

Global actions and investments fall far short of those needed to end the global TB epidemic.

# :: Executive Summary

### Background

The Sustainable Development Goals (SDGs) for 2030 were adopted by the United Nations in 2015. One of the targets is to end the global TB epidemic. The WHO End TB Strategy, approved by the World Health Assembly in 2014, calls for a 90% reduction in TB deaths and an 80% reduction in the TB incidence rate by 2030, compared with 2015.

This global TB report is the first to be produced in the era of the SDGs and the End TB Strategy. It provides an assessment of the TB epidemic and progress in TB diagnosis, treatment and prevention efforts, as well as an overview of TB-specific financing and research. It also discusses the broader agenda of universal health coverage, social protection and other SDGs that have an impact on health. Data were available for 202 countries and territories that account for over 99% of the world's population and TB cases.

## Main findings and messages

#### Status of the TB epidemic and MDR-TB crisis

The TB epidemic is larger than previously estimated, reflecting new surveillance and survey data from India. However, the number of TB deaths and the TB incidence rate continue to fall globally and in India.

In 2015, there were an estimated 10.4 million new (incident) TB cases worldwide, of which 5.9 million (56%) were among men, 3.5 million (34%) among women and 1.0 million (10%) among children. People living with HIV accounted for 1.2 million (11%) of all new TB cases.

Six countries accounted for 60% of the new cases: India, Indonesia, China, Nigeria, Pakistan and South Africa.<sup>1</sup> Global progress depends on major advances in TB prevention and care in these countries. Worldwide, the rate of decline in TB incidence remained at only 1.5% from 2014 to 2015. This needs to accelerate to a 4–5% annual decline by 2020 to reach the first milestones of the End TB Strategy.

In 2015, there were an estimated 480 000 new cases of multidrug-resistant TB (MDR-TB) and an additional 100 000 people with rifampicin-resistant TB (RR-TB) who were also newly eligible for MDR-TB treatment.<sup>2</sup> India, China and the Russian Federation accounted for 45% of the combined total of 580 000 cases.

There were an estimated 1.4 million TB deaths in 2015, and an additional 0.4 million deaths resulting from TB disease among people living with HIV.<sup>3</sup> Although the number of TB deaths fell by 22% between 2000 and 2015, TB remained one of the top 10 causes of death worldwide in 2015.

#### TB care and prevention results

TB treatment averted 49 million deaths globally between 2000 and 2015, but important diagnostic and treatment gaps persist.

In 2015, 6.1 million new TB cases were notified to national authorities and reported to WHO. Notified TB cases increased from 2013-2015, mostly due to a 34% increase in notifications in India. However, globally there was a 4.3 million gap<sup>4</sup> between incident and notified cases, with India, Indonesia and Nigeria accounting for almost half of this gap.<sup>5</sup>

The crisis of MDR-TB detection and treatment continues. In 2015, of the estimated 580 000 people newly eligible for MDR-TB treatment, only 125 000 (20%) were enrolled. Five countries accounted for more than 60% of the gap: India, China, the Russian Federation, Indonesia and Nigeria.<sup>5</sup> Globally, the MDR-TB treatment success rate was 52% in 2013.<sup>6</sup>

In 2015, 55% of notified TB patients had a documented HIV test result. The proportion of HIV-positive TB patients on antiretroviral therapy (ART) was 78%.

Access to TB preventive treatment needs to be expanded. A total of 910 000 people living with HIV were started on such treatment in 2015, as well as 87 000 children under five (7% of those eligible).

# TB financing, universal health coverage, social protection and social determinants

US\$ 6.6 billion was available for TB care and prevention in low and middle-income countries in 2016, of which 84% was from domestic sources. Nonetheless, national TB programmes (NTPs) in low-income countries continue to rely on international donors for almost 90% of their financing. Investments in low and middle-income countries fall almost US\$ 2 billion short of the US\$ 8.3 billion needed in 2016. This annual gap will widen to US\$ 6 billion in 2020 if current funding levels do not increase.

Improvements are also needed in overall health financing. Government expenditures on health in 2014 were less than the WHO benchmark of at least 6% of gross domestic product (GDP) in 150 countries. Out-of-pocket expenditures exceeded 45% of total health expenditures in 46 countries, including 11 of the 30 high TB burden countries.

#### TB research and development

Despite some progress in the pipeline for new diagnostics, drugs and regimens, and vaccines, TB research and development remains severely underfunded.

### Additional highlights from the report

#### A new era of global TB monitoring

The End TB Strategy has three high-level indicators: the TB incidence rate, the absolute number of TB deaths and the percentage of TB patients and their households that experience catastrophic costs as a result of TB disease. Targets for these indicators have been set for 2030 and 2035, with accompanying milestones for 2020 and 2025.

The 2020 milestones of the End TB Strategy are a 35% reduction in the absolute number of TB deaths and a 20% reduction in the TB incidence rate, compared with levels in 2015; and that no TB-affected households face catastrophic costs.

WHO has defined three lists of high burden countries for the period 2016–2020, for TB, TB/HIV and MDR-TB. Each list includes 30 countries.

#### TB disease burden

Upward revisions to estimates of the burden of TB disease in India for the period 2000–2015 follow accumulating evidence that previous estimates were too low. This evidence includes household surveys, a state-wide TB prevalence survey, studies of anti-TB drug sales in the private sector, notification data and new analysis of mortality data. Since India accounts for more than one quarter of the world's TB cases and deaths, these revisions have had a major impact on global estimates. Estimates for India are considered interim, pending a national TB prevalence survey scheduled for 2017/2018.

The proportion of TB cases living with HIV was highest in the WHO African Region (31%), and exceeded 50% in parts of southern Africa.

In addition to accelerating the annual decline in TB incidence, reaching the 2020 milestone for a 35% reduction in TB deaths requires reducing the global proportion of people with TB who die from the disease (the case fatality ratio or CFR) from 17% in 2015 to 10% by 2020.

The CFR in 2015 varied from under 5% in a few countries to more than 20% in most countries in the WHO African Region. This shows considerable inequalities among countries in access to TB diagnosis and treatment that need to be addressed. If everyone with TB had a timely diagnosis and high-quality treatment, the CFR would be low in all countries.

National notification and vital registration systems (with standard coding of causes of death) of high coverage and quality are needed in all countries. In the interim, national TB prevalence surveys will continue to provide the best method for directly measuring the burden of TB disease and identifying actions required to reduce that burden in an important subset of countries. In recent years, there has been enormous progress in implementing such surveys, with 22 completed between 2009 and August 2016.

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

The global male:female (M:F) ratio for notifications was 1.7, varying from 1.0 in Pakistan to 3.1 in Viet Nam among the 30 high TB burden countries. Results from national TB prevalence surveys of adults show higher M:F ratios, indicating that notification data understate the share of the TB burden accounted for by men in some countries. Globally, children (aged <15 years) accounted for 6.3% of the new cases that were notified in 2015.

In 2015, 30% of the 3.4 million new bacteriologically confirmed and previously treated TB cases notified globally were reported to have had drug susceptibility testing for rifampicin, with coverage of 24% for new TB patients and 53% for previously treated TB patients.

The only WHO-recommended rapid diagnostic test for detection of TB and rifampicin resistance currently available is the Xpert MTB/RIF® assay. Of the 48 countries in at least one of the three new lists of high burden countries, 15 had adopted national algorithms positioning Xpert MTB/ RIF as the initial diagnostic test for all people with signs and symptoms of pulmonary TB by the end of 2015. These countries accounted for 10% of the estimated global number of incident TB cases in 2015.

In 2015, the gap of 4.3 million between notifications of new cases and the estimated number of incident cases<sup>4</sup> reflects a mixture of underreporting of detected TB cases (especially in countries with large private sectors) and underdiagnosis (especially in countries where there are major geographic or financial barriers to accessing care). Ten countries accounted for 77% of the total estimated gap: India, Indonesia, Nigeria, Pakistan, South Africa, Bangladesh, the Democratic Republic of the Congo, China, the United Republic of Tanzania and Mozambique.<sup>5</sup>

In the African Region where the burden of HIVassociated TB is highest, 81% of notified TB patients had a documented HIV test result. The proportion of known HIV-positive TB patients on ART was above 90% in India, Kenya, Malawi, Mozambique, Namibia and Swaziland.

The latest treatment outcome data show a treatment success rate of 83% for TB (2014 cohort), 52% for MDR-TB (2013 cohort) and 28% for extensively drug-resistant TB (XDR-TB; 2013 cohort).

At least 23 countries in Africa and Asia have introduced shorter regimens for treatment of MDR-TB or RR-TB. These have achieved high treatment success rates (87-90%) under operational research conditions. A standardised regimen of 9-12 months is recommended by WHO for all patients (excluding pregnant women) with pulmonary MDR/RR-TB that is not resistant to second-line drugs.

As part of efforts to improve outcomes for MDR/XDR-TB, at least 70 countries had started using bedaquiline and 39 countries had introduced delamanid by the end of 2015.

#### **TB** prevention services

South Africa accounted for the largest share (45%) of people living with HIV who received TB preventive treatment for latent TB infection (LTBI) in 2015, followed by Malawi, Mozambique and Kenya. Ten countries reported data for the first time, including Kenya. Despite this progress, 21 of the 30 high TB/HIV burden countries did not report data.

The ratio of the TB notification rate among health-care workers to the TB notification rate in the general adult population is a good indicator of the impact of TB infection control in health facilities. In 16 countries, the number of TB cases per 100 000 health-care workers was more than double the notification rate in the general adult population in 2015.

BCG vaccination should be provided as part of national childhood immunization programmes according to a country's TB epidemiology. In 2015, 163 countries reported providing BCG vaccination as a standard part of these programmes; 102 reported coverage of above 90%.

# Universal health coverage, social protection and addressing social determinants: Implications for TB

In some high TB burden settings, emerging health financing schemes, including national health insurance, could lead to major reductions in out-of-pocket expenditures in lowincome populations. Thailand and a range of countries in the Region of the Americas are good pathfinding examples.

Building on established approaches to private engagement in TB care could help to address the burgeoning private sector in health-care delivery, especially in Asia. This includes a combination of provider incentives and regulation, and application of innovative institutional intermediaries and communications technologies. Such levers can help to assure the quality of services provided.

Social protection can be advanced through better models of care and social benefits. Many low- and middleincome countries have financed social and economic support for TB patients, but these support packages need to be better documented and evaluated. For overall impact and sustainability, using national social protection platforms is a priority.

WHO-recommended baseline national surveys are underway to assess the nature and severity of TB patient costs, and to improve service delivery and social protection accordingly. One country survey was conducted in 2015, eight began in 2016 and ten are planned for 2017-2018.

The available evidence about links between ending TB and ending poverty needs to be used to advocate for poverty elimination and action on related risk factors, such as noncommunicable disease prevention, food security, and housing.

### **TB** financing

The BRICS countries (Brazil, the Russian Federation, India, China and South Africa), which collectively account for about 50% of the world's TB cases, rely mostly or exclusively (the exception is India) on domestic funding.

In other countries with a high TB burden, international donor funding dominates, accounting for 75% of reported funding for NTPs in the group of 25 high TB burden countries outside BRICS, 87% of funding in low-income countries and 60% of funding in lower middle-income countries. The single largest source of international donor funding is the Global Fund to Fight AIDS, Tuberculosis and Malaria.

International donor funding for TB falls far short of donor contributions for HIV and malaria. The latest data from the Organisation for Economic Co-operation and Development (OECD) creditor reporting system show totals of US\$ 5.4 billion for HIV/AIDS, US\$ 1.7 billion for malaria and US\$ 0.7 billion for TB in 2014.

The cost per patient treated is usually in the range of US\$ 100-1000 for drug-susceptible TB and US\$ 2000-20 000 for MDR-TB.

#### TB research and development

At least US\$ 2 billion per year is needed for TB research and development. Funding during the decade 2005–2014 never exceeded US\$ 0.7 billion per year.

In 2016, four diagnostic tests were reviewed and recommended by WHO: the loop-mediated isothermal amplification test for TB (known as TB-LAMP), two line probe assays (LPAs) for the detection of resistance to the firstline anti-TB drugs isoniazid and rifampicin, and an LPA for the detection of resistance to second-line anti-TB drugs. A next-generation cartridge called Xpert Ultra and a new diagnostic platform called GeneXpert Omni are in development; assessment of both by WHO is expected in 2017.

There are nine drugs in advanced phases of clinical trials for the treatment of drug-susceptible TB, drug-resistant TB or LTBI. These are bedaquiline, delamanid, linezolid, PBTZ169, pretomanid, Q203, rifampicin (high-dose), rifapentine and sutezolid.

There are 13 vaccine candidates in clinical trials, including candidates for prevention of TB infection and candidates for prevention of TB disease in people with LTBI.

<sup>&</sup>lt;sup>1</sup> Countries are listed in descending order of their number of cases.

<sup>&</sup>lt;sup>2</sup> MDR-TB is defined as resistance to rifampicin and isoniazid. WHO recommends that all patients with rifampicin-resistant TB (RR-TB) are treated with a second-line MDR-TB regimen. Cases of MDR-TB and RR-TB are collectively referred to as MDR/RR-TB in this report.

<sup>&</sup>lt;sup>3</sup> When an HIV-positive person dies from TB disease, the underlying cause is classified as HIV in the International Classification of Diseases system (ICD-10).

<sup>&</sup>lt;sup>4</sup> i.e. 10.4 million minus 6.1 million.

Countries are listed in descending order of the size of their gap.

<sup>&</sup>lt;sup>6</sup> This is the latest year for which treatment outcome data are currently available.