efficacy of bedaquiline when used in combination with short MDR-TB regimens of nine and six months duration respectively is scheduled to start before the end of 2014. This will take place under the umbrella of the STREAM trial, in which a short regimen of nine months duration (Arm B) is being compared to the current WHO recommended standard of care for MDR-TB (Arm A). Two new bedaquiline-containing arms will be added: Arm C is a nine-month all oral regimen in which bedaquiline replaces kanamycin, and Arm D is a shortened simplified six-month regimen containing bedaquiline.

Delamanid (OPC-67683) is currently being tested in a Phase III clinical trial as an adjunct to an optimized background regimen (OBR) for the treatment of MDR-TB. The trial is comparing six months of treatment with delamanid plus OBR versus placebo plus OBR alone, including a full 24-month follow-up. Enrolment in the study was completed in November 2013 with the randomization of approximately 500 patients. Key features of this trial are the inclusion of once-daily dosing after a two-month induction phase, the inclusion of moxifloxacin in the optimized background regimen and the inclusion of HIV-positive patients on treatment with ART in a sub-study conducted in South Africa. The trial is expected to be completed in 2016.

Simultaneously, two trials are being conducted to evaluate delamanid for MDR-TB in children. The first trial is a 10-day open label pharmacokinetic (PK) study of delamanid plus OBR. Patients who successfully complete this trial may continue enrolment in a second, open-label study (Trial 242-12-233) to assess the safety, tolerability, PK, and efficacy of delamanid plus OBR over a six-month treatment period. These trials are expected to be completed in 2017.

9.2.4 Trials of new regimens for the treatment of drug-susceptible and/or drug-resistant TB

Besides individual compounds, new combinations of drugs are being tested in various Phase II trials. The NC-002 trial, conducted by the Global Alliance for TB Drug Development in South Africa and the United Republic of Tanzania, investigated the efficacy, safety and

tolerability of the combination of PA-824 (a nitroimidazole) + moxifloxacin + pyrazinamide (Pa-M-Z) after 8 weeks of treatment in adult patients with newly diagnosed drug-susceptible or smear-positive pulmonary MDR-TB. Two doses of PA-824 were tested (100 mg and 200 mg), but MDR-TB patients only received the regimen with the higher dose. The primary endpoint was the rate of change in colony forming units (CFU) from sputum on solid culture over eight weeks. Results of this trial, presented at the 20th International AIDS Conference in Melbourne, Australia in July 2014, showed that the Pa-M-Z regimen had active bactericidal activity against both drug-susceptible and MDR-TB over two months and that this bactericidal activity was significantly greater than that of HRZE therapy in patients with drug-susceptible TB using the Pa(200mg)-M-Z regimen.¹

The NC-003 trial has been testing the 14 day early bactericidal activity (EBA) of various combinations of clofazimine, bedaquiline, PA-824 and pyrazinamide in patients with drug-susceptible TB.² The trial randomized 105 subjects with newly diagnosed smear-positive pulmonary TB to seven parallel treatment arms: 1) (Control) (HRZE); 2) clofazimine (C) alone; 3) Z alone; 4) bedaquiline (B), PA-824 (PA), Z; 5) B, PA, Z, C; 6) B, PA, C; and 7) B, Z, C. Sputum was cultured on solid agar for counts of CFU and in liquid culture for time to positivity (TTP). The primary endpoint was the rate of change in logCFU per ml sputum over days 0–14. It was found that PA-824 with B and Z had robust EBA and should be tested in a trial of longer duration. Clofazimine did not have demonstrable EBA alone or in combination over 14 days of therapy. Further studies should be conducted over longer periods to determine if clofazimine contributes bactericidal or sterilizing activity to a regimen when administered for longer than 14 days.

The MAMS-TB-01 trial, conducted by the PanACEA consortium and funded by the European and Developing Countries Clinical Trials Partnership (EDCTP), is evaluating new combination regimens using a new adaptive study design. This design allows the efficient evaluation of multiple regimens by incorporating interim analyses that allow for the early exclusion of regimens that show little potential to shorten treatment.³ The drugs included in the combination regimens are H, R, Z, E, M and SQ-109. The end-point of the trial is time to culture conversion in liquid media. The trial started in May 2013.⁴ In March 2014,

¹ Everitt D, et al. *Randomized trial of the bactericidal activity of 8-weeks treatment with moxifloxacin, Pa-824, and pyrazinamide in drug sensitive and multi-drug resistant tuberculosis*. 20th International AIDS Conference, Melbourne, Australia, 2014 – Abstract B14TB.

² Everitt D et al. *14 Day EBA study of clofazimine alone and in combination*. 44th Union World Conference on Lung Health, Late-breaker session, Paris, 2013.

³ Phillips P et al. *Innovative trial designs are practical solutions for improving the treatment of tuberculosis*. *J Infect Dis*. 2012;205 Suppl 2:S250–7.

⁴ <http://clinicaltrials.gov/show/NCT01785186>

the independent data monitoring committee (IDMC) reviewed safety and efficacy data including several sensitivity analyses and secondary efficacy endpoints. Based on predefined stopping rules to allow for exclusion of regimens that were not likely to reach a set hazard ratio of at least 1.8 at the end of the trial, the IDMC recommended the termination of recruitment into the two arms including SQ-109 (H, Rstandard, Z, SQ-109 300 mg, and H, R 20 mg/kg, Z, SQ-109 300 mg), as there was insufficient evidence that these regimens could shorten treatment. Importantly, there was no evidence that either arm was inferior to standard treatment (the control arm) in terms of efficacy. There was, however, sufficient evidence that the other intervention arms using high doses of rifampicin with or without moxifloxacin (H, R 20 mg/kg, Z, M 400 mg; H, R 35 mg/kg, Z, E) could shorten treatment and thus patient enrolment in these other arms continues.¹

9.2.5 New developments in the treatment of latent TB infection

New drugs or drug regimens are also being tested for the treatment of latent TB infection (LTBI) in people without active TB disease (see *Global TB Report 2013*²). In 2011, CDC's TB Trials Consortium published its report of Study 26, demonstrating the non-inferiority of a 12-dose, once-weekly H/P regimen for treatment of LTBI.³ Further, the Study 26 authors have presented data supporting non-inferiority of the once-weekly LTBI regimen in both children aged 2–18 and in HIV-positive people aged >13 years not receiving concurrent ART.⁴ The Adult AIDS Clinical Trials Group began trial A5279 in May 2012; by July 2014, the trial had enrolled 2075 of its projected sample size of approximately 3000 participants. This trial compares 30 days of a daily dose of 300 mg of isoniazid plus rifapentine 600 mg with nine months of a daily dose of 300 mg of isoniazid. Enrollees are HIV-positive people with a positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) result, or residence in a country with an estimated TB prevalence of 60 or more per 100 000 population. The primary outcome is active TB, assessed in the intention-to-treat (ITT) population.

9.3 New vaccines to prevent TB

The slow decline in TB incidence globally and the growing problem of MDR-TB both highlight the critical need for new effective TB vaccines. The Bacille-Calmette-Guérin (BCG) vaccine for the prevention of TB is almost 100 years old, and while the vaccine protects against severe forms of TB in children (TB meningitis and miliary TB), its efficacy in preventing pulmonary TB in adults is highly variable. BCG is also not recommended for use in infants known to be infected with HIV, due to the risk of disseminated BCG disease. A recent meta-analysis, however, showed the efficacy of BCG in preventing *M. tuberculosis* infection in children.⁵ The development of techniques

for genetic manipulation of mycobacteria, completion of the genome sequence of *M. tuberculosis* in the 1990s, and recent advances in immunology and systems biology provide historic opportunities for developing a new generation of TB vaccines capable of achieving dramatically higher levels of impact.

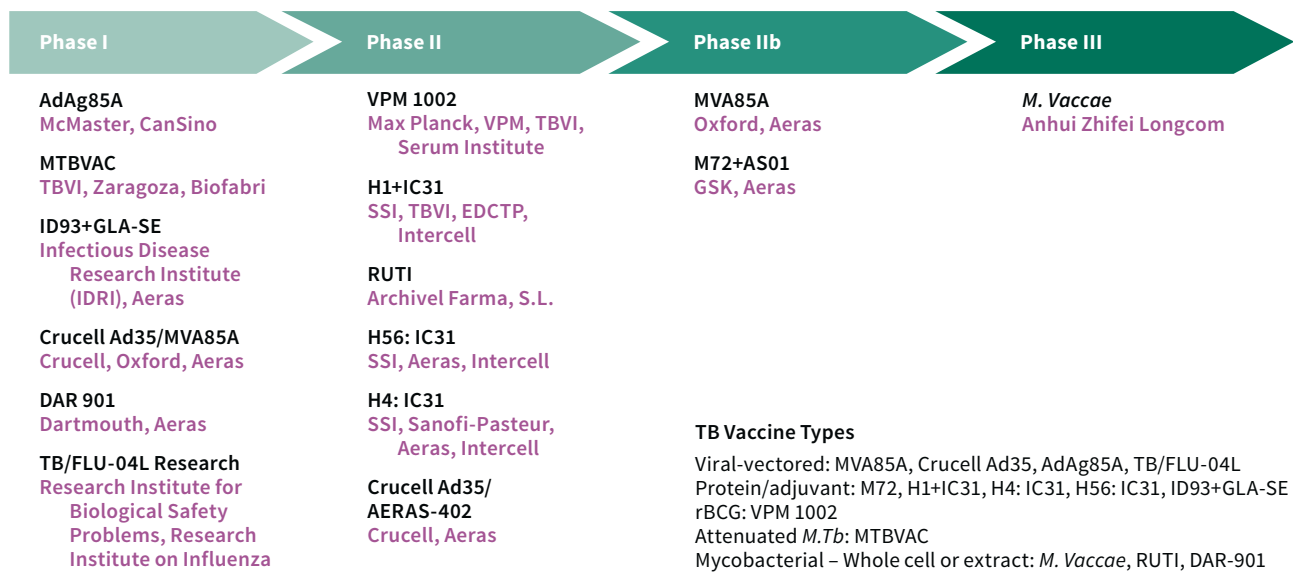
For the past decade, two major strategies have been used to develop new vaccines for prevention of TB.⁶ One approach has been to develop vaccines that would do better than BCG and replace it – such as an improved version of BCG or a new attenuated live *M. tuberculosis* vaccine. The second strategy has been a 'prime-boost' strategy in which BCG continues to be given to neonates (as is done currently, since it prevents TB in infants and children), and a new vaccine is given to adolescents and/or adults as a 'booster' dose to provide longer-term protection against TB disease or *M. tuberculosis* infection. Recent modelling of the public health impact at global level suggested that an adolescent and adult vaccine with 60% efficacy delivered to just 20% of the target population could avert up to 50 million new TB cases over 25 years.⁷ The potential for an adult/adolescent vaccine to have a rapid impact compared with an infant vaccine has shifted the focus of TB vaccine development towards a new paradigm in which the development of a diverse pipeline of new TB vaccine candidates that target the prevention of TB in this older population is emphasized. Scientific advances have also enabled the pursuit of more sophisticated approaches to vaccine design. The global pipeline of TB vaccine candidates in clinical trials is more robust than at any previous period in history, now including recombinant BCGs, attenuated *M. tuberculosis* strains, recombinant viral-vectored platforms, protein/adjuvant combinations, and mycobacterial extracts.

The status of the pipeline for new vaccines in August 2014 is shown in **Figure 9.3**. There are currently 15 vaccine candidates in clinical trials. Most are designed for prevention of TB, either to prevent infection (pre-exposure) or to prevent primary progression to disease or reactivation

- 1 <http://panacea-tb.net/mams-study-has-completed-first-interim-analysis/>
- 2 *Global Tuberculosis Report 2013*. Geneva, World Health Organization, 2013 (WHO/HTM/TB/2013.11). Available at: http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf
- 3 Sterling T et al. Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection. *N Engl J Med* 2011; 365;23: 2155–66.
- 4 Sterling T et al. *Three Months of Weekly Rifapentine + INH for M. tuberculosis Infection in HIV-infected Persons*. Poster presented at Conference on Retroviruses and Opportunistic Infections, Boston, Massachusetts, USA, March 3–6, 2014.
- 5 Roy A et al. Effect of BCG vaccination against Mycobacterium tuberculosis infection in children: systematic review and meta-analysis. *BMJ* 2014;349:g4643 doi: 10.1136/bmj.g4643.
- 6 Evans TG et al. Preventive vaccines for tuberculosis. *Vaccine* 2013; 31S: B223– B226.
- 7 A model of the global public health impact of new TB vaccines was commissioned by Aeras and developed by Applied Strategies. Publication is anticipated in 2015.

FIGURE 9.3

The development pipeline for new TB vaccines, August 2014



of latent TB (post-exposure). Two are BCG replacement vaccines and one is proposed as an immunotherapeutic agent, to improve responsiveness to chemotherapy or prevent relapse or re-infection. One vaccine has completed Phase II studies; another will soon enter a Phase IIb study.

MVA85A is an attenuated vaccinia virus-vectored vaccine candidate expressing Ag85A of *M. tuberculosis*. It was designed at Oxford University as a booster vaccine for BCG vaccinated infants and the first Phase IIb trial of this vaccine was conducted by the Oxford Emergent TB Consortium and Aeras in South Africa from 2009 to 2012, with results published in early 2013.¹ An additional Phase II trial of MVA85A, conducted in adults living with HIV in Senegal and South Africa, was recently completed. The study was a safety and immunogenicity trial in which 650 BCG-vaccinated, HIV-positive participants were enrolled. The results are expected to be available in early 2015.

M72 +AS01_E is a protein subunit vaccine from GSK, formulated in a novel adjuvant to enhance immunogenicity. It contains a fusion protein of the *M. tuberculosis* antigens 32A and 39A in the adjuvant AS01_E. BCG-vaccinated, interferon gamma release assay (IGRA) positive adults will be enrolled from three TB-endemic countries in Africa: South Africa, Kenya and Zambia. This large Phase IIb study, being conducted by GSK and Aeras, aims to enrol 3600 HIV-negative adults. The primary endpoint will be the protective efficacy of two doses of M72 + AS01_E against pulmonary TB disease. Secondary endpoints include safety and immunogenicity.

Crucell Ad35/AERAS-402 is an adenovirus-vectored

vaccine candidate expressing three *M. tuberculosis* antigens: Ag85A, Ag85B and TB10.4. It is designed as a booster vaccine for infants, adolescents and adults. Although started as a Phase IIb proof-of-concept trial in infants, the now completed trial was revised based on preliminary data to be a smaller Phase II study with safety and immunogenicity as primary endpoints.

Of note, **Crucell Ad35/AERAS-402 and MVA85A** are now being tested in early phase trials in *combination*, to try to drive a balanced CD4+/CD8+ immune response. One or two doses of Crucell Ad35 followed by a dose of MVA85A compared with 3 doses of Crucell Ad35 are being evaluated in a combined Phase I/Phase II trial in adults in the United Kingdom by Oxford University, Aeras and Crucell, for safety and immunogenicity.

Three vaccines are protein subunit adjuvanted vaccines, initially developed by the Statens Serum Institute in Copenhagen, Denmark. **Hybrid 1:IC31** contains Ag85B and ESAT-6 in an adjuvant, IC31. **H56:IC31** contains antigens 85B and ESAT6 as well as AgRv2660c, which is considered a “latency antigen”. **H4:IC31**, now being developed with Sanofi Pasteur and Aeras, is a fusion protein candidate that expresses Ag85B and TB10.4; the latter antigen is from the same gene family as ESAT-6. H4 and H56 are currently each being evaluated in Phase II studies in Africa with Aeras (and also with the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) network and the HIV Vaccine Trials Network (HVTN) in conjunction with NIAID). In addition, the **H4:IC31** candidate is being assessed in a Phase II proof of concept study for its ability to prevent *de novo* infection with *M. tuberculosis* among IGRA-negative, HIV-uninfected South African adolescents at high risk of acquiring *M. tuberculosis* infection (**Box 9.2**).

¹ Tameris MD, et al. Safety and efficacy of MVA85A, a new tuberculosis vaccine, in infants previously vaccinated with BCG: a randomised, placebo-controlled phase 2b trial. *Lancet*. 2013. 381:9871; 1021–1028.

VPM 1002, originally developed at the Max Planck Institute of Infection Biology with further development by Vakzine Projekt Management, the Tuberculosis Vaccine Initiative (TBVI), and Serum Institute of India, is a live recombinant vaccine. It has been derived from the Prague strain of BCG into which the listerolysin gene from *Listeria monocytogenes* has been cloned and the urease gene deleted to improve immunogenicity. A Phase IIa trial of this vaccine has recently been completed in South Africa. A second Phase II trial will assess the safety and immunogenicity of the vaccine in HIV exposed and unexposed newborns.

RUTI is a non-live vaccine based on fragmented, detoxified *M. tuberculosis* bacteria encapsulated in liposomes. RUTI is being developed by Archivel Pharma as an immunotherapeutic vaccine. A Phase II trial in South Africa was completed recently and a Phase III trial is planned.

In addition to the vaccine candidates described above, AnHui Longcom, a Chinese pharmaceutical company, is conducting a Phase III clinical trial in China to study the efficacy and safety of a lysate of *M. vaccae*, in the prevention of TB in high risk individuals (PPD>15mm). *Vaccae*TM is currently licensed in China as an adjunct to standard antimicrobial therapy.

There are five vaccine candidates in Phase I clinical trials:

- **MTBVAC** is being developed by the University of Zaragoza, Institut Pasteur, BIOFABRI and TBVI. It is a live *M. tuberculosis* strain attenuated via deletions of the *phoP* and *fadD26* genes. It is the first live attenuated *M. tuberculosis* vaccine to enter a Phase I clinical trial, a study which recently was completed. Phase II studies in neonates are being planned, with the potential for testing in adolescents and adults under consideration.
- **ID93+GLA-SE** is a recombinant fusion protein formulated in the novel adjuvant, GLA-SE. It is being developed by the Infectious Disease Research Institute (IDRI) in collaboration with Aeras. It expresses three *M. tuberculosis* virulence antigens (Rv2608, Rv3619 and Rv3620) and one *M. tuberculosis* latency antigen (Rv1813). A Phase I trial in adults in South Africa to assess safety and immunogenicity recently was completed. A Prevention of Recurrence trial (**Box 9.2**) is being planned with Aeras.
- **Ad5 Ag85A** is an adenovirus serotype 5 vector expressing Ag85A. It has been developed by McMaster University with support from CanSino, a Chinese biotechnology company based in Tianjin. The vaccine was recently evaluated in a Phase I trial that demonstrated no vaccine-related serious adverse events and showed greater immunogenicity in the study group primed with BCG. Further studies, including a Phase I safety and immunogenicity study of aerosol vaccine administration, are being planned.
- **DAR 901** is a heat-inactivated *M. obuense* strain of

mycobacteria. It has been developed by investigators at Dartmouth University and manufactured by Aeras. A Phase I safety and immunogenicity study in 77 BCG-vaccinated, HIV-infected and -uninfected individuals recently was initiated in the United States of America.

- **TB/FLU-04L** is a recombinant influenza vectored vaccine candidate developed by the Research Institute for Biological Safety Problems and the Research Institute on Influenza, with support and assistance from international experts. The influenza virus strain A/Puerto Rico/8/34 (H1N1) was used as a parent strain for construction of an attenuated replication-deficient vector expressing *M. tuberculosis* antigens Ag85A and ESAT-6. It was designed as a mucosal “boost” vaccine for infants, adolescents and adults. A Phase I trial in BCG-vaccinated QuantiFERON TB-Gold negative healthy adult volunteers using intranasal administration was recently completed, and a Phase IIa trial is planned.

Research on new TB vaccines is at a critical juncture. Despite the diversity that already exists in the global portfolio of TB vaccine candidates in clinical trials, there is growing recognition among scientists and researchers in the field that the immunological strategies being pursued are too similar.¹ In the absence of known immune correlates for either protective immunity against TB or control of infection, the portfolio must be further diversified so that candidates explore more immunological ‘space’. There is already a robust pipeline of candidates being evaluated pre-clinically – including nucleic acid-based (DNA and RNA) vaccines – and these pursuits may help to broaden the diversity of the clinical portfolio and fill the scientific gaps that currently exist. In addition to diversifying vaccine candidates, diversifying vaccine delivery strategies has also evolved into an important strategic concept. In particular, aerosol delivery of vaccines directly to the lungs via inhalation, either alone or in combination with an injected vaccine, has received increased attention, given that the primary route of *M. tuberculosis* infection is through the lungs. To rationalize and streamline the advancement of TB vaccine candidates, consensus has been developed among key stakeholders on ‘stage-gating’ criteria for new TB vaccines, and increased emphasis is being placed on global coordination among key stakeholders to advance a common research agenda.

To supplement these existing efforts, a re-prioritized focus on early stage, translational research is also underway. In accordance with this shift in emphasis, additional resources will be directed towards the pursuit of novel study designs. This will focus on testing hypotheses about immunological mechanisms, delivery methods, and candidate biomarkers, and on broadening preclinical scientific approaches, antigen selection strategies, and evaluation

¹ Evans TG et al. Preventive vaccines for tuberculosis. Vaccine 31S (2013) B223–B226.

BOX 9.2

Novel Clinical Trial Strategies for TB Vaccine Development

Clinical trials of TB vaccines are major undertakings that can be expensive and lengthy. Accordingly, new clinical research strategies are being undertaken that will more efficiently provide answers about *M. tuberculosis* pathophysiology relevant to the development of new TB vaccine concepts, and about the safety, immunogenicity and potential clinical impact of TB vaccine candidates. A greater emphasis on early experimental/translational medicine trials will answer focused basic hypotheses about TB vaccine immune responses and delivery methods. Simultaneously, mid-stage proof-of-biological activity trial designs are being implemented to evaluate a variety of efficacy endpoints, including prevention of *M. tuberculosis* infection in high risk populations and prevention of the recurrence of TB disease in people recently treated for TB. These proof-of-activity studies will assess, in a time- and cost-efficient way, whether vaccine candidates have a clinically-relevant biologic effect. Together, these strategies will inform basic TB vaccinology and vaccine portfolio management decisions in a resource- and time-efficient manner.

Experimental medicine studies

Several small, early-phase human studies of TB vaccine concepts are currently underway (with more planned) to address specific scientific questions and provide data to inform future vaccine development. Examples of questions to be addressed in such studies include assessments of mucosal versus systemic immune responses resulting from different delivery methods and vaccine platforms; comparisons of various dosing regimens; immune responses to 'non-dominant' mycobacterial antigens; and the potential role of antibodies in TB prevention. These experimental medicine studies will allow comparative evaluation of current vaccine candidates with novel vaccine concepts, such as non-protein antigens or varied antigen/adjuvant compositions. Low dose *M. tuberculosis* challenge studies in nonhuman primates (NHPs) and other animal models will be carried out in parallel to these small

clinical studies with identical assessment of immunogenicity, to learn more about protective immunity and the predictive value of various animal models in an iterative manner. Innovative studies are also underway in an effort to develop a safe yet predictive human challenge model for future vaccine evaluations.

Prevention of infection

The first Phase II prevention of infection proof-of-activity study has been initiated in South Africa. This study, which is being conducted by the South African Tuberculosis Vaccine Initiative (SATVI) and Aeras, with support from Sanofi Pasteur, Statens Serum Institut and multiple funders, will evaluate the safety, immunogenicity and ability to prevent de novo *M. tuberculosis* infection of the H4:IC31 protein-adjuvant combination vaccine. The study also will evaluate the effect of BCG revaccination on these endpoints. The study is being conducted among approximately 1000 South African adolescents, a much smaller number than would normally be required due to the high annual rate of *M. tuberculosis* infection in this population. A series of prevention of infection studies, utilizing various new vaccine candidates, is being planned.

Prevention of recurrent disease

Planning is underway to initiate a Phase II proof-of-concept trial of two adjuvanted recombinant protein candidates: H56:IC31 and ID93+GLA-SE. This trial will assess the ability of these vaccine candidates compared with placebo to prevent recurrent TB disease in adults recently completing successful treatment for active, drug-sensitive pulmonary tuberculosis. Approximately 450 subjects per arm will be enrolled in this proof-of-activity trial, a much smaller sample size than would be required for a classic Phase IIb prevention of disease efficacy trial in the broader population. This is due to the relatively high rate of recurrent TB in this population.

strategies to ensure that a more diverse pipeline of new TB vaccine candidates moves forward into clinical trials.¹

9.4 The post-2015 global TB strategy: the critical role of research and development

The new WHO post-2015 global TB strategy, endorsed in May 2014 by the WHA, includes the target of a 95% reduction in TB mortality by 2035 worldwide (compared with 2015 levels) and a 90% reduction in TB incidence (compared with 2015 levels). These reductions will require novel tools for TB control allowing quicker and better diagnosis, treatment and prevention, with simultaneous efforts to optimize the use of existing technologies

for TB prevention, diagnosis and treatment globally. To highlight the crucial role of research in ending the global TB epidemic, the WHO post-2015 global TB strategy includes "Intensified Research and Innovation" as one of three fundamental pillars (Chapter 1). This is further subdivided into two essential and complementary areas: (1) Discovery, development and rapid uptake of new tools, interventions and strategies; and (2) Research to optimize implementation and impact.

The "research pillar" addresses research across its full continuum, from fundamental research for better understanding of human TB and discovery of new diagnostics, drugs and vaccines, to operational research for effective introduction and scale up of new tools and strategies within the larger context of improved health systems. The "research pillar" will be essential to the success of the two other pillars and the achievement of post-2015 global TB targets.

¹ Brennan MJ and Thole J, Eds. Tuberculosis vaccines: A strategic blueprint for the next decade. *Tuberculosis*. 2012; 92: Supplement 1; S6–S13.

Fundamental science is necessary to drive innovations in new tools for improved TB care and control. Research is required to better characterize *M. tuberculosis* and to improve understanding of the interaction between the bacillus and the human host, as a basis for maintaining the flow of new technologies into the product pipeline. Researchers are making great strides in redefining the spectrum of TB disease and the transition from latent to active TB, and developing a better understanding of the behaviour of *M. tuberculosis* within the host. This progress is expected to deliver better knowledge about pathogenesis and identification of biomarkers and bio-signatures relevant to new TB diagnostics. It is also expected to point to new targets for anti-TB drugs as well as early indicators of protective immunity, vaccine efficacy and early

response to treatment. Such developments will facilitate the selection and testing of new interventions.

Biomedical research will need to be integrated as a critical component of the post-2015 global TB strategy. Although collaboration and consultation already exist, creating even closer connections among scientific disciplines (for example, biomedical research, epidemiology and operational research) will further support this integration.

The need for more and expanded operational research to optimize implementation and adopt innovations will require extensive work at the country level, for example to generate essential data on the epidemiology of TB and universal health coverage. Similarly, adaptation of global recommendations and policies at the national level will be necessary.

ANNEX 1

**Access to
the WHO global
TB database**

Accessing TB data using the WHO Global TB Programme website

Most of the data collected annually for the production of the WHO global TB report are available online on the WHO website at www.who.int/tb/data. This page gives you access to the following resources:

1. Country profiles

You can view and download profiles for all 216 countries and territories that report TB data to WHO each year, and not just the 22 high burden countries shown in the global TB report. The profiles are generated on-demand directly from the global TB database and therefore may include updates received after publication of the global TB report.

You can also view and download TB financial profiles for over 100 countries and territories that report detailed TB financial data to WHO.

2. CSV data files

This is a primary resource for anyone interested in conducting their own analyses of the records in the global TB database.

You can download data reported by countries such as time series for case notifications and treatment outcomes and also WHO's estimates of TB burden as comma-separated value (CSV) files covering all years for which we have data. You can import these CSV files into many spreadsheet, statistical analysis and database packages.

You can also download a data dictionary which defines each of the variables available in the CSV files.

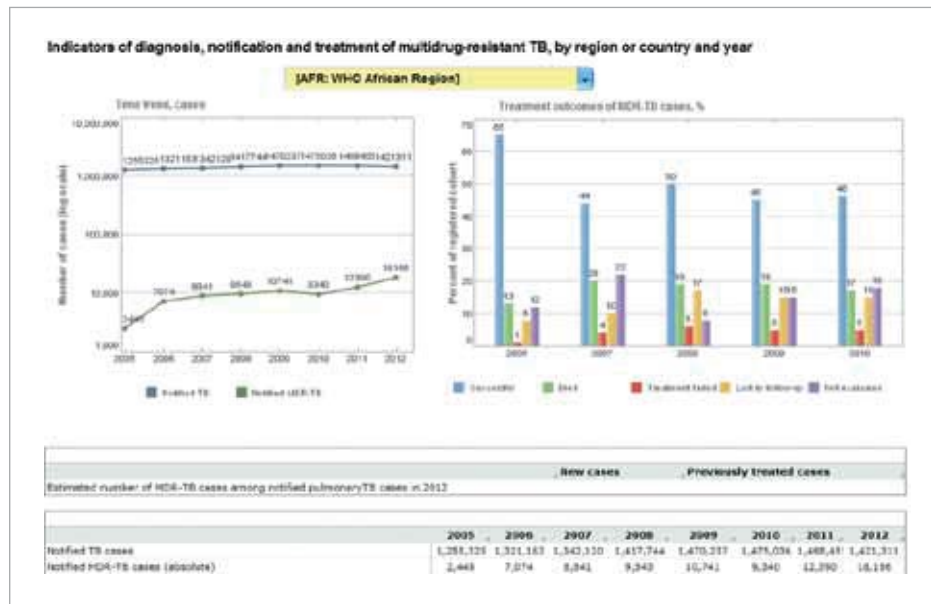
The CSV files are generated on-demand directly from the global TB database, and therefore may include updates received after publication of the global TB report.

3. Data visualisations

You can choose from a number of interactive web pages to view maps, graphs and underlying data on TB case notifications, drug-resistant TB cases and treatment outcomes, laboratory capacity and WHO estimates of TB incidence, prevalence and mortality (**Figure A.1**).

FIGURE A.1

Interactive page to view MDR-TB indicators by region or country and year



Accessing TB data using the WHO Global Health Observatory

The WHO Global Health Observatory (GHO) at www.who.int/research/ is WHO's portal, providing access to data and analyses for monitoring the global health situation. It includes a data repository.

You can view, filter, aggregate and download key data from WHO's global TB database from within the GHO Data Repository at apps.who.int/gho/data/node.main.1315

The GHO data table headers include links to variable and indicator definitions. You can download the data in many formats, including CSV and Excel. You can also embed data tables within your own website using a simple HTML fragment (Figure A.2).

The GHO also provides a data query Application Programme Interface (API) (see <http://apps.who.int/gho/data/node.resources.api>) which allows analysts and programmers to use GHO data directly in their own software applications.

FIGURE A.2

A data table in the GHO Data Repository



ANNEX 2

Country profiles

Afghanistan

HIGH TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	13 (8.4–16)	42 (27–53)
Mortality (HIV+TB only)	0.082 (0.065–0.1)	0.27 (0.21–0.33)
Prevalence (includes HIV+TB)	100 (54–170)	340 (178–554)
Incidence (includes HIV+TB)	58 (51–65)	189 (167–212)
Incidence (HIV+TB only)	0.2 (0.17–0.22)	0.64 (0.57–0.72)
Case detection, all forms (%)	53 (47–60)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	3.7 (2.5–4.9)	20 (13–27)
MDR-TB cases among notified pulmonary TB cases	820 (560–1 100)	460 (300–610)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	14 277	1 154
Pulmonary, clinically diagnosed	8 020	
Extrapulmonary	7 056	

Total new and relapse 30 507

Previously treated, excluding relapses 1 115

Total cases notified 31 622

Among 30 507 new and relapse cases:

3 454 (11%) cases aged under 15 years; male:female ratio: 0.7

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	7 (<1%)	38 (2%)	45
Laboratory-confirmed RR-/MDR-TB cases			73
Patients started on MDR-TB treatment			49

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	8 247	(26)
HIV-positive TB patients	9	(<1)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)		
HIV-positive TB patients on antiretroviral therapy (ART)		
HIV-positive people screened for TB	100	
HIV-positive people provided with IPT	12	

Treatment success rate (%)

New and relapse cases registered in 2012	88
Previously treated cases, excluding relapse, registered in 2012	65
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	29
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	2.2
Culture (per 5 million population)	0.5
Drug susceptibility testing (per 5 million population)	0
Sites performing Xpert MTB/RIF	1
Is second-line drug susceptibility testing available?	Yes, outside country

Financing TB control 2014

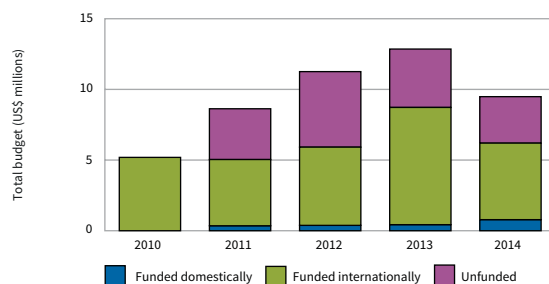
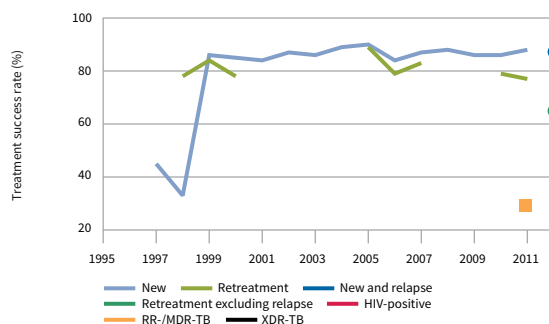
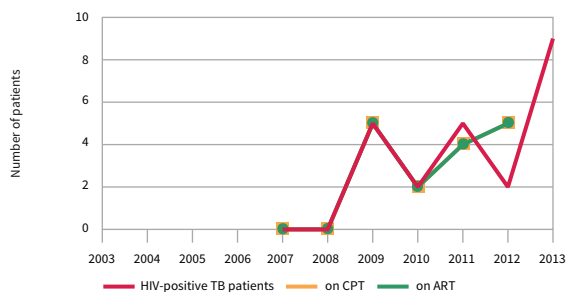
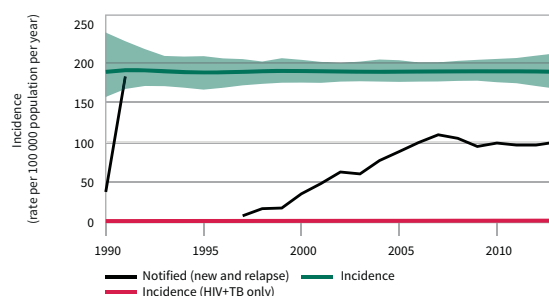
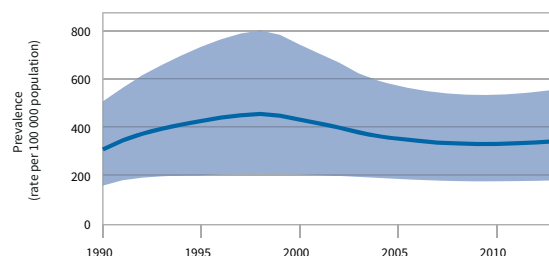
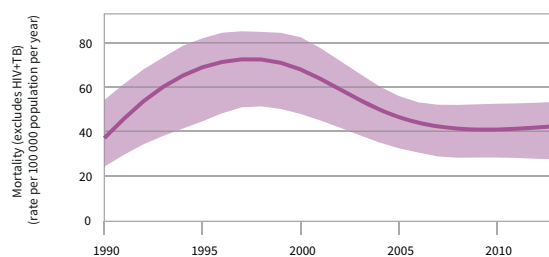
National TB programme budget (US\$ millions)	9.5
% Funded domestically	8%
% Funded internationally	57%
% Unfunded	35%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **31 million**



Bangladesh

HIGH TB BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	80 (51–110)	51 (33–69)
Mortality (HIV+TB only)	0.16 (0.1–0.24)	0.1 (0.07–0.15)
Prevalence (includes HIV+TB)	630 (330–1 000)	402 (210–656)
Incidence (includes HIV+TB)	350 (310–400)	224 (199–253)
Incidence (HIV+TB only)	0.41 (0.18–0.46)	0.26 (0.12–0.3)
Case detection, all forms (%)	53 (47–59)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.4 (0.7–2.5)	29 (24–34)
MDR-TB cases among notified pulmonary TB cases	2 100 (1 000–3 700)	2 600 (2 200–3 200)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	105 539	2 869
Pulmonary, clinically diagnosed	42 394	0
Extrapulmonary	33 704	0

Total new and relapse 184 506

Previously treated, excluding relapses 6 385

Total cases notified 190 891

Among 181 637 new cases:

5 051 (3%) cases aged under 15 years; male:female ratio: 1.5

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	446 (<1%)	4 611 (50%)	11 219
Laboratory-confirmed RR-/MDR-TB cases			1 024
Patients started on MDR-TB treatment			684

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	2 067	(1)
HIV-positive TB patients	68	(3)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	61	(90)
HIV-positive TB patients on antiretroviral therapy (ART)	68	(100)
HIV-positive people screened for TB	607	
HIV-positive people provided with IPT	0	

Treatment success rate (%)

New and relapse cases registered in 2012	92
Previously treated cases, excluding relapse, registered in 2012	82
HIV-positive TB cases, all types, registered in 2012	81
RR-/MDR-TB cases started on second-line treatment in 2011	68
XDR-TB cases started on second-line treatment in 2011	100

Laboratories 2013

Smear (per 100 000 population)	0.7
Culture (per 5 million population)	<0.1
Drug susceptibility testing (per 5 million population)	<0.1
Sites performing Xpert MTB/RIF	26
Is second-line drug susceptibility testing available?	Yes, in and outside country

Financing TB control 2014

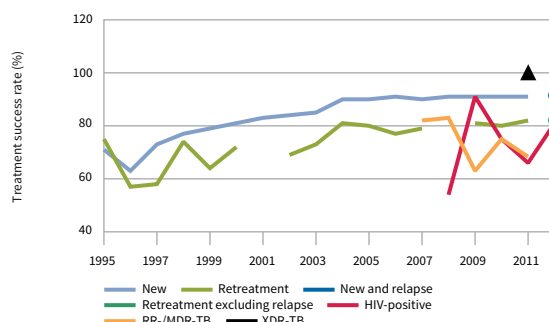
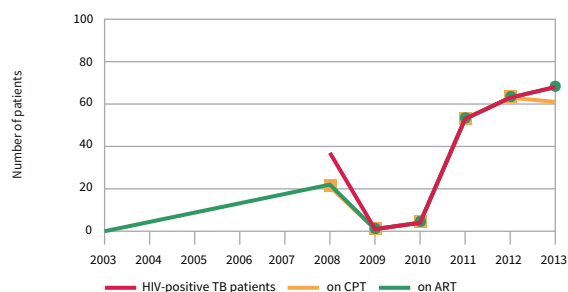
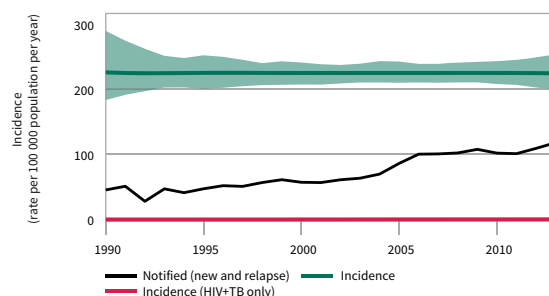
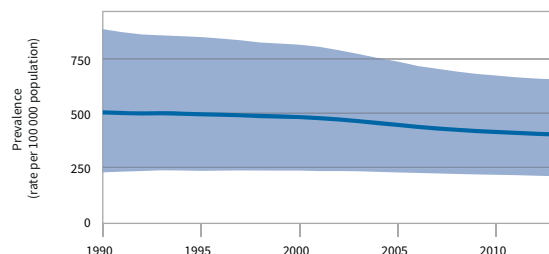
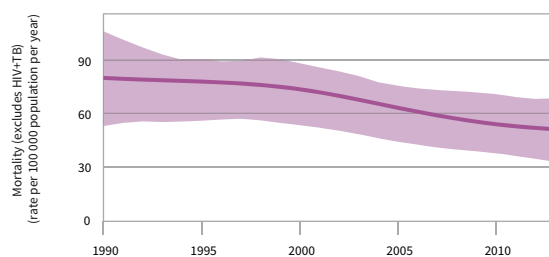
National TB programme budget (US\$ millions)	57
% Funded domestically	5%
% Funded internationally	33%
% Unfunded	62%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals. Estimates of TB disease burden have not been approved by the national TB programme in Bangladesh and a joint reassessment will be undertaken following the completion of the prevalence survey planned for 2015.

^b Includes cases with unknown previous TB treatment history

Population 2013 **157 million**



Brazil

HIGH TB BURDEN | HIGH HIV BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	4.4 (2.5–6.8)	2.2 (1.3–3.4)
Mortality (HIV+TB only)	2.1 (1.5–2.7)	1 (0.77–1.4)
Prevalence (includes HIV+TB)	110 (54–200)	57 (27–99)
Incidence (includes HIV+TB)	93 (83–110)	46 (41–52)
Incidence (HIV+TB only)	13 (13–13)	6.5 (6.5–6.6)
Case detection, all forms (%)	82 (72–92)	

Estimates of MDR-TB burden^a 2013

	NEWRETREATMENT	
% of TB cases with MDR-TB	1.4 (1–1.8)	7.5 (5.7–9.9)
MDR-TB cases among notified pulmonary TB cases	840 (600–1 100)	940 (710–1 200)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	41 885	3 613
Pulmonary, clinically diagnosed	18 303	1 604
Extrapulmonary	10 148	467

Total new and relapse 76 020

Previously treated, excluding relapses 7 290

Total cases notified 83 310

Among 76 020 new and relapse cases:

2 647 (3%) cases aged under 15 years; male:female ratio: 2.0

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	670 (2%)	217 (2%)	895
Laboratory-confirmed RR-/MDR-TB cases			706
Patients started on MDR-TB treatment			717

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	54 213	(65)
HIV-positive TB patients	9 340	(17)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)		
HIV-positive TB patients on antiretroviral therapy (ART)		
HIV-positive people screened for TB		
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	72
Previously treated cases, excluding relapse, registered in 2012	36
HIV-positive TB cases, all types, registered in 2012	48
RR-/MDR-TB cases started on second-line treatment in 2011	56
XDR-TB cases started on second-line treatment in 2011	21

Laboratories 2013

Smear (per 100 000 population)	1.5
Culture (per 5 million population)	8.6
Drug susceptibility testing (per 5 million population)	1.0
Sites performing Xpert MTB/RIF	0
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

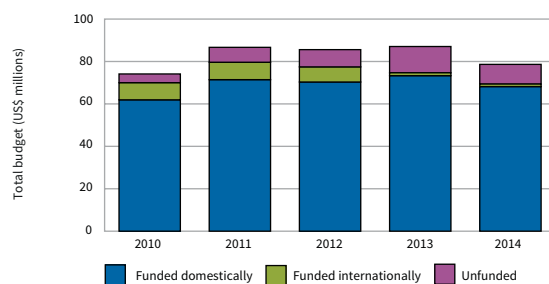
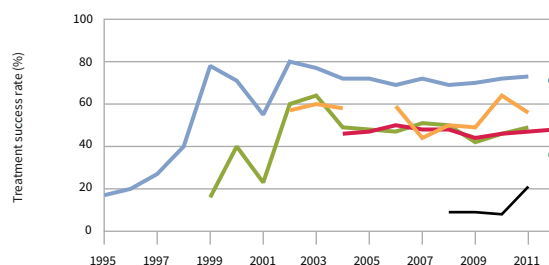
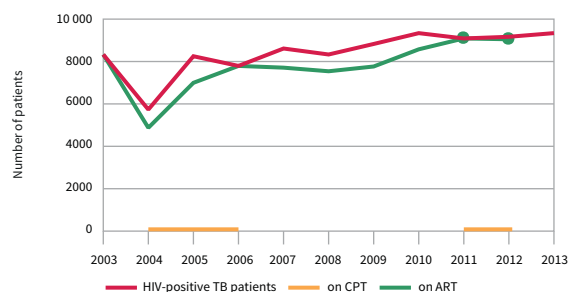
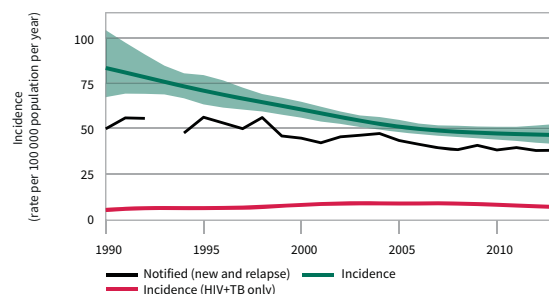
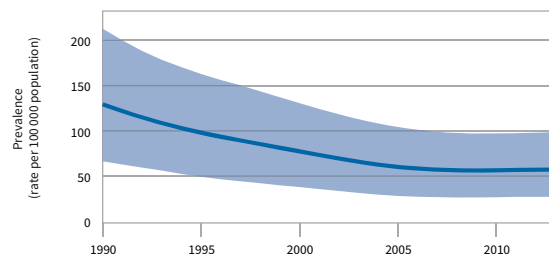
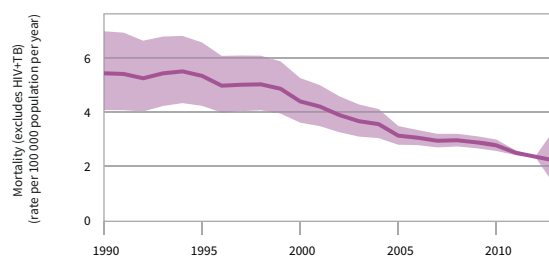
National TB programme budget (US\$ millions)	79
% Funded domestically	87%
% Funded internationally	2%
% Unfunded	12%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **200 million**



Cambodia

HIGH TB BURDEN | HIGH HIV BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	10 (6.3–14)	66 (42–92)
Mortality (HIV+TB only)	0.59 (0.45–0.76)	3.9 (3–5)
Prevalence (includes HIV+TB)	110 (91–130)	715 (604–834)
Incidence (includes HIV+TB)	61 (55–67)	400 (366–444)
Incidence (HIV+TB only)	2.3 (2.1–2.6)	15 (14–17)
Case detection, all forms (%)	62 (56–68)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.4 (0.7–2.5)	11 (4–22)
MDR-TB cases among notified pulmonary TB cases	320 (160–580)	180 (68–370)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	14 082	389
Pulmonary, clinically diagnosed	9 069	0
Extrapulmonary	14 203	0

Total new and relapse

37 743

Previously treated, excluding relapses

1 312

Total cases notified

39 055

Among 14 083 new cases:

64 (<1%) cases aged under 15 years; male:female ratio: 1.2

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	338 (2%)	1 255 (74%)	1 593
Laboratory-confirmed RR-/MDR-TB cases			121
Patients started on MDR-TB treatment			121

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	32 176	(82)
HIV-positive TB patients	1 241	(4)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	1 107	(89)
HIV-positive TB patients on antiretroviral therapy (ART)	1 100	(89)
HIV-positive people screened for TB	1 241	
HIV-positive people provided with IPT	1 343	

Treatment success rate (%)

New and relapse cases registered in 2012	94
Previously treated cases, excluding relapse, registered in 2012	88
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	86
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	1.4
Culture (per 5 million population)	1.3
Drug susceptibility testing (per 5 million population)	0.3
Sites performing Xpert MTB/RIF	10
Is second-line drug susceptibility testing available?	No

Financing TB control 2014

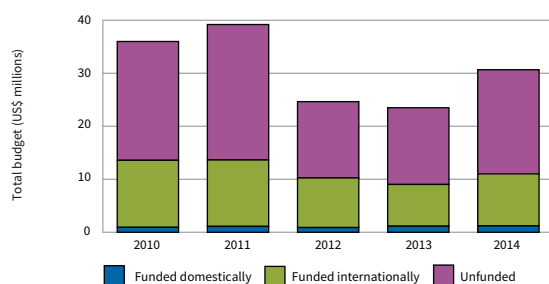
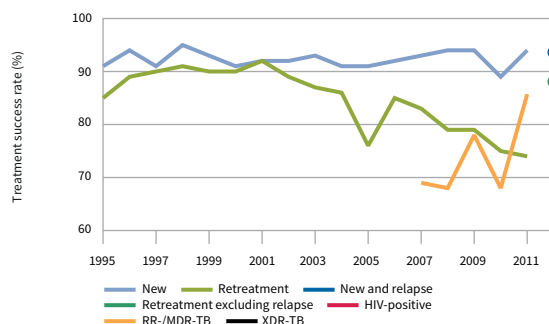
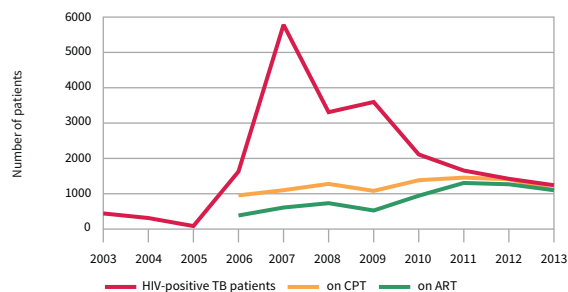
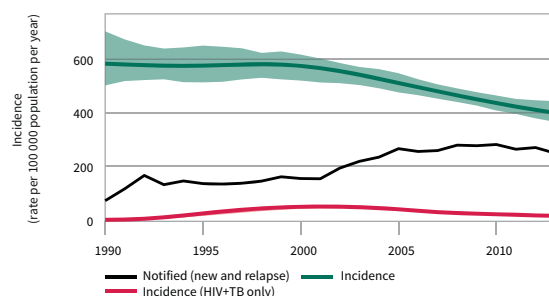
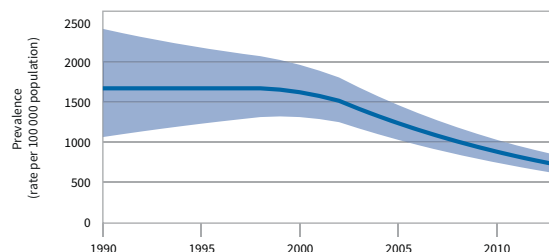
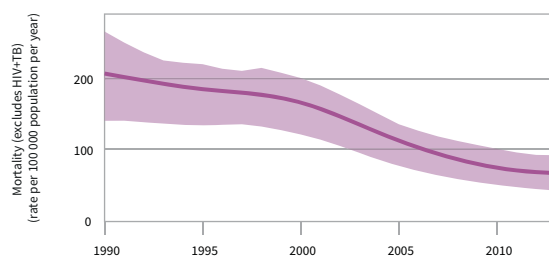
National TB programme budget (US\$ millions)	31
% Funded domestically	4%
% Funded internationally	32%
% Unfunded	64%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **15 million**



China

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	41 (40–43)	3 (2.9–3.1)
Mortality (HIV+TB only)	0.67 (0.23–1.3)	0.05 (0.02–0.1)
Prevalence (includes HIV+TB)	1 300 (1 100–1 500)	94 (82–107)
Incidence (includes HIV+TB)	980 (910–1 100)	70 (66–77)
Incidence (HIV+TB only)	4.5 (4.3–9.9)	0.33 (0.31–0.72)
Case detection, all forms (%)	87 (79–93)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	5.7 (4.5–7)	26 (22–30)
MDR-TB cases among notified pulmonary TB cases	45 000 (35 000–55 000)	9 200 (7 800–11 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	275 915	28 025
Pulmonary, clinically diagnosed	512 469	
Extrapulmonary	30 767	

Total new and relapse 847 176

Previously treated, excluding relapses 8 065

Total cases notified 855 241

Among 847 176 new and relapse cases:

4 830 (<1%) cases aged under 15 years; male:female ratio: 2.2

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	30 156 (11%)	11 656 (32%)	41 812
Laboratory-confirmed RR-/MDR-TB cases			4 183
Patients started on MDR-TB treatment			2 184

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	329 415	(39)
HIV-positive TB patients	4 649	(1)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)		
HIV-positive TB patients on antiretroviral therapy (ART)	3 127	(67)
HIV-positive people screened for TB	358 345	
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	95
Previously treated cases, excluding relapse, registered in 2012	90
HIV-positive TB cases, all types, registered in 2012	47
RR-/MDR-TB cases started on second-line treatment in 2011	50
XDR-TB cases started on second-line treatment in 2011	25

Laboratories 2013

Smear (per 100 000 population)	0.2
Culture (per 5 million population)	4.6
Drug susceptibility testing (per 5 million population)	0.9
Sites performing Xpert MTB/RIF	160
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

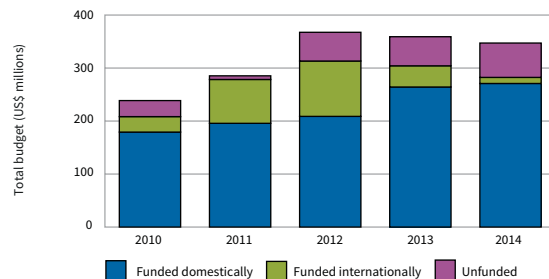
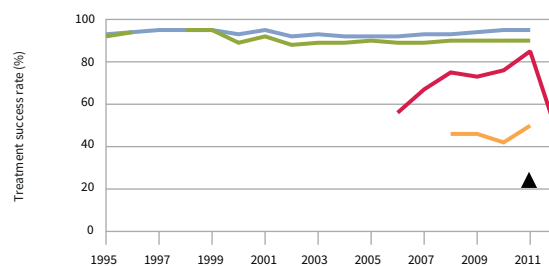
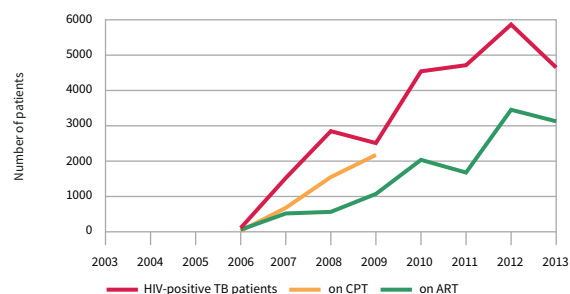
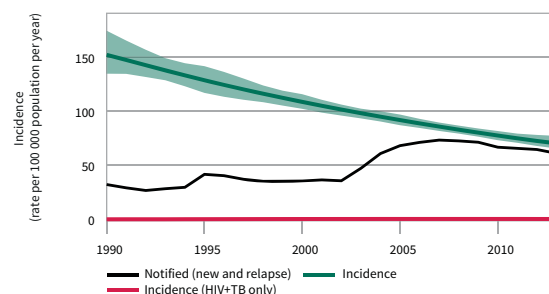
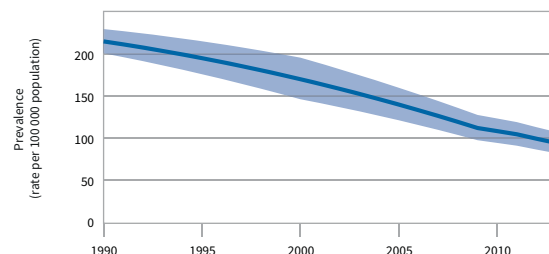
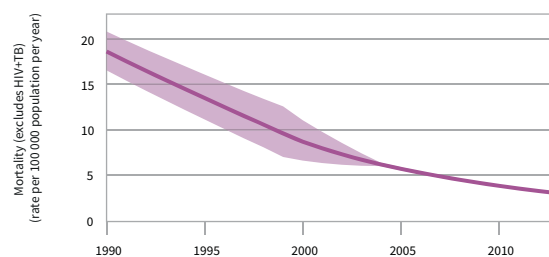
National TB programme budget (US\$ millions)	347
% Funded domestically	78%
% Funded internationally	3%
% Unfunded	19%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **1 386 million**



Democratic Republic of the Congo

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	46 (22–53)	68 (33–78)
Mortality (HIV+TB only)	6.4 (0.17–24)	9.5 (0.25–35)
Prevalence (includes HIV+TB)	370 (190–610)	549 (285–898)
Incidence (includes HIV+TB)	220 (200–240)	326 (297–356)
Incidence (HIV+TB only)	16 (9.8–75)	24 (14–111)
Case detection, all forms (%)	51 (47–56)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2.6 (0.01–5.5)	13 (0.2–28)
MDR-TB cases among notified pulmonary TB cases	2 200 (9–4 700)	900 (14–2 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	71 526	3 981
Pulmonary, clinically diagnosed	13 887	1 943
Extrapulmonary	20 297	805

Total new and relapse 112 439

Previously treated, excluding relapses 1 164

Total cases notified 113 603

Among 71 526 new cases:

3 086 (4%) cases aged under 15 years; male:female ratio: 1.3

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	344 (<1%)	1 070 (14%)	1 426
Laboratory-confirmed RR-/MDR-TB cases			272
Patients started on MDR-TB treatment			147

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	49 816	(44)
HIV-positive TB patients	6 984	(14)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	4 866	(70)
HIV-positive TB patients on antiretroviral therapy (ART)	3 371	(48)
HIV-positive people screened for TB		
HIV-positive people provided with IPT		

Treatment success rate (%)

New cases registered in 2012	88
Previously treated cases registered in 2012	74
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	59
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	2.3
Culture (per 5 million population)	0.1
Drug susceptibility testing (per 5 million population)	<0.1
Sites performing Xpert MTB/RIF	26
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

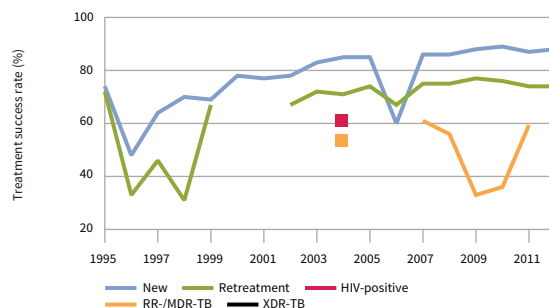
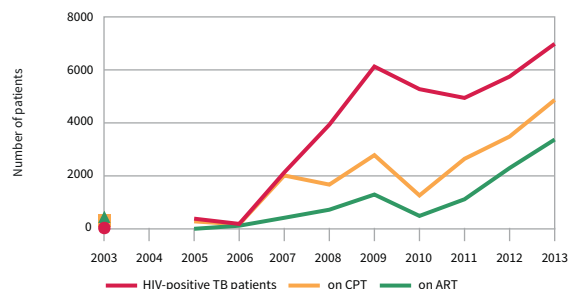
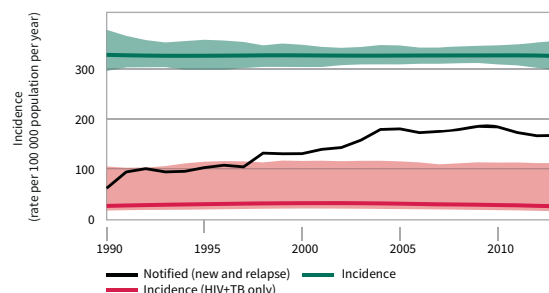
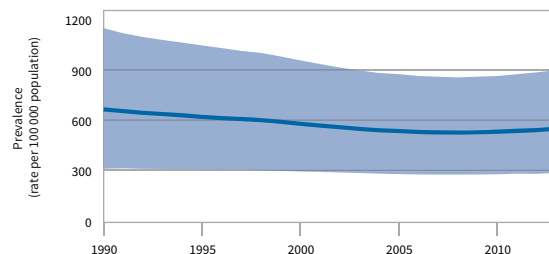
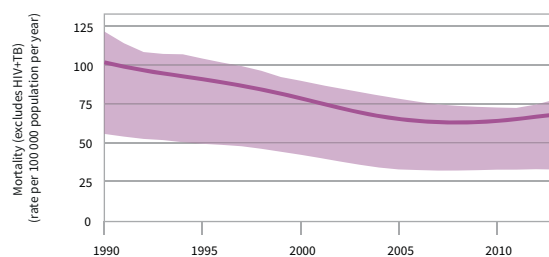
National TB programme budget (US\$ millions)	66
% Funded domestically	3%
% Funded internationally	21%
% Unfunded	75%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **68 million**



Ethiopia

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	30 (16–47)	32 (17–50)
Mortality (HIV+TB only)	5.6 (3.6–8)	5.9 (3.8–8.5)
Prevalence (includes HIV+TB)	200 (160–240)	211 (170–257)
Incidence (includes HIV+TB)	210 (180–260)	224 (188–276)
Incidence (HIV+TB only)	22 (19–32)	24 (21–33)
Case detection, all forms (%)	62 (51–74)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.6 (0.9–2.8)	12 (5.6–21)
MDR-TB cases among notified pulmonary TB cases	1 400 (800–2 500)	

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	43 860	
Pulmonary, clinically diagnosed	45 464	
Extrapulmonary	42 353	

Total new and relapse 131 677

Previously treated, excluding relapses

Total cases notified 131 677

Among 131 677 new cases:

21 317 (16%) cases aged under 15 years; male:female ratio: 1.2

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	212 (<1%)	1 095	3 071
Laboratory-confirmed RR-/MDR-TB cases			558
Patients started on MDR-TB treatment			413

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	93 356	(71)
HIV-positive TB patients	10 374	(11)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)		
HIV-positive TB patients on antiretroviral therapy (ART)	7 055	(68)
HIV-positive people screened for TB	324 674	
HIV-positive people provided with IPT	15 424	

Treatment success rate (%)

New cases registered in 2012	91
Previously treated cases registered in 2012	43
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	72
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	2.2
Culture (per 5 million population)	0.4
Drug susceptibility testing (per 5 million population)	0.4
Sites performing Xpert MTB/RIF	23
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

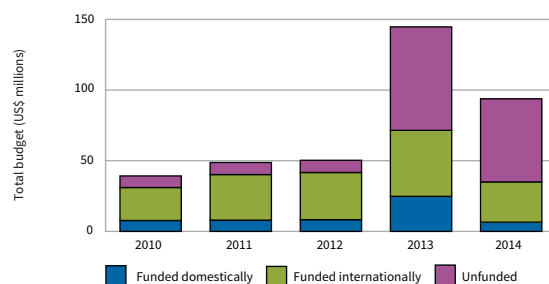
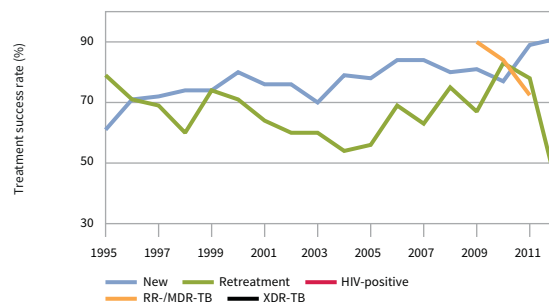
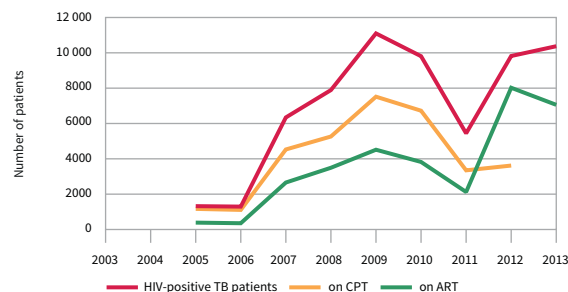
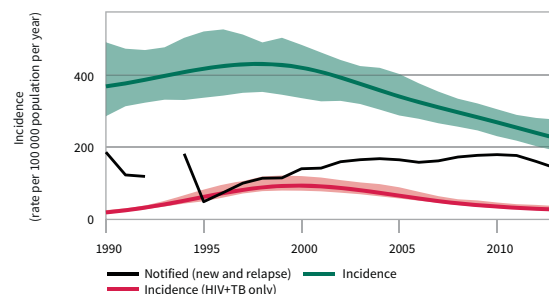
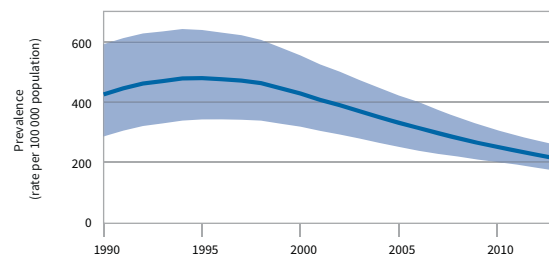
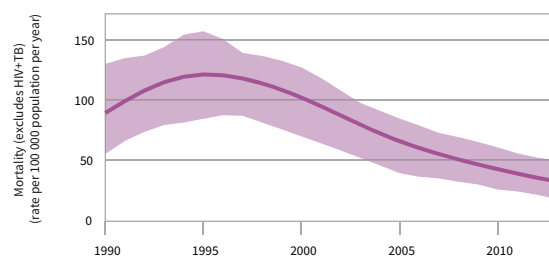
National TB programme budget (US\$ millions)	94
% Funded domestically	7%
% Funded internationally	30%
% Unfunded	63%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals. Estimates of TB disease burden for Ethiopia are provisional pending a joint review by WHO and the MOH in early 2015.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **94 million**



India

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	240 (150–350)	19 (12–28)
Mortality (HIV+TB only)	38 (31–44)	3 (2.5–3.5)
Prevalence (includes HIV+TB)	2 600 (1 800–3 700)	211 (143–294)
Incidence (includes HIV+TB)	2 100 (2 000–2 300)	171 (162–184)
Incidence (HIV+TB only)	120 (100–140)	9.7 (8.3–11)
Case detection, all forms (%)	58 (54–61)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2.2 (1.9–2.6)	15 (11–19)
MDR-TB cases among notified pulmonary TB cases	20 000 (17 000–24 000)	41 000 (30 000–52 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	621 762	102 660
Pulmonary, clinically diagnosed	292 926	
Extrapulmonary	226 557	

Total new and relapse 1 243 905

Previously treated, excluding relapses 171 712

Total cases notified 1 415 617

Among 1 243 905 new and relapse cases:

64 726 (5%) cases aged under 15 years

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB			248 341
Laboratory-confirmed RR-/MDR-TB cases			35 385
Patients started on MDR-TB treatment			20 763

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	887 903	(63)
HIV-positive TB patients	44 027	(5)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	41 827	(95)
HIV-positive TB patients on antiretroviral therapy (ART)	38 754	(88)
HIV-positive people screened for TB	1 063 644	
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	88
Previously treated cases, excluding relapse, registered in 2012	74
HIV-positive TB cases, all types, registered in 2012	77
RR-/MDR-TB cases started on second-line treatment in 2011	50
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	1.0
Culture (per 5 million population)	0.2
Drug susceptibility testing (per 5 million population)	0.2
Sites performing Xpert MTB/RIF	54
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

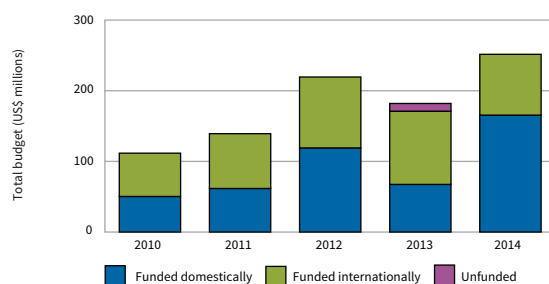
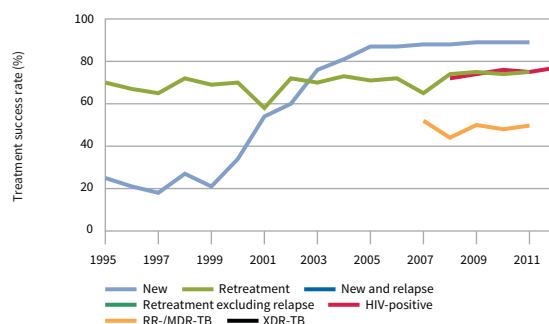
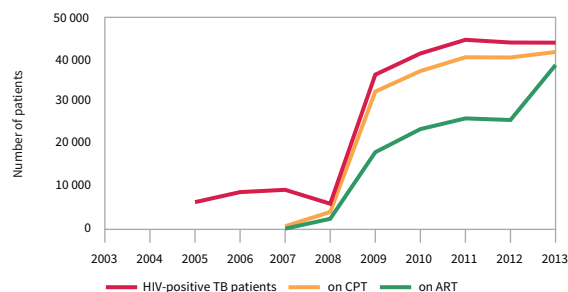
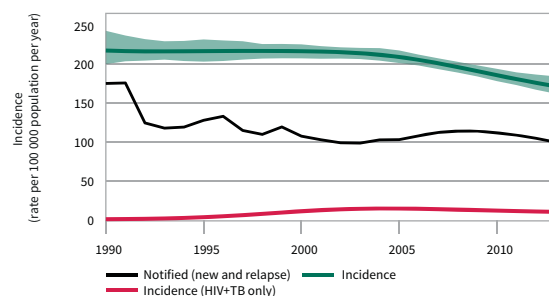
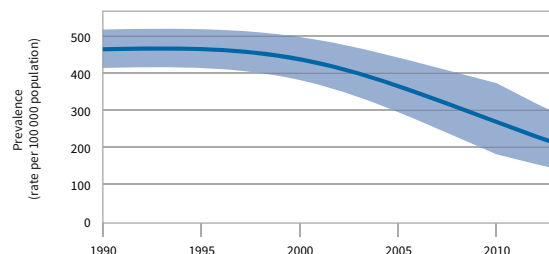
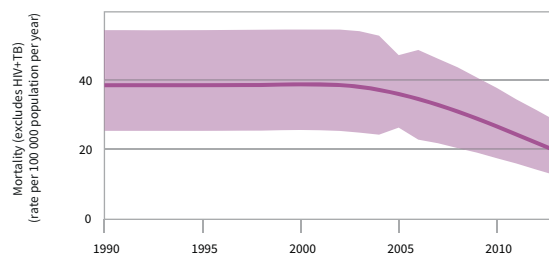
National TB programme budget (US\$ millions)	252
% Funded domestically	66%
% Funded internationally	34%
% Unfunded	0%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals. Estimates for India have not yet been officially approved by the Ministry of Health & Family Welfare, Government of India, and should therefore be considered provisional.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **1 252 million**



Indonesia

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	64 (36–93)	25 (14–37)
Mortality (HIV+TB only)	3.9 (2.2–6.2)	1.6 (0.87–2.5)
Prevalence (includes HIV+TB)	680 (340–1 100)	272 (138–450)
Incidence (includes HIV+TB)	460 (410–520)	183 (164–207)
Incidence (HIV+TB only)	15 (8.7–20)	5.8 (3.5–7.8)
Case detection, all forms (%)	71 (63–80)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.9 (1.4–2.5)	12 (8.1–17)
MDR-TB cases among notified pulmonary TB cases	5 700 (4 200–7 500)	1 100 (770–1 600)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	196 310	6 406
Pulmonary, clinically diagnosed	103 888	1 558
Extrapulmonary	17 420	

Total new and relapse 325 582

Previously treated, excluding relapses 1 521

Total cases notified 327 103

Among 325 582 new and relapse cases:

26 054 (8%) cases aged under 15 years; male:female ratio: 1.4

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	53 (<1%)	3 740 (39%)	3 838
Laboratory-confirmed RR-/MDR-TB cases			912
Patients started on MDR-TB treatment			809

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	7 631	(2)
HIV-positive TB patients	1 599	(21)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	477	(30)
HIV-positive TB patients on antiretroviral therapy (ART)	332	(21)
HIV-positive people screened for TB	22 190	
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	86
Previously treated cases, excluding relapse, registered in 2012	71
HIV-positive TB cases, all types, registered in 2012	49
RR-/MDR-TB cases started on second-line treatment in 2011	60
XDR-TB cases started on second-line treatment in 2011	50

Laboratories 2013

Smear (per 100 000 population)	2.2
Culture (per 5 million population)	0.4
Drug susceptibility testing (per 5 million population)	0.2
Sites performing Xpert MTB/RIF	23
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

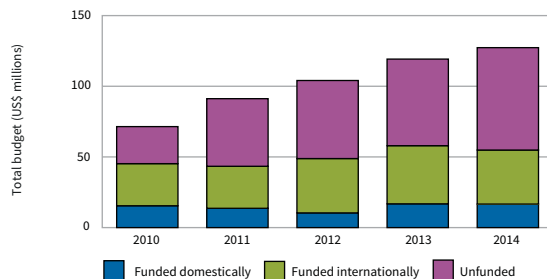
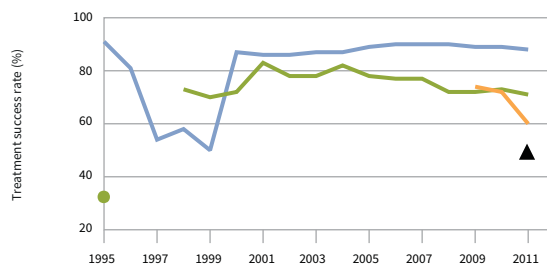
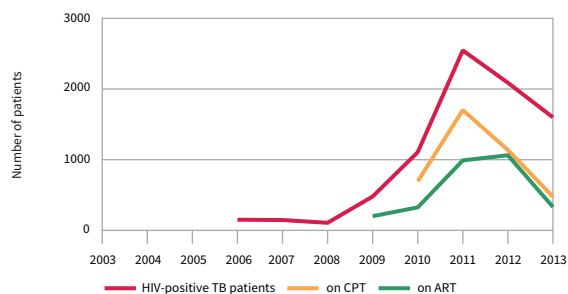
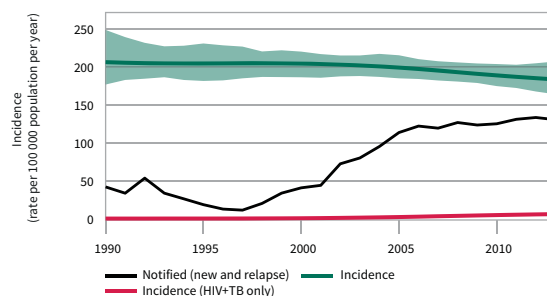
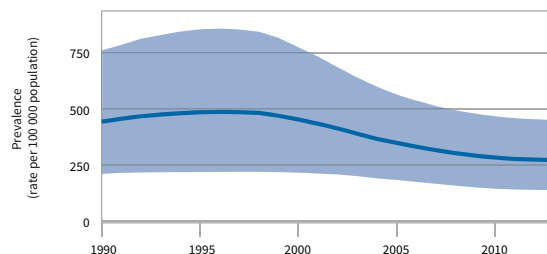
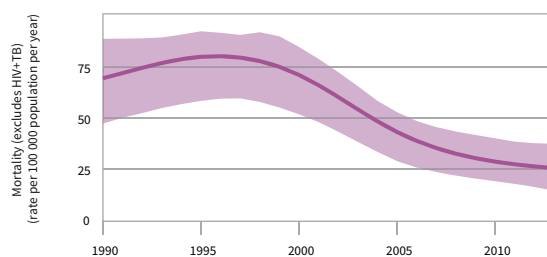
National TB programme budget (US\$ millions)	127
% Funded domestically	13%
% Funded internationally	30%
% Unfunded	57%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **250 million**



Kenya

HIGH TB BURDEN | HIGH HIV BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	9.1 (5.5–12)	20 (12–27)
Mortality (HIV+TB only)	9.5 (7.5–12)	21 (17–27)
Prevalence (includes HIV+TB)	130 (69–200)	283 (156–447)
Incidence (includes HIV+TB)	120 (120–120)	268 (261–275)
Incidence (HIV+TB only)	48 (47–50)	109 (105–112)
Case detection, all forms (%)	75 (74–77)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2.6 (0.01–5.5)	13 (0.2–28)
MDR-TB cases among notified pulmonary TB cases	1 700 (7–3 700)	1 100 (17–2 300)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	34 686	4 632
Pulmonary, clinically diagnosed	32 153	3 847
Extrapulmonary	14 478	0

Total new and relapse **89 796**

Previously treated, excluding relapses

Total cases notified **89 796**

Among 74 335 new cases:

4 383 (6%) cases aged under 15 years; male:female ratio: 1.4

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	127 (<1%)	1 846 (22%)	2 116
Laboratory-confirmed RR-/MDR-TB cases			160
Patients started on MDR-TB treatment			290

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	84 178	(94)
HIV-positive TB patients	31 650	(38)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	31 380	(99)
HIV-positive TB patients on antiretroviral therapy (ART)	26 431	(84)
HIV-positive people screened for TB		
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	86
Previously treated cases, excluding relapse, registered in 2012	78
HIV-positive TB cases, all types, registered in 2012	83
RR-/MDR-TB cases started on second-line treatment in 2011	70
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	4.2
Culture (per 5 million population)	0.8
Drug susceptibility testing (per 5 million population)	0.7
Sites performing Xpert MTB/RIF	21
Is second-line drug susceptibility testing available?	No

Financing TB control 2014

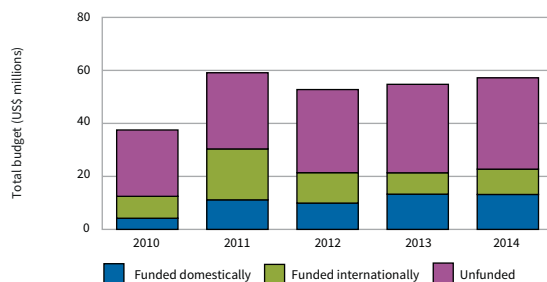
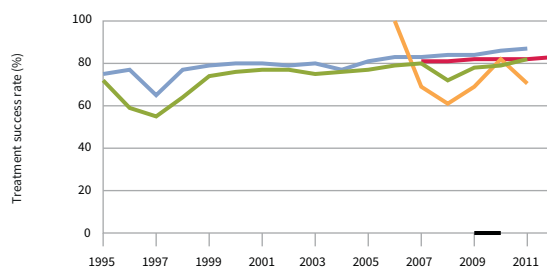
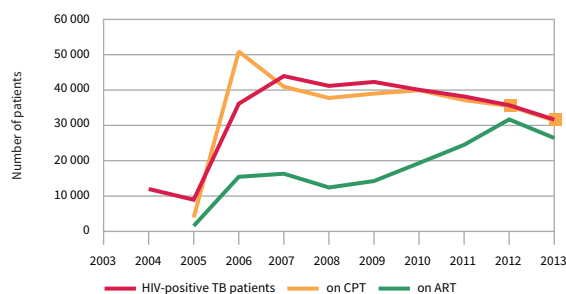
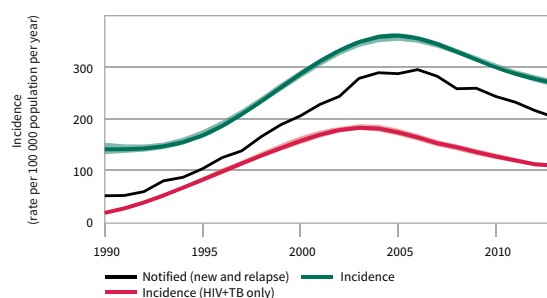
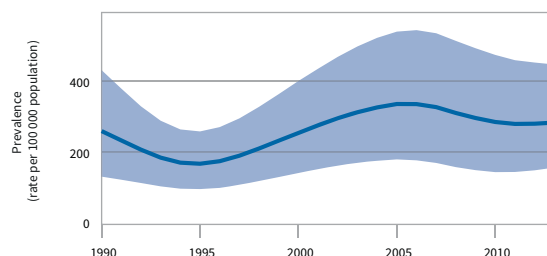
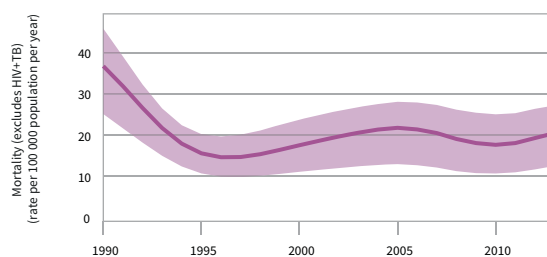
National TB programme budget (US\$ millions)	57
% Funded domestically	23%
% Funded internationally	17%
% Unfunded	60%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **44 million**



Mozambique

HIGH TB BURDEN | HIGH HIV BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	18 (9.4–26)	69 (36–101)
Mortality (HIV+TB only)	38 (27–51)	148 (105–198)
Prevalence (includes HIV+TB)	140 (78–230)	559 (303–893)
Incidence (includes HIV+TB)	140 (110–180)	552 (442–680)
Incidence (HIV+TB only)	81 (64–100)	312 (248–388)
Case detection, all forms (%)	37 (30–47)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	3.5 (2.2–4.8)	11 (0–25)
MDR-TB cases among notified pulmonary TB cases	1 500 (950–2 100)	830 (0–1 900)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	23 115	2 081
Pulmonary, clinically diagnosed	20 131	2 422
Extrapulmonary	5 523	

Total new and relapse 53 272

Previously treated, excluding relapses 2 948

Total cases notified 56 220

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	634 (3%)	653 (9%)	1 287
Laboratory-confirmed RR-/MDR-TB cases			444
Patients started on MDR-TB treatment			313

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	51 172	(91)
HIV-positive TB patients	28 585	(56)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	27 624	(97)
HIV-positive TB patients on antiretroviral therapy (ART)	20 449	(72)
HIV-positive people screened for TB		
HIV-positive people provided with IPT	48 188	

Treatment success rate (%)

New cases registered in 2012	87
Previously treated cases registered in 2012	
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	31
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	1.3
Culture (per 5 million population)	0.6
Drug susceptibility testing (per 5 million population)	0.4
Sites performing Xpert MTB/RIF	14
Is second-line drug susceptibility testing available?	Yes, outside country

Financing TB control 2014

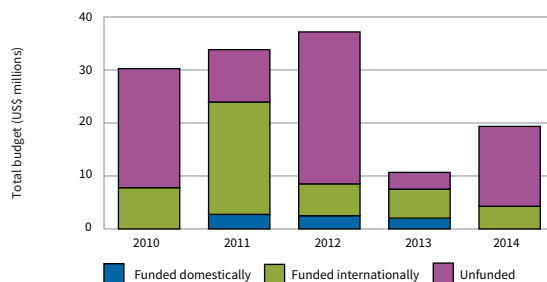
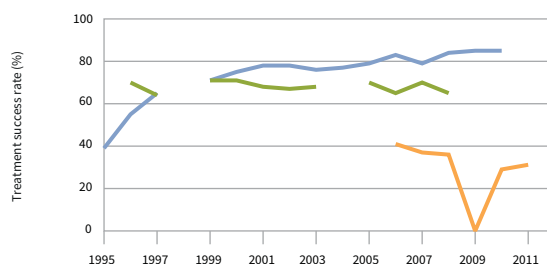
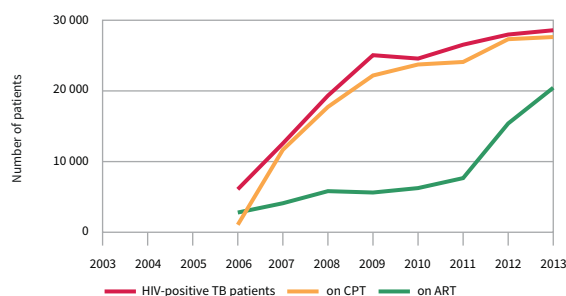
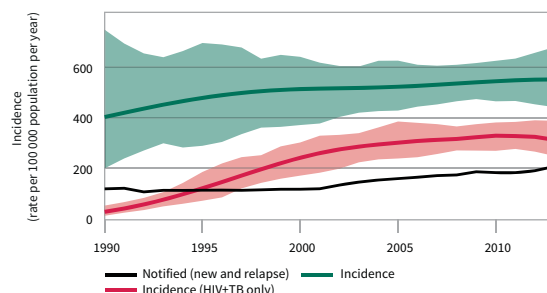
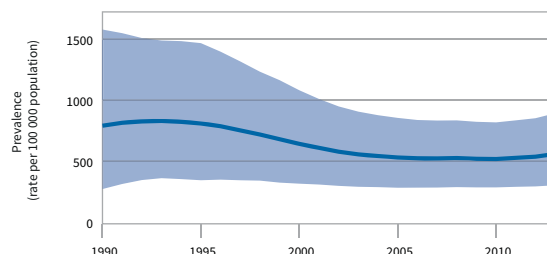
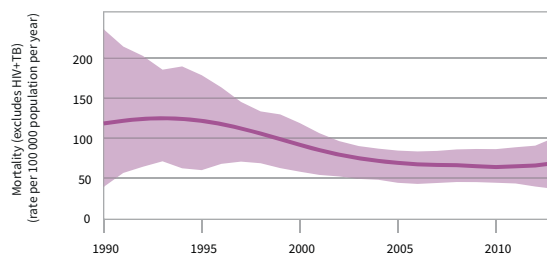
National TB programme budget (US\$ millions)	19
% Funded domestically	
% Funded internationally	22%
% Unfunded	78%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **26 million**



Myanmar

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	26 (16–38)	49 (29–71)
Mortality (HIV+TB only)	4.3 (3.3–5.3)	8 (6.3–9.9)
Prevalence (includes HIV+TB)	250 (190–320)	473 (364–595)
Incidence (includes HIV+TB)	200 (180–220)	373 (340–413)
Incidence (HIV+TB only)	17 (16–18)	33 (30–34)
Case detection, all forms (%)	68 (61–74)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	5 (3.1–6.8)	27 (15–39)
MDR-TB cases among notified pulmonary TB cases	5 700 (3 500–7 700)	3 300 (1 800–4 800)

TB case notifications 2013^b

	NEW ^c	RELAPSE
Pulmonary, bacteriologically confirmed	42 595	4 854
Pulmonary, clinically diagnosed	70 519	
Extrapulmonary	16 887	

Total new and relapse 134 855

Previously treated, excluding relapses 7 307

Total cases notified 142 162

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^c
Cases tested for RR-/MDR-TB	5 527 (13%)	8 551 (70%)	14 246
Laboratory-confirmed RR-/MDR-TB cases			1 984
Patients started on MDR-TB treatment			667

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	16 882	(12)
HIV-positive TB patients	5 413	(32)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	4 826	(89)
HIV-positive TB patients on antiretroviral therapy (ART)	3 987	(74)
HIV-positive people screened for TB	45 337	
HIV-positive people provided with IPT	468	

Treatment success rate (%)

New cases registered in 2012	89
Previously treated cases registered in 2012	70
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	71
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	0.9
Culture (per 5 million population)	0.3
Drug susceptibility testing (per 5 million population)	0.2
Sites performing Xpert MTB/RIF	24
Is second-line drug susceptibility testing available?	Yes, outside country

Financing TB control 2014

National TB programme budget (US\$ millions)	36
% Funded domestically	15%
% Funded internationally	49%
% Unfunded	35%

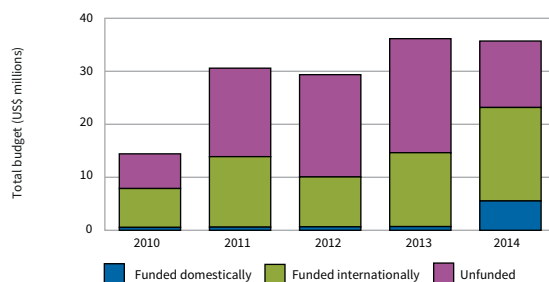
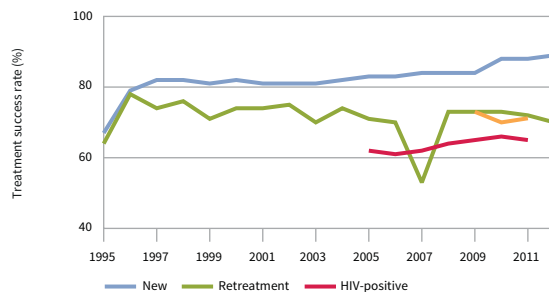
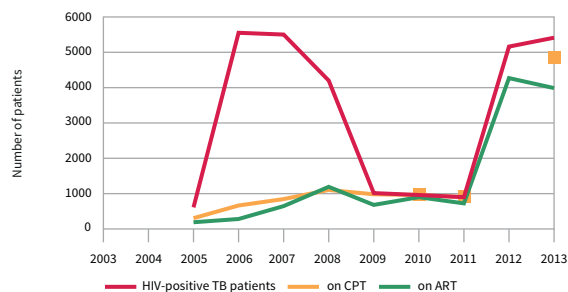
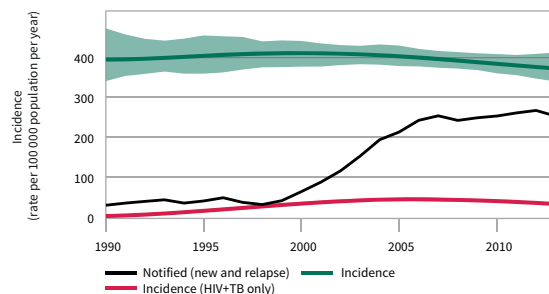
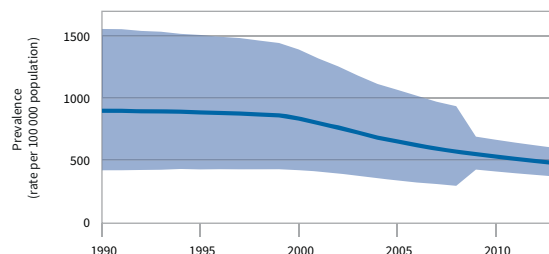
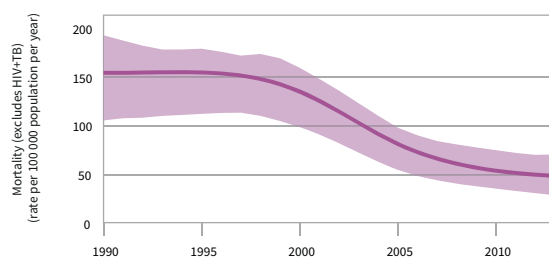
Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Case notifications were updated after TB burden estimates had already been produced.

^c Includes cases with unknown previous TB treatment history.

Population 2013 **53 million**



Nigeria

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	160 (68–270)	94 (39–156)
Mortality (HIV+TB only)	85 (47–140)	49 (27–78)
Prevalence (includes HIV+TB)	570 (430–730)	326 (246–418)
Incidence (includes HIV+TB)	590 (340–880)	338 (194–506)
Incidence (HIV+TB only)	140 (81–220)	81 (47–124)
Case detection, all forms (%)	16 (11–28)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2.9 (2.1–4)	14 (10–19)
MDR-TB cases among notified pulmonary TB cases	2 500 (1 800–3 500)	1 200 (860–1 600)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	52 811	2 828
Pulmonary, clinically diagnosed	33 873	
Extrapulmonary	5 313	

Total new and relapse 94 825

Previously treated, excluding relapses 5 576

Total cases notified 100 401

Among 100 401 new and relapse cases:

5 776 (6%) cases aged under 15 years; male:female ratio: 1.5

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB			10 410
Laboratory-confirmed RR-/MDR-TB cases			669
Patients started on MDR-TB treatment			426

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	88 317	(88)
HIV-positive TB patients	19 423	(22)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	16 948	(87)
HIV-positive TB patients on antiretroviral therapy (ART)	12 923	(67)
HIV-positive people screened for TB	435 216	
HIV-positive people provided with IPT	7 973	

Treatment success rate (%)

New cases registered in 2012	86
Previously treated cases registered in 2012	83
HIV-positive TB cases, all types, registered in 2012	79
RR-/MDR-TB cases started on second-line treatment in 2011	63
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	0.9
Culture (per 5 million population)	0.1
Drug susceptibility testing (per 5 million population)	<0.1
Sites performing Xpert MTB/RIF	49
Is second-line drug susceptibility testing available?	Yes, outside country

Financing TB control 2014

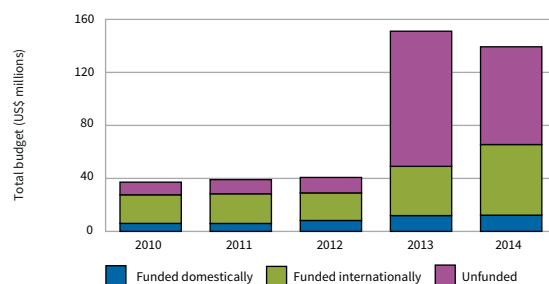
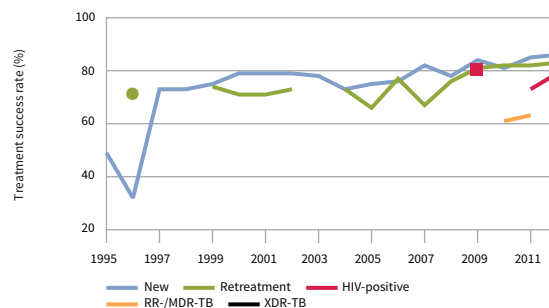
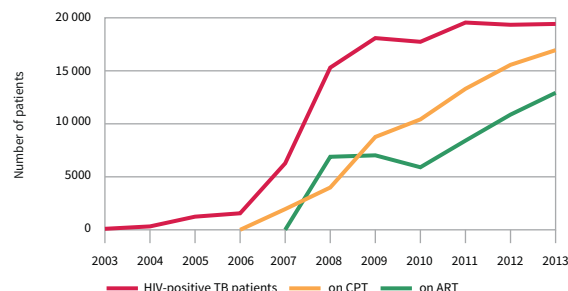
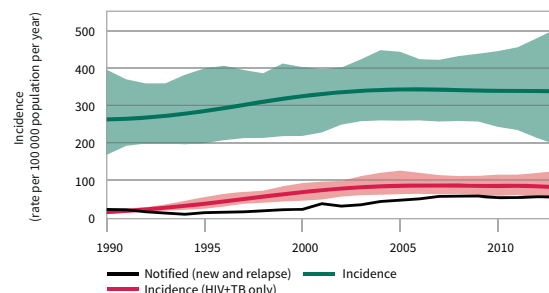
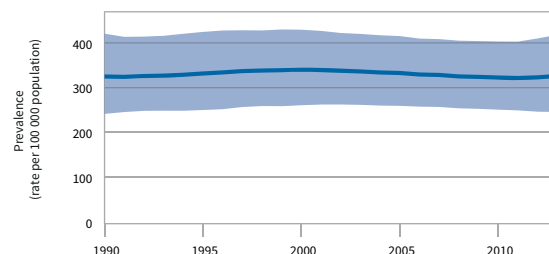
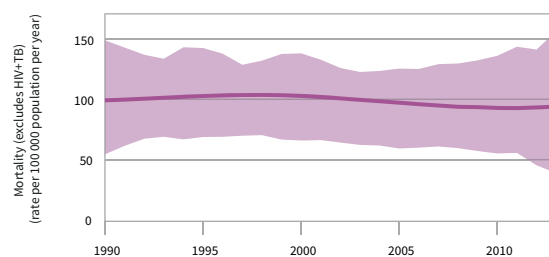
National TB programme budget (US\$ millions)	139
% Funded domestically	9%
% Funded internationally	38%
% Unfunded	53%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **174 million**



Pakistan

HIGH TB BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	100 (45–170)	56 (25–92)
Mortality (HIV+TB only)	0.97 (0.52–1.6)	0.53 (0.28–0.86)
Prevalence (includes HIV+TB)	620 (520–740)	342 (284–406)
Incidence (includes HIV+TB)	500 (370–650)	275 (205–357)
Incidence (HIV+TB only)	2.6 (1.2–3.4)	1.4 (0.64–1.9)
Case detection, all forms (%)	58 (44–78)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	4.3 (2.8–5.7)	19 (14–25)
MDR-TB cases among notified pulmonary TB cases	9 900 (6 400–13 000)	3 100 (2 200–4 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	111 682	6 303
Pulmonary, clinically diagnosed	118 279	0
Extrapulmonary	52 646	0

Total new and relapse 288 910

Previously treated, excluding relapses 9 536

Total cases notified 298 446

Among 282 607 new cases:

28 113 (10%) cases aged under 15 years; male:female ratio: 1.0

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	5 161 (5%)	3 510 (22%)	12 777
Laboratory-confirmed RR-/MDR-TB cases			2 596
Patients started on MDR-TB treatment			1 495

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	8 306	(3)
HIV-positive TB patients	36	(<1)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)		
HIV-positive TB patients on antiretroviral therapy (ART)		
HIV-positive people screened for TB		
HIV-positive people provided with IPT		

Treatment success rate (%)

New cases registered in 2012	91
Previously treated cases registered in 2012	81
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	70
XDR-TB cases started on second-line treatment in 2011	43

Laboratories 2013

Smear (per 100 000 population)	0.8
Culture (per 5 million population)	0.3
Drug susceptibility testing (per 5 million population)	0.2
Sites performing Xpert MTB/RIF	32
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

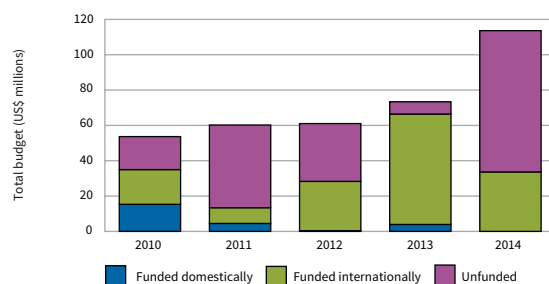
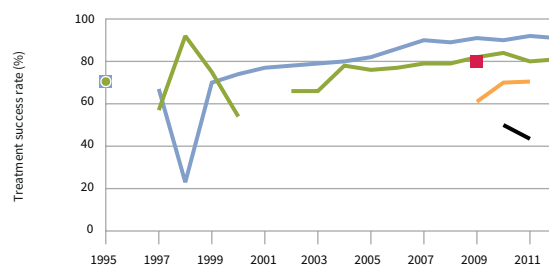
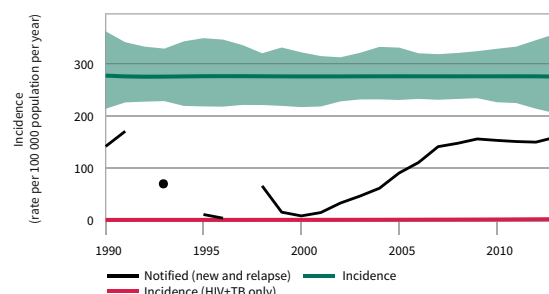
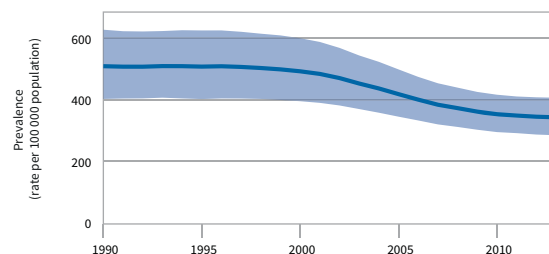
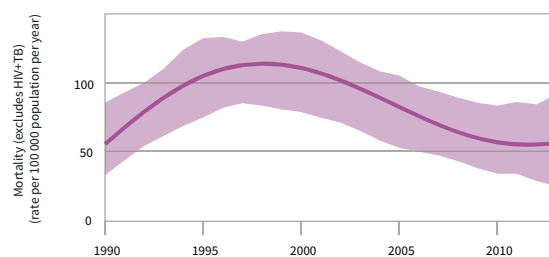
National TB programme budget (US\$ millions)	114
% Funded domestically	
% Funded internationally	30%
% Unfunded	70%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **182 million**



Philippines

HIGH TB BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	27 (25–29)	27 (25–29)
Mortality (HIV+TB only)	0.058 (0.042–0.077)	0.06 (0.04–0.08)
Prevalence (includes HIV+TB)	430 (380–490)	438 (385–495)
Incidence (includes HIV+TB)	290 (260–330)	292 (261–331)
Incidence (HIV+TB only)	0.31 (0.18–0.34)	0.32 (0.18–0.35)
Case detection, all forms (%)	80 (71–90)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2 (1.4–2.7)	21 (16–29)
MDR-TB cases among notified pulmonary TB cases	4 400 (3 100–6 000)	4 100 (3 000–5 500)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	97 353	4 669
Pulmonary, clinically diagnosed	123 510	0
Extrapulmonary	4 386	0

Total new and relapse	229 918
Previously treated, excluding relapses	14 474
Total cases notified	244 392

Among 97 221 new cases:

2 065 (2%) cases aged under 15 years; male:female ratio: 2.3

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	3 137 (3%)	13 419 (70%)	17 241
Laboratory-confirmed RR-/MDR-TB cases			3 962
Patients started on MDR-TB treatment			2 262

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	5 034	(2)
HIV-positive TB patients	26	(<1)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)		
HIV-positive TB patients on antiretroviral therapy (ART)		
HIV-positive people screened for TB	3 006	
HIV-positive people provided with IPT		

Treatment success rate (%)

New cases registered in 2012	88
Previously treated cases registered in 2012	
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	41
XDR-TB cases started on second-line treatment in 2011	67

Laboratories 2013

Smear (per 100 000 population)	2.6
Culture (per 5 million population)	0.9
Drug susceptibility testing (per 5 million population)	0.2
Sites performing Xpert MTB/RIF	16
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

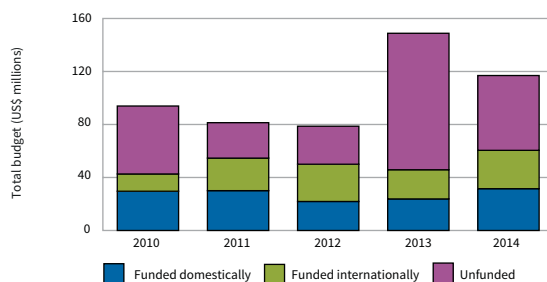
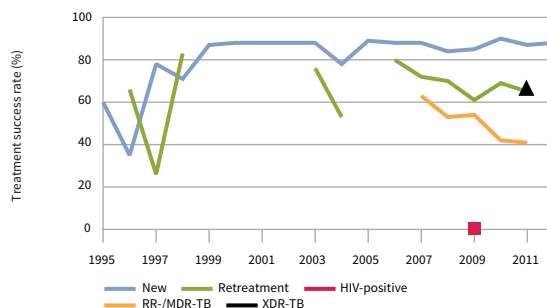
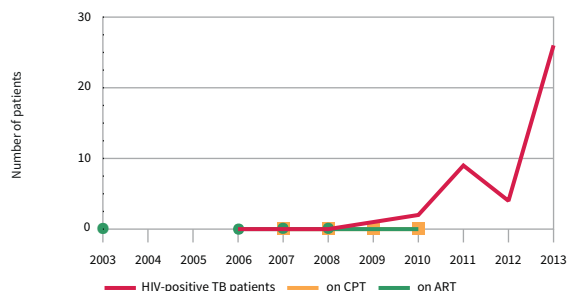
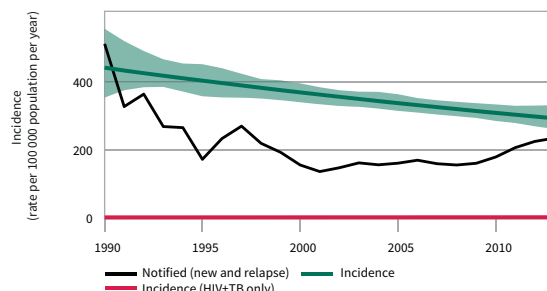
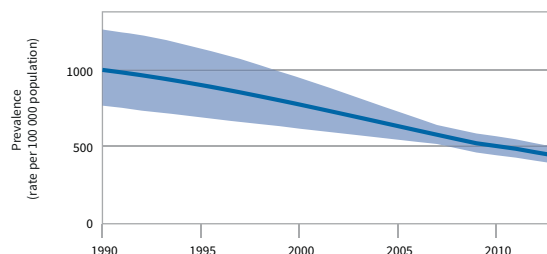
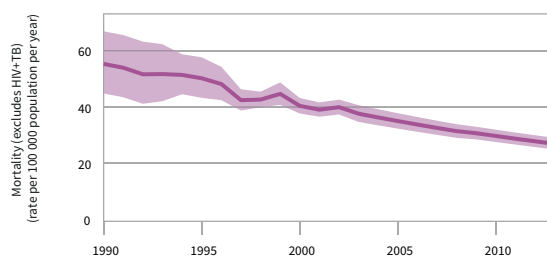
National TB programme budget (US\$ millions)	117
% Funded domestically	27%
% Funded internationally	25%
% Unfunded	48%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **98 million**



Russian Federation

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	17 (17–18)	12 (12–13)
Mortality (HIV+TB only)	1.4 (1–1.9)	0.98 (0.7–1.3)
Prevalence (includes HIV+TB)	160 (74–290)	114 (51–201)
Incidence (includes HIV+TB)	130 (120–140)	89 (82–100)
Incidence (HIV+TB only)	7.9 (6.9–9.1)	5.5 (4.8–6.4)
Case detection, all forms (%)	83 (74–91)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	19 (14–25)	49 (40–59)
MDR-TB cases among notified pulmonary TB cases	16 000 (11 000–20 000)	25 000 (20 000–30 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	37 779	7 866
Pulmonary, clinically diagnosed	43 859	7 194
Extrapulmonary	8 789	566

Total new and relapse 106 053

Previously treated, excluding relapses 36 480

Total cases notified 142 533

Among 90 427 new cases:

3 298 (4%) cases aged under 15 years; male:female ratio: 2.2

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	31 677 (84%)	12 066 (23%)	43 743
Laboratory-confirmed RR-/MDR-TB cases			13 521
Patients started on MDR-TB treatment			20 372

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status ^c	69 724	
HIV-positive TB patients	4 990	
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)		
HIV-positive TB patients on antiretroviral therapy (ART)		
HIV-positive people screened for TB		
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	69
Previously treated cases, excluding relapse, registered in 2012	37
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	37
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	3.7
Culture (per 5 million population)	11.6
Drug susceptibility testing (per 5 million population)	7.6
Sites performing Xpert MTB/RIF	72
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

National TB programme budget (US\$ millions)	1 827
% Funded domestically	100%
% Funded internationally	
% Unfunded	0%

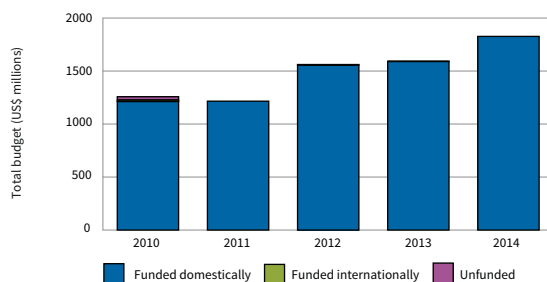
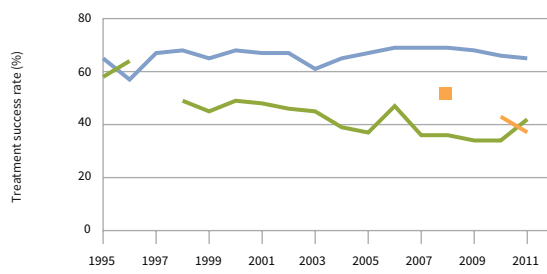
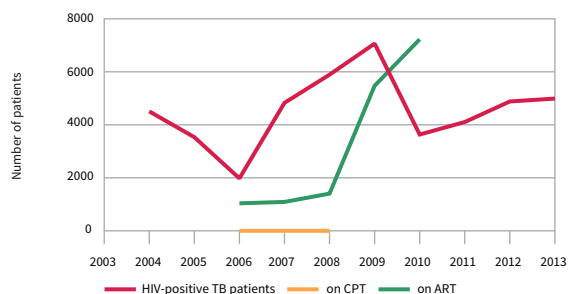
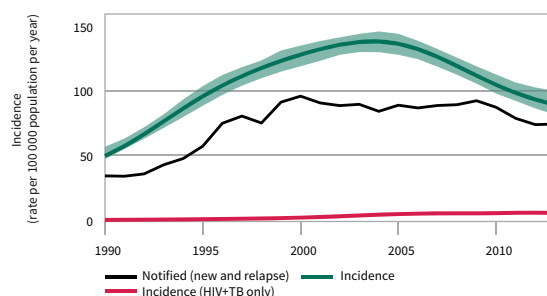
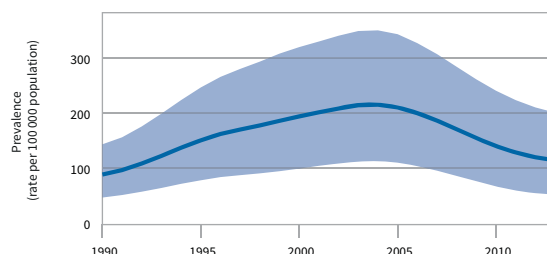
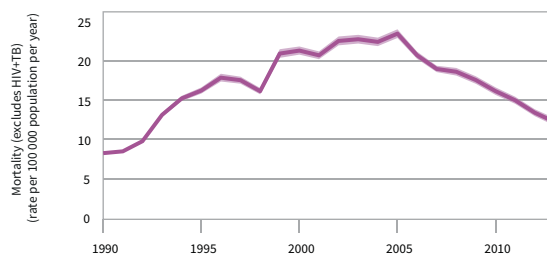
Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

^c The reported number of TB patients with known HIV status is for new TB patients in the civilian sector only. It was not possible to calculate the percentage of all TB patients with known HIV status.

Population 2013 **143 million**



South Africa

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	25 (15–38)	48 (28–73)
Mortality (HIV+TB only)	64 (47–83)	121 (90–158)
Prevalence (includes HIV+TB)	380 (210–590)	715 (396–1 126)
Incidence (includes HIV+TB)	450 (410–520)	860 (776–980)
Incidence (HIV+TB only)	270 (240–310)	520 (464–594)
Case detection, all forms (%)	69 (60–76)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.8 (1.4–2.3)	6.7 (5.4–8.2)
MDR-TB cases among notified pulmonary TB cases	4 600 (3 600–5 900)	2 200 (1 800–2 700)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	109 630	7 751
Pulmonary, clinically diagnosed	148 658	8 627
Extrapulmonary	37 709	5

Total new and relapse 312 380

Previously treated, excluding relapses 16 516

Total cases notified 328 896

Among 312 380 new and relapse cases:

36 671 (12%) cases aged under 15 years; male:female ratio: 1.2

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB			258 401
Laboratory-confirmed RR-/MDR-TB cases			26 023
Patients started on MDR-TB treatment			10 663

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	294 504	(90)
HIV-positive TB patients	181 736	(62)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	146 973	(81)
HIV-positive TB patients on antiretroviral therapy (ART)	120 298	(66)
HIV-positive people screened for TB	961 967	
HIV-positive people provided with IPT	339 518	

Treatment success rate (%)

New and relapse cases registered in 2012	77
Previously treated cases, excluding relapse, registered in 2012	64
HIV-positive TB cases, all types, registered in 2012	74
RR-/MDR-TB cases started on second-line treatment in 2011	45
XDR-TB cases started on second-line treatment in 2011	15

Laboratories 2013

Smear (per 100 000 population)	0.4
Culture (per 5 million population)	1.4
Drug susceptibility testing (per 5 million population)	1.4
Sites performing Xpert MTB/RIF	207
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

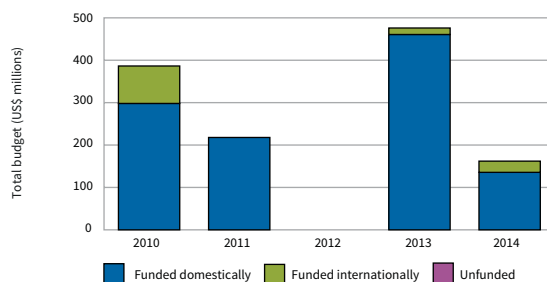
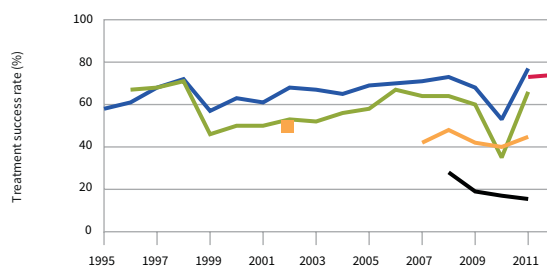
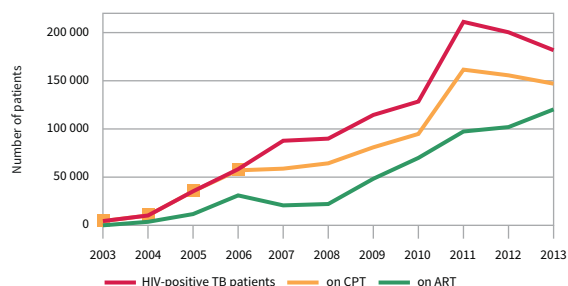
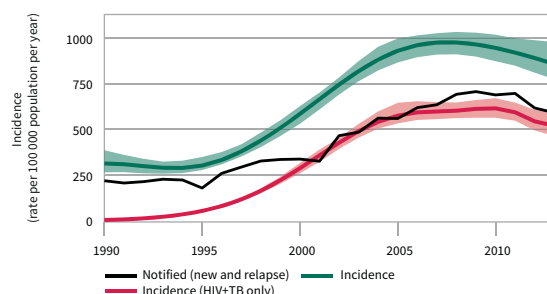
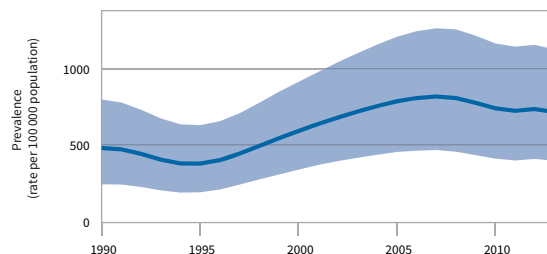
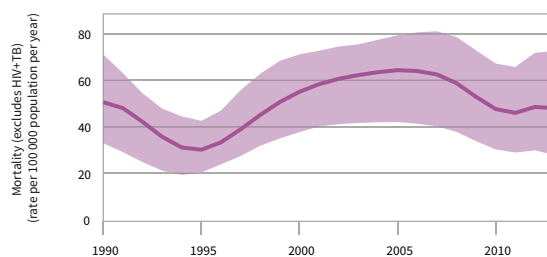
National TB programme budget (US\$ millions)	162
% Funded domestically	84%
% Funded internationally	16%
% Unfunded	0%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **53 million**



Thailand

HIGH TB BURDEN | HIGH HIV BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	8.1 (4.9–12)	12 (7.3–18)
Mortality (HIV+TB only)	1.9 (1.3–2.4)	2.8 (2–3.6)
Prevalence (includes HIV+TB)	100 (48–170)	149 (72–252)
Incidence (includes HIV+TB)	80 (71–90)	119 (106–134)
Incidence (HIV+TB only)	12 (10–13)	17 (15–19)
Case detection, all forms (%)	80 (71–89)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2 (1.4–2.8)	19 (14–25)
MDR-TB cases among notified pulmonary TB cases	1 000 (730–1 500)	880 (640–1 200)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	32 887	1 802
Pulmonary, clinically diagnosed	19 559	0
Extrapulmonary	9 293	0

Total new and relapse

63 541

Previously treated, excluding relapses

2 874

Total cases notified

66 415

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	3 246 (10%)	540 (12%)	3 866
Laboratory-confirmed RR-/MDR-TB cases			230
Patients started on MDR-TB treatment			230

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	54 991	(83)
HIV-positive TB patients	8 245	(15)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	5 206	(63)
HIV-positive TB patients on antiretroviral therapy (ART)	4 890	(59)
HIV-positive people screened for TB		
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	81
Previously treated cases, excluding relapse, registered in 2012	63
HIV-positive TB cases, all types, registered in 2012	70
RR-/MDR-TB cases started on second-line treatment in 2011	
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	1.6
Culture (per 5 million population)	4.8
Drug susceptibility testing (per 5 million population)	1.3
Sites performing Xpert MTB/RIF	14
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

National TB programme budget (US\$ millions)	16 ^c
% Funded domestically	54%
% Funded internationally	33%
% Unfunded	13%

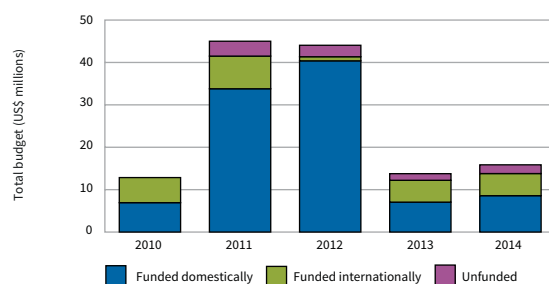
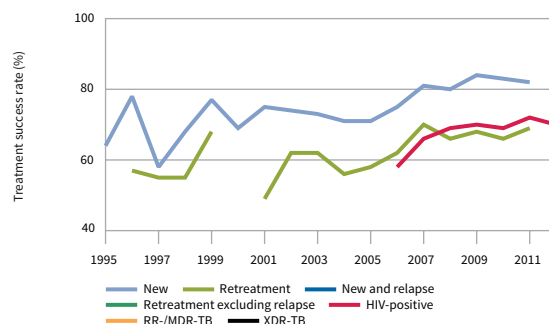
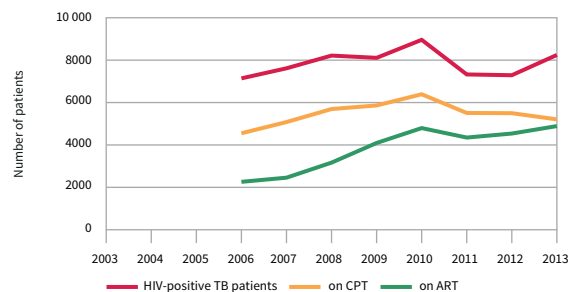
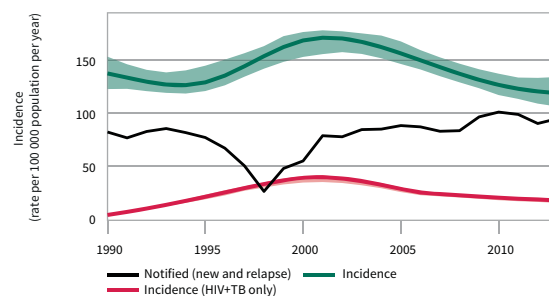
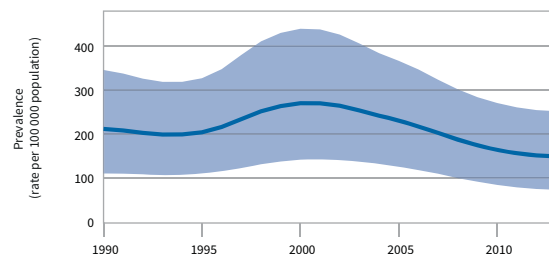
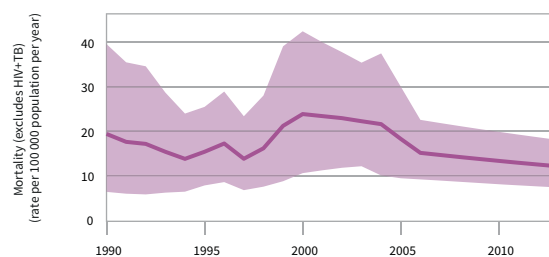
Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

^c Data reported are only national level budgets for the Bureau of TB and the National Health Security Office, and do not include provincial, local and private sector budgets.

Population 2013 **67 million**



Uganda

HIGH TB BURDEN | HIGH HIV BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	4.1 (2.2–6.6)	11 (5.8–18)
Mortality (HIV+TB only)	7.2 (5–9.9)	19 (13–26)
Prevalence (includes HIV+TB)	58 (32–91)	154 (85–243)
Incidence (includes HIV+TB)	62 (56–73)	166 (149–193)
Incidence (HIV+TB only)	32 (29–38)	86 (77–102)
Case detection, all forms (%)	73 (63–81)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.4 (0.6–2.2)	12 (6.8–19)
MDR-TB cases among notified pulmonary TB cases	540 (230–840)	490 (270–780)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	25 442	1 312
Pulmonary, clinically diagnosed	12 852	615
Extrapulmonary	5 328	

Total new and relapse 45 549

Previously treated, excluding relapses 2 101

Total cases notified 47 650

Among 25 408 new cases:

649 (3%) cases aged under 15 years; male:female ratio: 1.9

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	92 (<1%)	397 (10%)	549
Laboratory-confirmed RR-/MDR-TB cases			117
Patients started on MDR-TB treatment			199

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	43 318	(91)
HIV-positive TB patients	20 648	(48)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	19 902	(96)
HIV-positive TB patients on antiretroviral therapy (ART)	13 399	(65)
HIV-positive people screened for TB	675 373	
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	77
Previously treated cases, excluding relapse, registered in 2012	66
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	77
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	3.5
Culture (per 5 million population)	0.5
Drug susceptibility testing (per 5 million population)	0.5
Sites performing Xpert MTB/RIF	37
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

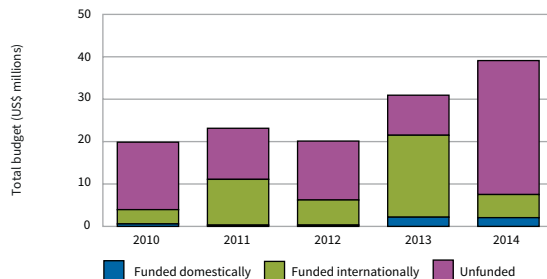
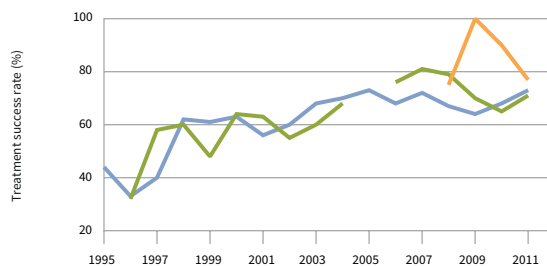
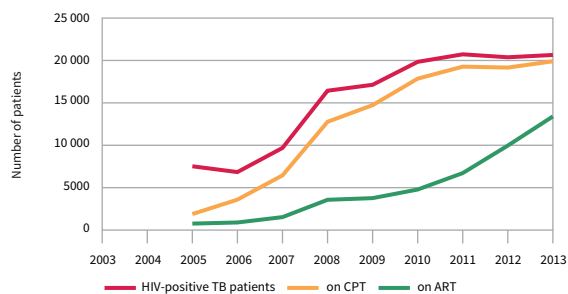
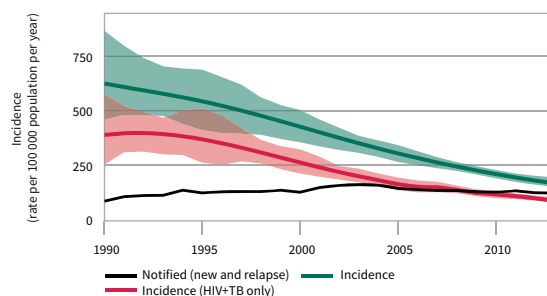
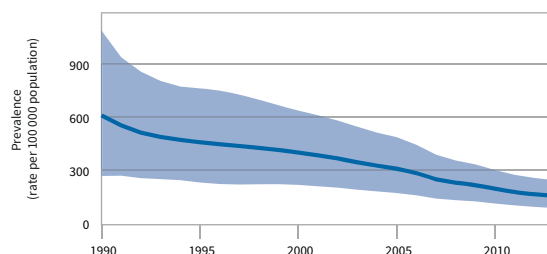
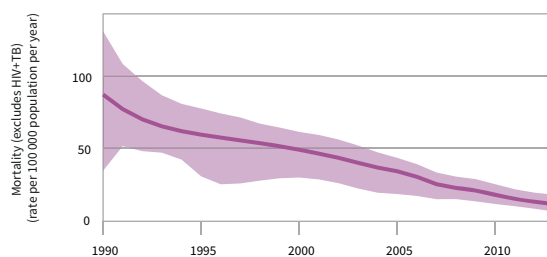
National TB programme budget (US\$ millions)	39
% Funded domestically	5%
% Funded internationally	14%
% Unfunded	81%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **38 million**



United Republic of Tanzania

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	6 (3.4–8.2)	12 (7–17)
Mortality (HIV+TB only)	6.1 (4.8–7.5)	12 (9.8–15)
Prevalence (includes HIV+TB)	85 (45–140)	172 (92–277)
Incidence (includes HIV+TB)	81 (77–84)	164 (157–170)
Incidence (HIV+TB only)	30 (29–31)	61 (58–63)
Case detection, all forms (%)	79 (77–83)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.1 (0.5–2)	3.1 (0.9–7.9)
MDR-TB cases among notified pulmonary TB cases	530 (240–960)	86 (25–220)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	24 565	1 101
Pulmonary, clinically diagnosed	23 371	
Extrapulmonary	15 016	

Total new and relapse 64 053

Previously treated, excluding relapses 1 679

Total cases notified 65 732

Among 62 952 new cases:

6 658 (11%) cases aged under 15 years; male:female ratio: 1.4

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	1 192 (5%)	728 (26%)	2 020
Laboratory-confirmed RR-/MDR-TB cases			64
Patients started on MDR-TB treatment			28

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	54 504	(83)
HIV-positive TB patients	20 320	(37)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	19 835	(98)
HIV-positive TB patients on antiretroviral therapy (ART)	14 864	(73)
HIV-positive people screened for TB	457 901	
HIV-positive people provided with IPT	166	

Treatment success rate (%)

New and relapse cases registered in 2012	90
Previously treated cases, excluding relapse, registered in 2012	80
HIV-positive TB cases, all types, registered in 2012	77
RR-/MDR-TB cases started on second-line treatment in 2011	75
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	1.9
Culture (per 5 million population)	0.5
Drug susceptibility testing (per 5 million population)	0.1
Sites performing Xpert MTB/RIF	35
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

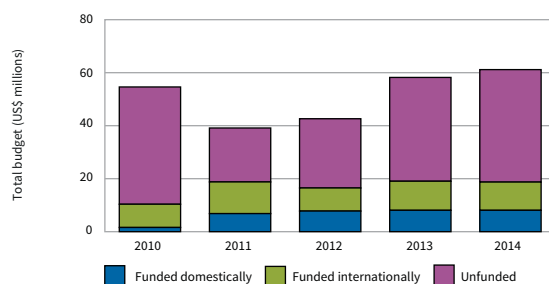
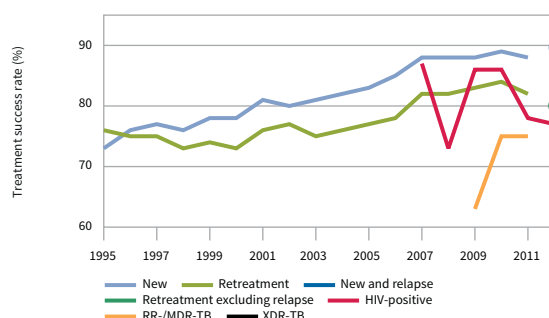
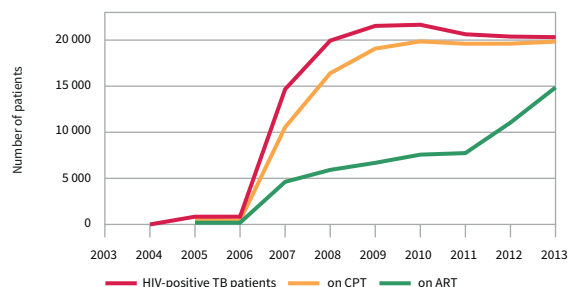
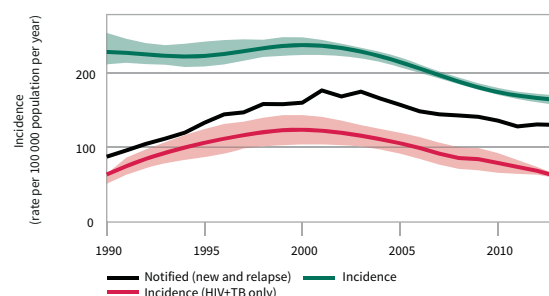
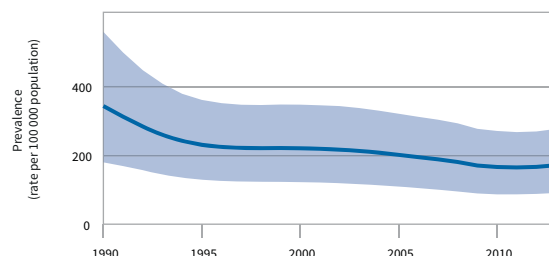
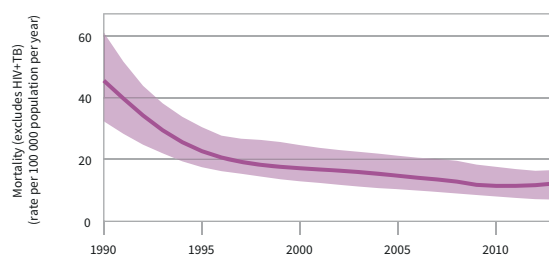
National TB programme budget (US\$ millions)	61
% Funded domestically	13%
% Funded internationally	17%
% Unfunded	69%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **49 million**



Viet Nam

HIGH TB BURDEN | HIGH HIV BURDEN | HIGH MDR-TB BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	17 (12–24)	19 (13–26)
Mortality (HIV+TB only)	2 (1.2–2.9)	2.1 (1.3–3.2)
Prevalence (includes HIV+TB)	190 (79–350)	209 (86–384)
Incidence (includes HIV+TB)	130 (110–160)	144 (121–174)
Incidence (HIV+TB only)	9.4 (8–12)	10 (8.7–13)
Case detection, all forms (%)	76 (63–91)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	4 (2.5–5.4)	23 (17–30)
MDR-TB cases among notified pulmonary TB cases	3 000 (1 900–4 100)	2 100 (1 500–2 600)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	50 607	7 059
Pulmonary, clinically diagnosed	24 403	
Extrapulmonary	18 326	

Total new and relapse 100 395

Previously treated, excluding relapses 1 801

Total cases notified 102 196

Among 50 607 new cases:

143 (<1%) cases aged under 15 years; male:female ratio: 2.9

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	353 (<1%)	3 955 (45%)	4 531
Laboratory-confirmed RR-/MDR-TB cases			1 204
Patients started on MDR-TB treatment			948

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	71 374	(70)
HIV-positive TB patients	4 438	(6)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	3 205	(72)
HIV-positive TB patients on antiretroviral therapy (ART)	2 715	(61)
HIV-positive people screened for TB		
HIV-positive people provided with IPT		

Treatment success rate (%)

New and relapse cases registered in 2012	91
Previously treated cases, excluding relapse, registered in 2012	
HIV-positive TB cases, all types, registered in 2012	72
RR-/MDR-TB cases started on second-line treatment in 2011	72
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	1.1
Culture (per 5 million population)	1.3
Drug susceptibility testing (per 5 million population)	0.1
Sites performing Xpert MTB/RIF	27
Is second-line drug susceptibility testing available?	Yes, in country

Financing TB control 2014

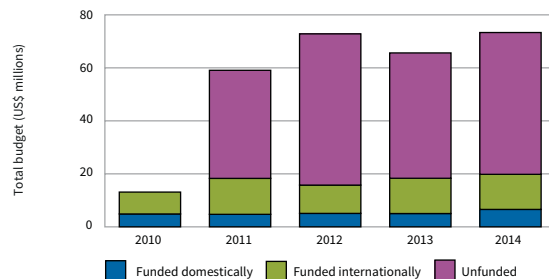
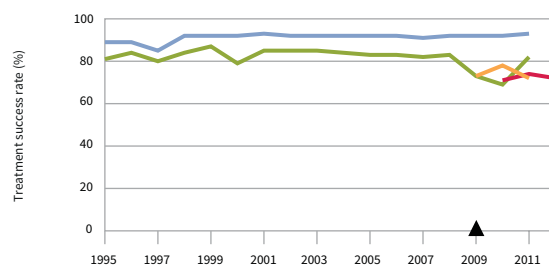
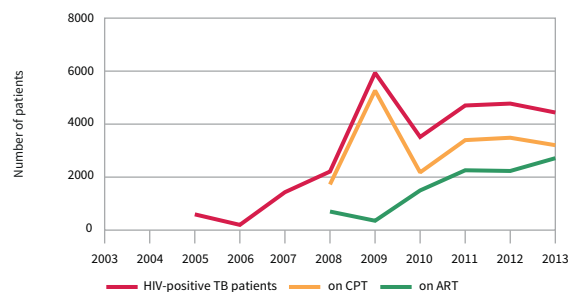
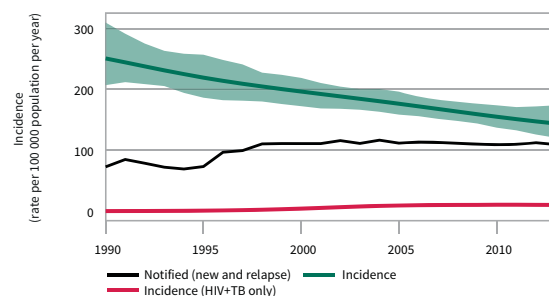
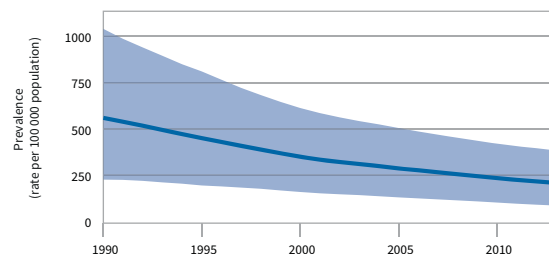
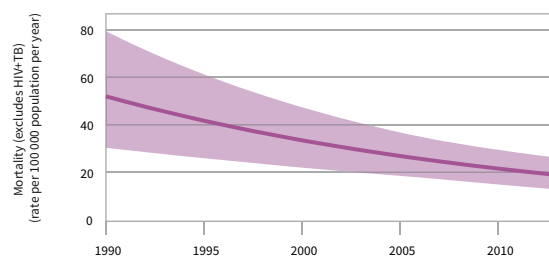
National TB programme budget (US\$ millions)	73
% Funded domestically	9%
% Funded internationally	18%
% Unfunded	73%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **92 million**



Zimbabwe

HIGH TB BURDEN | HIGH HIV BURDEN

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	5.7 (3.6–7.4)	40 (25–52)
Mortality (HIV+TB only)	22 (17–27)	153 (121–189)
Prevalence (includes HIV+TB)	58 (33–89)	409 (235–630)
Incidence (includes HIV+TB)	78 (67–91)	552 (474–643)
Incidence (HIV+TB only)	56 (48–66)	395 (341–464)
Case detection, all forms (%)	42 (36–49)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	1.9 (1–3.3)	8.3 (1.8–23)
MDR-TB cases among notified pulmonary TB cases	520 (270–900)	300 (66–820)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	11 404	1 275
Pulmonary, clinically diagnosed	15 807	
Extrapulmonary	4 413	

Total new and relapse	32 899
Previously treated, excluding relapses	2 379
Total cases notified	35 278

Among 32 899 new and relapse cases:
2 567 (8%) cases aged under 15 years; male:female ratio: 1.3

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB			4 276
Laboratory-confirmed RR-/MDR-TB cases			433
Patients started on MDR-TB treatment			351

TB/HIV 2013

	NUMBER	(%)
TB patients with known HIV status	32 460	(92)
HIV-positive TB patients	22 442	(69)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	17 267	(77)
HIV-positive TB patients on antiretroviral therapy (ART)	17 267	(77)
HIV-positive people screened for TB	323 431	
HIV-positive people provided with IPT	10 926	

Treatment success rate (%)

New cases registered in 2012	81
Previously treated cases registered in 2012	
HIV-positive TB cases, all types, registered in 2012	
RR-/MDR-TB cases started on second-line treatment in 2011	81
XDR-TB cases started on second-line treatment in 2011	

Laboratories 2013

Smear (per 100 000 population)	1.5
Culture (per 5 million population)	0.7
Drug susceptibility testing (per 5 million population)	0.7
Sites performing Xpert MTB/RIF	58
Is second-line drug susceptibility testing available?	Yes, in and outside country

Financing TB control 2014

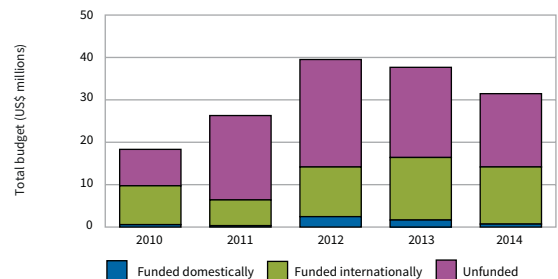
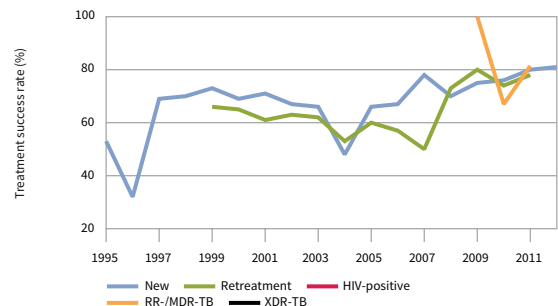
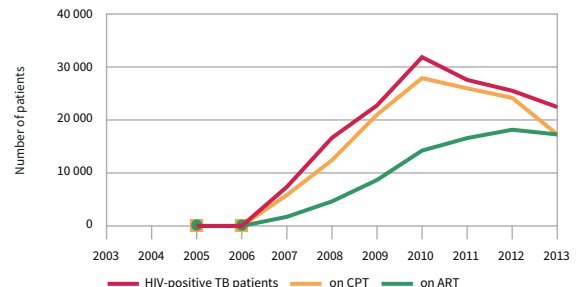
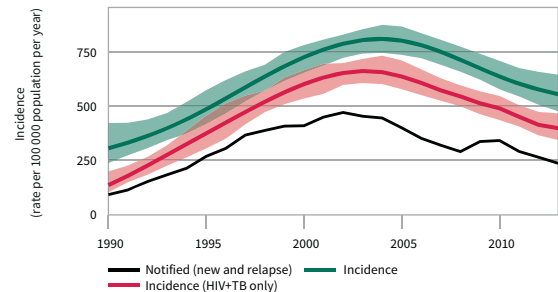
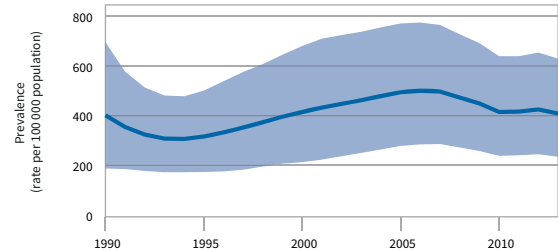
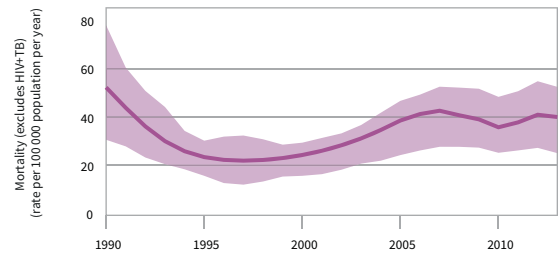
National TB programme budget (US\$ millions)	31
% Funded domestically	2%
% Funded internationally	43%
% Unfunded	55%

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

Population 2013 **14 million**



ANNEX 3

Regional profiles

WHO African Region

WHO MEMBER STATES 47

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	390 (300–500)	42 (32–54)
Mortality (HIV+TB only)	300 (250–350)	32 (27–38)
Prevalence (includes HIV+TB)	2 800 (2 400–3 200)	300 (263–341)
Incidence (includes HIV+TB)	2 600 (2 300–2 900)	280 (251–311)
Incidence (HIV+TB only)	870 (790–960)	94 (86–104)
Case detection, all forms (%)	52 (46–57)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2.4 (0.2–5)	13 (0.02–27)
MDR-TB cases among notified pulmonary TB cases	25 000 (2 100–52 000)	18 000 (28–37 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	591 519	45 232
Pulmonary, clinically diagnosed	457 249	18 093
Extrapulmonary	224 742	1 368

Total new and relapse 1 338 203

Previously treated, excluding relapses 75 882

Total cases notified 1 414 085

Among 1 050 607 reported new and relapse^c cases disaggregated by age, 95 764 (9.1%) cases were aged < 15 years

Among 1 036 642 reported new and relapse^c cases disaggregated by sex, male:female ratio = 1.4

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	5 083 (<1%)	9 925 (7.1%)	292 797
Laboratory-confirmed RR-/MDR-TB cases			32 480
Patients started on MDR-TB treatment			14 418

TB/HIV 2013

	NUMBER	(%) ^d
TB patients with known HIV status	1 068 146	(76)
HIV-positive TB patients	432 994	(41)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	362 883	(87)
HIV-positive TB patients on antiretroviral therapy (ART)	295 278	(69)
HIV-positive people screened for TB	3 933 281	
HIV-positive people provided with IPT	539 381	

Treatment success rate (%)

New and relapse ^c cases registered in 2012	81
Previously treated cases, excluding relapse, registered in 2012	48
HIV-positive TB cases, all types, registered in 2012	68
RR-/MDR-TB cases started on second-line treatment in 2011	47
XDR-TB cases started on second-line treatment in 2011	16

Laboratories 2013

	NUMBER OF MEMBER STATES ^e
Smear (per 100 000 population) > 1	26 out of 44
Culture (per 5 million population) > 1	14 out of 44
Drug susceptibility testing (per 5 million population) > 1	10 out of 44

Financing TB control (low- and middle-income countries)^{e,f} 2014

National TB programme budget (US\$ millions)	917
% Funded domestically	29
% Funded internationally	31
% Unfunded	41

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

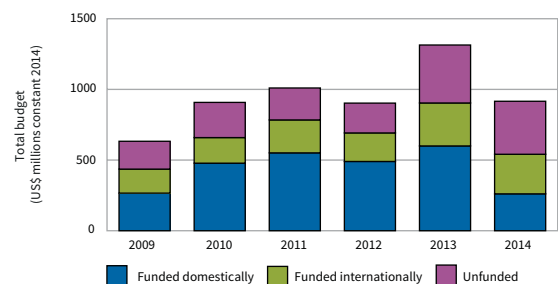
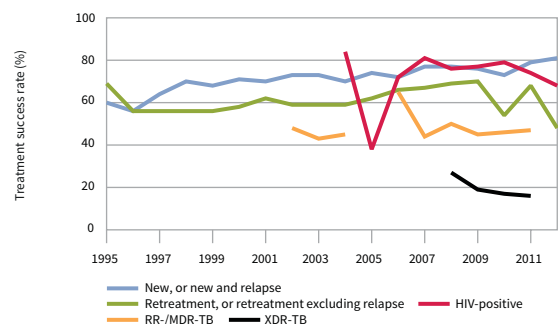
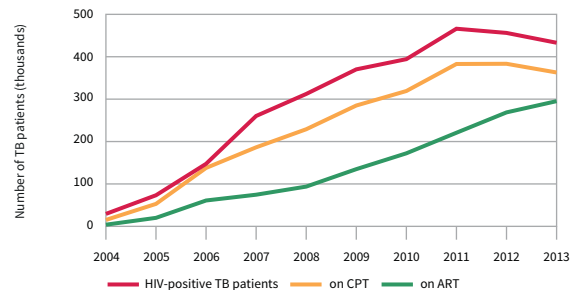
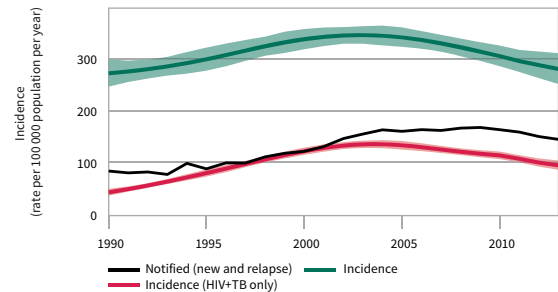
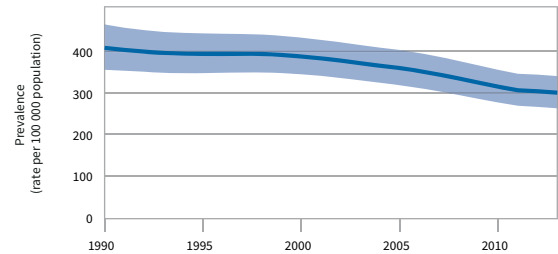
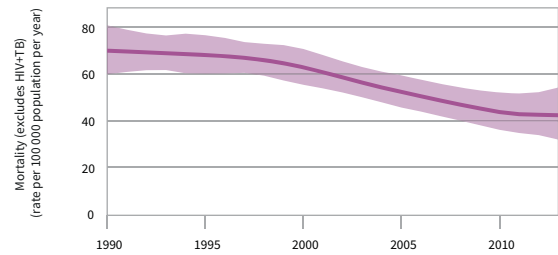
^c Some countries reported on new cases only.

^d Calculations exclude countries with missing numerators or denominators.

^e Data are not collected from all Member States.

^f Financing indicators exclude funding for general healthcare services provided outside NTPs.

Population 2013 **927 million**



WHO/PAHO Region of the Americas

Population 2013 **971 million**

WHO MEMBER STATES 35
OTHER COUNTRIES AND TERRITORIES 11

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	14 (12–17)	1.5 (1.2–1.7)
Mortality (HIV+TB only)	6 (6–7)	0.63 (0.56–0.71)
Prevalence (includes HIV+TB)	370 (290–460)	38 (30–48)
Incidence (includes HIV+TB)	280 (270–300)	29 (28–31)
Incidence (HIV+TB only)	32 (31–33)	3.3 (3.2–3.4)
Case detection, all forms (%)	77 (73–80)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2.2 (1.3–3)	13 (4.9–22)
MDR-TB cases among notified pulmonary TB cases	3 800 (2 200–5 200)	3 300 (1 200–5 400)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	129 469	10 004
Pulmonary, clinically diagnosed	42 365	2 416
Extrapulmonary	33 777	844

Total new and relapse	218 875
Previously treated, excluding relapses	12 455
Total cases notified	231 330

Among 212 141 reported new and relapse^c cases disaggregated by age, 11 271 (5.3%) cases were aged < 15 years
Among 214 005 reported new and relapse^c cases disaggregated by sex, male:female ratio = 1.7

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	27 922 (22%)	6 252 (24%)	40 769
Laboratory-confirmed RR-/MDR-TB cases			3 362
Patients started on MDR-TB treatment			2 977

TB/HIV 2013

	NUMBER	(%) ^d
TB patients with known HIV status	159 784	(69)
HIV-positive TB patients	21 290	(14)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	4 434	(51)
HIV-positive TB patients on antiretroviral therapy (ART)	6 651	(65)
HIV-positive people screened for TB	9 281	
HIV-positive people provided with IPT	23 858	

Treatment success rate (%)

New and relapse ^c cases registered in 2012	76
Previously treated cases, excluding relapse, registered in 2012	46
HIV-positive TB cases, all types, registered in 2012	54
RR-/MDR-TB cases started on second-line treatment in 2011	56
XDR-TB cases started on second-line treatment in 2011	27

Laboratories 2013

	NUMBER OF MEMBER STATES ^e
Smear (per 100 000 population) > 1	19 out of 23
Culture (per 5 million population) > 1	21 out of 23
Drug susceptibility testing (per 5 million population) > 1	9 out of 23

Financing TB control (low- and middle-income countries)^{e,f} 2014

National TB programme budget (US\$ millions)	187
% Funded domestically	70
% Funded internationally	11
% Unfunded	19

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

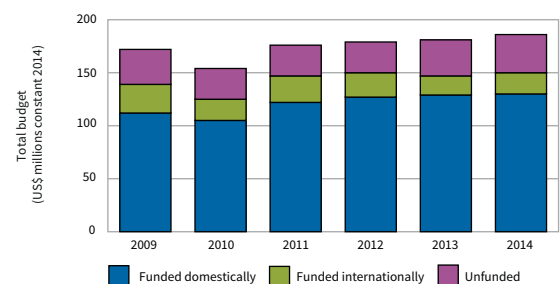
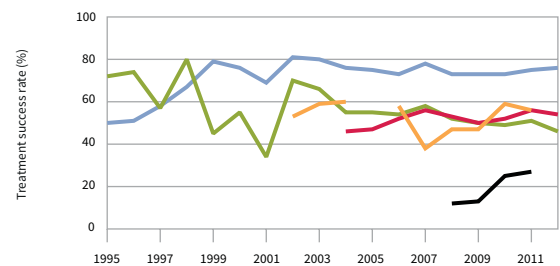
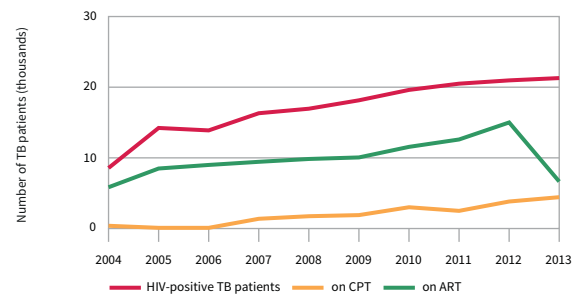
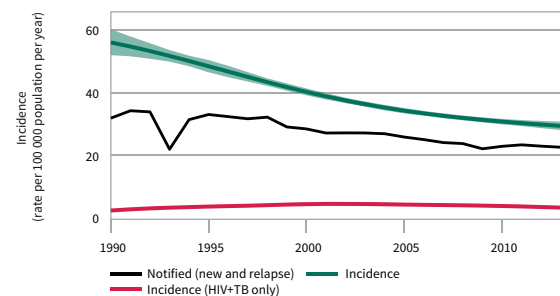
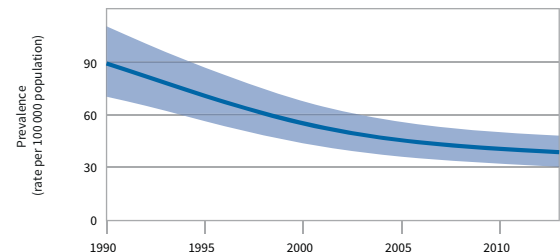
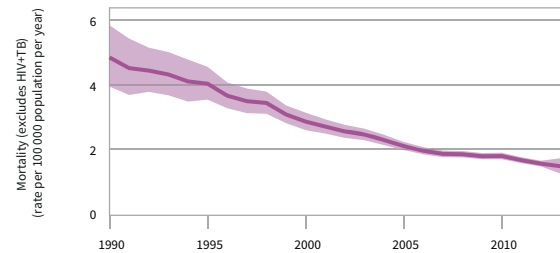
^b Includes cases with unknown previous TB treatment history.

^c Some countries reported on new cases only.

^d Calculations exclude countries with missing numerators or denominators.

^e Data are not collected from all Member States.

^f Financing indicators exclude funding for general healthcare services provided outside NTPs.



WHO Eastern Mediterranean Region

Population 2013 **617 million**

WHO MEMBER STATES 21
OTHER COUNTRIES AND TERRITORIES 1

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	140 (90–210)	23 (15–34)
Mortality (HIV+TB only)	2 (1–2)	0.3 (0.21–0.4)
Prevalence (includes HIV+TB)	1 000 (880–1 200)	165 (143–189)
Incidence (includes HIV+TB)	750 (620–890)	121 (100–144)
Incidence (HIV+TB only)	5 (4–6)	0.83 (0.64–1)
Case detection, all forms (%)	58 (49–71)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	3.6 (2.3–5)	22 (12–32)
MDR-TB cases among notified pulmonary TB cases	12 000 (7 400–16 000)	5 700 (3 200–8 200)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	173 949	11 251
Pulmonary, clinically diagnosed	148 748	112
Extrapulmonary	99 897	476

Total new and relapse 434 433

Previously treated, excluding relapses 14 164

Total cases notified 448 597

Among 409 034 reported new and relapse^c cases disaggregated by age,

39 697 (9.7%) cases were aged < 15 years

Among 417 244 reported new and relapse^c cases disaggregated by sex,

male:female ratio = 1.0

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	13 584 (7.8%)	5 452 (21%)	23 503
Laboratory-confirmed RR-/MDR-TB cases			3 687
Patients started on MDR-TB treatment			2 013

TB/HIV 2013

	NUMBER	(%) ^d
TB patients with known HIV status	51 362	(11)
HIV-positive TB patients	1 244	(2.4)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	400	(57)
HIV-positive TB patients on antiretroviral therapy (ART)	364	(38)
HIV-positive people screened for TB	12 860	
HIV-positive people provided with IPT	265	

Treatment success rate (%)

New and relapse ^c cases registered in 2012	87
Previously treated cases, excluding relapse, registered in 2012	76
HIV-positive TB cases, all types, registered in 2012	53
RR-/MDR-TB cases started on second-line treatment in 2011	64
XDR-TB cases started on second-line treatment in 2011	38

Laboratories 2013

	NUMBER OF MEMBER STATES ^e
Smear (per 100 000 population) > 1	4 out of 15
Culture (per 5 million population) > 1	8 out of 15
Drug susceptibility testing (per 5 million population) > 1	4 out of 15

Financing TB control (low- and middle-income countries)^{e,f} 2014

National TB programme budget (US\$ millions)	237
% Funded domestically	30
% Funded internationally	29
% Unfunded	41

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

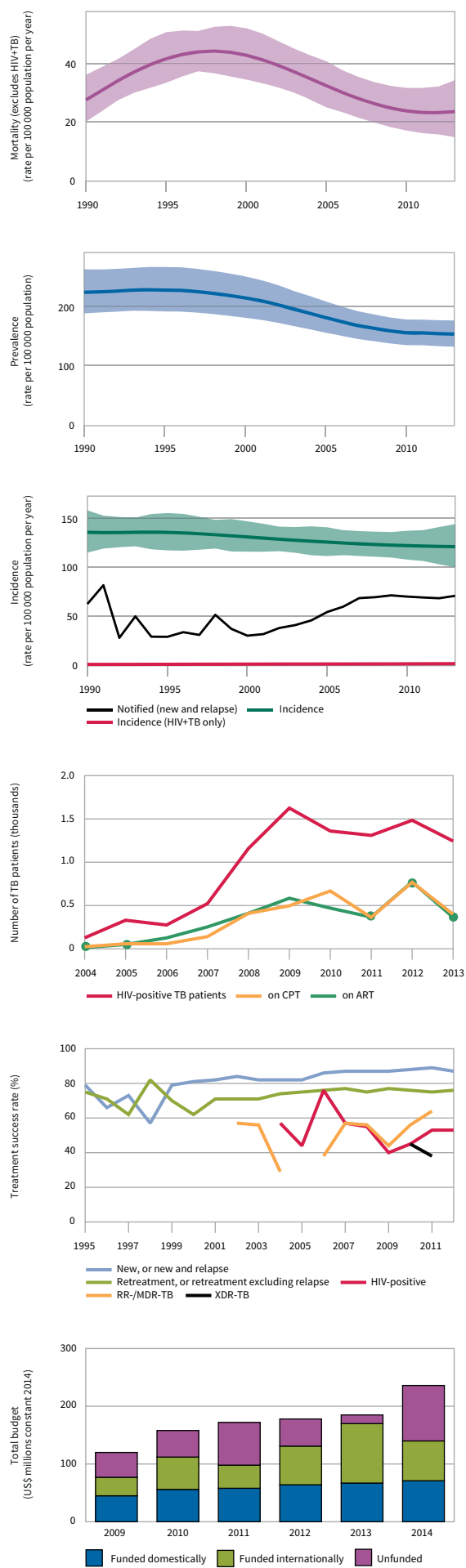
^b Includes cases with unknown previous TB treatment history.

^c Some countries reported on new cases only.

^d Calculations exclude countries with missing numerators or denominators.

^e Data are not collected from all Member States.

^f Financing indicators exclude funding for general healthcare services provided outside NTPs.



WHO European Region

WHO MEMBER STATES 53
OTHER COUNTRIES AND TERRITORIES 1

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	38 (37–39)	4.1 (4–4.2)
Mortality (HIV+TB only)	4 (3–4)	0.42 (0.35–0.48)
Prevalence (includes HIV+TB)	460 (350–590)	51 (39–65)
Incidence (includes HIV+TB)	360 (340–370)	39 (38–41)
Incidence (HIV+TB only)	21 (20–22)	2.3 (2.2–2.5)
Case detection, all forms (%)	80 (77–84)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	14 (9.7–19)	44 (36–52)
MDR-TB cases among notified pulmonary TB cases	29 000 (20 000–38 000)	45 000 (37 000–53 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	116 082	27 162
Pulmonary, clinically diagnosed	87 583	12 726
Extrapulmonary	41 245	2 217

Total new and relapse	287 015
Previously treated, excluding relapses	62 730
Total cases notified	349 745

Among 262 521 reported new and relapse^c cases disaggregated by age, 10 902 (4.2%) cases were aged < 15 years
Among 264 979 reported new and relapse^c cases disaggregated by sex, male:female ratio = 2.0

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	95 161 (82%)	43 027 (41%)	156 669
Laboratory-confirmed RR-/MDR-TB cases			45 136
Patients started on MDR-TB treatment			46 517

TB/HIV 2013

	NUMBER	(%) ^d
TB patients with known HIV status	206 650	(59)
HIV-positive TB patients	16 747	(8.0)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	6 026	(56)
HIV-positive TB patients on antiretroviral therapy (ART)	6 149	(54)
HIV-positive people screened for TB	30 628	
HIV-positive people provided with IPT	18 714	

Treatment success rate (%)

New and relapse ^c cases registered in 2012	75
Previously treated cases, excluding relapse, registered in 2012	57
HIV-positive TB cases, all types, registered in 2012	56
RR-/MDR-TB cases started on second-line treatment in 2011	46
XDR-TB cases started on second-line treatment in 2011	27

Laboratories 2013

	NUMBER OF MEMBER STATES ^e
Smear (per 100 000 population) > 1	11 out of 53
Culture (per 5 million population) > 1	39 out of 53
Drug susceptibility testing (per 5 million population) > 1	35 out of 53

Financing TB control (low- and middle-income countries)^{e,f} 2014

NATIONAL TB PROGRAMME BUDGET (US\$ MILLIONS)	2 413
% FUNDED DOMESTICALLY	93
% FUNDED INTERNATIONALLY	3.8
% UNFUNDED	3.3

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

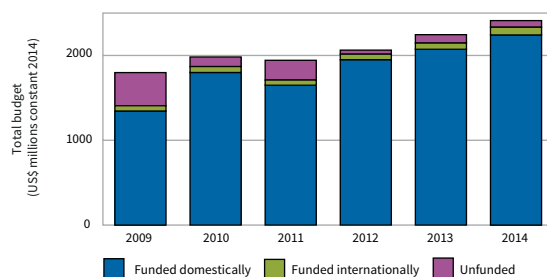
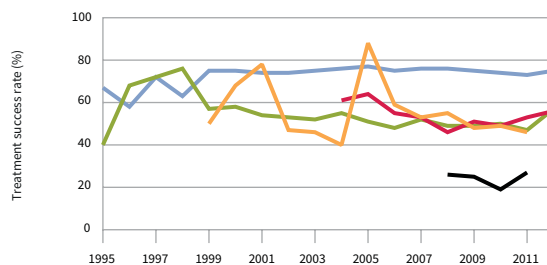
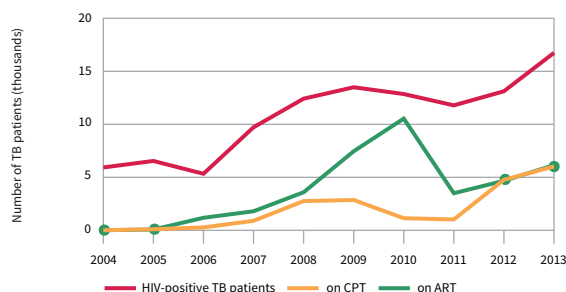
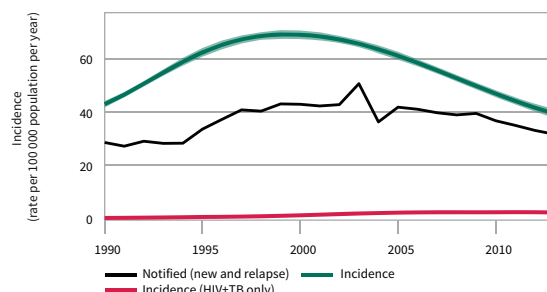
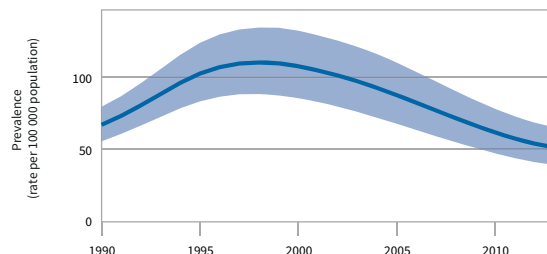
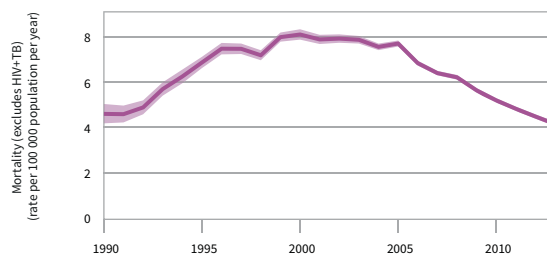
^c Some countries reported on new cases only.

^d Calculations exclude countries with missing numerators or denominators.

^e Data are not collected from all Member States.

^f Financing indicators exclude funding for general healthcare services provided outside NTPs.

Population 2013 **907 million**



WHO South-East Asia Region

WHO MEMBER STATES 11

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	440 (330–550)	23 (18–30)
Mortality (HIV+TB only)	48 (42–55)	2.6 (2.2–3)
Prevalence (includes HIV+TB)	4 500 (3 500–5 700)	244 (188–307)
Incidence (includes HIV+TB)	3 400 (3 200–3 600)	183 (175–192)
Incidence (HIV+TB only)	170 (150–190)	9 (8.1–10)
Case detection, all forms (%)	62 (59–65)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	2.2 (1.8–2.7)	16 (12–20)
MDR-TB cases among notified pulmonary TB cases	36 000 (29 000–44 000)	53 000 (41 000–66 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	1 054 316	128 256
Pulmonary, clinically diagnosed	580 374	1 558
Extrapulmonary	333 666	0

Total new and relapse 2 098 170

Previously treated, excluding relapses 198 863

Total cases notified 2 297 033

Among 1 868 824 reported new and relapse^c cases disaggregated by age, 102 196 (5.5%) cases were aged < 15 years

Among 624 919 reported new and relapse^c cases disaggregated by sex, male:female ratio = 1.5

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	12 333 (1.2%)	19 018 (5.8%)	286 323
Laboratory-confirmed RR-/MDR-TB cases			40 335
Patients started on MDR-TB treatment			23 766

TB/HIV 2013

	NUMBER	(%) ^d
TB patients with known HIV status	980 559	(43)
HIV-positive TB patients	59 462	(6.1)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	52 441	(88)
HIV-positive TB patients on antiretroviral therapy (ART)	48 141	(81)
HIV-positive people screened for TB	1 149 974	
HIV-positive people provided with IPT	1 142	

Treatment success rate (%)

New and relapse ^c cases registered in 2012	88
Previously treated cases, excluding relapse, registered in 2012	75
HIV-positive TB cases, all types, registered in 2012	76
RR-/MDR-TB cases started on second-line treatment in 2011	54
XDR-TB cases started on second-line treatment in 2011	39

Laboratories 2013

	NUMBER OF MEMBER STATES ^e
Smear (per 100 000 population) > 1	9 out of 11
Culture (per 5 million population) > 1	3 out of 11
Drug susceptibility testing (per 5 million population) > 1	2 out of 11

Financing TB control (low- and middle-income countries)^{e,f} 2014

National TB programme budget (US\$ millions)	551
% Funded domestically	41
% Funded internationally	35
% Unfunded	23

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

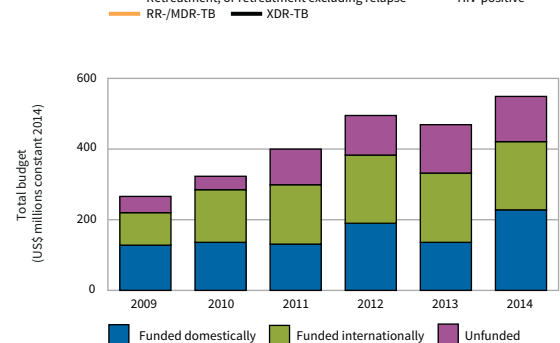
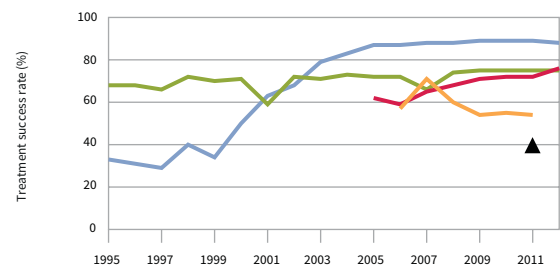
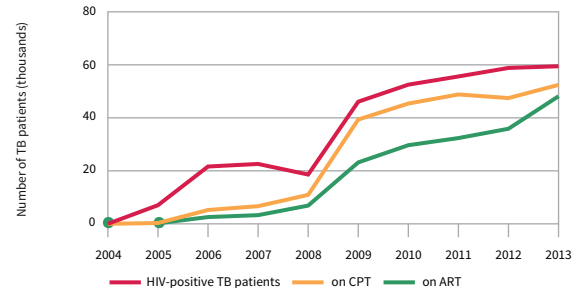
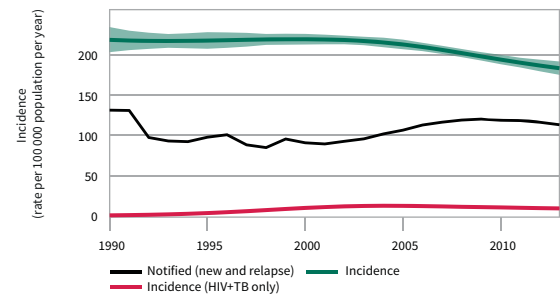
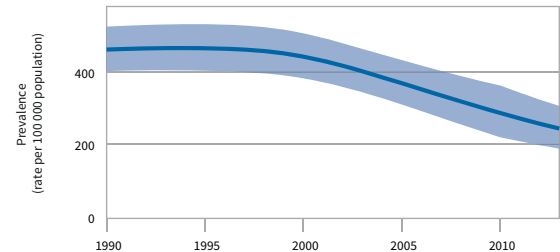
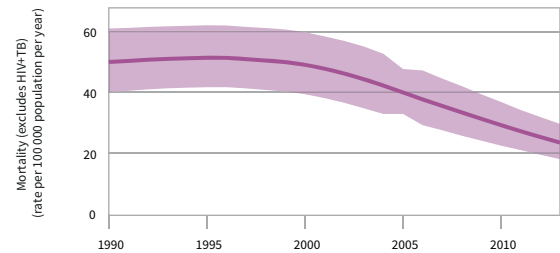
^c Some countries reported on new cases only.

^d Calculations exclude countries with missing numerators or denominators.

^e Data are not collected from all Member States.

^f Financing indicators exclude funding for general healthcare services provided outside NTPs.

Population 2013 **1855 million**



WHO Western Pacific Region

WHO MEMBER STATES 27
OTHER COUNTRIES AND TERRITORIES 9

Estimates of TB burden^a 2013

	NUMBER (thousands)	RATE (per 100 000 population)
Mortality (excludes HIV+TB)	110 (100–120)	5.8 (5.4–6.3)
Mortality (HIV+TB only)	5 (4–6)	0.26 (0.2–0.32)
Prevalence (includes HIV+TB)	2 300 (2 000–2 500)	121 (109–134)
Incidence (includes HIV+TB)	1 600 (1 500–1 700)	87 (82–92)
Incidence (HIV+TB only)	23 (19–26)	1.2 (1–1.4)
Case detection, all forms (%)	83 (79–88)	

Estimates of MDR-TB burden^a 2013

	NEW	RETREATMENT
% of TB cases with MDR-TB	4.4 (2.6–6.3)	22 (18–26)
MDR-TB cases among notified pulmonary TB cases	53 000 (31 000–75 000)	18 000 (15 000–21 000)

TB case notifications 2013

	NEW ^b	RELAPSE
Pulmonary, bacteriologically confirmed	496 303	46 025
Pulmonary, clinically diagnosed	700 129	2 440
Extrapulmonary	96 838	1 322

Total new and relapse	1 343 057
Previously treated, excluding relapses	32 689
Total cases notified	1 375 746

Among 1 136 370 reported new and relapse^c cases disaggregated by age, 15 170 (1.3%) cases were aged < 15 years
Among 1 114 062 reported new and relapse^c cases disaggregated by sex, male:female ratio = 2.2

Reported cases of RR-/MDR-TB 2013

	NEW	RETREATMENT	TOTAL ^b
Cases tested for RR-/MDR-TB	63 512 (13%)	38 593 (47%)	115 224
Laboratory-confirmed RR-/MDR-TB cases			11 412
Patients started on MDR-TB treatment			6 926

TB/HIV 2013

	NUMBER	(%) ^d
TB patients with known HIV status	480 489	(35)
HIV-positive TB patients	13 100	(2.7)
HIV-positive TB patients on co-trimoxazole preventive therapy (CPT)	4 777	(58)
HIV-positive TB patients on antiretroviral therapy (ART)	7 711	(60)
HIV-positive people screened for TB	369 779	
HIV-positive people provided with IPT	2 566	

Treatment success rate (%)

New and relapse ^c cases registered in 2012	92
Previously treated cases, excluding relapse, registered in 2012	82
HIV-positive TB cases, all types, registered in 2012	57
RR-/MDR-TB cases started on second-line treatment in 2011	52
XDR-TB cases started on second-line treatment in 2011	39

Laboratories 2013

	NUMBER OF MEMBER STATES ^e
Smear (per 100 000 population) > 1	13 out of 17
Culture (per 5 million population) > 1	10 out of 17
Drug susceptibility testing (per 5 million population) > 1	4 out of 17

Financing TB control (low- and middle-income countries)^{e,f} 2014

National TB programme budget (US\$ millions)	618
% Funded domestically	55
% Funded internationally	12
% Unfunded	33

Data are as reported to WHO. Estimates of TB and MDR-TB burden are produced by WHO in consultation with countries.

^a Ranges represent uncertainty intervals.

^b Includes cases with unknown previous TB treatment history.

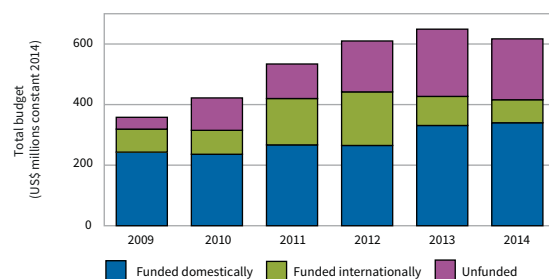
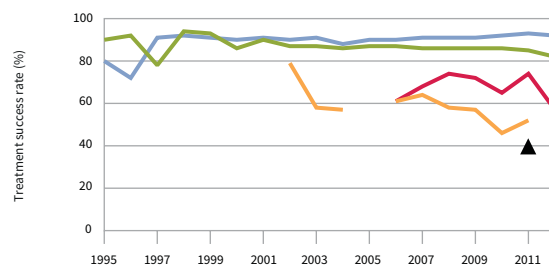
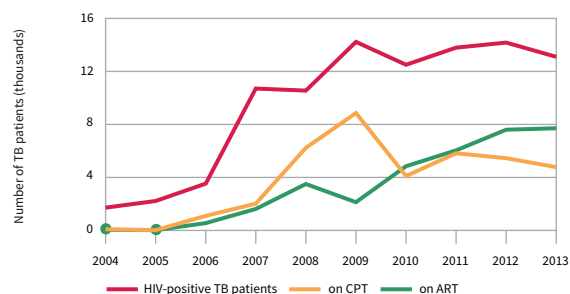
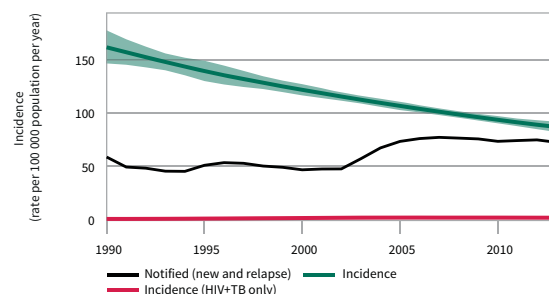
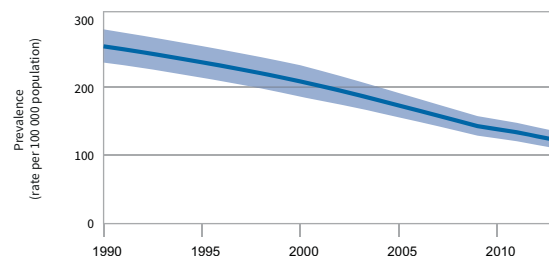
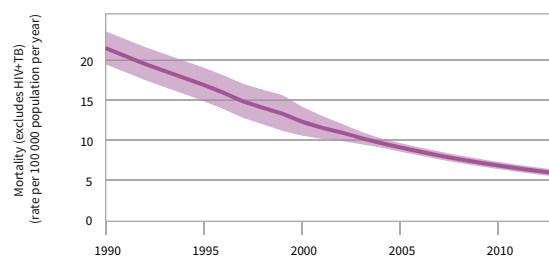
^c Some countries reported on new cases only.

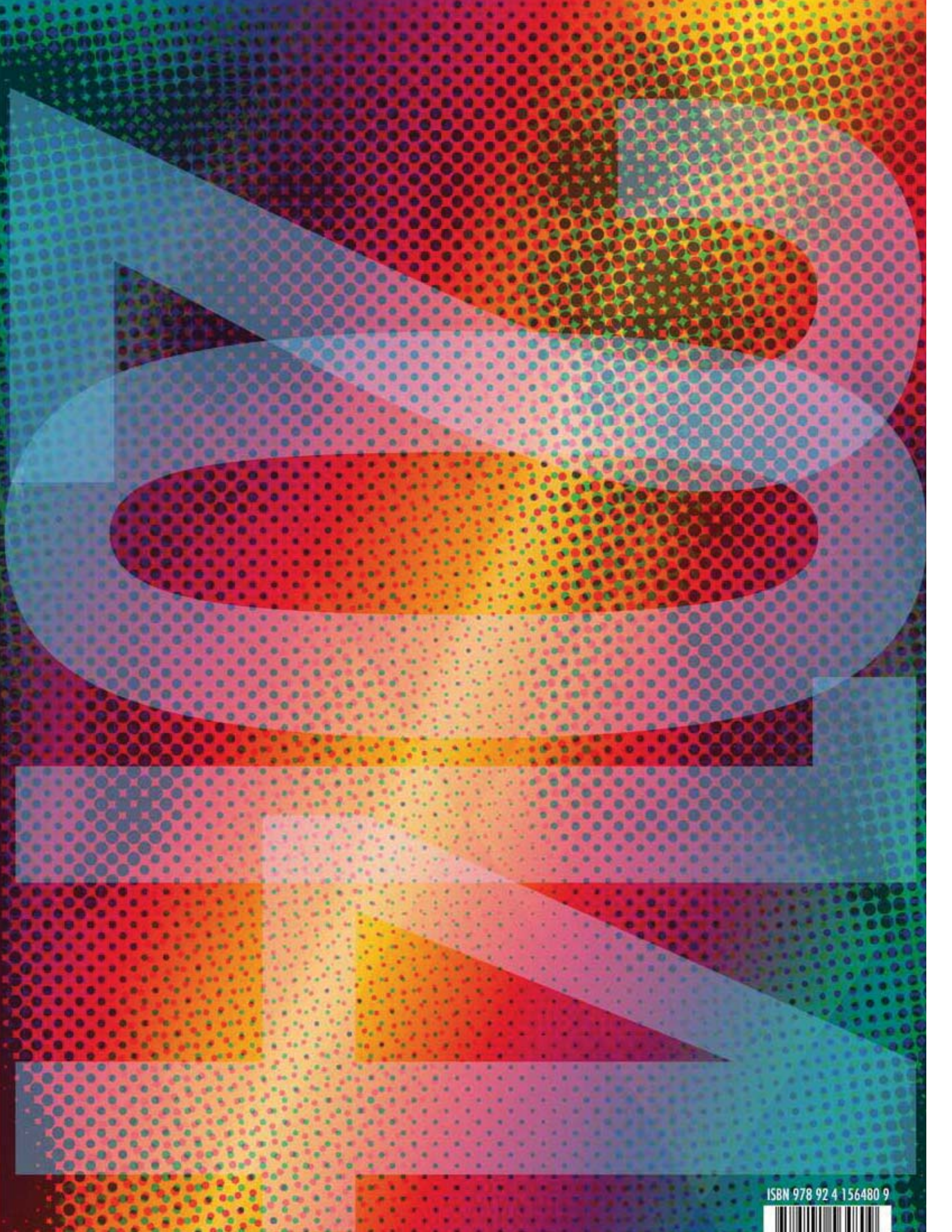
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Population 2013 **1858 million**





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