

It's Time to End Drug-Resistant Tuberculosis

The case for action

A report by The Economist Intelligence Unit



Contents

Executive summary	2
A problem long in the making	3
High-burden countries	4
An under-resourced global health threat	5
The societal costs of inaction	14
Preparing for success	21
The time to act is now	27
References	28
Appendix 1: About this report	33
Appendix 2. Analysis methods	36

Executive summary

Tuberculosis (TB) is an ancient disease that has killed over 2 billion people in the past 200 years. More recently, drug-resistant strains of TB which are resistant to one or more of the drugs normally used to treat it have emerged and spread. Drug-resistant TB (DR-TB) is the only major airborne drug-resistant epidemic. It is harder and more costly to treat than drug-susceptible TB (DS-TB), and affects more than half a million people across the globe annually, mostly in low and middle income countries.

Only about one in three people with DR-TB is diagnosed and one in four is treated. Even with treatment, only about half of people who contract the disease are cured and some strains are becoming resistant to even more drugs. In addition to the suffering that DR-TB causes among people affected by the disease, it is predicted that DR-TB will cost the global economy approximately US\$17 trillion by 2050 if the problem is not addressed.

DR-TB is not invincible—yet. Comprehensive approaches can turn the tide on DR-TB, and the benefits gained from defeating it would be vast. In this report, through a synthesis of insights from in-depth research, more than 20 expert interviews and engagement with an expert advisory panel, The Economist Intelligence Unit (EIU) assesses the urgent economic and health threats posed by DR-TB, and highlights the importance of taking action now to end it.

More specifically, the case for increased action on DR-TB focuses on three important considerations:

DR-TB poses a significant threat to global health security, yet efforts to fight it are acknowledged as being under-resourced. The ability of bacteria and viruses to develop resistance to drugs—called antimicrobial resistance (AMR)—is a major threat to global health security, as it undermines the ability to treat infectious diseases. DR-TB is estimated to cause a third of deaths due to AMR worldwide, resulting in about 230,000 deaths in 2017. It has been predicted that deaths attributable to AMR could rise more than ten-fold to 10 million annually by 2050. Unless action is taken now, DR-TB could be responsible for about 2.5 million of these deaths. Public awareness of the extent of this threat is minimal and funding and commitment to tackle it is inadequate.

DR-TB incurs major economic costs from an individual to a global level. Our analysis suggests that the deaths attributed to DR-TB in one year will cost the global economy at least US\$17.8 billion in future GDP (PPP) loss. Work absences necessitated by DR-TB treatment were estimated to have resulted in a loss to global GDP (PPP) of at least US\$3 billion in 2018 alone. These figures are conservative estimates: they do not capture losses linked to the estimated 400,000 people with this disease who are not diagnosed or treated, or the 70,000 undocumented deaths from DR-TB. As well as its global impact, affected households can face catastrophic costs as a result of the disease, locking generations into a cycle of poverty.

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

Recent advances have coincided with a growing global commitment to fight DR-TB—but this must now be translated into effective action on the ground. Bold action is needed to support the delivery of comprehensive approaches and continued research and development (R&D) efforts. Done correctly, this could leave a legacy of strengthened health systems, as the battle against DR-TB will largely be fought where healthcare provision is traditionally weakest. Finally, widespread advocacy and comprehensive accountability measures are needed to ensure that political commitment from global, regional and national leaders translates into tangible results.

A problem long in the making

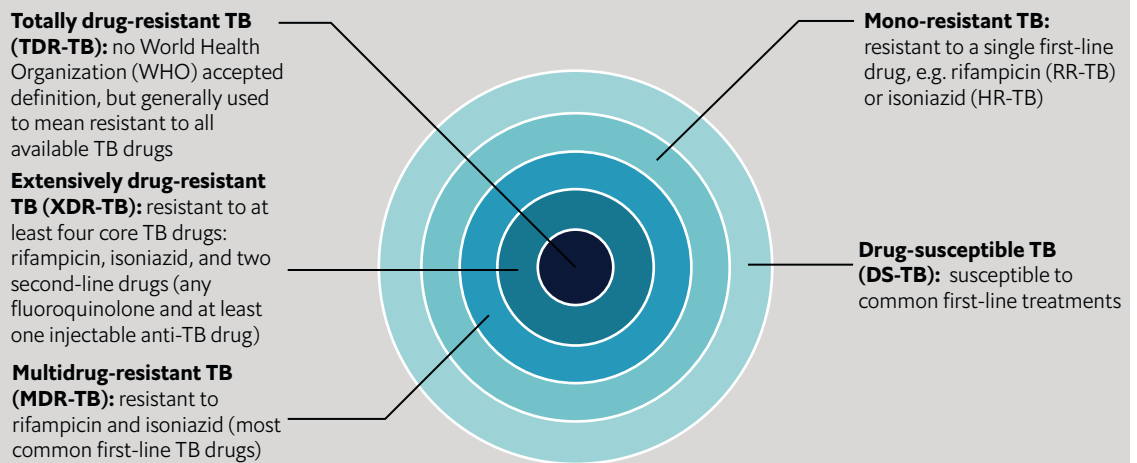
Tuberculosis (TB), despite being an ancient disease, is still among the top ten causes of death worldwide today.¹ It causes significantly more deaths than HIV or malaria, and is the leading single infectious cause of death globally.² Stubbornly persistent and infectious (spread through breathing in airborne droplets containing the bacteria), TB continues to pose a major global public health threat.

The approximately 10 million people that developed TB in 2017 represent only the tip of the iceberg. Many people do not develop symptoms but still carry the bacteria, called latent TB infection (LTBI). In 2017, just under a quarter of the world's population—1.7 billion people—were estimated to

have LTBI.³ Up to 15% of those carrying LTBI will go on to develop active TB in their lifetimes.¹

Currently, so-called “first-line” antibiotics can successfully treat most cases of TB (these are known as drug-susceptible TB, or DS-TB). But the TB bacteria can become resistant to one or more of these drugs, resulting in what is known as drug-resistant TB (DR-TB), a form of antimicrobial resistance (AMR). As shown in Figure 1, there are different forms of DR-TB, which are classified based on number of the drugs to which the TB bacteria are resistant.^{4,5} In this report, the term “DR-TB” is used to describe all forms of TB with some level of drug resistance. Where evidence specifically pertains to a specific sub-type of DR-TB, this is reflected in the terminology used.

Figure 1: The different forms of TB



Source: WHO.^{4,5}

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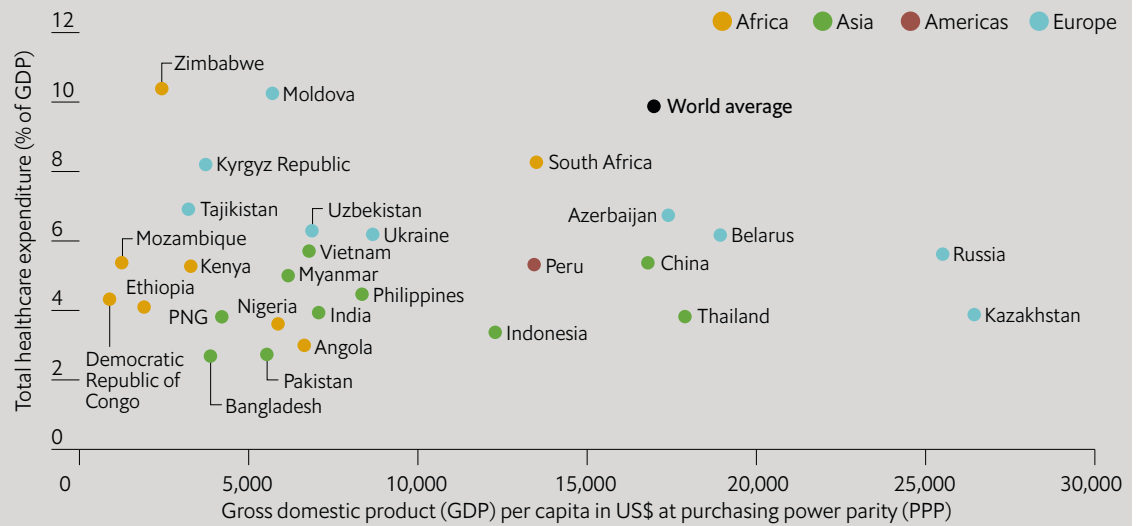
THE CASE FOR ACTION

High-burden countries

DR-TB (and TB) can infect anyone, but it disproportionately affects people of low socioeconomic status, and incidence is highest in low- and middle-income countries (LMICs).³ Poverty and its effects, such as overcrowding and undernourishment, increase the risk of transmission

and development of the disease, as do smoking, diabetes and HIV, among other factors.³ Figure 2 shows that the countries with the highest burden of DR-TB almost all fall below the world average for both GDP per capita and total healthcare expenditure. It also illustrates that there are high-burden countries in all regions of the world.

Figure 2: Healthcare expenditure versus GDP per capita in 28 high burden countries



A costly and under-resourced global health threat

“The reason [DR-TB] is serious is because it is transmissible from human to human. If we don't tackle it now what's going to happen, and models have shown this, is that over time the proportion of DR-TB keeps increasing, and it becomes more and more difficult and more and more expensive to treat.”

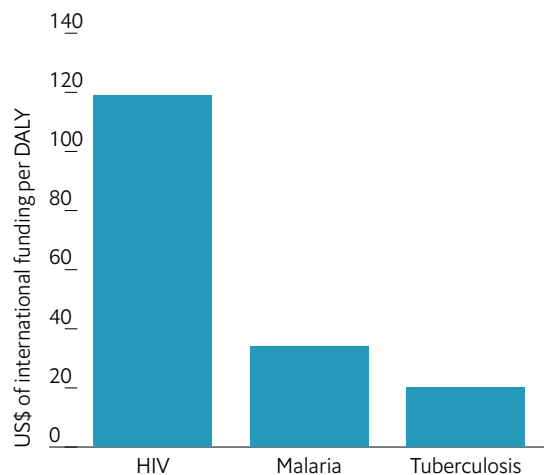
*Dr Soumya Swaminathan,
Chief Scientist, World
Health Organization*

In the early-to-mid 20th century improved living conditions, the development of a vaccine effective against some forms of TB, and the advent of antibiotics reduced rates of TB in the developed world.⁷ This has led to deprioritisation, failure to innovate and a misguided sense that TB is “under control”. Consequently, although TB rates are declining, at the current rate the disease will not be eliminated for more than 160 years, a far cry from the Sustainable Development Goal (SDG) of achieving this by 2030.⁸

The emergence of drug-resistant strains has further slowed progress, and, in combination with HIV, fuelled a resurgence of TB in the early 1990s.⁹⁻¹⁰ Less than a third of the people that are estimated to develop DR-TB each year are diagnosed and recorded (notified), and only one in four start treatment.³ Those who are not treated can continue to spread the disease, and one untreated person with active disease can infect 10-15 other people in a year through close contact.¹ Even among those who are treated, only 55% are cured.³

DR-TB represents a significant threat to global health security. Yet the TB community has long struggled to get different stakeholders to understand the urgency of dealing with this form of AMR. Financing for overall TB management continues to fall short of what is required to meet the TB targets established by the World Health Organization (WHO).^{*} For instance, in low- and middle-income countries (LMICs), which account for 97% of notified TB cases, there was an estimated US\$3.5 billion shortfall in the US\$10.4 billion total budget required to effectively address TB in 2018.³ TB—and consequently DR-TB—receives much less international donor funding than HIV and malaria, despite having a similar detrimental impact on years of healthy life lost (see Figure 3).³ TB gets about an eighth of the amount of international funding that HIV does, and about half of the funding of malaria.

Figure 3: International funding for HIV, malaria and TB per disability-adjusted life year (DALY) lost to these diseases in 2017



Source: WHO.³

DR-TB: A complex problem that could get more difficult to solve

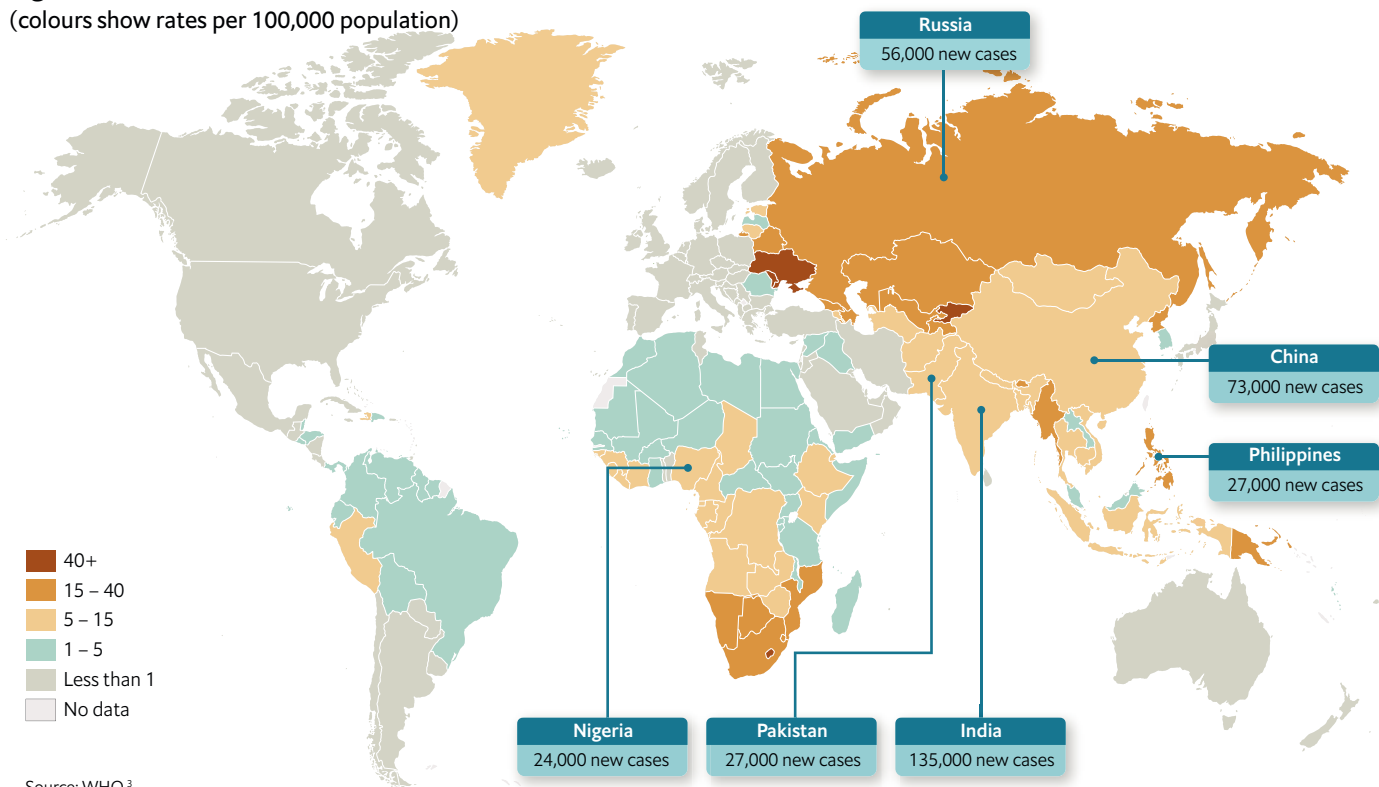
Compared with drug-susceptible tuberculosis (DS-TB), DR-TB requires treatment that is longer in duration and more toxic.^{3, 11, 12} Treating DR-TB is also more costly; the median cost per patient treated in 2017 was almost six times that for DS-TB (these costs include treatment for the disease and for side effects, as well as costs for inpatient and outpatient care).³ This results in DR-TB using a disproportionate amount of resources. In South Africa, for example, although DR-TB only accounts for about 7% of new TB cases, its diagnosis and treatment requires 65% of the national TB budget.¹³

* The ultimate targets are a 90% reduction in TB incidence rate and a 95% reduction in TB deaths (compared with a 2015 baseline), and no families experiencing TB-related catastrophic costs by 2035. Interim milestones for 2020 and 2025 have also been set out.

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

Figure 4: Estimated incidence rates of DR-TB in 2017
(colours show rates per 100,000 population)



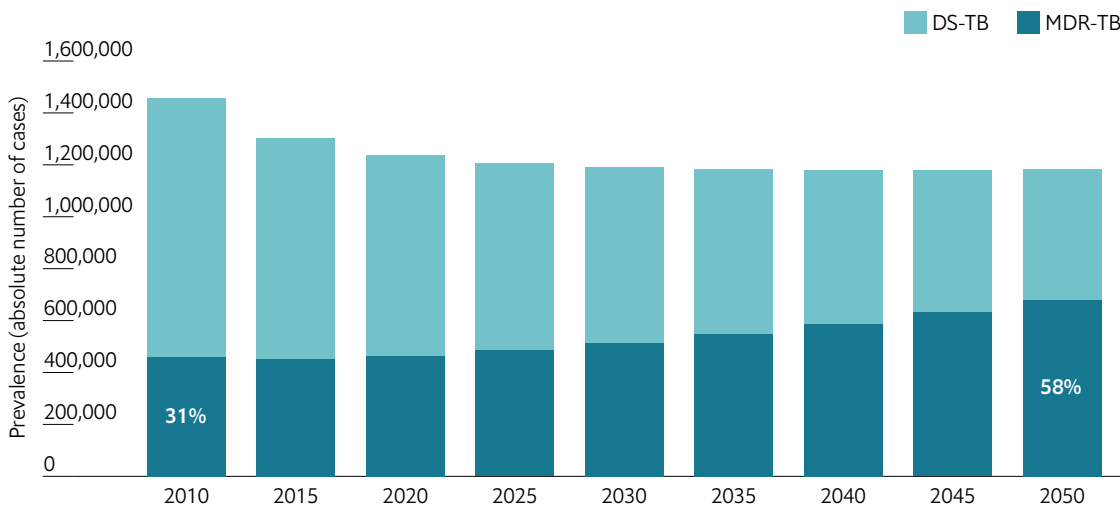
Source: WHO³

As well as gaps in diagnosis and treatment, there are gaps in data collection that hinder understanding of the DR-TB epidemic. Data on DR-TB were still not systematically being collected in 34 WHO member states in 2017.³ Rather than routinely carrying out testing for drug resistance in all cases of TB, many countries only collect data through intermittent surveys of patient samples.

Only 22 of the 40 countries with the highest TB or DR-TB burdens have official DR-TB incidence data covering more than one year, and only ten have at least three years' worth.³ The WHO reports that the data from these ten countries shows a slight increase over time in the proportion of multidrug-resistant TB (MDR-TB) cases among all TB cases, and in all but one of these countries (Tajikistan) the MDR-TB incidence rate is increasing at a faster rate—or at least decreasing more slowly—than TB rates as a whole.³ Essentially, in these countries TB is becoming increasingly multidrug-resistant.

For some high-burden countries, modelled predictions of DR-TB trends are available. India has the highest number of DR-TB cases in the world, with the WHO estimating 135,000 new cases in 2017.³ Current predictions show that the proportion of TB cases that are MDR-TB will more than double by 2032, while untreated MDR-TB cases will more than triple and the mortality rate will quadruple if the management of TB in India remains unchanged.¹⁴ Perhaps even more alarmingly, a 2013 model projected that MDR-TB would overtake DS-TB as the most prevalent form of TB in China by 2050 (see Figure 5).¹⁵ Increasing proportions of MDR-TB and extensively drug-resistant TB (XDR-TB) have also been predicted in other high-burden countries such as the Philippines, Russia and South Africa.¹⁶

Figure 5. Predicted trajectory of MDR-TB in China 2010-2050



Source: Mehra 2013.¹⁵

Case study: Starting from scratch—tackling DR-TB in post-Soviet Russia

After the breakdown of the Soviet Union, poverty, unemployment, crime, conflict and a degraded healthcare system contributed to increasing rates of TB in Russia.²⁰ The disease became particularly prevalent in the country’s crowded prisons, where as many as seven of every 100 prisoners were affected. MDR-TB rates rose to some of the highest in the world, exacerbated by poor quality care (largely due to poor availability and accessibility of medicines).

As a result, a project targeting MDR-TB was initiated in the Tomsk region in the early 2000s.^{17,18} In its initial phase, 630 prisoners and civilians with MDR-TB were provided with a comprehensive programme of diagnosis and treatment.¹⁷ Owing to the severity of the MDR-TB problem and

the collection of robust data on the impact of the project, it gained support and buy-in from multiple levels of government. Early successes among the first patient cohort with individualised treatment regimens also led to integration of DR-TB management into Russia’s national TB control strategies.

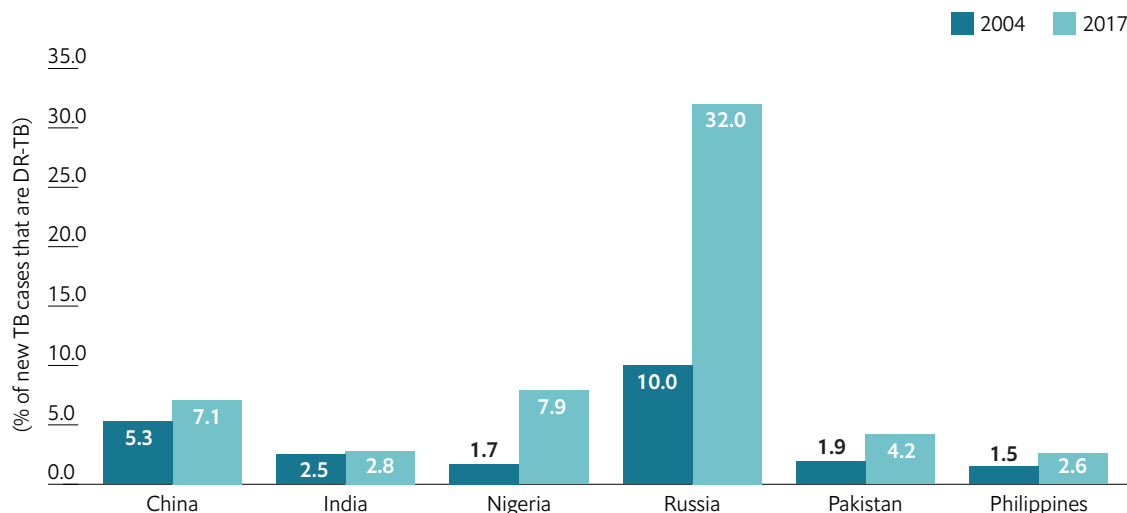
Between 2005 and 2011, an average of 67% of MDR-TB patients being treated as part of the project were cured,¹⁷ far higher than the average achieved globally today (55%).³ In addition, drug susceptibility testing was performed with nearly 100% of new TB patients in the Tomsk region.¹⁷ The prevalence of MDR-TB was more than halved between 2002 and 2012 (from 823 cases to 328).¹⁹ Although challenges remain on the national level (MDR-TB rates have been increasing by 1% per year nationwide since 2011³), Tomsk provides an important blueprint for a local approach that could be replicated elsewhere.

DR-TB is more common among patients who have had active TB before, as incomplete treatment can allow the TB bacteria to become resistant to the drugs that they were exposed to. However, DR-TB is gradually becoming more common among people who have active TB for the first time, and have never been exposed to TB drugs before. These people have caught DR-TB directly from another person

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

Figure 6: Change in estimated percentage of new TB cases that were drug-resistant between 2004 and 2017



Source: WHO.^{3,21}

with the disease (called primary transmission). Figure 6 shows this trend across the six highest DR-TB burdened countries between 2004 and 2017.^{20, 21}

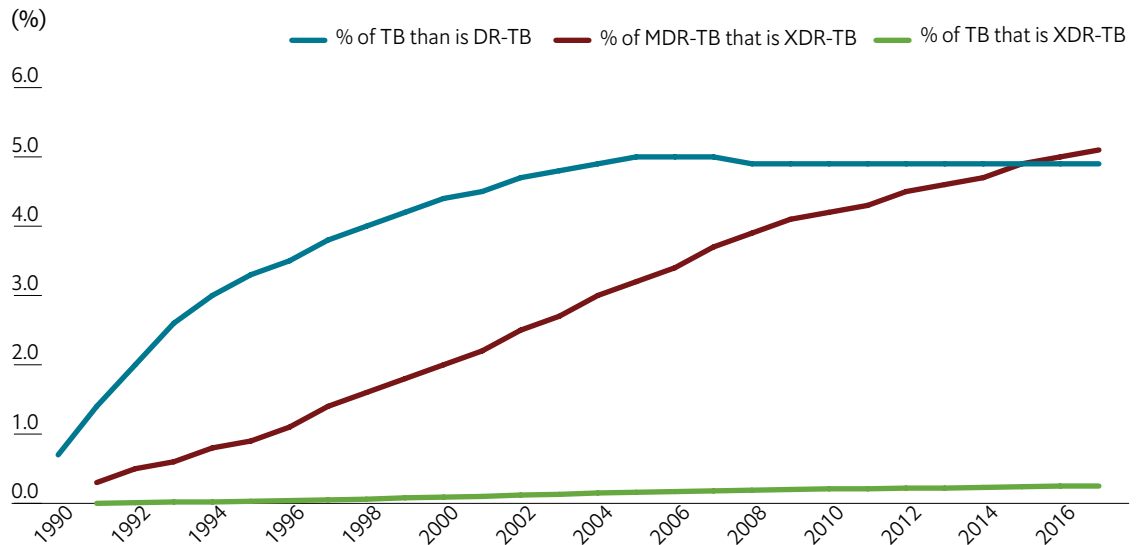
The increase in person-to-person transmission is not surprising, given that 75% of people with DR-TB are not currently treated and each untreated person can spread the disease to 10-15 people in a year through close contact.^{1,3} Even if most of these people develop latent DR-TB, these figures show how easily DR-TB can spread once it is being passed person-to-person.

Models have predicted that this trend will continue. For example, if management of TB does not improve in India, 85% of MDR-TB cases will be caused by people passing on DR-TB by 2032 – a massive increase from the 15% seen in 2012.²⁷

Furthermore, as time goes on and TB bacteria are exposed to more drugs, resistance to additional drugs can develop, making the disease increasingly harder to treat. While most DR-TB cases currently involve resistance to two common first-line drugs, a small proportion of these—known as XDR-TB—are also resistant to at least two second-line drugs. In the early 2000s the first cases of XDR-TB were recorded; between 2000 and 2004 XDR-TB was estimated to account for about 2% of MDR-TB cases.²² By 2017, XDR-TB prevalence had been reported in 127 countries and had increased to 8.5% of all MDR-TB cases according to WHO figures.³ Figure 7 illustrates the dramatic increase in XDR-TB over this time.²³ Currently only about a third (34%) of XDR-TB cases are cured as a result of treatment, much lower than the 55% for MDR-TB.³

In 2007, the first reports emerged of cases of TB that were resistant to all first-line and second-line drugs; since then small clusters of cases have been reported in Iran, India and South Africa.^{5, 24} Unless these highly resistant forms of DR-TB are stopped from spreading, an untreatable epidemic could become a reality.

Figure 7: Steep growth of XDR-TB as a proportion of incident MDR-TB cases*



Source: Global Burden of Disease study.²¹

* Data are from the Global Burden of Disease study from the Institute for Health Metrics and Evaluation (IHME). The IHME uses different methods to the WHO, therefore estimates do have some differences, but overall are broadly similar.

DR-TB poses a major threat to global health security

Antimicrobial resistance (AMR) has been widely recognised as a major global public health threat; the UN deems it a global health emergency and the WHO lists it as one of the top threats to global health in 2019.^{25, 26} According to one forecast, unless action is taken, AMR will cause about 10 million deaths per year by 2050, and cost the global economy US\$100 trillion.²⁷ DR-TB is the only major airborne drug-resistant epidemic, and is currently estimated to be responsible for almost one in three AMR-related deaths.^{27, 28} The forecast described above predicts that by 2050, DR-TB could be responsible for 2.5 million deaths a year.²⁷

When placed alongside other acknowledged global health security hazards, the evidence of the threat wielded by DR-TB is even more stark. Between 2013 and 2016 there were just under 29,000 reported cases of Ebola and just over 11,000 deaths in West Africa.²⁹ In 2017 alone there were estimated to be about twenty times as many cases and deaths globally from DR-TB (558,000 cases and 230,000 deaths).³ These figures suggest that mortality rates of the diseases are similar (about 40%) but the number of DR-TB deaths is far greater.

Despite the strong link between DR-TB and AMR, some suggest that historically DR-TB has been left out of the AMR response. They have been perceived as distinct issues and funding and programming to combat them are largely kept separate. This seems to be changing. For example, the TB Europe Coalition, a regional advocacy network of civil society organisations established in 2009, published a policy paper in 2017 highlighting that DR-TB is the cornerstone of the AMR threat, and calling for governments to ensure that TB is prioritised as a key component of the AMR response.²⁸

Lack of action also wields an economic threat

As more people become aware of DR-TB and the threat of AMR more broadly, tourism, trade and foreign investment could be significantly impacted, with people and companies choosing not to visit

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

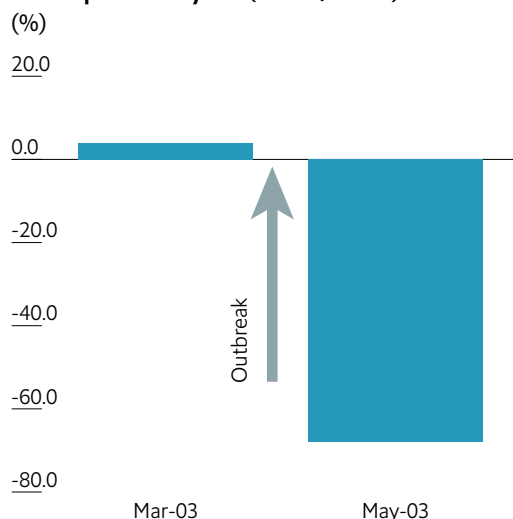
THE CASE FOR ACTION

or invest in high-burden countries and cities. This impact has been recognised in a number of other infectious disease outbreaks. For instance, the emergence of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) in Asia led to people in the affected countries shunning public transport and other public venues for fear of contracting these diseases, which had a significant negative impact on local economies.^{30, 31}

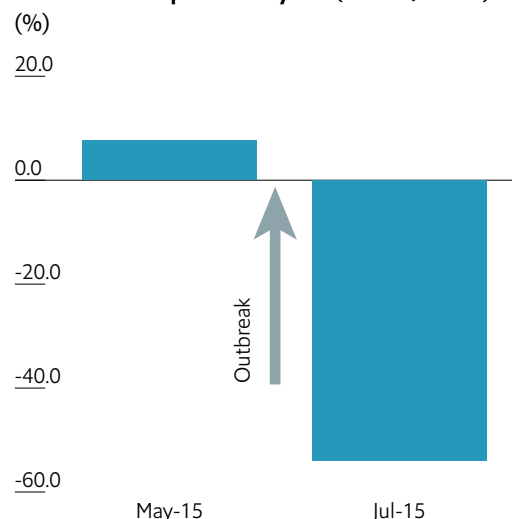
Figure 8 shows the short-term impact of SARS and MERS on tourism in the two months after the outbreaks started in Hong Kong and South Korea as global awareness of the epidemics grew (changes are versus the same month in the previous year).³² Beyond the striking short-term impact on tourism arrivals, these diseases reduced overall tourism arrivals by a total of 6-7% in both 2003 in Hong Kong and in 2015 in South Korea.³²

Figure 8: Impact of infectious disease outbreaks on tourism arrivals

(a) Percent change in tourism arrivals in Hong Kong compared with the same month in the previous year (SARS, 2003)



(b) Percent change in tourism arrivals in South Korea compared with the same month in the previous year (MERS, 2015)



Source: Fazeli 2016.³²

Conversely, modelling shows that the eradication of disease can significantly boost tourism. One study showed that eradicating malaria, dengue, yellow fever and Ebola alone could result in 10 million more tourists visiting the disease-affected countries, adding US\$12 billion in tourism revenue.³³

Beyond tourism, failing to address infectious disease threats can also exacerbate challenges with trade and foreign investment, as foreign companies may be cautious of investing in a country or city that fails to contain an epidemic or exposes workers to these threats.³⁴

As awareness of DR-TB grows, impacts on tourism, trade and investment will be felt in high-burden areas unless the disease is brought under control. As one expert the Economist Intelligence Unit interviewed put it: "I don't think we are there yet, because there is not enough awareness. But, frankly, there are some places in the world where there is a lot of MDR-TB, and people ought to be worried about it. I don't think people quite realise how nasty it is."

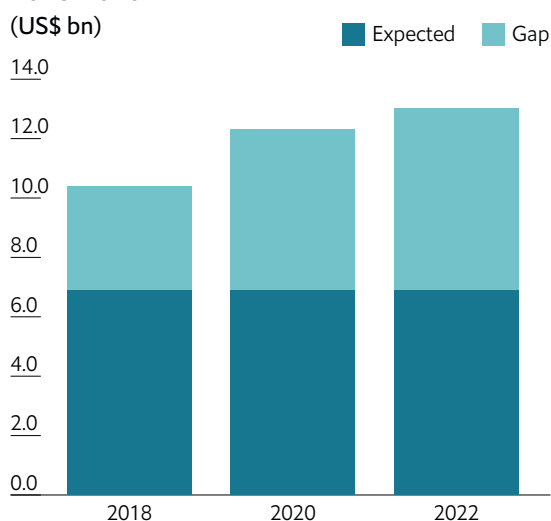
A major UK review on AMR estimated the impact of an additional 40% of global TB cases becoming resistant to first-line drugs.^{35, 36} In this scenario an additional 75 million people would lose their lives to MDR-TB between 2015 and 2050, with India, Nigeria, China, Indonesia and South Africa accounting for over half of these deaths. The study predicted that MDR-TB would cost the global economy US\$16.7 trillion in total over this period, owing to illness, death and other related costs. This figure was equivalent to the total economic output of the EU in the year after the estimation was made.

Resources for DR-TB fall far short of what is needed

Despite posing a grave economic and global health threat, DR-TB—as with TB as a whole—faces a significant funding shortfall. The Stop TB Partnership has estimated that at least US\$13 billion will be needed for the implementation of TB programmes globally by 2022, to meet the targets of their Global Plan to End TB.³ The funding requirement is increasing, so unless the available funding increases the gap will widen (see Figure 9); the shortfall is currently US\$3.5 billion, with a gap of US\$0.5 billion for addressing DR-TB specifically.^{3, 37} The total funding requirement for DR-TB is also expected to increase, rising from US\$2.5 billion in 2018 to US\$3.6 billion in 2020.³ According to the WHO, national TB programmes tend to report smaller funding needs than those estimated by the Stop TB Partnership, as many countries have different, less ambitious targets than those laid out by The Global Plan.³ This lack of alignment increases the likelihood that elimination targets will not be met, and may also exacerbate the critical funding challenges.

Four of the BRICS group of countries (Russia, India, China and South Africa) had the highest

Figure 9. Forecasted global funding need for TB prevention, diagnosis and treatment, highlighting gaps in expected funding, 2018-2020



Source: WHO.³

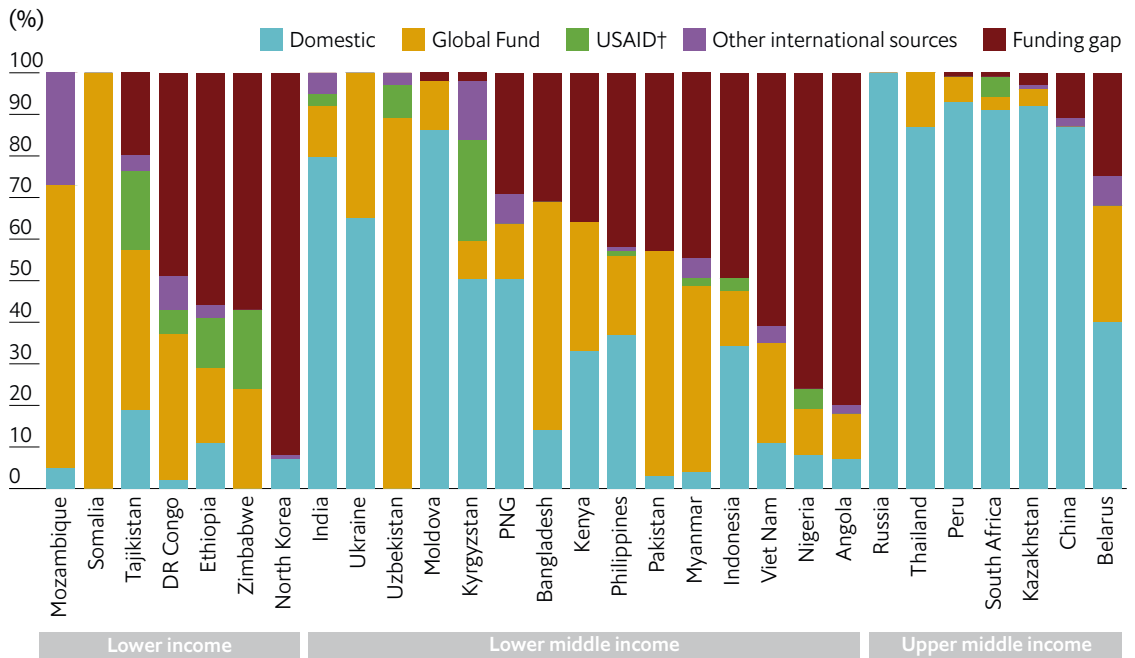
numbers of DR-TB cases in 2017, and accounted for 60% of notified MDR-TB cases globally. BRICS includes strong emerging economies and almost all of their TB funding (96%) comes from domestic sources. However, their levels of DR-TB imply that even in these countries more still needs to be done to defeat this disease.³

Other high-burden, lower-income countries rely heavily on international donor funding (see Figure 10). Donor funding for TB dropped slightly in 2018, to below US\$1 billion, leaving a shortfall in the US\$2.6 billion estimated to be needed from these sources.³ The Global Fund to Fight AIDS, TB and Malaria (the Global Fund) provided 74% of this funding in 2018. As mentioned earlier, international donor funding for TB is noticeably less than that for HIV and malaria (see Figure 3).

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

Figure 10. Sources of funding and gaps in 2017 for the 30 high-burden MDR-TB countries* by income group

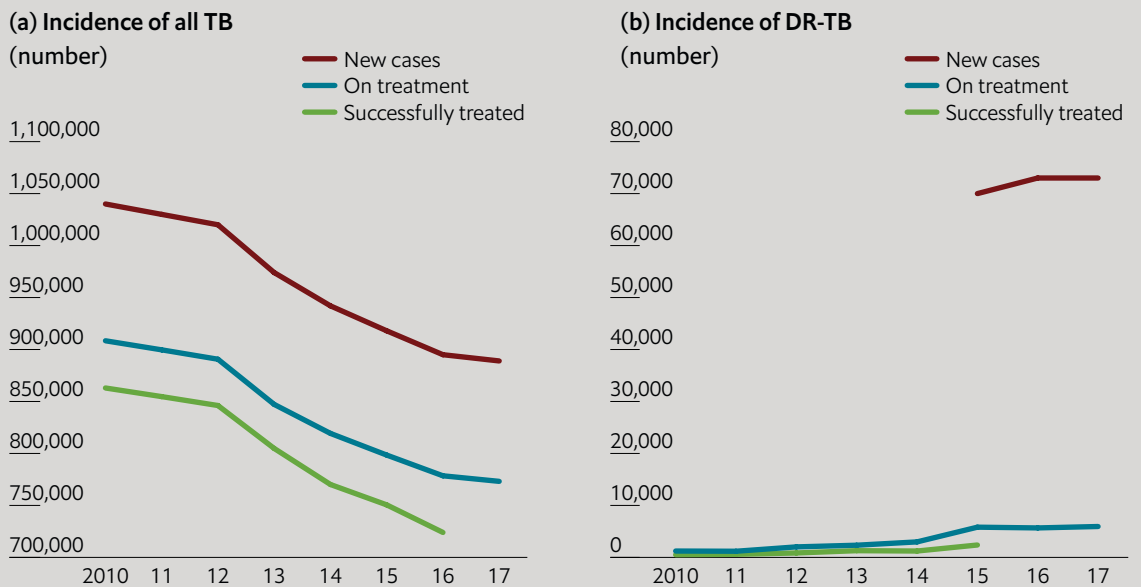


*Excluding Azerbaijan, for which funding data was not available. †United States Agency for International Development
Source: WHO.³⁸

Case study: Undoing the hard work—what happens if DR-TB control lags behind DS-TB control

Despite making notable progress on tackling DS-TB, China has historically had less success in dealing with DR-TB (see Figure 11). After the Ministry of Health established a national TB control network to

Figure 11. All TB vs DR-TB incidence and treatment in China 2010-2017



Source: WHO.³⁸

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS THE CASE FOR ACTION

standardise diagnosis and treatment in the early 2000s, the country achieved the global TB control target set by the WHO in 2005, becoming one of the only countries to do so. Since then, China has diagnosed at least 80% of TB patients and successfully treated more than 90%.³⁹ Between 1990 and 2010 China achieved the TB control targets of the Millennium Development Goals, halving prevalence and mortality.³⁹

However, increasing prevalence of DR-TB due to factors such as delays in drug susceptibility testing and poor treatment, particularly in less developed areas, is undermining these successes (see Figure 11).⁴⁰ China comes second only to India in estimated numbers of DR-TB cases (73,000 in 2017). Modelling performed in 2013 suggested that DR-TB could become more prevalent than DS-TB by 2035.¹⁵ China's MDR-TB treatment success rate was 41% in 2017, well below the global average of 55%.³

Although domestic DR-TB funding in China has increased steadily since 2006 to nearly US\$530 million in 2018, gaps remain. There was a reported funding deficit of over US\$60 million (11% of the total budget) in 2018, nearly half of which was related to DR-TB-specific funding.³⁸ Despite rapidly expanding social health insurance schemes, the costs not covered by these lead to catastrophic health expenditures and prevent people from accessing care.^{40,41} For example, in 2013 92% of MDR-TB patients in the city of Tianjin experienced catastrophic costs (>40% non-food household costs).⁴⁰ None of the Chinese TB budget is reported to be specifically earmarked for patient support.³⁸

The government of China has stepped up efforts to address DR-TB and improve quality of care.^{40,42} However, success will be dependent on sustainably filling funding gaps and continued government commitment.

R&D is a particular area of concern

The erosion of the effective drug pool as resistance increases emphasises the need for an R&D pipeline full of new anti-TB drugs. In addition to using existing tools in the fight against DR-TB, new tools—such as new vaccines, diagnostics and treatments—need to be developed.

Without a strong developed-world demand for new TB drugs, companies' incentives to invest in such research have historically been limited, as evidenced by only two new TB drugs emerging in nearly half a century.^{37,43} Initiatives such as the Stop TB Partnership's Working Group on New Drugs and the TB Alliance were set up to encourage cross-sectoral collaboration to accelerate the development of new TB drugs. There are now 20 TB drugs in trials, including 11 new compounds and 12 vaccine candidates.³ Efforts must be made to ensure that this pipeline expands, particularly as not all of these products will be successful in trials and make it to the market. New drugs are also needed for cases that are resistant to all existing treatments.

In contrast, there has been limited activity in the diagnostics pipeline. Only one rapid diagnostic test for drug susceptibility in TB is recommended by the WHO, and it currently only detects resistance to one drug (rifampicin).³ Rapid, point-of-care tests that can detect resistance to multiple drugs are needed. More operational research is also needed to understand how best to introduce, scale up, assess and, if needed, modify available interventions and approaches in the field.^{3,44}

However, declining industry investment and flat expenditures from public and philanthropic sources have been widening the TB R&D funding gap over the past five years. This gap is currently estimated at almost US\$1.3 billion.³ Whereas TB accounts for almost 2% of all of the healthy years of life lost to any condition globally, it receives only 0.25% of the estimated annual spend on medical research.⁴⁵

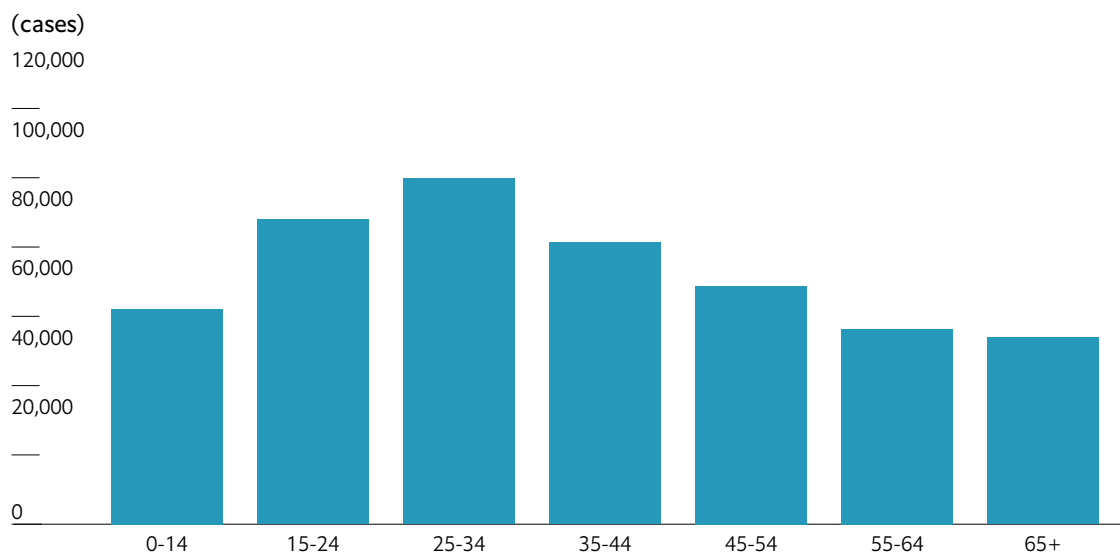
The societal costs of inaction

Although the costs of effectively addressing DR-TB are significant, they are outweighed by the economic and human impact of inaction. DR-TB is not just a public health problem; it consumes vast resources and has a wide-reaching economic impact. Its impacts are borne by affected individuals and their households, as well as at the country level, and globally. Beyond the cost of inaction, there are clear benefits to be gained from addressing DR-TB.

The global economic impact of DR-TB

DR-TB largely impacts people in their most economically productive years, affecting their ability to participate in the workforce.⁴⁶ The number of cases peaks in the 25 to 34 year-old age group, and over three-quarters of those affected (77%) are between the ages of 15 and 64 (see Figure 12).

Figure 12. Incidence of DR-TB by age group in 2017



Source: Global Burden of Disease study.²³

Treatment for DR-TB can require daily visits to a health clinic or hospital in the first six to eight months (called the intensive phase), particularly if the patient is being treated with medicines given by injection. Although outpatient and community treatment are becoming more common and an all-oral regimen is recommended by the WHO, some countries still opt for costly inpatient treatment during the intensive phase. In 2017 for example, 33 countries reported that all MDR/XDR-TB patients were treated in a hospital, with an average stay of about 3.5 months.³⁸

Not only does the condition itself lead to disability, but regimens of 20 months or more can have severe side effects including hearing loss and psychosis.³ If DR-TB treatment is successful, some studies have suggested that post-TB lung disease and permanent side effects from treatment are common.⁴⁷

These combined impacts of DR-TB can make it challenging for patients to maintain employment. In

“You start to realise that the cost of not treating a single patient is in the thousands of dollars to an economy like the Indian economy.”

Professor Salmaan Keshavjee, Department of Global Health and Social Medicine and Department of Medicine, Harvard Medical School

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

a 2013 survey of people with MDR-TB in Ethiopia, 79% reported income loss as a result of the disease, and 72% reported losing their jobs.⁴⁸ Even when treatment is successful, patients may need reskilling to ensure that they can re-enter the workforce, and programmes that offer this are few and far between.

Work absences from DR-TB reduce countries' productivity

Analysis by the Economist Intelligence Unit suggests that work absences due to hospitalisation or clinic visits resulted in global GDP losses of US\$3 billion (PPP) in 2018, with 80% of this due to absences among patients who are hospitalised (see Appendix 2 for analysis methods). Table 1 summarises the countries with the greatest losses. Russia's losses are valued at US\$1.2 billion, the largest of all countries in absolute terms. This is due, in part, to the fact that it had the second-highest number of people with DR-TB starting treatment in 2018, and that all MDR-TB patients receiving treatment are reportedly hospitalised for an average of seven months.³⁸

Furthermore, these calculations are likely to have significantly underestimated the impact of work absences, as they do not account for the 75% of people with DR-TB who do not get treatment, but are still likely to need to take time off work owing to their illness. They also exclude reduced productivity if a person works while ill (sometimes referred to as presenteeism), in addition to time off work for family members who become caregivers.⁴⁹

Table 1. Top 10 countries by GDP loss due to work absences for treatment for DR-TB (MDR-TB and XDR-TB) in 2018

Country	Absolute GDP loss, billion (US\$ PPP)	% of global loss
Russia	1.2	41%
India	0.6	22%
Kazakhstan	0.3	9%
Philippines	0.1	4%
South Africa	0.1	4%
Indonesia	0.1	3%
Ukraine	0.09	3%
Nigeria	0.06	2%
Peru	0.06	2%
Belarus	0.05	2%

Source: The Economist Intelligence Unit.

Taking action in the workplace

Employers in high-burden countries can play an important role in reducing the stigma associated with TB, as well as enabling early diagnosis and treatment among staff.

Some employers are taking up this challenge. Brihanmumbai Electric Supply and Transport Undertaking, Mumbai's state-run public transport and electricity provider, reportedly provides paid leave of up to one year for employees suffering from TB.⁴⁶ This type of progressive approach should encourage employees to seek treatment, as well as help employers to retain and attract staff and protect their wider workforce.

The government of South Africa has joined with workers' unions and employers in the mining

industry to launch annual TB screening among mine workers, who are known to have high TB rates.⁵⁰ In 2017, 94% of the more than 400,000 workers were screened. As well as screening, most mining companies also offer testing, treatment and contact tracing to workers.⁵¹

Some groups of workers may be particularly hard to reach: the Kavach Project in India, run by the Transport Corporation of India (TCI) Foundation, is an example of a project aiming to combat TB among such a group.⁵² The project was set up to screen truck drivers for sexually transmitted infections, and is now being extended to TB. TCI's existing clinics are identifying truckers with TB, ensuring that they receive treatment and education about the condition as part of the TB Free India campaign.⁵³

Deaths from DR-TB have a sizeable impact on GDP

Beyond losses from work absences, deaths from DR-TB also put a strain on economies. We estimate that the 163,000 deaths attributed by the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease (GBD) study to DR-TB in 2017²³ will result in future GDP (PPP) losses of at least US\$17.8 billion globally.* These figures are likely to underestimate the true cost as deaths from DR-TB are under-reported; the WHO estimates that the actual number of deaths in 2017 could have been about 67,000 higher than the GBD figures.³ It is also roughly equivalent to, for example, total annual health care spend for countries such as New Zealand (about US\$16.9 billion at PPP in 2017).⁶

India alone accounts for 41% of losses globally, at US\$7.3 billion in PPP terms. This drastically outweighs the less than US\$0.6 billion budgeted for TB care as a whole (not just DR-TB) in India in 2018.³

Figure 13 shows global losses highlighted by region, magnitude of the loss, and losses as a percentage of GDP. Regionally, South-East Asia—which the WHO categorises as including India—accounts for just under half of the losses (45%), and Europe accounts for a quarter (see Figure 13). Overall, the ten countries with the highest absolute GDP losses together account for 80% of the global impact on GDP (see Table 2).

These figures can be put into perspective by relating them to the size of each country's economy. Looking at future GDP losses as a proportion of the economies of the individual countries, those in Sub-Saharan Africa are disproportionately impacted. Zimbabwe shows the greatest impact of any

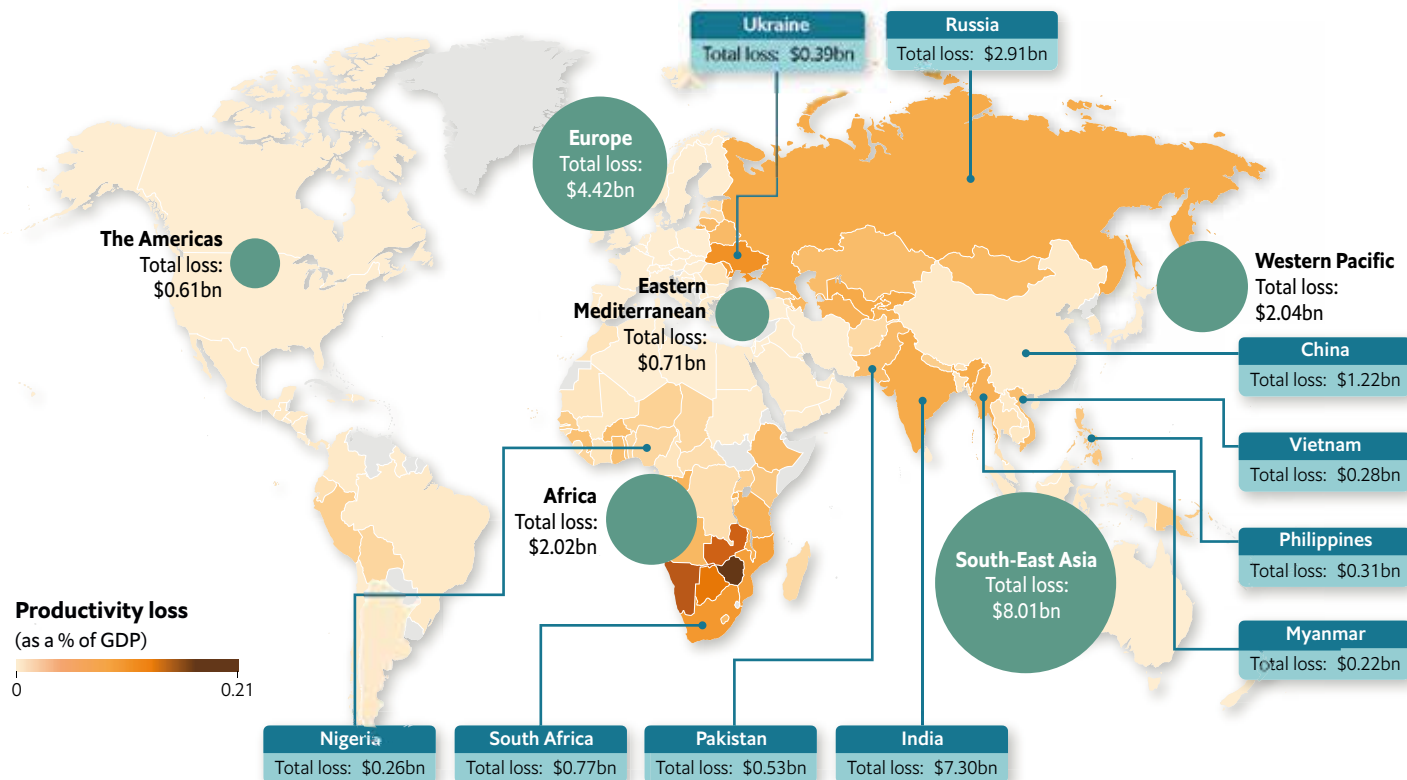
* US\$6.4 billion at market exchange rates

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

Figure 13: Future GDP (PPP) losses due to early mortality from DR-TB in 2017

Includes deaths due to MDR-TB and XDR-TB in 2017 according to Global Burden of Disease study data.²³



Source: The Economist Intelligence Unit.

Table 2: Countries with the largest absolute future GDP (PPP) losses due to early mortality from DR-TB in 2017

Country	Absolute GDP loss, billion (US\$ PPP)	Loss as a % of GDP	% of total global GDP loss
India	7.3	0.08%	41.0%
Russia	2.9	0.08%	16.4%
China	1.2	0.01%	6.9%
South Africa	0.8	0.10%	4.3%
Pakistan	0.5	0.05%	3.0%
Ukraine	0.4	0.11%	2.2%
Philippines	0.3	0.03%	1.7%
Vietnam	0.3	0.04%	1.6%
Nigeria	0.3	0.02%	1.4%
Myanmar	0.2	0.07%	1.3%

Source: The Economist Intelligence Unit

nation globally (future losses represent 0.21% of 2017 GDP), while six other Sub-Saharan African countries also feature in the top 10. Ukraine and Moldova are the only European countries among the top 10, with respective losses of 0.11% and 0.09%.

These figures show the high cost of inaction on DR-TB from a single year alone. For TB as a whole, the cost is even higher. For every year that this disease is not eliminated these losses will accumulate, creating an ongoing drain on the economies of high-burden countries.

DR-TB can have a catastrophic impact on affected households, and perpetuates inequity

TB often puts a significant financial strain on households, owing both owing to costs directly associated with receiving care and indirect costs such as loss of earnings.⁵⁴⁻⁵⁸ Although TB diagnosis and treatment are provided free of cost to the patient in most high-burden countries, this is often not the case for non-medical costs (such as transport, accommodation and food during treatment).⁵⁹ Costs incurred for care before a TB diagnosis is received also often have to be paid for out-of-pocket by the patient. One systematic review across 33 low- and middle- income countries found that, on average, 60% of costs to TB patients come from income loss, 20% come from direct medical costs (such as consultation fees, diagnosis and treatment costs, and hospitalisation) and the remaining 20% from direct non-medical costs.⁶⁰ Half of the costs were incurred before receiving a TB diagnosis. On average, TB claimed 58% of each patient's annual income and 39% of their total household income.⁶⁰

A patient survey in Kenya found that the proportion of people living below the poverty line more than doubled among those who had contracted TB, rising from 14% to 31%.⁶¹ In addition, children in 9% of TB-affected households faced disruption to their education; up to half of households experienced food insecurity; and 28% were forced to use coping strategies such as loans, sale of assets or use of savings.

The survey of Kenyan patients also found that drug-resistance amplified the impact of TB. Just under two-thirds (63%) of people with DR-TB lost their jobs, compared with 39% of those with DS-TB.⁶¹ Overall, 86% of households affected by DR-TB incurred catastrophic costs (defined as costs amounting to more than 20% of household income), compared with 26% of households affected by DS-TB. Results from surveys in other countries such as Ethiopia, Indonesia, and Kazakhstan suggest similarly high levels of income loss and job loss among those with DR-TB.⁵⁹

Millions of the poorest patients face catastrophic costs

If the status quo in TB care continues, over 20 million households in India and over 1 million households in South Africa are predicted to experience catastrophic costs between 2016 and 2035.⁶² Catastrophic healthcare costs are defined as healthcare costs of more than 20% household income. This disproportionately affects households with the lowest incomes: 30-40% of Indian households affected and nearly 80% in South Africa fall in the lowest income quintile. However, higher income households do not emerge unscathed. In India, over 300,000 households in the highest income quintile will also experience catastrophic costs.

Out-of-pocket costs for DR-TB patients may initiate a spiral into poverty or exacerbate existing poverty.⁶³ This phenomenon, referred to as the "medical poverty trap", locks generations of families into a cycle of poverty that is difficult to escape. Successfully eliminating DR-TB will require shielding those affected from the economic impact of the disease. Vital to this will be effective social protection strategies, such as social welfare programmes, food support, disability grants, transport vouchers, housing support and job security policies.⁶⁴

The fight against DR-TB is a worthwhile use of resources

Based on existing research on the cost-effectiveness of MDR-TB treatment, a systematic review extrapolated findings to 14 WHO subregions* covering 193 countries.⁶⁵ It estimated that cost per disability-adjusted life year (DALY) saved was an average of US\$725 for an outpatient care model, and US\$1,812 for an inpatient model of care. For both models the cost per DALY was less than the GDP per capita in every region which is an indicator of providing good value for money.⁶⁶

The significant return on investment (ROI) from addressing TB is also widely recognised. The Stop TB Partnership has estimated that if sufficient investment is made to achieve Global Plan targets by 2025,⁶⁵ a ROI of US\$530 billion could be achieved—this equates to US\$27 per dollar invested.³⁷ If this investment were accelerated, and targets achieved by 2020, the ROI could more than double, to US\$1.2 trillion, equivalent to US\$85 for every dollar invested.

The Copenhagen Consensus Center, a Denmark-based think-tank, looked at the ROI associated with the 169 targets linked to the 17 SDGs adopted by all UN Member States in 2015, quantifying the potential social, economic, and environmental benefit per dollar spent between 2016 and 2030.⁶⁷ Investment in reducing TB incidence by 90% and deaths by 95% was estimated to provide US\$43 of social and economic benefit for every dollar spent, placing it among the top 20 best value-for-money SDG targets.⁶⁷ The estimated benefit-to-cost ratio for investing in diagnosis and treatment of MDR-TB specifically was up to US\$23 for every dollar invested.⁶⁸

The Stop TB Partnership estimates that fully funding TB programmes so that the WHO's End TB targets can be met would prevent up to 45 million TB cases and save up to 10 million lives.³⁷ Similarly, providing the US\$9 billion of funding needed by 2020 for R&D to develop new tools such as drugs, diagnostics and vaccines to fight TB would lead to:

- 8.4 million fewer TB cases;
- 1.4 million fewer TB deaths;
- US\$181 billion in productivity gains; and
- US\$5.3 billion reduction in TB treatment costs by 2030.

In addition, DR-TB is not just a medical issue, it has broader societal impacts. Investing in DR-TB strongly aligns with other important health and societal priorities, such as reducing poverty and inequality, furthering universal health coverage (UHC), and improving global health security. Also, building up capacity to address DR-TB can leave a legacy of stronger and more equitable health systems, as the battle against DR-TB will largely be fought where healthcare provision is traditionally weakest.

Finally, since TB can be eliminated, control programs in theory present only a temporary cost. Once under control, savings can be redirected to tackle other health priorities.

* The subregions included two within Africa, three within the Americas, two within the Eastern Mediterranean, three within Europe, two within South-East Asia, and two in the Western Pacific region. Costs were adjusted by the review to 2005 US\$ values.

⁶⁵ Reaching at least 90% of all people with TB (including the most vulnerable and underserved populations) and treating them appropriately, achieving at least 90% treatment success.

“If we really want to achieve the SDG ambition of ending the epidemic by 2030, we have to step up the fight. We have to do more, better. That’s not just about money, it’s innovation, it’s collaboration, it’s better execution, better use of data. But it also takes more money.”

Mr Peter Sands, Executive Director, The Global Fund to Fight AIDS, TB, and Malaria

Case study: front-loaded investment in New York City

When New York City had an outbreak of MDR-TB in the late 1980s and early 1990s the city mobilised US\$1 billion to tackle this crisis. This led to a notable decline in both incidence (from a peak of 437 cases in 1992 to under 50 cases in 1998, and around 11 cases in 2016) and funding needs (in 2017-18 the budget was just under US\$15 million).^{69,70}

Surveillance systems still need to be kept

in place once the epidemic is brought under control, and New York City illustrates this. In 2017 it reported the largest increase in TB seen in 25 years. This included 14 patients with MDR-TB, one of whom had XDR-TB. Because the increase has been detected early, and the resources and infrastructure are in place to deal with it, the city is likely to be able to contain the outbreak. This example highlights the fact that as long as DR-TB remains in someone, somewhere, it can still spread.⁷¹

Preparing for success

There was wide consensus among the experts the Economist Intelligence Unit interviewed that it is now possible to eliminate TB, including DR-TB. In recent years, technological improvements, along with other innovations in DR-TB care and increasing global attention for TB, have put us in a far better place to escalate the fight against DR-TB compared to five years ago.

With many of the key elements of improved care already available, these now need to be implemented as part of comprehensive treatment strategies targeting all forms of TB; there is not the luxury of waiting for perfect data or treatments. As one expert put it, “Before, the thinking was that the only way to sort out TB was to sort out the drug-susceptible cases first, as that way you stop the majority of cases. [...] But I think people are now realising there is a balance between the two. Therefore, even if your programme against DS-TB isn’t perfect, you can still invest in DR-TB.”

The time is now

The situation could be at a promising tipping point. In March 2018 Narendra Modi, the prime minister of India (the country facing by far the highest DR-TB burden), publicly committed to eradicate TB in the country by 2025—five years ahead of the UN’s 2030 target.⁷⁴ Later in 2018, the first UN High Level Meeting (UNHLM) on TB took place.⁷⁵ The positive message presented by such events, combined with the availability (and the ongoing development) of long-awaited new diagnostic tools and treatments, arguably puts us in a better position than ever to change the trajectory of DR-TB.

“One in two TB patients that could be easily saved is dying today...because of bad treatment, bad diagnosis, late or missed diagnosis, not getting the drugs on time, or not getting the support they need to complete TB treatment. This is just absolutely unacceptable. This is the lowest hanging fruit anyone can hope to find in global health.”

Professor Madhukar Pai, Director, McGill International TB Centre

Success stories: Decisive action in a Micronesian State

Comprehensive, patient-centered care packages that include prevention measures can reduce TB and DR-TB. One example of this was seen in Chuuk State in the Federated States of Micronesia (FSM). The FSM are made up of over 600 islands spread over 1 million square miles of the Pacific Ocean. Chuuk State is its most populated state, with about 50,000 inhabitants living on multiple islands.

In 2007 the TB incidence rate in Chuuk State was about 30 times the US rate (127 per 100,000, versus 4.4 per 100,000). There was only one hospital where TB could be diagnosed, extremely limited TB programme staffing (two nurses and a part-time doctor), and testing for TB drug susceptibility had only recently become available through US laboratories.²²

Starting in late 2007, the first MDR-TB cases were identified in Chuuk State. As no second-line treatments were available in the FSM at that point, five people died. With high-level political commitment in the FSM, and technical and financial support from multiple national and international governments and agencies (mainly the US Department of the Interior), a comprehensive plan was put into action to trace the contacts of those affected, and diagnose and treat all cases identified, both active and latent.⁷² A year later, TB mortality in Chuuk dropped from 11% of all TB cases to less than 1% (the US rate at that time was 5%)—a 90% reduction.⁷³ In 2017, there were only four cases of DR-TB across the whole of the FSM, and the treatment success rate was 100%.³

To take advantage of the opportunity to eliminate DR-TB, a three-pronged approach is needed: **political commitment** supported by **rigorous accountability measures** and greater **public advocacy** will ensure that public support and political will can be sustained for as long as it takes for the fight against DR-TB to be successful.

Political commitment is essential

The eradication of smallpox, finally achieved in 1979, demonstrates the power of political commitment. As one expert put it, "That final push occurred when heads of state, particularly in the low-burden countries, acknowledged that they needed to be accountable to end the epidemic as well as those high-burden countries. The "free-rider" excuse that someone else is going to pick up the tab ceased to be acceptable at a global level. So countries like the US [a low-burden country] invested in ending the epidemic. The US invested US\$200 million in the late 1970s and they make back that investment every 26 days in terms of savings to the healthcare system. The same is true for TB. If we could drive down incidence, the health savings to both high- and low-income countries would be tremendous."

Growing international momentum needs to be translated to the national level, particularly in high-burden countries. Strong national leadership is vital to making this happen. One of the most compelling arguments for governments is that dealing with DR-TB is achievable, and provides health, social and economic benefits, as outlined in this report.

IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

Success stories: The Zero TB Initiative in Pakistan

Pakistan had an estimated 27,000 new cases of DR-TB in 2017, the fourth-highest estimated burden worldwide.³ Only 13% of these cases were notified and 11% started treatment. Relatively weak health infrastructure and lack of controls over prescriptions and drug quality present challenging barriers to achieving success in DR-TB in Pakistan.

The Zero TB Initiative, a Global Fund-supported project, is showing what is possible in overcoming these barriers. The initiative aims to create “islands of elimination” in high-burden settings using a comprehensive evidence-based, cross-sectoral programme to proactively identify and treat people with TB (including those with DR-TB; see Figure 15 for details).⁷⁶ The project has been rolled out in Karachi, a city of almost 15 million people.

Over 3 million people have been screened for TB as part of the project, and mobile X-ray vans

Figure 15: Components of the Zero TB approach in Karachi



Source: Khan 2019.¹⁸

have been used to take chest X-rays from almost a million people.¹⁸ The initiative takes advantage of modern technology, using an integrated TB information management system that allows advanced collection and storage of data. Integrated screening for other diseases such as diabetes and depression are also being offered. Girls in high schools are being trained to assist with case finding in their communities, a strategy that should raise awareness among the next generation of adults.¹⁸

For DR-TB specifically, around 1,700 patient contacts have been evaluated, and those infected

started on preventive treatment.¹⁸ Project leaders believe that this is the largest implementation of preventive treatment in any city. In the town where the project has been running longest, the numbers of cases revealed through screening declined in 2018, and there was a 20% drop in TB notifications, showing how rapidly progress can be made when the right tools are in place.¹⁸ This may be the first sign of a decrease in incidence as a result of the programme. Data collection continues, and it is hoped that figures on return on investment will be published this year.

High-burden countries must lead from the front

One of the most frequently cited examples of successful national action is South Africa, where a progressive approach reflects strong government commitment. In addition to dealing with a high burden of HIV, the country has also risen to the challenge of tackling TB. The country now has “one of the most vibrant, progressive, forward-thinking TB programmes that you could come up with”, as one expert the Economist Intelligence Unit interviewed put it. The minister of health of South Africa, Dr Aaron Motsoaledi, has been recognised for his outstanding leadership in galvanising effective action on TB within South Africa, and also for increasing the profile of TB internationally.⁷⁷

South Africa has been ahead of the curve in mobilising domestic resources to scale up new diagnostic tools, uses improved regimens for DR-TB and implements a person-centered approach. In 2017 all individuals notified as having bacteriologically confirmed TB were reported to have been tested for rifampicin susceptibility. In addition, 73% of people with MDR-TB in South Africa started treatment, which is the second-highest rate among the high-burden DR-TB countries (with Kazakhstan achieving 82%).³

Case study: Innovative funding, steps to social welfare and private-sector engagement—India's quest for results

Backing its ambitious target to eliminate TB by 2025, India has significantly scaled up TB funding, more than tripling its budget between 2016 and 2018.³ About US\$175 million (30%) of the country's overall 2017 TB budget was for DR-TB-specific costs, despite DR-TB only accounting for about 2%

of notified cases. The majority of the (fully-funded)³ budget is coming from domestic sources (79%).

The government is also using an innovative blended finance approach—through an International Bank for Reconstruction and Development loan, with the Global Fund committing to providing grant funding to pay a part of the loan (called a buy-down).^{78,79} This loan is in part to finance diagnostics for DR-TB, alongside patient support, and aims for at least a 60% improvement in treatment outcomes.⁷⁹ Funding for TB initiatives is also being provided by the private

sector. The India Health Fund, a collaboration between the Tata Trusts and the Global Fund, has made a multi-million-dollar commitment to provide seed funding for innovation.⁸⁰

Finally, the government has also begun to introduce measures to reduce catastrophic costs faced by the most vulnerable members of society, as well as encouraging treatment completion—it has committed to provide 500 Indian rupees (INR) per month directly to notified TB patients

during treatment for nutritional support.⁷⁸ The government has also incentivised reporting by private providers by offering 500 INR at TB notification and 500 INR for reporting treatment outcome. This is very important, given that the private sector is the first point of contact for roughly 70% of all patients.⁸¹ Steps will also be needed to ensure consistent, high-quality TB treatment in the private sector.

In Nigeria the TB budget has been drastically underfunded in recent years. In 2018, for example, the budget needed for TB was US\$409 million, but only about a quarter of this (US\$96.6 million) was available. This funding gap included a US\$95 million gap in the budget for DR-TB-specific treatment and programmes.³

However, Nigeria is showing early signs of commitment for much-needed improvement in TB funding and care. The health budget is set to increase in 2019,⁸² and the minister of health, Professor Isaac Adewole, has stated that this budget will show greater commitment to TB.⁸³ TB care will be part of the basic primary care health package offered to all Nigerians. The government aims to fund these improvements through a public-private financing model. The size and buoyancy of Nigeria's economy (by 2050 it is predicted to grow to become the world's 14th largest⁸⁴) gives the country a significant opportunity to take control of its DR-TB situation and reap the benefits of doing so. It will be critical that leadership in Nigeria is held accountable for a strong response to DR-TB.

Governments must act quickly to mobilise resources

The speed and scale of the response to DR-TB directly affects its outcome. For instance, both Russia and New York City experienced a growing burden of DR-TB in the early 1990s.⁷⁰ Whereas New York City quickly mobilised the resources needed and brought the outbreak under control, Russia was unable to fund a full response or secure sufficient international support to bring down rates of DR-TB. Russia now has the third highest number of cases of DR-TB, with 56,000 cases estimated in 2017.³ DR-TB accounts for about 31% of all notified cases of TB in Russia, and over half of cases of TB in people who have been treated previously—among the highest rates in the world.

Governments need to be held to account for progress on DR-TB

The UNHLM has produced some strong commitments from governments, including \$1.5 million to fight DR-TB, but there is some concern whether these will be met without rigorous accountability mechanisms in place. The Moscow Declaration to End TB from 2017 called for strengthened national and global accountability for TB response.⁸⁵ As a result, a multisectoral framework is being developed by the WHO, and this framework is due to be in place before the World Health Assembly in May 2019. It aims to provide an important incentive for leaders to act—or provide disincentives for not doing so.

Effective advocacy is key to driving a sustained battle against DR-TB

Many experts interviewed for this report discussed the detrimental impact of a lack of sufficient advocacy on the fight against DR-TB. One reason why this is critical is that some of the ROI in DR-TB is likely to manifest in timescales beyond the terms of specific government's administrations. In this sense, advocates must fight to ensure that public awareness is at such a level that DR-TB elimination remains a priority for governments, even if benefits of doing so do not arise in time to ease short-term political pressures.

The progress made for other health challenges, specifically HIV/AIDS, can guide a route for DR-TB elimination. Those engaged in the fight against HIV/AIDS faced problems gaining political commitment owing to short political terms and a lack of long-term mindset. However, the HIV/AIDS community was able to overcome this with strong advocacy. A similar grassroots advocacy movement would keep the pressure on leaders to act in the fight against DR-TB. One expert punctuates this comparison: "You think about massive strides that have been made in response to the HIV epidemic, and that those strides have been made in large part because of the noisy, vociferous activists. For the better part of the last 20 years, those activists have been silent in TB. We want to make the case for having them be part of the social and political agenda around TB elimination." Another expert also raised the importance of the TB community advocating within the wider global health community, and engaging in the broader resource allocation debate with health planners and finance ministers.

All of us—not just TB patients and survivors or those in high-burden countries—have a responsibility to take part in the advocacy agenda. Key stakeholders such as civil society, communities, and the private sector must send clear messages to governments and policymakers.

"A lot of people across the world need to understand the time bomb we are sitting on. I don't think everybody knows the seriousness of this problem."

Mr Manoj Kumar, CEO, India Health Fund

The time to act is now

“It is not a problem that should vex us for the next two millennia. We have the potential right now to address this problem, whether it is DR-TB or the [TB] epidemic at large... with enough science, with enough rigorous, intellectual engagement, with enough bright minds, TB is a solvable problem.”

*Assistant Professor
Michael Reid of the Lancet
Commission on TB and the
University of California San
Francisco*

This report summarises the economic and human impacts of DR-TB, showing that scaling up DR-TB control represents a good use of resources, and can contribute to economic growth and strengthen global health security. The case for addressing DR-TB is clear, and progress on different fronts made in recent years signals a greater chance of success than ever before. To help chart a course for the elimination of DR-TB, this report arrives at five key conclusions:

To eliminate DR-TB the world must act now. Although DR-TB is largely preventable and curable, almost a quarter of a million people die each year from this disease—almost one every two minutes. Moreover, the burden of DR-TB is predicted to grow in some areas. Experts agree that, in light of the recent UNHLM, innovations in diagnostics and treatments, and other advances in DR-TB care, now is the time to accelerate efforts to end this disease. To do so, a rapid scale-up of resourcing by governments in high-burden countries and the international donor community is required to implement existing effective interventions and develop new and improved approaches.

The cost of inaction is high. The evidence captured in this report shows that accepting the status quo is simply not an option—it costs thousands of lives and is harmful to economies. Underestimating the threat of DR-TB could have serious consequences for global health security, particularly if the trend of increasing extensive drug-resistance continues.

Addressing DR-TB aligns with other important health, economic and societal priorities. Efforts to move closer to UHC, strengthen health systems and improve global health security can be bolstered by actions to address DR-TB. In addition, once elimination of DR-TB is achieved this can create wider fiscal space for broader health priorities.

National leaders, in partnership with other stakeholders, must be held accountable for progress to end DR-TB.

The growing threat of DR-TB can be directly traced to a legacy of complacency and lack of political will. Although there are signs that this is changing, international and national accountability frameworks and the voice of the wider public are needed to ensure that governments and other stakeholders take effective, concerted action to end DR-TB.

Stronger public advocacy is required to increase the commitment to end DR-TB. As shown by its success against other major health threats such as HIV, strong advocacy will be critical to ensuring that governments and policymakers remain committed to the fight against DR-TB. The voice of the TB community is critical for engaging a wider group of stakeholders to come together to drive change.

Millions of lives can be saved over the coming years, and the very real threat of DR-TB can be ended by a combination of increased investment, commitment and coordination at the local, national and global levels. This disease can be ended, and we all have a role to play.

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IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

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IT'S TIME TO END DRUG-RESISTANT TUBERCULOSIS

THE CASE FOR ACTION

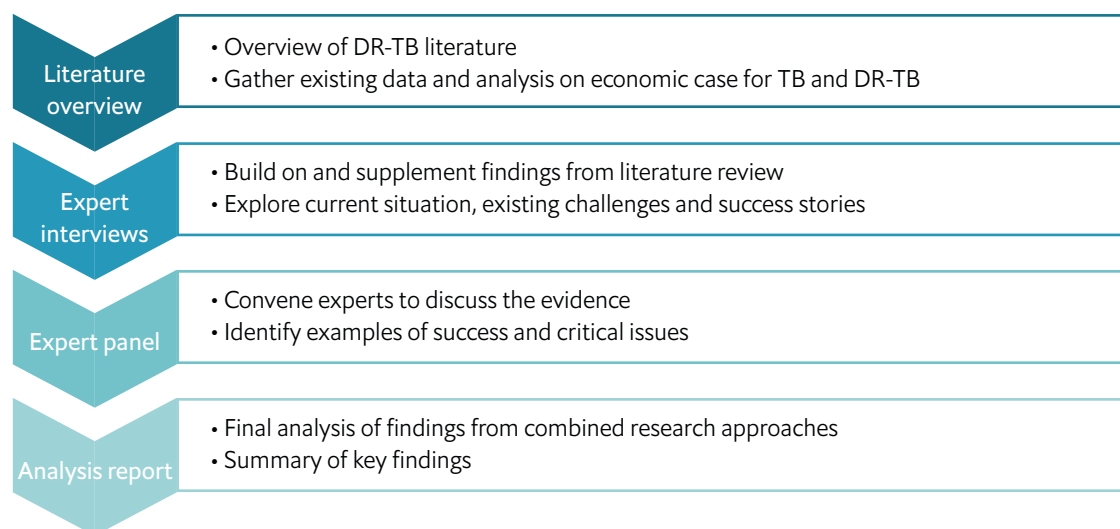
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Appendix 1: About this report

This is an Economist Intelligence Unit (EIU) report, sponsored by Johnson & Johnson Global Public Health. The report focuses on policy and system-level aspects of DR-TB, rather than on specific interventions.

Our approach to this research programme comprised the following components:

Figure A1. Summary of the research programme



In concert with interviews of leading researchers, clinicians, financiers, and other stakeholders in the field, we performed a structured literature search based around factors related to both micro- and macroeconomics of DR-TB. We supplemented our search results with studies found in the extensive library of the TB Modelling and Analysis Consortium (TB-MAC), various policy documents, reports from the TB community and data on epidemiological trends. We limited our search to studies relating to cost and economics within the past 5 years (2014-2018) to account for the changing nature of consumer and treatment costs, new policy guidelines at the national and international level, and critical advancements in TB treatments and diagnostic tools that have fundamentally shifted the TB landscape within this time period.

Our initial searching, combined with articles that met our criteria from TB-MAC, resulted in a combined library of 464 articles, excluding articles that did not mention DR-TB, or information related to cost or economics in their title or abstract. This resulted in 81 articles. We looked at the full texts of these articles, excluding any that again did not contain a component specific to DR-TB, focused specifically on individual treatments or diagnostic tools, cited data that was known to be outdated, or were duplicate articles published in other journals. Our final reference library contained 49 articles. From the 49 included articles, we extracted specific costs by country, and analysed common themes and findings. In addition to published articles we conducted extensive reviews of publically available datasets and grey literature sources.

To explore key gaps and questions, and add to the narrative richness of existing data, we conducted approximately 20 expert interviews with researchers, advocates, financiers and other stakeholders. We also conducted a half-day expert panel meeting in December 2018 with nine experts to discuss interim findings and the economic case for ending DR-TB. The meeting was held under Chatham House rules, meaning that discussions can be reported but not attributed. We supplemented these insights with our own economic analyses. The methods for our analyses are detailed in Appendix 2. Combined findings from our evidence review, interviews, expert panel and our analysis are summarised in this report.

Contributors

The findings and views expressed in this report are those of the EIU and do not necessarily reflect the views of expert panel members, interviewees or project sponsors.

Our thanks go to many people for both their time and contributions to our work as members of our expert panel or interview participants (in alphabetical order):

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- **Dr Shelly Batra**, Co-Founder and President, Operation Asha
- **Dr Grania Brigden**, Deputy Director, Department of Tuberculosis, International Union Against Tuberculosis and Lung Disease
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In addition, we are grateful for many informal conversations and opportunities to share ideas on this topic with various stakeholders in the TB community over the past several months that may not be listed here. The wealth of insight gathered through these activities was much broader than could be included in this report, but all of the contributions developed our thinking about the issues.

This report was researched, written and edited by Dr Alicia White and Amanda Stucke, with additional editing by Paul Tucker, literature review input from Elly Vaughan, data analysis led by Darshni Nagaria and overall guidance from Dr Rob Cook. While every effort has been taken to verify the accuracy of this information, the EIU cannot accept any responsibility of liability for reliance by any person on this report or any of the information, opinions or conclusions set out in this report.

Appendix 2. Analysis methods

Estimation of future non-health GDP losses due to early mortality

To calculate the future losses to the economy due to a single year of deaths from DR-TB, we followed the method from Kirigia and Muthuri,⁸⁶ which used a human capital approach. This method calculates the amount that a person could have contributed to the economy in terms of non-health GDP had they not died prematurely. These losses in the macroeconomic outputs of countries result from the erosion of future labour and productivity, as well as the reduction in investments in human and physical capital formation. Figures are expressed in US\$ at purchasing power parity (PPP). PPP is a way of presenting values so that irrelevant variations in exchange rates do not distort international comparisons or year-on-year comparisons. A value in US\$ PPP takes into account the purchasing power of different currencies when converting into US dollars.

The key variables utilised in these calculations and their sources included (most recent available data used):

Variable	Source
Deaths from MDR-TB and XDR-TB by age (0-14, 15-59 and 60+) in people with and without HIV	Global Burden of Disease data for 2017
Life expectancy at birth	World Bank
GDP per capita	World Bank
Health expenditure per capita	World Bank

Key assumptions included that:

- People's contribution to GDP starts from age 15+ and continues throughout their lifetime
- The rate used to discount future losses was 3%
- The average age of death being the mid-point of the age bracket
- Non-health GDP is calculated by subtracting health expenditure per capita from GDP per capita

Methodology for one-year losses for absences

We also quantified the annual indirect impact on the economy of working days lost owing to receiving treatment for DR-TB.

We estimated the number of employed people infected with DR-TB who were receiving treatment by multiplying the number of people starting treatment by the labour force participation rate. This figure was multiplied by GDP per employed person per working day to calculate the cost from losing one day of work because of treatment for DR-TB. The number of days lost from health facility visits and hospitalisations was estimated based on data from the WHO TB database for 2017.³⁸ We made the assumption that half a working day was lost for a health facility visit⁸⁷ and a full day was lost for hospitalisation.

Data for the labour participation rate, labour force, GDP estimates and population figures came from the World Bank. We assumed 235 working days in a year, as per the assumption made in the RAND report³⁶ quantifying the impact of AMR that was part of the AMR review.

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