K4D | Knowledge, evidence and learning for development

Ending Tuberculosis

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About this report

The K4D Emerging Issues report series highlights research and emerging evidence to policy-makers to help inform policies that are more resilient to the future. K4D staff researchers work with thematic experts and DFID to identify where new or emerging research can inform and influence policy.

This report is based on twelve days of desk-based research.

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from the British people

Health is a human right. No one should get sick or die just because they are poor, or because they cannot access the services they need.

Dr Tedros Adhanom Ghebreyesus, Director-General of WHO
(Adhanom Ghebreyesus, 2017)

We have never before seen this level of political commitment to making TB history. Now is the time to make sure that commitment becomes action.

Dr Tedros Adhanom Ghebreyesus, Director-General of WHO
(Adhanom Ghebreyesus, 2018)

The economic case, put simply, is that TB treatment is low cost and highly effective, and on average may give an individual in the middle of their productive life around 20 additional years of life…

Professor Anna Vassall, London School of Hygiene & Tropical Medicine
(Vassall, 2014)

I went totally blind and I went to the National Tuberculosis Programme and they said that prevention of disability is not part, disability rehabilitation is not part and counselling is not their job. So, I described to my parents and of course I had no more friends at that time because they were having all this stigma regarding the disease.

Ms Eloisa Zepeda-Teng, TB survivor, Philippines
(Zepeda-Teng, 2018)

Contents

1. Summary

This report examines the challenges facing ending tuberculosis (TB). TB is preventable and curable, and yet it continues to affect over 10 million people a year and is the world's deadliest infectious disease. TB affects those most vulnerable and threatens livelihoods, perpetuating poverty and undermining economic development. The spread of drug-resistant TB, against which we are ill-equipped to respond to, threatens global health security. Current global efforts in tackling TB means that the 2015 Sustainable Development Goal (SDG) Three to end TB by 2030 will not be met for over a century. Optimising use and implementation of current and new tools emerging from the pipeline in the provision of equitable TB care and prevention within the broader context of universal health coverage (UHC) and social protection can be done now to accelerate progress. New tools will need to be available by 2025 to accelerate progress further but investment needs to happen now to ensure a vaccine, point-of-care diagnostic and new drugs are ready. Partnerships and reaching out to all key populations vulnerable to TB will help to find and treat the four million people with TB missed by the health system each year. The United Nations General Assembly High Level Meeting (UN HLM) on TB on 26 September 2018 offers a once-in-a-lifetime opportunity for the global TB community led by heads of state and government to prioritise, invest, partner and reach out to all to cure and prevent TB contributing to the good health and well-being of people, eliminating poverty and enabling work and economic growth. Substantial investment will not only deliver a world free of TB but will also strengthen health systems to respond to diseases beyond TB, help move towards UHC, widen social protection and address social and economic determinants of poverty.

TB burden

In 2016, an estimated 10.4 million people fell ill with TB worldwide. This disease killed 1.7 million people that year being the ninth leading cause of death globally. Forty per cent of all TB cases globally are let down by health systems which fail to complete the full sequence of quality assured diagnosis, notification, and treatment, i.e. four million people with TB disease are missed each year. The burden of TB is higher in men than in women, requiring new thought on gender-sensitive strategies which address the specific vulnerabilities and needs of both males and females not accessing and committing to complete care. It is estimated that one million children under the age of 15 became sick with TB in 2016 with less than half (43 per cent) reported to national TB programmes (NTPs). One quarter of children who became sick with TB—253,000—died. Treatment of drug-sensitive TB is effective, low cost and prevents onwards transmission. Children with TB rarely die when they receive standard treatment for the disease, but 90 per cent of children who died from TB worldwide went untreated thus neglecting children's right to health and equal access to healthcare. TB is the only major drug-resistant infection transmitted through the air and is the leading cause of death due to antimicrobial resistance (AMR), thus threatening global health security. Patients accessing public and private healthcare services are vulnerable to poor-quality care, catastrophic care-seeking costs and a lack of wider health and financial support. If efforts to tackle TB continue at the current rate of progress, it is predicted that between the years 2015 and 2030, 28 million people will die of TB at a global economic cost of $983 billion.

Prioritise

The burden of TB is falling but not quickly enough to reach the 2015 Sustainable Development Goal to End TB by 2030 and the targets set in World Health Organization (WHO) End TB Strategy. Much can be done now to steepen the trajectory and reach global goals: optimising the use of

current tools, ensuring all TB care is people-centred and pursuing universal health coverage and social protection. However, new tools will need to be introduced by 2025 to reach the 2030 targets of a 90 per cent reduction in TB deaths and 80 per cent reduction in TB incidence compared with 2015 levels.

TB is now receiving heightened political attention due to the first ever UN HLM, attended by heads of state and government, devoted solely to TB on 26 September 2018 in New York. The resulting political declaration will only accelerate progress to End TB if commitments are turned into action, investments and partnerships. All stakeholders—academics, civil society, communities—have a role to play in holding politicians to account on their promises as well as helping to deliver them. A multi-sectoral accountability framework to accelerate progress to end TB that enables the monitoring, reporting, review, and actions needed for effective accountability of government and all stakeholders at global, regional, and country levels will be essential in this respect. Later in 2018, the *Lancet* Commission on TB will publish its report which aims to identify decisive global and country-specific actions necessary to ensure success (Goosby, Jamison, Swaminathan, Reid, & Zuccala, 2018). This report will include recommendations for the global community to be bold, prioritise investment in research and development (R&D), create an enabling environment, and dedicate substantial resources to implement strategies to end TB (Goosby, Jamison, Swaminathan, Reid, & Zuccala, 2018).

Fund

Funding for TB reached US$6.9 billion in 2017. This falls US$2.3 billion short of the Stop TB Partnership's Global Plan to End TB estimated requirement of US$9.2 million. Funding from domestic sources dominated in the BRICS countries (with 48 per cent of the world's notified TB cases), whilst low-income countries (LICs) depended heavily on international donor funding. The Global Plan estimates that at least US$56 billion will be required for implementing the first 5 years of the End TB Strategy (2016-2020). This investment would treat 29 million people for TB, prevent 45 million people from developing TB, save 10 million lives and avert 144.7 million Disability Adjusted Life Years (DALYs). The overall return on the accelerated investment plan would be US$1.2 trillion, or US$85 for each dollar invested. The TB community is looking to politicians to mobilise, increase and focus funding dedicated to ending the TB epidemic. Cost savings on the price of TB medicines also offers an opportunity to free up funds to diagnose and treat more cases.

Partner

Partnerships between multiple stakeholders will be essential to reaching out to all key populations vulnerable to TB. Private providers of TB care are diverse in type and scale and operate in formal and informal settings. Private provision of care can delay diagnosis, be of low-quality, inefficient, lead to high loss to follow-up and can impoverish patients. NTPs in key high-burden countries where initial care seeking from private providers is high, are now changing their approach and working with, rather than in parallel to, the private sector. Public sector engagement with the private sector at scale has been shown to be cost-effective and can reduce the financial burden of TB care for patients, but a lack of prioritisation; low investment relative to the scale of private healthcare provision; limited understanding at the local level of the different types of private health providers and their business models and priorities; and a lack of understanding of care-seeking behaviours has limited progress on how to manage a large, fragmented, and non-homogenous sector at scale, with much research to be done. Lessons emerging suggest that efforts must go into the development and deployment of enablers and motivators to encourage private provider

participation, communication, and trust, as well as building system capacity for strategic purchasing, roll-out of digital data systems, mandatory notification decrees, and other regulatory approaches. Partnership with civil society and communities affected by TB is crucial to transform policies and practice, help mobilise resources and stimulate and support local action.

Reach

TB often has the worst outcomes amongst the most vulnerable. The Global Plan defines *key populations* to whom it is essential to reach out to for ending TB as they have increased exposure to TB, limited access to quality TB services, or are at increased risk of developing TB disease once infected due to biological or behavioural factors that compromise their immune system (Stop TB Partnership & UNOPS, 2015). Focusing on key populations at high risk of TB who are underserved and marginalised means not conducting business as usual. Costs of care-seeking for TB to patients and their households can be catastrophic, especially for the poorest who spend proportionately more on care-seeking than the less poor, with loss of income often contributing the highest proportion of costs experienced by households affected by TB.

Prevent

Finding and treating 40 per cent of the world's TB cases missed by the health system is pivotal to preventing the ongoing spread of this disease through the air. National notification and vital registration systems need to be strengthened to directly count TB incidence and mortality in all countries. Working with people with TB and TB survivors to identify, measure and eliminate stigma will help address barriers in care seeking and isolation of those affected. Development of strong contact tracing and relationships with communities during the long treatment regimens of TB will provide a firm foundation to rapidly respond to other infectious diseases. Providing TB preventive treatment to those eligible realises their human rights.

Research and innovate

New tools will need to be introduced by 2025 to reach the 2030 targets of the End TB Strategy, which means that investment needs to be increased now to ensure those tools are available. Priorities are for a rapid, affordable, easy-to-use point-of-care tests for diagnosing TB and detecting drug resistance; shorter and safer drug regimens for treating drug-sensitive, drug-resistant, and latent forms of the disease; and a new universally applicable, effective vaccine for pre-exposure and post-exposure prophylaxis. The importance of applied health research to ensure new tools are successfully implemented and strengthening of health systems to deliver new tools and innovative approaches must not be underestimated. Substantial increased funding, required to address the chronic underfunding of TB research, from a more diverse base is critical to ensure that scientific progress reaches all those affected by TB and will need to be complimented by a research-enabling environment for research and design (R&D) on TB at country level. The new Global Strategy for TB research being developed should enhance the cooperation and coordination of research; mobilise resources; and promote sharing of data and information to rapidly advance implementation. Learning can be drawn from other new and existing research and development initiatives, such as the Global Antimicrobial Resistance Research and Development Hub. Decisive action by all governments working in concert with the private and philanthropic sectors, civil society, and communities affected by TB is needed to make TB research and innovation a real priority.

2. TB facts

An estimated 10.4 million people developed TB in 2016 (WHO, 2017c) but only 6.6 million cases were reported to NTPs and to the WHO, missing four million people with TB. Thirty countries are defined by the WHO as high-TB burden countries (HBCs) on three new HBC lists for the period 2016-2020 (one for TB, one for TB/HIV, and one for MDR-TB); 20 in terms of the absolute number of estimated incident cases, plus an additional 10 countries not already listed with the most severe burden in terms of incidence rates per capita (WHO, 2017c, p.17). These 30 HBCs accounted for 87 per cent of estimated incident cases worldwide in 2016 with five countries alone accounting for 56 per cent of the global total (in descending order): India, Indonesia, China, the Philippines, and Pakistan. Most of the 30 HBCs have an incidence rate that ranges from 150-300 cases per 100,000 people, rising to above 500 cases per 100,000 people in a few countries. Globally in 2016, 90 per cent of estimated TB incidence was in adults, 65 per cent in males, with 18 per cent (1.9 million) attributable to undernourishment, 10 per cent (1 million) to HIV infection, 8 per cent (0.8 million) to smoking and 8 per cent (0.8 million) to diabetes. It is estimated that one million children under the age of 15 became sick with TB in 2016 with less than half (43 per cent) reported to NTPs.

An estimated 1.3 million people died from TB among HIV-negative people in 2016 and an additional 374,000 among HIV-positive people (estimates are presented separately given that the cause of TB deaths among HIV-positive people is classified as HIV by the WHO's International Classification of Disease and Related Health Problems 10th Revision (as cited in WHO, 2017c)). TB is the leading cause of death in people living with HIV and the ninth leading cause of death worldwide, causing more deaths than any other infectious disease. Almost one in four children, 253,000, who developed TB died, 90 per cent of whom were untreated. The case-fatality rate (CFR i.e. the proportion of people with TB who die from the disease) in 2016 was 16 per cent, varying widely from under 5 per cent in a few countries to more than 20 per cent in most countries in the WHO African Region, highlighting the inequity of access to diagnosis and treatment among countries. Most of these deaths could be prevented with early diagnosis and appropriate treatment. For example, in 2015 the treatment success rate among people whose TB was detected, reported, and treated was 83 per cent globally and can be over 95 per cent in high-income countries (HICs) with UHC.

TB is the only major drug-resistant infection transmitted through the air and is the leading cause of death due to AMR (Abdullahi et al., 2016). There were 490,000 cases of multi-drug-resistant TB (MDR-TB) in 2016 and an additional 110,000 cases that were susceptible to isoniazid but resistant to rifampicin (RR-TB), the most effective first-line anti-TB drug. It is estimated that 79 per cent of patients with drug-resistant TB (DR-TB) go without treatment, and among those who are treated, only 54 per cent are cured. The median cost per patient treated in 2016 was US$1,253 for drug-susceptible TB and over 7 times higher for MDR-TB (US$9,529) (WHO, 2017c). Although age-disaggregated data on MDR-TB is not yet reported to NTPs, it is estimated that less than 10 percent of the estimated 30,000 children who develop MDR-TB every year are detected and treated (Dodd, Sismanidis, & Seddon, 2016; Jenkins et al., 2014).

Current health interventions for preventing TB are prevention of infection and prevention of disease through finding and treating missed cases, infection control, vaccination, with Bacillus Calmette-Guérin (BCG), and treatment of latent TB infection (LTBI) in specific at-risk groups. Twenty-three of the HBCs reported data on TB preventive treatment in 2016 for people living with HIV (coverage ranging from 2.4 to 73 per cent) and/or children under 5 years of age who were household contacts of a bacteriologically confirmed pulmonary TB case. Despite an 85 per cent increase between

2015 and 2016 (from 87,242 to 161,740) in the number of children in this risk group reported to have been started on TB preventive treatment, this was still only 13% of the 1.3 million children estimated to be eligible. The ratio of the TB notification rate among healthcare 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. Globally in 2016, 8,144 healthcare workers were reported with TB with the number of TB cases per 100,000 healthcare workers more than double the notification rate in the general adult population in seven countries (Burkina Faso, Columbia, Dominican Republic, Georgia, Lithuania, Mexico and Venezuela). BCG vaccination should be provided as part of national childhood immunisation programmes according to a country's TB epidemiology. In 2016, 154 countries reported providing BCG vaccination as standard part of these programmes, of which 111 reported coverage above 90 per cent.

Whilst the TB burden remains bad, it is better than it has been. Consistent with previous years, the number of incident cases is falling slowly, in both absolute terms and per capita. Globally, the average rate of decline in the TB incidence rate was 1.9 per cent between 2015 and 2016. Likewise, globally the number of TB deaths among HIV-negative people also fell by 3.4 per cent between 2015 and 2016. However, trends in mortality rates in the 30 HBCs vary substantially. Whilst some countries have rates of decline exceeding 6 per cent per year since 2010 (e.g. Ethiopia, the United Republic of Tanzania, Viet Nam, and Zimbabwe), other countries show limited changes (e.g. Angola, Congo, and South Africa). Between 2000 and 2016, TB treatment prevented an estimated 44 million deaths among HIV-negative people and, supported by Antiretroviral therapy (ART), averted an additional 8.5 million deaths among HIV-positive people. (WHO, 2017c)However, from 2000 to 2015, 33 million people died of TB at a global economic cost of US$617 billion (Global TB Caucus, 2017).

Despite progress, the pace of decline in TB is too slow to reach goals set by the global community. The annual decline in the global TB incidence rate needs to accelerate to 4-5 per cent per year by 2020, and then to 10 per cent per year by 2025. Declines of 10 per cent per year have only been documented in the context of UHC combined with broader social and economic development. The global CFR needs to be reduced to 10 per cent by 2020 and then to 6.5 per cent by 2025, a rate similar to the current level in many HICs.

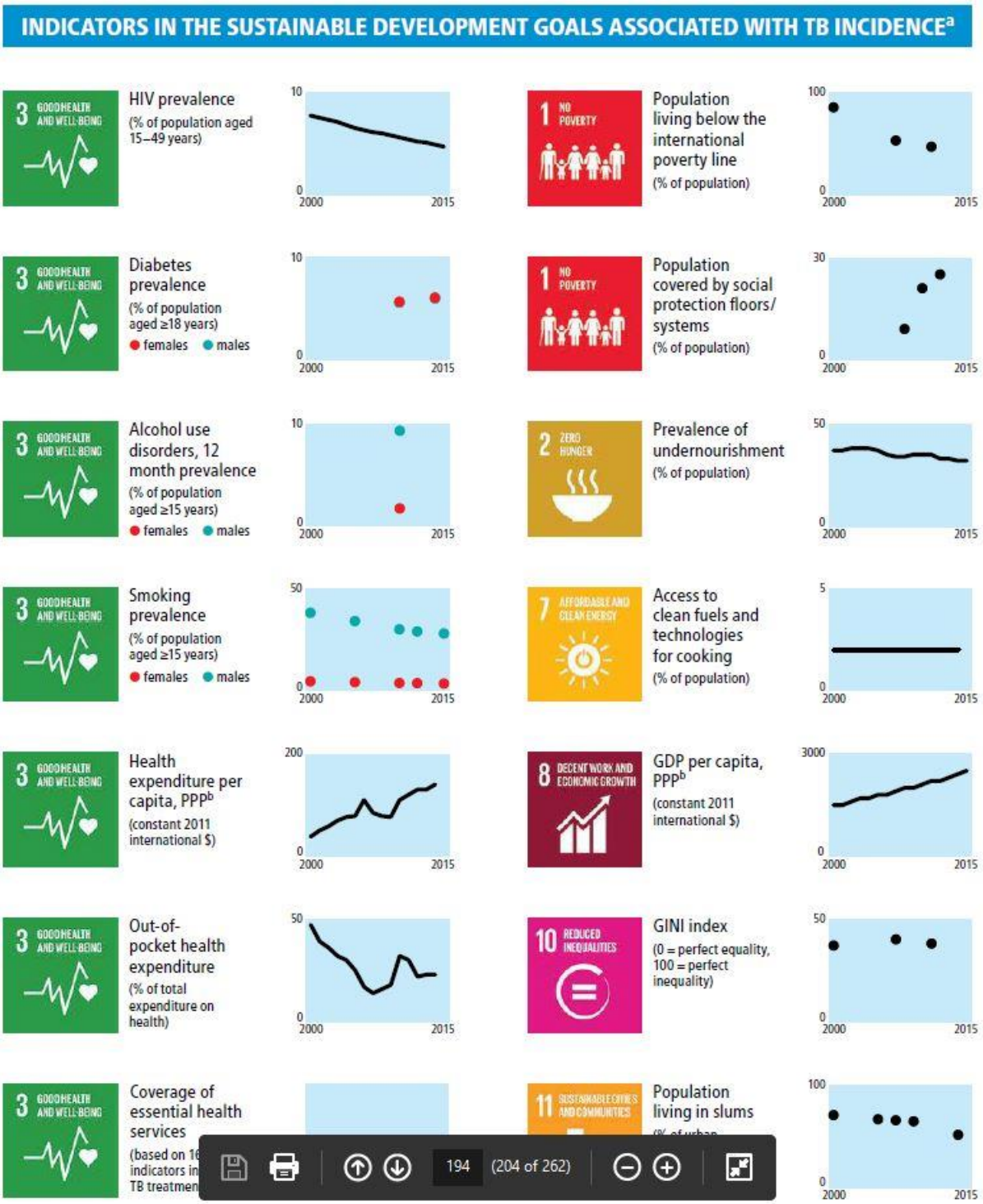
3. Prioritise

The Sustainable Development Goals

Seventeen Sustainable Development Goals (SDGs) were adopted by the UN Member States in September 2015. Ending the TB epidemic falls under the health SDG Three.

In the SDG goal**, Ensure healthy lives and promote well-being for all at all ages,** TB is specifically mentioned under target 3.3: 'By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases'. To end the epidemic of TB requires progress in reducing health-related risk factors for TB infection and disease, as well as broader social and economic determinants of TB infection and disease. WHO has therefore expanded its TB monitoring and developed a TB-SDG monitoring framework that comprises 14 indicators under seven SDGs for which there is evidence of an association with TB incidence. This will provide analysis and inform broader actions in the health sector and beyond that will be necessary to end the TB epidemic.

Figure 1: TB-SDG monitoring framework for the United Republic of Tanzania



Source: WHO Global TB Report 2017 (WHO, 2017c, p.193)

The End TB Strategy

The WHO has also developed a new global End TB Strategy post-2015 which shares a common goal with SDG target 3.3 to end the global TB epidemic (WHO, 2015d). This is defined as 10 new (incident) cases per 100,000 population per year (WHO, 2015d). This Strategy has three high-

level, overarching indicators with targets set for 2030 (linked to the SDGs) and 2035, and milestones for 2020 and 2025. Targets are: reduce TB deaths by 95 per cent; cut new cases by 90 per cent by 2035; eliminate catastrophic costs that TB-affected families face by 2020. To achieve these targets and milestones, the End TB Strategy has four underlying principles and three pillars. The prevalence of TB disease is not an indicator in the SDGs or a high-level indicator of the End TB strategy. Ending the TB epidemic depends on high-quality TB care and prevention to all whilst also pursuing universal access to healthcare and social protection and rapidly improving nutrition and economic conditions (Uplekar et al., 2015).

Figure 2: The WHO End TB Strategy

THE END TB STRATEGY: *AT A GLANCE*

VISION: A WORLD FREE OF TB

Zero deaths, disease and suffering due to tuberculosis

GOAL: END THE GLOBAL TB EPIDEMIC

INDICATORS	MILESTONE		TARGETS	
	2020	2025	**2030***	**2035**
Reduction in number of TB deaths compared with 2015	35%	75%	**90%**	**95%**
Reduction in TB incidence rate compared with 2015	20% (<85/100 000)	50% (<55/100 000)	**80%** (<20/100 000)	**90%** (<10/100 000)
TB-affected families facing catastrophic costs due to TB (%)	0	0	**0**	**0**

PRINCIPLES

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

PILLARS AND COMPONENTS

1. INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION

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

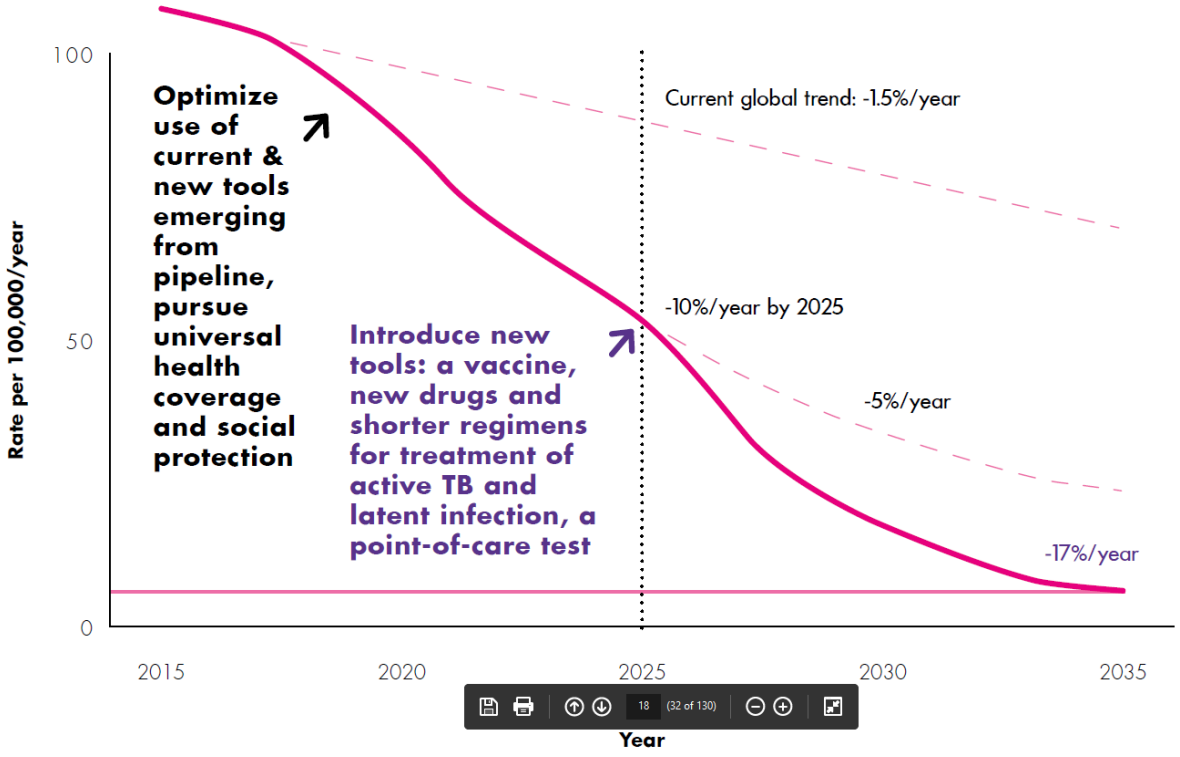
* Targets for the United Nations Sustainable Development Goals.

Source: WHO Implementing the End TB Strategy: The Essentials (WHO, 2015c, p.3)

High-level meetings

Optimising the use of current and new tools emerging from the pipeline along with pursuing UHC and social protection will start to accelerate the decline in the TB incidence rate (WHO, 2015c). Aggressive scale-up of any single intervention or merely expanding the coverage of TB services will not be enough to achieve the post-2015 End TB Strategy targets (R. Houben et al., 2016). Through comparison of multiple TB models, expansion of existing interventions should enable South Africa to reach the 2025 targets; however, in India and China—although full scale-up of all interventions in TB-programme performance would result in major reductions in the TB burden—additional country-specific activities are likely to be needed to achieve the 2025 targets (R. Houben et al., 2016). After 2025, reaching the 2030 and 2035 targets for the rate at which TB incidence falls globally will depend on: prevention of new infections and a technological breakthrough that can prevent progression from infection to disease and substantially reduce the risk of developing TB disease among the approximately 1.7 billion people who are already infected with *Mycobacterium tuberculosis*. At the current rate of progress, it will take 150 years to achieve the SDG target 3.3 to end the TB epidemic.

Figure 3: Projected global trajectory of TB incidence rate 2015-2035 required to reach 2035 targets (log scale)



Source: WHO Implementing the End TB Strategy: The Essentials (WHO, 2015c, p. 18)

Political leaders have started to recognise the need for a paradigm shift and acceleration in tackling TB. In July 2017, the G20 leaders recognised that acting on priority pathogens, including TB, is a crucial part of global efforts to combat AMR (Leaders of the G20 Nations, 2017). In September 2017, BRICS leaders committed to combat TB together, including advancing TB research (Press Information Bureau, 2017). The first global ministerial conference on TB was hosted by WHO and

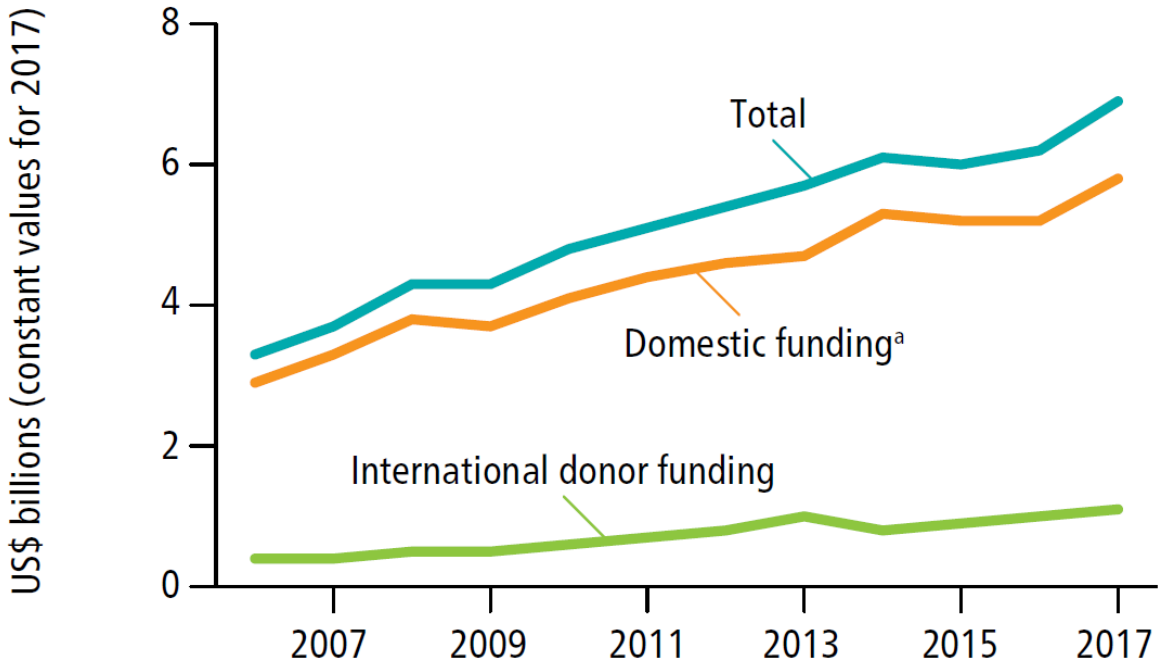
the Russian Federation in Moscow on 16-17 November 2017. In the Moscow Declaration, all 120 participating delegations committed themselves to advancing the TB response within the SDG agenda; ensuring sufficient and sustainable financing; pursuing science, research and innovation; and developing a multi-sectoral accountability framework to fundamentally transform the fight against TB (Ministry of Health of the Russian Federation, 2017). This meeting was a significant milestone to inform the United Nations High Level Meeting (UNHLM) on TB which will take place on 26 September 2018, during the second day of general debate of the General Assembly at its seventy-third session in New York (NY, USA) (WHO, 2018a). The UN HLM meeting will be attended by heads of state, permanent missions to the United Nations, ministers of health, national delegations to the UNHLM, parliamentarians, and other relevant officials. This meeting provides a once-in-a-generation opportunity at a critical juncture in the epidemic to drive a step-change in the response to TB to end this disease by 2030 (Global TB Caucus, 2017) with calls for turning commitments into action (Herbert et al., 2018a; Herbert, 2018b).

4. Fund

Current funding

Overall, most funding during the period 2006-2017 was provided by domestic sources (WHO, 2017c). In 2017, US$5.8 billion (84 per cent) of the total funding of US$6.9 billion for TB was from domestic sources (WHO, 2017c, p.112).

Figure 4. Funding for TB prevention, diagnosis and treatment by funding source, 2006-2017, 118 countries with 97 per cent of reported TB cases

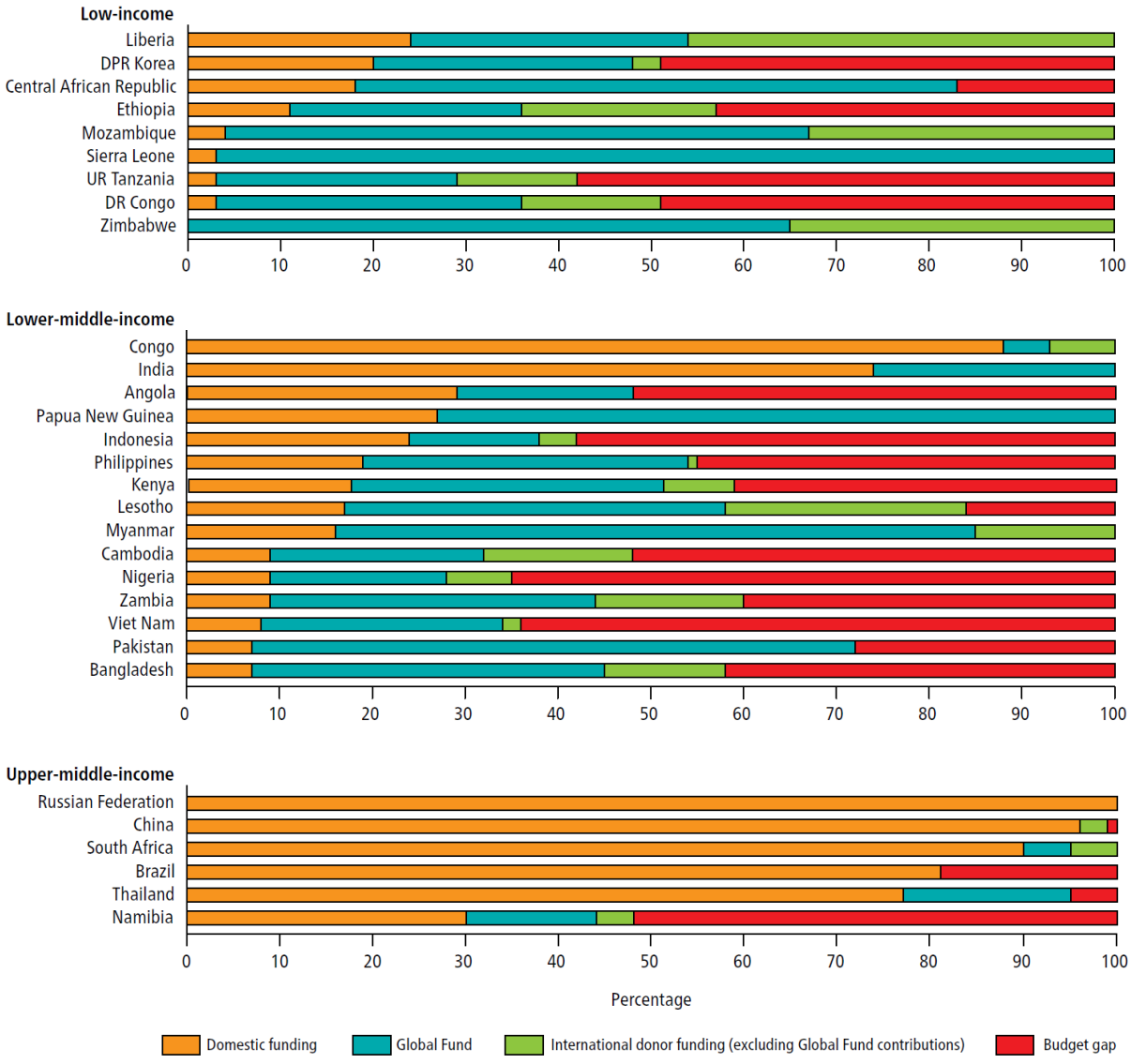


Source: WHO Global TB Report 2017, (WHO, 2017c, p. 112)

However, these aggregated figures for the 118 LICs and middle-income countries (MICs) conceal substantial variation among countries. For example, while domestic funding dominates in BRICS,

accounting for 95 per cent of total funding in 2017, international donor funding exceeds funding from domestic sources in LICs (56 per cent of the total in 2017) and is similar to levels of domestic funding in the 25 HBCs outside BRICS (48 per cent of the total in 2017) (WHO, 2017c). The importance of international donor funding in HBCs is clear: 80 per cent of funding of TB-specific budgets included in national strategic plans for TB were from international donors in 2017 (WHO, 2017c).

Figure 5. Sources of funding and funding gaps for the TB-specific budgets included in national strategic plans for TB in 2017, 30 HBCs



Source: WHO Global TB Report (WHO, 2017c, p.116)

Funding gaps

Progress against TB requires adequate and sustained funding over many years. The Stop TB Partnership's Global Plan to End TB is a 5-year investment plan covering 2016-2020 which represents a roadmap to accelerating progress to achieve the 2020 milestones of End TB Strategy:

- to reduce TB deaths by 35 per cent compared to 2015;
- to reduce the TB incidence rate by 20 per cent compared to 2015; and
- no TB patients and their households face catastrophic costs as a consequence of TB disease (Stop TB Partnership & UNOPS, 2015).

Two investment scenarios are considered in the Global Plan to End TB: standard and accelerated. In the standard scenario, investments are gradually increased to ensure that the 2020 End TB Strategy milestones are reached. In the accelerated investment scenario, investment increases sooner but with less investment overall owing to the reduced number of people needing TB care and lower implementation costs. The accelerated scenario is more cost-effective, requires less overall investment (US$56.1 billion instead of US$58.4 billion), would significantly increase the number of lives saved and return on investment in the period covered by the Global Plan. For these reasons, the accelerated investment scenario is recommended by the Global Plan (Stop TB Partnership & UNOPS, 2015). An additional US$9 billion would be needed for global TB R&D.

Table 1. Resource requirements for the accelerate investment scenario (in US$ billions)

Country	2016	2017	2018	2019	2020	Total
Global	9.9	12.0	12.4	11.4	10.4	56.1
LICs	1.0	1.6	1.6	1.4	1.2	6.8
Lower-middle income	2.4	3.2	3.3	2.9	2.5	14.3
Upper-middle income	2.6	2.9	2.8	2.7	2.5	13.5
HICs	3.9	4.4	4.6	4.4	4.2	21.5
BRICS	4.5	5.3	5.4	5.2	4.9	25.3

Source: Stop TB Partnership Global Plan (Stop TB Partnerships & UNOPS, 2015, p. 105)

Accelerated investment would treat 29 million people for TB, prevent 45 million people from getting TB, save 10 million lives and avert 144.7 million DALYs. The overall economic return on the accelerated investment plan would be US$1.2 trillion, or US$85 for each dollar invested. Health systems would also see permanent gains as a result of investing in TB in the following ways (Stop TB Partnership & UNOPS, 2015):

1. Investing in early and effective TB diagnosis builds lasting diagnostic, laboratory, and case-finding capacity in the health system.
2. Investments that strengthen contact investigations for TB will create a system that can be reliably called upon during infectious disease outbreaks, such as Ebola outbreak in West Africa in 2014, which demanded the rapid mobilisation of both health facilities and communities to conduct extensive contact investigations.
3. Fighting TB requires investment in airborne infection control practices building capacity of health systems to quickly respond to other airborne infection outbreaks such as influenza.

4. TB treatment requires lengthy interaction with patients and communities. TB investments can strengthen overall engagement with these communities to the benefit of other health programmes.
5. Lengthy TB treatment demands strong and reliable drug supply chain systems. Improvement in and greater integration of these systems will improve supply chains for other diseases.
6. Costs besides commodity-based or direct costs make up a large proportion of the costs. These costs involve laboratory strengthening, the improvement of the health system components, and human resource development, all of which have the potential to make a lasting, positive impact on the overall strength of health systems.

Despite growth in funding since 2006, from both domestic and international donor sources, many NTPs continue to be unable to mobilise all the funding required for full implementation of their national strategic plans. The funding gap in 2017 between national TB budgets and funding mobilised was US$0.9 billion (WHO, 2017c). However, in many countries, national strategic plans for TB are less ambitious than the targets set in the Global Plan, and so funding mobilised for TB prevention, diagnosis, and treatment of US$6.9 billion in 2017, falls US$2.3 billion short of the Global Plan's estimated requirement of US$9.2 billion.

Expansion of TB services could be cost-effective for HBCs and could generate substantial health and economic benefits for patients, despite requiring substantially increased funding compared with current practice (Menzies, Cohen, Lin, Murray, & Salomon, 2012). Wide differences exist though in the effect and efficiency of different approaches, implying that countries will need to carefully consider the approaches taken to service expansion (Menzies et al., 2016). In Nigeria, to reach 90 per cent reduction in TB deaths and an 80 per cent reduction in new cases by 2030, about 81 billion Naira per year would need to be spent to increase detection rates, strengthen primary healthcare provision, and treat many more patients (Vassall & Mustapha, 2015). This would give each TB patient on average about another 22 years of life and overall would produce about 2.8 million additional years of life (Vassall & Mustapha, 2015).

The impact of BRICS countries and their capacity to fund their national programmes

The incidence and mortality rates for the upper-middle-income countries (UMICs) of the 30 HBCs and their share of the global burden are shown in Table 2. In the Russian Federation, the burden of TB disease is falling but the incidence of MDR-TB is increasing (WHO, 2017c).

Table 2. Estimated epidemiological burden of TB in 2016 for the UMICs of the 30 high TB burden countries and their share of the global burden.

Country	HIV-negative TB mortality (thousands)	% global burden	HIV-positive TB mortality (thousands)	% global burden	Incidence (thousands)	% global burden
Brazil	5.4	0.4	1.9	0.5	87	0.8
Russian Federation	12	0.9	1.7	0.5	94	0.9
India	423	32.5	12	3.2	2790	26.8
China	50	3.8	1.8	0.5	895	8.6
South Africa	23	1.8	101	27	438	4.2
Thailand	8.6	0.7	3.9	1	119	1.1
Namibia	0.75	0.1	0.87	0.2	11	0.1

Source: WHO Global TB Report (WHO, 2017c, p.29)

TB financing for the UMICs of the 30 HBCs in 2017 is shown in Table 3.

Table 3. TB financing, 2017

Country	National TB budget (US$ millions)	Funding source %		
		Domestic	International	Unfunded
Brazil	67	81	<1	19
Russian Federation	1175	100	0	0
India	525	74	26	0
China	384	96	3	1
South Africa	244	90	10	0
Thailand	20	77	18	6
Namibia	56	30	18	52

Source: WHO Global TB Report (WHO, 2017c, pp.156-215)

Specifically, Brazil, the Russian Federation, India, China, and South Africa (BRICS) accounted for 46 per cent of the available funding for TB in 2017 (and 48 per cent of the world's notified TB cases), with 95 per cent (range 89-100 per cent) of their funding coming from domestic sources (WHO, 2017c). Prospects for increasing domestic funding include: increased political commitment, increased budget available; and cost savings on medicines.

India—the country with the largest burden of TB disease—accounts for 27 per cent of the world's 10.4 million new TB cases, 26 per cent of the 1.6 million TB deaths globally, and 16 per cent of the estimated 490,000 new cases of MDR-TB. India has tripled domestic funding for TB in 2017 from US$124 million in 2016 (WHO, 2017c). The budget in 2017 was US$525 million (almost double the 2016 budget of US$280 million) and was fully funded, including 74 per cent from domestic sources. This increase followed high-level (Prime Ministerial) political commitment to an ambitious goal of ending TB by 2025, and the development of a new National Strategic Plan for TB Elimination 2017-2025 that aims to accelerate progress towards this goal (Central TB Division, 2017). Suggestions for turning this ambition into reality are offered by Pai, Bhaumik, and Bhuyan (2016).

Cost savings through new agreements between the Stop TB Partnership's Global Drug Facility and medicine manufacturers have substantially lowered the prices of medicines used in the treatment of TB and offer potential savings of approximately US$31 million in the April 2018 to March 2019 period. If these savings were used to purchase additional medicines, the savings would be sufficient to provide 960,000 people with drug-sensitive TB medicines, 53,000 people with shorter regimens for DR-TB, or up to 37,000 people with conventional regimens for DR-TB (Stop TB Partnership, 2018a). Country-level negotiation can also offer savings and lead other countries to follow. South Africa has negotiated a price drop of around 50 per cent for the MDR-TB injection-free drug bedaquiline (replacing painful kanamycin injections which can lead to irreversible hearing-loss) from US$750 to US$400 for a 6-month treatment course, which will also be made available for all TB programmes procuring from the Global Drug Facility (Stop TB Partnership, 2018b). The Minister of Health of South Africa claims that this decrease in price over the next eight months will lead to savings of more than US$36 million for the South African health budget (Stop TB Partnership, 2018b). Although formal evidence from randomised controlled trials of bedaquiline and other new TB drugs is only just emerging, the Minister now calls on the WHO to urgently update the MDR-TB treatment guidelines to reflect the body of evidence available on the use of bedaquiline in the treatment of DR-TB.

The impact of low income countries and their capacity to fund their national programmes

International donor funding remains crucial, accounting for 48 per cent of the funding available in the 25 other HBCs outside BRICS (which have 38 per cent of the world's notified TB cases) and for 56 per cent of funding in LICs (WHO, 2017c). International donor funding reported by NTPs amounts to US$1.1 billion in 2017. The single largest source (80 per cent of the total) is the Global Fund to Fight AIDS, TB and Malaria. The largest bilateral donor is the United States government, which also provides about one-third of the contributions received by the Global Fund. Estimates of the funding needed to be mobilised from domestic and international donor sources from countries eligible to apply to the Global Fund to Fight AIDS, TB, and Malaria (this does not include Brazil, China or the Russian Federation) for the period 2016-2020 is US$29.4 billion (US$16 billion domestic and the rest from international donors) (Stop TB Partnerships & UNOPS, 2015). These figures do not include the broader investments required to increase the overall coverage and

quality of healthcare services or to remove financial barriers to accessing care (Pillar 2 of the End TB Strategy).

Many NTPs continue to be unable to mobilise all the funding required for full implementation of their national strategic plans. In 2017, the largest funding gaps among LICs were for the HBCs of the United Republic of Tanzania (US$40 million), Ethiopia (US$36 million), the Democratic Republic of Congo (US$28 million) and the Democratic People's Republic of Korea (US$13 million). Half of the total reported funding gap in 2017 was accounted for by countries in the WHO African Region (US$502 million), with Nigeria reporting the largest gap (US$215 million) (WHO, 2017c).

5. Partner

Multi-sector collaboration is key to successful implementation of the End TB Strategy. The required mix of biomedical, public health and socioeconomic interventions combined with research and innovation go far beyond the remit of NTPs. NTP leadership will need to coordinate broad engagement across and beyond government, ranging from ministries such as social welfare, labour, justice, education, transport, and science and technology; technical and scientific institutions; financial partners and development agencies; civil society; and the private sector (WHO, 2015c). Cross-border collaboration is also necessary if progress in one country is not to be undone by a neighbouring epidemic (Global TB Caucus, 2017).

Partnering with the private sector

Most global TB prevention and care efforts have focussed on the public-sector role. However, in South Asia over 80 per cent of all patients with TB start their care seeking in the private or informal sector (M. S. Khan, Salve, & Porter, 2015). The private health sector is complex and diverse in its service provision, motivations, level of training, and fees charged. Private providers operate in formal and informal settings, ranging from large hospitals to roadside stalls, and include doctors, diagnostic laboratories, and pharmacies. Seeking private provision of care can delay diagnosis, be of low-quality, inefficient, and potentially expensive for the patient (Sreeramareddy, Qin, Satyanarayana, Subbaraman, & Pai, 2014; Wells, Uplekar, & Pai, 2015).

Whilst expectations for quality standards of TB care have been laid out by the Institute of Scientific and Technical Communicators (ISTC) (TB CARE I., 2014), quality of care in both the public and private sector often falls short of these international standards (Cazabon et al., 2017). The loss of TB patients along the TB care pathway from diagnosis to starting treatment has been shown to be alarmingly high in Pakistan, with 64 per cent of bacteriologically confirmed TB cases diagnosed at public-private mix (PPM) facilities in Lahore never starting treatment (B. J. Khan et al., 2017). This was higher among males (68 per cent) and the elderly (79 per cent) (B. J. Khan et al., 2017). Additionally, the outcome of patients started on treatment was unfavourable for 19 per cent of cases (B. J. Khan et al., 2017). This pre-treatment loss to follow-up is higher than what has been observed in studies conducted in the public sector of five Asian countries, including Pakistan (4 to 28 per cent) (MacPherson, Houben, Glynn, Corbett, & Kranzer, 2014). From patient-pathway analyses in five countries, 66 per cent of patients initially sought care in private facilities; only 7 per cent of notified cases were from the private sector (Hanson, Osberg, Brown, Durham, & Chin, 2017). Patient-centred care will require engaging with the private sector with differentiated approaches to patient-centred care relevant to subnational differences (Hanson et al., 2017).

Accelerating tailored strategic engagement of private healthcare providers in TB care and prevention will be essential to achieving the global goals by reducing transmission by shortening delays in starting treatment, ensuring quality treatment completion, and slowing the emergence of drug-resistance caused by substandard care, reducing catastrophic costs and impoverishment, and accelerating uptake of new tools. The need to engage private healthcare providers for TB has been acknowledged since the early 1990s and featured in many global and national strategies, not least the most recent WHO End TB Strategy (WHO, 2015d), and research has significantly increased information on how to successfully engage private providers for TB care (Lei et al., 2015) and for those co-infected with HIV and TB (Hudson, Rutherford, Weiser, & Fair, 2018). Indeed, PPM implementation on a large scale has been shown to be cost-effective and can reduce the financial burden of TB for patients (Pantoja et al., 2009b). However, whilst numerous initiatives have been launched and piloted, less research has been conducted on which elements of private-sector engagement strategies work well and are successfully scaled up. A lack of prioritisation, a lack of investment relative to the scale of private healthcare provision, limited understanding at the local level of the different types of private health providers and their business models and priorities, and limited understanding of care-seeking behaviours are some of the challenges being faced in successfully engaging with private providers. With only a few countries including India, Bangladesh, Myanmar, and Pakistan achieving significant scale in private provider engagement, understanding of how to manage a large, fragmented and non-homogenous sector at large is limited. Lessons learnt so far suggest that efforts must go into the development and deployment of enablers and motivators that encourage private provider participation, communication, and trust as well as build system capacity for strategic purchasing, roll-out of digital data systems, mandatory notification decrees, and other regulatory approaches.

There are now new opportunities to introduce more systemic, scalable, and innovative approaches in the form of social businesses, national health insurance schemes, payment reform, regulatory regimes, digital technologies (e.g. digital vouchers for drugs and diagnostics, adherence monitoring technologies), and consolidation of other healthcare structures. Changes in health financing due to economic growth also provide an opportunity for engaging the private sector. In Pakistan, novel approaches, such as using laypeople as cough screeners, mobile phone software, incentives, and communication campaigns have been shown to substantially increase case notifications from the private sector (A. J. Khan et al., 2012). In urban projects in Mumbai, Patna, and Mehsana, the Indian NTP, in collaboration with intermediary agencies such as PATH (Furtwangler & Malaviya, 2016) has engaged large numbers of private providers and greatly increased the number of notifications from the private sector. Wells, Uplekar, and Pai (2015) review newer private sector engagement models and highlight the complex choices policy makers face but provide motivations to promote initiatives that will benefit the entire health sector. The authors note several successful elements and enablers of going to scale. This includes allowing private sector providers to manage TB patients (instead of referring them to the NTP); offering free services to private patients, including digital e-vouchers for free diagnostics and treatment; using intermediary agencies to network a diverse range of private providers; and ensure notification and link to care and adherence monitoring and support to all TB patients to help them complete treatment. ICT services were used in all these pilot programmes which enabled the projects to scale as well as track patients to monitor treatment completion and facilitate retention. The paper focuses on Asia (based on the large private sector and evidence base), but the authors expect many conclusions to be broadly applicable (Wells et al., 2015).

India

Engagement of the Revised National TB Control Programme (RNTCP) with the private sector is an overarching theme in the Government of India's National Strategic Plan for TB Elimination 2017-2025 (Central TB Division, 2017). At least half of those treated for TB in India first attend the largely unorganised and unregulated private sector. Systematic and large-scale engagement of the RNTCP assisting the private sector to provide high-quality care replaces the previous approach of private providers directing people to the RNTCP to receive their care in the public sector. In 2012, India rolled out a web-based TB case notification system (called *Nikshay*). It started by using SMS services to communicate with patients, issued decrees banning serological tests, made TB notifications mandatory for both the public and private sectors, and aligned RNTCP regimens with those commonly used in the private sector by adopting daily fixed-dose combination drugs. Payment to private providers for notification and adherence will be linked to integrated patient notification and social welfare payments. Notably, the mandatory notification of all people with TB in the country has contributed to a 37 per cent increase in notifications of new TB cases from 2013 to 2016 (WHO, 2017c). In 2017, India began to scale-up digital adherence monitoring and direct cash transfer to patients and private providers. India's National Strategic Plan for TB (2017-2020) has set an ambitious target of 2 million private TB notifications per year by 2020 (56 per cent of total case notifications), allocating substantial budget and mobilising strong political support at all levels. If these targets are reached, this success could inspire NTPs in other countries to be more ambitious and set higher targets. India is conducting pilot projects with Private Provider Interface Agencies in Mehsana, Mumbai, and Patna and have shown that notifications from the private sector can be dramatically increased, with improvements in quality and patient outcomes. Lessons from these projects can be used to develop a comprehensive plan to engage with the private sector to improve quality of care and better regulate this sector. In March 2018 at the Delhi End TB Summit, the prime minister of India, His Excellency Narendra Modi, reaffirmed his government's commitment to End TB by 2025 in India, a country which carries the world's greatest burden of TB (Modi, 2018).

Partnering with civil society and communities

Civil society and community-based organizations have a critical role to play in raising awareness and understanding of the issues facing End TB: advocating for increased investment; ensuring that the commitments made at the UN HLM are translated into real investments and actions at the country level; and ensuring that human rights established in numerous international human rights treaties and instruments are mainstreamed in the TB response—these are the rights to health, life, non-discrimination, information, privacy, participation, and enjoyment of the benefits of scientific progress and its applications. For example, the Treatment Action Group (TAG) and partners educated key decision-makers on TB needs, securing US legislative commitments to increasing funding for both the domestic and global TB response, even in an oppositional political environment, which will help resource-equitable access to the benefits of research (Treatment Action Group, 2017). TAG has also advocated for improved availability of a specific key diagnostic (TB-LAM), prevention treatment (once-weekly isoniazid-rifapentine for 12 weeks, 3HP for treatment of LTBI), and newer drugs (bedaquiline, delamanid and child-friendly formulations) at the global level and empowered in-country advocates to do the same at national and regional levels (Treatment Action Group, 2017).

A policy paper on TB research funding for the WHO, *Global Investments in TB Research and Development: Past, Present and Future*, was prepared together with various stakeholders from civil society groups, academia, and product development partnerships to inform the WHO's First Global Ministerial Conference on TB in the Sustainable Development Era – *A Multisectoral Response* in Moscow in November 2017 (WHO, 2017b). This paper describes how some of the research funded in the past has delivered benefits to patients and influenced policy and decision-making, but how little is being invested in TB R&D in comparison with other diseases, such as HIV and malaria. Research funded in the past has delivered benefits to patients and influenced policy- and decision-making, but progress has not been sufficient to tackle difficult TB challenges, such as MDR-TB and the development and successful implementation of new tools. This policy paper recommends the development of a global strategy for TB research to foster collaboration, improve efficiency, and increase R&D financing (WHO, 2017b).

Partnering with other sectors

Tackling the many challenges of facing TB requires the engagement of a diverse range of stakeholders. This includes partnership of NTPs with the social and employment sectors addressing living and working environments and providing support during absence from work due to TB. Partnership with prisons and providing services to those migrating are also important steps to reaching out to key populations.

6. Reach

TB often has the worst outcomes amongst the most vulnerable. The Global Plan defines *key populations* to whom it is essential to reach out to for ending TB as they have increased exposure to TB, limited access to quality TB services, or are at increased risk of developing TB disease once infected due to biological or behavioural factors that compromise their immune system (Stop TB Partnership & UNOPS, 2015). People who fall into one of the key population categories listed in the figure below are also likely to intersect with one or both other groups. Focusing on key populations at high risk of TB who are underserved and marginalised means not conducting business as usual.

Figure 6. The Global Plan Key populations for TB

Source: The Global Plan to End TB, 2016-2020 (Stop TB Partnership & UNOPS, 2015, p.53)

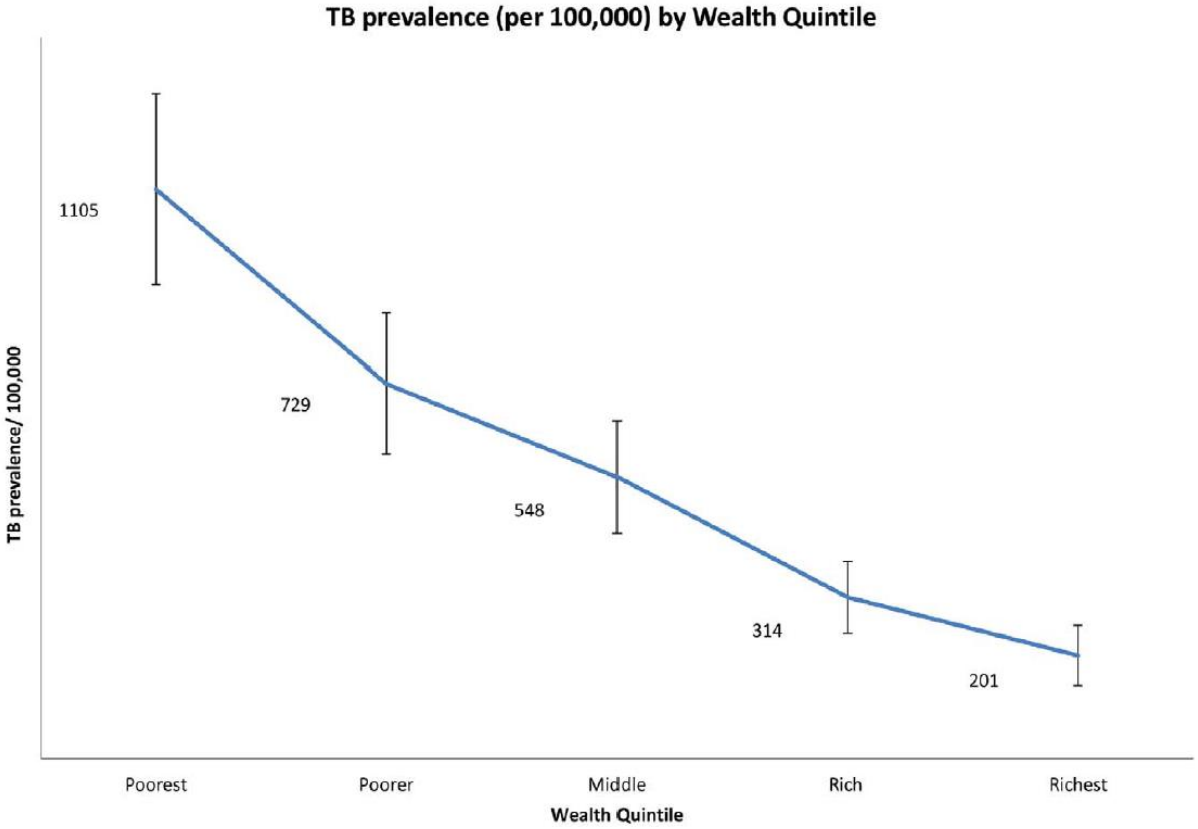
Poverty

TB is both a cause and consequence of poverty and can impose profound costs on families, communities, and countries. Many vulnerable poor do not have access to affordable health services of sufficient quality. Costs faced by patients with TB can exacerbate poverty even more by affecting health-seeking behaviour and delaying diagnosis, jeopardising treatment completion further worsening their disease, encouraging the emergence of DR-TB strains, and increasing the risk of disease transmission.

At the household level, assessing socioeconomic factors and TB disease can be difficult due to the small numbers of cases usually detected in TB prevalence surveys (Siroka et al., 2016). However, Oxlade and Murray (2012) found that the prevalence of TB was substantially higher in the poorest stratum in India as shown in the figure below. Most of the proximate risk factors for TB are associated with social conditions. People from low socioeconomic status groups typically have more frequent contact with people with active disease, a higher likelihood of crowded living and working conditions, greater food insecurity, lower levels of health awareness or less power to act on existing knowledge concerning healthy behaviours, and less access to quality healthcare than those from high socioeconomic groups (Lonnroth et al., 2010).

The influence of various social and economic determinants on the TB epidemic, including the links between TB and poverty, social protection, the prevalence of undernutrition, diabetes, HIV, alcohol use, smoking, indoor air pollution, and income per capita, have long been recognised, but the WHO has provided up-o-date data on the scale of the problem. New WHO estimates of the number of incident TB cases that were attributable to selected risk factors are provided in the WHO TB Report (WHO, 2017c). The continuing development of drug resistant strains of TB could absorb increasing proportions of national budgets. Co-infection epidemics with HIV—already widespread—could be exacerbated by joint epidemics of TB and non-communicable diseases like diabetes. Air pollution, overcrowded urban environments, and poor nutrition could increase the susceptibility of millions of people to a disease which has consistently shown itself ready to make the most of any vulnerability.

Figure 7: Self-reported TB prevalence (per 100,000) by wealth quintile



Source: Oxlade and Murray (2012)

The economic burden on households affected by TB through costs to patients and their households can be catastrophic (more than 20 per cent of household income), especially for the poorest who spend proportionately more on care seeking than the less poor (Tanimura, Jaramillo, Weil, Raviglione, & Lonnroth, 2014). In low- and middle-income countries, patients with TB face costs that, on average, amount to half their annual income (Tanimura et al., 2014) and considerable costs can be incurred seeking diagnosis through the private sector (Pantoja et al., 2009a). Costs incurred are not only for direct medical payments for diagnosis and treatment of TB patients (which can include traditional healers and private providers), but also direct non-medical payments (such as for transportation, food, and hospitalisation) and indirect costs (such as time accessing healthcare or lost income) for TB patients and their caregivers. Loss of income often contributes the highest proportion of costs experienced by households affected by TB. Education can also be

negatively affected. In one study in Malawi, children replaced 12.7 per cent of all household activities—mostly female children (11.5 per cent)—resulting in possible days lost from school (Kemp, Mann, Simwaka, Salaniponi, & Squire, 2007). Even where TB treatment is provided free by the government, such as in India, the costs of TB have been estimated to be up to 30,000 rupees per household in terms of treatment costs and lost earnings. Coping mechanisms include taking a loan or borrowing from family and friends, asset selling, and diversifying income-generating activities (Barter, Agboola, Murray, & Barnighausen, 2012).

One of the three targets of the End TB Strategy is to eliminate catastrophic costs due to TB in TB-affected households by 2020 (WHO, 2015d). WHO aims to annually report on results from national surveys of costs faced by TB patients and their households to document the magnitude and main drivers of different types of costs incurred by TB patients and their households to guide policy and monitor progress to the End TB Strategy target. A WHO handbook for conducting these surveys including a protocol was published in 2017 (WHO, 2017d) with surveys already completed, ongoing, or planned for a number of countries. The first national survey conducted in Viet Nam in 2016 of costs faced by TB patients and their households found that 63 per cent of households affected by TB or MDR-TB experienced costs that were above 20 per cent of their annual household income costing on average US$1,068 for an episode of TB (of which 49 per cent was reported household income loss) and US$4,289 for an episode of MDR-TB (WHO, 2017c).

TB predominantly affects people of working-age, reducing productivity and their ability to participate in the formal and informal economies, as well as within households. Country studies document that between three and four months of work time can be lost annually to TB with lost earnings of 20 to 30 per cent of household income.

The economic case for investment in TB control is that TB has a high mortality rate if left untreated; TB is the leading infectious cause of death globally; TB treatment is low cost and highly effective, and on average may give an individual in the middle of their productive life around 20 additional years of life, resulting in substantial economic and health returns (Vassall, 2014). Yet TB control continues to be chronically under-funded despite the costs of addressing TB being reasonable compared to other development and health investments (Vassall, 2014).

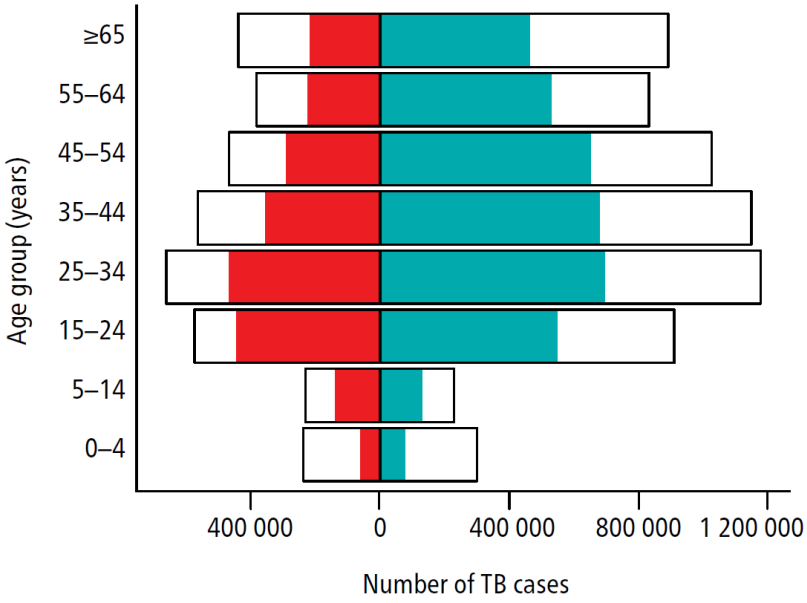
Aggressive expansion of TB services in India and South Africa could lessen financial hardship on many patients and their households, but improved social protection for people with TB will still be needed to eliminate catastrophic costs (Verguet et al., 2017). This includes appropriate income replacement as income loss often constitutes the largest financial risk for patients (Tanimura et al., 2014). The percentage of TB patients and their households facing catastrophic costs is a good tracer for progress towards UHC as well as social protection. If UHC and social protection are in place, then people with TB should be able to access high-quality diagnosis and treatment without incurring catastrophic costs.

Gender equity

Globally, in 2016, 65 per cent of TB incident cases were among men (an estimated 6.7 million). Globally in 2016, 55 per cent of deaths among HIV-negative people were among men (an estimated 718,000) and 55 per cent of deaths among HIV-positive people were among men (an estimated 207,000) (WHO, 2017c). The prevalence-to-notification ratios from surveys implemented in 2007-2016 show that men are accessing available diagnostic and treatment services less effectively than women (WHO, 2017c). Thus, more men than women remain undetected, are undiagnosed, and die from TB. The male: female ratio of incident TB cases for

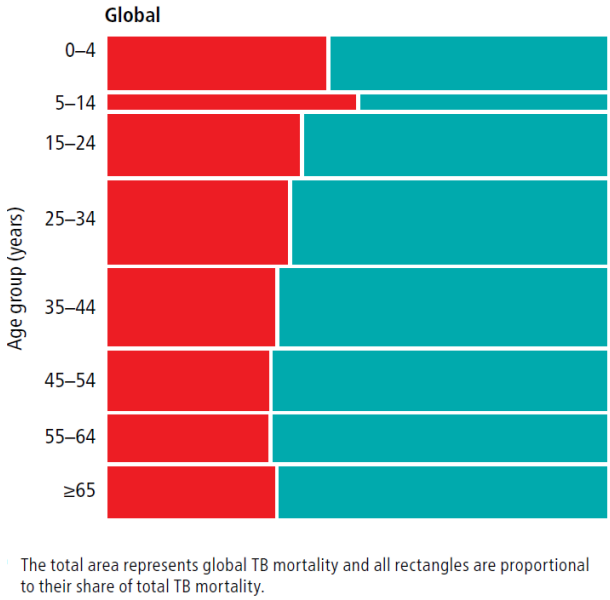
adults ranged from 1.3 to 2.1, whereas for children the male: female ratio was close to 1.1. Global estimates of TB incidence and mortality disaggregated by sex and age are shown in the figures below but represent consistently higher TB burden amongst men than women across most of the 30 HBCs (WHO, 2017c).

Figure 8. Global estimates of TB incidence (black line) and case notification disaggregated by age and sex (female in red; male in green), 2016



Source: Global TB report 2017 (WHO, 2017c, p. 57)

Figure 9. Global distribution of TB mortality in HIV-negative people by age group and sex (female in red; male in green), 2016



Source: Global TB report 2017 (WHO, 2017c, p. 59)

The excess of notified cases among men has often been explained as due to the barriers faced by women in seeking care for and being diagnosed with TB (Long et al., 1999; Weiss et al., 2006). However, a systematic review and meta-analysis of sex differences in TB burden and notifications in low and middle-income countries found that whilst case notifications continue to be higher in men than in women, TB prevalence was also higher among men than in women, including higher in settings with high HIV prevalence, suggesting a higher incidence of TB rather than a more complete registration for treatment by men (Horton, MacPherson, Houben, White, & Corbett, 2016). Moreover, on average, the ratio of prevalent-to-notified cases of TB was 1.5 times higher among men than women, suggesting that men take longer to seek or access care than women (Horton et al., 2016). Men therefore remain infectious in the community for a longer period than women, and in combination with social mixing patterns, are responsible for most infections in men, women, and children (Dodd et al., 2016). Greater effort and investment in addressing male-specific barriers to diagnosis and treatment is therefore not only an individual issue but also a public health issue. Addressing barriers that men may face in accessing care—such as the lack of awareness, loss of income, stigma, admission of illness, and feelings of inadequacy—by offering convenient access to care while maintaining men's sense of control could help ensure gender equitable access to diagnosis and treatment (Horton et al., 2016) and play a critical part of the solution to finding missing TB patients. Given that undiagnosed TB is the key driver of transmission in communities, targeting men as a high-risk group will be necessary to reduce the burden of TB in the whole population.

A UNDP discussion paper summarises the body of evidence on gender and TB, highlighting the lack of sex-disaggregated data, gender analysis, and gender-responsive programming (UNDP, 2015). Recommendations for responding to the gender-specific needs and vulnerabilities of people affected by or at risk of TB are also provided in the paper.

Children

Most children with TB contract the disease from family members in a household setting. Isoniazid preventive therapy has been recommended for children aged under five years exposed to patients with newly diagnosed, bacteriologically confirmed TB for many years, yet only 13 per cent of children eligible for preventive therapy received it in 2016, highlighting a substantial gap between policy and practice (WHO, 2017c). Reaching out to children through community-based contact tracing and isoniazid provision to children has been shown to be feasible under programme settings in Ethiopia and can achieve high adherence and completion rates (Datiko, Yassin, Theobald, & Cuevas, 2017). TB is a preventable under-five cause of death in TB-endemic countries, and TB care and prevention can be integrated with maternal and child health services (Black et al., 2016). Children with TB are at high risk of developing severe forms of the disease and dying if undetected and untreated. It is estimated that over 96 per cent of children who die from TB never access treatment (Dodd, Yuen, Sismanidis, Seddon, & Jenkins, 2017) despite the availability of child-friendly formulations for drug-sensitive TB and pre-qualified child-friendly formulations for second-line medicines (Detjen et al., 2018). The same child-friendly, water-dispersible tablets used during the continuation phase of treatment can also be used for preventive therapy if given for a period of 3 months, but this practice is rarely encouraged or implemented (Detjen et al., 2018). It is suggested that health systems neglect children with TB because children are less contagious than adults (stopping the spread of TB is a priority), and TB is difficult to diagnose in children with currently available tools (The Union, 2018).

Progress in the development of better tools to detect TB in children has been minimal. All existing diagnostic tests remain inadequate to diagnose TB in young children, especially those aged below five years, who cannot expectorate and usually have paucibacillary TB (fewer bacteria making them harder to diagnose). Isoniazid and rifapentine, a 3-month, once-weekly regimen for TB prevention; and bedaquiline and delamanid, two new drugs to treat TB, remain mostly inaccessible to children and no data are available on the performance and safety of the shorter MDR-TB regimen in children (Detjen et al., 2018).

There is a call for new resolutions from the upcoming UNHLM on TB to also benefit children (Detjen et al., 2018). The Child and Adolescent TB Working Group of the Stop TB Partnership proposes countries commit to four targets specific to childhood TB, in-line with other global goals (Detjen et al., 2018). The Decentralise TB Services and Engage Communities to Transform Lives of Children with TB, or DETECT Child TB, is a health-systems model being trialled in Uganda. The DETECT Child TB is applicable at different levels of the health system from higher-level facilities equipped with technology to volunteer community members who interact with their neighbours to help identify potential illnesses and encourage people to go for treatment (Green, 2015). TB services for adolescents also need to be improved to better serve this age-group, who frequently develop adult-type TB and therefore may contribute to disease transmission (Detjen et al., 2018).

Disability

Understanding the combined and complex impact of individual, social, contextual, and systems barriers to accessing TB services for vulnerable groups in poor populations is necessary to reach equity in health. A qualitative study conducted in a district in southern Malawi found that a lack of information combined with confusion related to TB, its cause, and how to protect oneself were major barriers to accessing health and TB services for individuals with disability (Grut, Sanudi, Braathen, Jurgens, & Eide, 2015). Health systems need to become more inclusive and strengthened to be more responsive to the priorities of disabled people.

CASE STUDY

Why TB research matters to Eloisa who lost her sight when recovering from TB

In 2007, Eloisa Zepeda-Teng was paralysed and nearly died from DR-TB meningitis in the Philippines. She was misdiagnosed multiple times but eventually was correctly diagnosed and started treatment. She then started to lose her vision through treatment but was told that that it is just the way it is. After 24 months of treatment she was completely blind. The NTP did not provide any support for her disability. She lost her friends through stigma of the disease. In June 2018, Eloise spoke at the civil society hearing at UN headquarters to ask for support of prevention of disability during treatment of TB and for social protection to those who develop a disability through their TB journey. Because of her disability, Eloise will no longer be able to work as an architect but dreams of her sight returning so she can see her daughter (**Zepeda-Teng, 2018).**

7. Prevent

Progress to achieve the End TB Strategy targets set for 2030 and 2035 can be accelerated with prevention of new infections of *Mycobacterium tuberculosis* and a reduction in the current lifetime risk of progressing to TB disease of 5-15 per cent (Vynnycky & Fine, 2000) amongst the estimated

1.7 billion people already infected (R. M. Houben & Dodd, 2016). Every infection prevented is one that needs no treatment, and this approach is in line with the Global AMR action plan principle of prevention first (WHO, 2015a). Prevention of infection can be cost-effective and implemented in all settings and sectors, even where resources are limited. Currently three health interventions are available for TB prevention:

1. Prevention of transmission through finding and treating missing cases and through infection control;
2. Vaccination of children with BCG;
3. Prevention of developing TB disease through treatment of LTBI.

Finding and treating missing cases of TB

Four million people who get sick with TB are missed by health systems after failing to be diagnosed, treated, or reported. Missing cases are people without access to services, are hard to reach, such as migrants, miners, refugees, children and people living with HIV, or patients who were treated but never reported to NTPs. National notification and vital registrations systems need to be strengthened towards the goal of direct measurement of TB incidence and mortality in all countries (WHO, 2017c). Too many people have undetected TB for too long, and these people will continue to be sick and may have poorer health outcomes and transmit TB, die, or, if treated with improper drugs, could develop AMR.

Diagnosis of TB in a person can lead to rejection by their family, friends, and community and is likely to be one of the reasons why those who fall ill do not seek care. TB-related stigma and discrimination is not systematically measured yet understanding and measuring the scale of TB stigma would enable TB stakeholders to go beyond medical interventions to fully address the suffering of TB-affected individuals (Jaramillo, Sahu, & Van Weezenbeek, 2017). A supplement of 11 papers published in 2017 presents the latest evidence on TB-related stigma and offers tools to develop indicators to measure TB stigma. Rood, Mergenthaler, Bakker, Redwood, and Mitchell (2017), Sommerland et al. (2017), and Chikovore et al. (2017) show that stigma impedes the utilisation of TB testing and treatment services in some groups and affects men and women differently (Chikovore et al., 2017; Rood et al., 2017; Sommerland et al., 2017). Tools to develop indicators to measure stigma and to incorporate social justice into cost-effectiveness analysis for MDR-TB are presented in several papers, see: Bond et al. (2017); Wouters et al. (2017); Zwerling, Dowdy, von Delft, Taylor, and Merritt (2017). The TB Stigma Measurement Guidance developed by the TB Foundation, KNCV, determines the level of stigma among, for example, patient groups or healthcare workers, and then presents a means to monitor trends that can help capture the outcomes of TB stigma reduction efforts. This was developed following a TB stigma-measurement meeting held in The Hague, The Netherlands in 2016 on how tools can be used to lead to a greater understanding of what causes TB stigmas to emerge and thrive, to tackle the complexity in measuring stigma, and to develop stigma-specific interventions that simply increasing the quality of TB services and care would not address (Macintyre et al., 2017). Following the principle of *nothing about us without us,* the instruments used to identify, measure, and eliminate stigma are recommended to be developed with people with TB and TB survivors (Maleche, Citro, Tisile, & Abdullaev, 2017).

Actively finding cases through, for example, house-to-house screening for active TB or organising TB diagnostic clinics nearer to where people live and work, may increase TB case detection in settings where the prevalence of undiagnosed disease is high (Mhimbira, Cuevas, Dacombe,

Mkopi, & Sinclair, 2017). These people may also have higher levels of treatment success and lower levels of default from treatment. The provision of services at the community level has been shown to increase case detection, treatment acceptance, and treatment completion at scale in Ethiopia (Datiko et al., 2017). However, there is insufficient evidence to determine if health promotion activities alone increase TB case detection or to determine if sustained improvements in case detection impact on long-term TB prevalence (Mhimbira et al., 2017). Reaching missing patients calls for expanding programmes that support integrated community and family-based approaches to TB and DR-TB care. This can include investing in strengthening and better equipping primary healthcare services to accelerate case detection. This also necessitates closer engagement with private and public-sector providers.

TB infection control

TB infection control is part of the End TB Strategy. The risk of TB transmission is high in healthcare settings, workplaces, schools, transportation systems, incarceration systems and other congregate settings. In the latest revision of WHO guidance on monitoring and evaluation of collaborative TB/HIV activities (WHO, 2015b), the risk of TB among healthcare workers relative to the risk in the general adult population is one of the global indicators recommended to measure the impact of TB infection control activities in healthcare facilities. If TB infection control measures are effective, the relative risk of TB in healthcare workers compared with the general adult population should be close to 1. In 2016, 8,144 TB cases among healthcare workers were reported from 60 countries, with the notification rate, where calculable, ranging from zero to 701 cases per 100,000 populations, with the highest rate observed in Mozambique (WHO, 2017c).

Treatment of latent TB infection

Latent TB infection (LTBI) is defined as a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB. WHO recommends specific efforts to treat LTBI in particular at-risk groups: HIV-negative household contacts of bacteriologically confirmed pulmonary TB cases, people living with HIV, and other HIV-negative at-risk groups whose immune systems are or could be compromised (patients initiating anti-TNF treatment, patients receiving dialysis, patients preparing for an organ or haematological transplant and patients with silicosis) (WHO, 2018b). There is no gold standard diagnostic test for LTBI but either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) can be used to test for LTBI. However, diagnosis of infection is not required for initiating preventive treatment in people living with HIV or child household contacts younger than 5 years old (WHO, 2018b). Contact tracing and delivery of preventive treatment in young children exposed to TB in HBCs is considered a highly cost-effective intervention (Mandalakas et al., 2013). Globally in 2016, there were an estimated 1.3 million children under 5 years who were household contacts of bacteriologically confirmed pulmonary TB and who were eligible for TB preventive treatment, yet only 13 per cent received treatment. At least 1.3 million people living with HIV were started on TB preventive treatment in 2016. Of the 30 high TB/HIV burden countries, 18 did not report any provision of preventive treatment in 2016. In the 12 high TB/HIV burden countries that did report data, coverage among people newly enrolled in HIV care ranged from 2.4 per cent to 73 per cent. A substantial scale-up of LTBI screening and treatment is necessary to realise the targets of the End TB Strategy but with greater engagement with community members to avoid stigmatisation (Fox, Dobler, Marais, & Denholm, 2017). Innovative approaches include WHO's newly developed mobile phone application to facilitate monitoring and evaluation of the programmatic management

of LTBI. Randomised studies to evaluate the effectiveness of regimens to prevent MDR-TB are underway.

TB vaccination

BCG is the only available vaccine against TB. BCG vaccination is recommended as part of national childhood immunization programmes according to a country's TB epidemiology. The vaccine has been shown to prevent disseminated disease, including TB meningitis and millary TB, which are associated with high mortality in infants and young children and thus proof that vaccine-mediated protection against TB is possible. In the 154 countries that reported data, 111 reported coverage of more than 90 per cent. Among the 30 HBCs, coverage ranged from 58 per cent to 99 per cent (WHO, 2017c).

There is a clear need for a new vaccine that is more effective than the BCG vaccine to reduce the risk of infection with *Mycobacterium tuberculosis* and the risk of progression from infection to active TB disease. Antigens and immune correlates of risk of TB disease have been identified, animal models standardised, and novel approaches to later stage clinical trials are being developed (Voss et al., 2018). However, despite scientific progress, few vaccine candidates have entered clinical trials in the last 5 years, and few are progressing along the pipeline. Progression of vaccine candidates will benefit from learning from *failed* trials, less risk aversion, and more confidence in funding an inevitable part of the package needed to End TB (Voss et al., 2018).

8. Research and innovate

The essential role of applied health research

Existing and new tools will only be successful if there is support to deliver them. It is important for global policy makers and funders (and the analysts supporting them) to consider the uncertainty caused by implementation constraints when making recommendations for guidelines and investing in new tools. This importance is highlighted by post-hoc, real-world economic analyses of new technologies to validate initial predictions (Vassall, Mangham-Jefferies, Gomez, Pitt, & Foster, 2016). Vassall et al (2017) investigated the cost-effectiveness of a new diagnostic test for TB, Xpert MTB/RIF during phased national roll-out in South Africa (Vassall et al., 2017). This test had received conditional programmatic recommendation from WHO in 2010 (WHO, 2010) and several model-based economic evaluations predicted that Xpert would be cost-effective across sub-Saharan Africa (Abimbola et al., 2012; Langley et al., 2014; Menzies et al., 2012; Vassall et al., 2011). However, Vassall et al. (2017) found that Xpert introduction in South Africa was cost-neutral (the additional cost of Xpert equipment and tests was mitigated by a reduction in costs elsewhere in the TB cascade of care) and combining with the absence of any mortality effect, Xpert did not improve the cost-effectiveness of drug-susceptible TB diagnosis and treatment in the context of routine implementation. The authors conclude that this study, along with other research from South Africa (Churchyard et al., 2015) and Brazil (Trajman et al., 2015), suggests that the incremental costs, effect, and cost-effectiveness of Xpert MTB/RIF might be fundamentally affected by real world issues such as empirical treatment practices, availability of HIV treatment, and provider and patient adherence. This evidence, from the initial roll-out of Xpert in South Africa, does not mean though that Xpert will not be cost-effective in other settings, or in South Africa in the future, but rather suggests that policy-makers need to consider the context that Xpert (and other TB diagnostics) are placed in before providing large-scale investment.

Strengthening health systems, universal health coverage and social protection

Achieving the TB milestones and targets of the SDGs and End TB Strategy requires provision of TB care and prevention within the broader context of universal health coverage (UHC), social protection, and multi-sectoral action to address the social and economic determinants and consequences of TB. Commitment to strengthening inclusive health systems is an essential pillar of the TB response, including surveillance systems and access to diagnostic technologies for drug resistance, infection prevention and control, community-based health service delivery systems, medicines procurement and distribution, and robust health information and financial management systems. Substantial investments are needed in infrastructure, health workforce and equipment to provide essential health services. It was estimated in 2017 that middle-income countries can mobilise the resources to self-finance the investment required to strengthen their health systems and progress to UHC and reach other SDG related health targets by 2030, but LICs face a financing gap and will continue to need external financial support throughout the period of the SDGs (Stenberg et al., 2017). Improved revenue generation and management of public expenditures as well as increased public health budgets are needed (WHO, 2017c). However, even the poorest countries can reach some level of universality (Stenberg et al., 2017). Integrated, inclusive people-centred diagnosis, treatment, care and prevention, psychosocial support and socioeconomic support are all necessary for all people, including vulnerable and key populations, living with, at risk of, or affected by TB to receive the quality and affordable services they need under UHC. These services should include integrated care for related health conditions, such as HIV, under-nutrition, non-communicable diseases including diabetes and chronic lung disease, mental health, and, tobacco use, harmful use of alcohol and other substance abuse, including drug injection with access to existing and new tools, stewardship of antimicrobials and infection control, and be more responsive to the priorities of disabled people.

TB patients should be able to receive the health services they need, while ensuring that the use of these services does not expose them or their household to financial hardship. However, TB patients and their households often face high economic and financial burdens due to TB disease. Some of the main cost drivers could be reduced or eliminated through improved models of care, while others require use of new tools and social support. Most HBCs have national policies that provide the foundation for expanding social protection, including cash transfer programmes for some poor and vulnerable populations. Finding ways to link TB patients into these schemes is important.

The WHO guide to implementing the End TB Strategy (WHO, 2015c) provides examples e.g. in Kenya, of general social protection systems, including cash transfer programmes for poor and vulnerable populations along with key implementation steps. Basic components of social protection policy and cash transfer schemes that exist in the 30 HBCs can be found in the WHO TB Report (WHO, 2017c).

Antimicrobial resistance

TB is treated with a combination of drugs to prevent the development of resistance. Current effective treatment of drug-sensitive TB consists of four medicines (the first-line drugs HRZE) administered for a period of 6 to 9 months. Many people with TB struggle to take their medication daily over the long treatment period. If patients are not cured and their disease becomes resistant to rifampicin (RR-TB) and isoniazid (MDR-TB), or patients are newly infected with a resistant strain,

second-line drugs are administered, commonly for 2 years or longer consisting of more than 14,000 pills plus daily injections for six months (TB Alliance, 2018). Many of these second-line drugs are toxic and have severe side effects. The complexity and prohibitive cost of MDR-TB treatment means that few of the world's MDR-TB patients receive proper treatment. If treatment for MDR-TB fails, a person can develop extensively drug-resistant TB (XDR-TB), treatment for which is even lengthier, more complex and more expensive making it extremely difficult and sometimes impossible to treat in resource-limited settings.

AMR threatens global health security and economic stability (WHO, 2015a). Globally in 2016, an estimated 490,000 people developed MDR-TB with an additional 110,000 RR-TB cases; an estimated 4.1 per cent of new cases and 19 per cent of previously treated cases (WHO, 2017c). An estimated one quarter of all deaths due to AMR annually are caused by DR-TB (Abdullahi et al, 2016). Drug-resistant cases place additional burden on health and community systems and could reverse progress made against eliminating TB.

New tools

The End TB Strategy indicates that it is critical that new tools are introduced by 2025 to reach the 2030 targets. Specifically, the End TB Strategy calls for the introduction of rapid, affordable, easy to use point-of-care tests for diagnosing TB and detecting drug resistance; shorter and safer drug regimens for treating drug-sensitive, drug-resistant and latent forms of the disease; and a new universally applicable, effective vaccine for pre-exposure and post-exposure prophylaxis. Taking into account the time it takes to develop and test diagnostic, drug, and vaccine candidates increased investment is required **today** to ensure new tools will be available by 2025. TB receives less funding for research than other global health problems, such as HIV and malaria, in absolute terms and relative to its share of DALYs and premature mortality.

When adequately funded, many TB research efforts over the past decade have met with success (WHO, 2017a); however, insufficient investment in operational research has compromised the scale-up of new technologies limiting TB patients right to enjoy the benefits of scientific progress and its applications (UN General Assembly, 1948, 1966). Chronic underfunding of TB research as a whole has slowed the pace of product development and created challenges in translating advances in basic science into new interventions (WHO, 2017a). Funding for TB R&D peaked in 2013 at US$686.3 million and in several recent years fell compared with the year before (WHO, 2017a). The Global Plan estimates that an additional US$9 billion needs to be invested in research between 2016 and 2020 to address the most urgent gaps in diagnosis, treatment, and prevention. Based on recent analyses, TB is responsible for nearly 2 per cent of DALYs but receives only 0.25 per cent of the estimated US$265 billion spent on medical research each year (WHO, 2017a). Over the period 2009-2015, 61 per cent of total TB R&D funding came from the public sector, 17 per cent from the private sector, 21 per cent from the philanthropic sector, and 1 per cent from multi-lateral funding relying on a few donors for the majority of support. From 2009-2015, the UK was the second largest contributor of country funding for TB R&D, but still nearly seven times less that the US, which contributed US$1.8 billion. Expenditure did not grow significantly over this period for either country but in the US funding jumped by US$142.8 million from 2008 to 2009 under the American Recovery and Reinvestment Act, an economic stimulus package released by the US Government in response to the 2008 financial crisis (WHO, 2017a). This was the biggest increase in TB R&D funding in recent history (WHO, 2017a). The UK spent more on TB research as a percentage of its annual gross domestic expenditure on R&D (GERD) (WHO, 2017a). This funding landscape though is vulnerable to political will (Frick, 2017) and the world cannot depend

on a few wealthy countries to support all the research that is required to tackle TB. High-burden, MICs have the potential to transform the global TB research agenda through increased domestic funding, collaborative networks, and trans-national research partnerships (Pai, 2018).

Creating a research-enabling environment for R&D on TB at the country level through the development of country-specific strategic plans where TB research often faces complex and lengthy regulatory processes in countries with limited capacity to conduct efficient, adequate reviews of new studies or products, is equally important to increasing funding (WHO, 2017a). At the international level, governments have agreed to work with WHO and global partners to develop a novel Global Strategy for TB Research to enhance research for the development of new tools and innovative strategies for patient-centred services grounded in the principles of human rights and health equity. This global strategy should enhance the cooperation and coordination of research to promote efficient use of available resources; mobilise resources for TB research, including through innovative financing mechanisms, incentive strategies, and a more diverse funding base; and promote sharing of data and information to rapidly advance implementation (Lienhardt et al., 2018). Governments recommended drawing on new and existing research and development initiatives, such as the AMR R&D Collaboration Hub proposed in the 2017 G20 Leaders' Declaration (Leaders of the G20 Nations, 2017) and the TB Research Network described in the BRICS ministers of health Xiamen Declaration (Press Information Bureau, 2017).

9. Conclusions

The burden of TB continues to decline but at a pace that is too slow to reach the time-bound targets set by the global community. If efforts to tackle TB continue at the same rate of progress, 28 million people will die from TB at a global economic cost of US$983 billion over the period 2015-2030 (Global TB Caucus, 2017). Milestones, targets, and goals have been set in the UN's 2030 Agenda for Sustainable Development and the WHO's End TB Strategy. A Global plan for 2016-2020 has been laid out, and a Global Strategy for TB research is being developed. But none of this will be achieved without prioritisation, funding, partnership, reach, prevention, research, and innovation. The spotlight is starting to shine on TB, presenting a one-in-a-lifetime opportunity to accelerate progress through action. A multi-sectoral accountability framework is urgently required to ensure effective accountability of promises made by governments and all stakeholders at global, regional, and country levels (WHO, 2018c).

Today remarkable progress could be made against the disease with available tools by simply diagnosing and treating everyone who has TB. However, new diagnostics, shorter and safer drug regimens, and a new vaccine will need to enter the arena by 2025 to ensure a quicker pace of decline. For those tools to be ready investment in research needs to happen now. Existing and new tools and innovative approaches will only work if national health systems are strengthened. Patients and their families will only avoid financial hardship if broader support is available, including social protection. Realising TB goals will guide progress on many other SDGs and in achieving UHC. AMR TB threatens progress made and progress that could be made unless shorter, cheaper, less toxic treatments become available for adults and children.

The investment in people-centred prevention and care of TB and in research and innovation required is substantial but reflects the burden of the disease and the chronic underfunding of years past. The economic case for TB is clear and convincing: TB has a high mortality rate if left untreated; it is the leading infectious cause of death globally; it primarily affects people of working age; treatment of drug-sensitive TB is low; effective treatment prevents onwards spread;

healthcare costs are greater than prevention costs; and care-seeking costs can be catastrophic for people with TB and their households, further perpetuating poverty. The sooner action is taken more lives will be saved at a reduced overall cost. Engaging with the private sector in key HBCs, where initial care seeking from private providers is high, will be essential to reach all and ensure an equitable, fair, and quality regulated service is delivered.

The distribution of the burden of TB needs to be fully appreciated in political resolutions to reach and benefit all those vulnerable and to ensure that no one in left behind. Strategies need to address the needs of men, women, and children, including key populations, such as persons with disabilities before or caused by treatment of TB and those who face catastrophic costs, primarily through loss of income, which can delay care-seeking and impoverish patients and their households. To encourage patients with TB to seek care, TB-related stigma needs to be better understood, measured, and addressed.

Continuing to miss cases of TB will continue to fuel the spread of the disease through the community. Prevention through finding cases, vaccinating, and treating latent TB is key to winning this battle. Providing equitable access to the best available healthcare at all levels, including at the primary and community level, is the right of every TB patient who became infected simply by breathing the same air as someone else who had TB.

10. References

Abdullahi, M., Adams, E., Anderson, J., Arinaminpathy, N., Balasegeram, M., Barder, O., ,…Zowawi, H.M. (2016, May). Tackling drug-resistant infections globally: final report and recommendations. In J. O'Neill (Chair), *The review on antimicrobial resistance*. Retrieved from https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

Abimbola, T. O., Marston, B. J., Date, A. A., Blandford, J. M., Sangrujee, N., & Wiktor, S. Z. (2012). Cost-effectiveness of tuberculosis diagnostic strategies to reduce early mortality among persons with advanced HIV infection initiating antiretroviral therapy. *J Acquir Immune Defic Syndr, 60*(1), e1-7. doi:10.1097/QAI.0b013e318246538f

Adhanom Ghebreyesus, T. (2017, December 10). *Health is a fundamental human right* [Statement]. Retrieved from http://www.who.int/mediacentre/news/statements/fundamental-human-right/en/

Adhanom Ghebreyesus, T. (2018, March 23). *WHO: Director-General Dr Tedros message for World TB Day 2018* [Video]. Retreived from https://www.youtube.com/watch?v=T_F2NWTNf9Y

Barter, D. M., Agboola, S. O., Murray, M. B., & Barnighausen, T. (2012). Tuberculosis and poverty: the contribution of patient costs in sub-Saharan Africa--a systematic review. *BMC Public Health, 12*, 980. doi:10.1186/1471-2458-12-980

Black, R. E., Levin, C., Walker, N., Chou, D., Liu, L., Temmerman, M., & Group, D. R. A. (2016). Reproductive, maternal, newborn, and child health: key messages from Disease Control Priorities 3rd Edition. *Lancet, 388*(10061), 2811-2824. doi:10.1016/S0140-6736(16)00738-8

Bond, V., Floyd, S., Fenty, J., Schaap, A., Godfrey-Faussett, P., Claassens, M., . . . Hargreaves, J. R. (2017). Secondary analysis of tuberculosis stigma data from a cluster randomised trial in Zambia and South Africa (ZAMSTAR). *Int J Tuberc Lung Dis, 21*(11), 49-59. doi:10.5588/ijtld.16.0920

Cazabon, D., Alsdurf, H., Satyanarayana, S., Nathavitharana, R., Subbaraman, R., Daftary, A., & Pai, M. (2017). Quality of tuberculosis care in high burden countries: the urgent need to address gaps in the care cascade. *Int J Infect Dis, 56*, 111-116. doi:10.1016/j.ijid.2016.10.016

Central TB Division, Directorate General of Health Services, Ministry of Health with Family Welfare. (2017). *National Strategic Plan for Tuberculosis Elimination 2017-2025* Retrieved from Government of India website: https://www.tbfacts.org/wp-content/uploads/2018/01/NSP-Draft-2017-2025.pdf

Chikovore, J., Hart, G., Kumwenda, M., Chipungu, G., Desmond, N., & Corbett, E. L. (2017). TB and HIV stigma compounded by threatened masculinity: implications for TB health-care seeking in Malawi. *Int J Tuberc Lung Dis, 21*(11), 26-33. doi:10.5588/ijtld.16.0925

Churchyard, G. J., Stevens, W. S., Mametja, L. D., McCarthy, K. M., Chihota, V., Nicol, M. P., . . . Fielding, K. L. (2015). Xpert MTB/RIF versus sputum microscopy as the initial diagnostic test for tuberculosis: a cluster-randomised trial embedded in South African roll-out of Xpert MTB/RIF. *Lancet Glob Health, 3*(8), e450-e457. doi:10.1016/S2214-109X(15)00100-X

Datiko, D. G., Yassin, M. A., Theobald, S. J., Blok, L., Suvanand, S., Creswell, J., & Cuevas, L. E. (2017). Health extension workers improve tuberculosis case finding and treatment

outcome in Ethiopia: a large-scale implementation study. *BMJ Glob Health, 2*(4), e000390. doi:10.1136/bmjgh-2017-000390

Datiko, D. G., Yassin, M. A., Theobald, S. J., & Cuevas, L. E. (2017). A community-based isoniazid preventive therapy for the prevention of childhood tuberculosis in Ethiopia. *Int J Tuberc Lung Dis, 21*(9), 1002-1007. doi:10.5588/ijtld.16.0471

Detjen, A. K., McKenna, L., Graham, S. M., Marais, B. J., Amanullah, F., Child, W. S. T. P., & Adolescent, T. B. W. G. (2018). The upcoming UN general assembly resolution on tuberculosis must also benefit children. *Lancet Glob Health, 6*(5), e485-e486. doi:10.1016/S2214-109X(18)30108-6

Dodd, P. J., Looker, C., Plumb, I. D., Bond, V., Schaap, A., Shanaube, K., . . . White, R. G. (2016). Age- and Sex-Specific Social Contact Patterns and Incidence of Mycobacterium tuberculosis Infection. *Am J Epidemiol, 183*(2), 156-166. doi:10.1093/aje/kwv160

Dodd, P. J., Sismanidis, C., & Seddon, J. A. (2016). Global burden of drug-resistant tuberculosis in children: a mathematical modelling study. *Lancet Infect Dis, 16*(10), 1193-1201. doi:10.1016/S1473-3099(16)30132-3

Dodd, P. J., Yuen, C. M., Sismanidis, C., Seddon, J. A., & Jenkins, H. E. (2017). The global burden of tuberculosis mortality in children: a mathematical modelling study. *Lancet Glob Health, 5*(9), e898-e906. doi:10.1016/S2214-109X(17)30289-9

Fox, G. J., Dobler, C. C., Marais, B. J., & Denholm, J. T. (2017). Preventive therapy for latent tuberculosis infection-the promise and the challenges. *Int J Infect Dis, 56*, 68-76. doi:10.1016/j.ijid.2016.11.006

Frick, M. (2017). Funding for tuberculosis research-an urgent crisis of political will, human rights, and global solidarity. *Int J Infect Dis, 56*, 21-24. doi:10.1016/j.ijid.2016.11.412

Furtwangler, T., & Malaviya, S. (2016). A new approach to battling TB in Mumbai's crowded slums [Web log blog]. Retrieved from http://blog.path.org/2016/02/a-new-approach-to-battling-tb-in-mumbais-crowded-slums

Leaders of the G20 Nations. (2017). *G20 leaders' declaration: shaping an interconnected world*. Retrieved from Hamburg: http://www.g20.utoronto.ca/2017/2017-G20-leaders-declaration.html

Global TB Caucus. (2017) *Price of a pandemic*. Retrieved from https://docs.wixstatic.com/ugd/309c93_56d4ef0e87d24667b1d3edae55f6eeb5.pdf

Goosby, E., Jamison, D., Swaminathan, S., Reid, M., & Zuccala, E. (2018). The Lancet Commission on tuberculosis: building a tuberculosis-free world. *Lancet, 391*(10126), 1132-1133. doi:10.1016/S0140-6736(18)30666-4

Green, A. (2015). Tackling childhood tuberculosis in Uganda. *Lancet Respir Med, 3*(4), 273. doi:10.1016/S2213-2600(15)00107-1

Grut, L., Sanudi, L., Braathen, S. H., Jurgens, T., & Eide, A. H. (2015). Access to tuberculosis services for individuals with disability in rural Malawi, a qualitative study. *PLoS One, 10*(4), e0122748. doi:10.1371/journal.pone.0122748

Hanson, C., Osberg, M., Brown, J., Durham, G. & Chin, D.P. (2017) Finding the Missing Patients with Tuberculosis: Lessons Learned From Patient-Pathway Analyses in 5 Countries. The Journal of Infectious Diseases, 216 (Suppl 7): S686-95doi: 10.1093/infdis/jix388

Herbert, N., Masham, B. S., Suttie, B. A., Sharma, V., Albani, S., Domenti, O., . . . Zumla, A. (2018a). Advancing political will to end the tuberculosis epidemic. *Lancet Infect Dis,* 18(7), 711-712. doi:10.1016/S1473-3099(17)30679-5

Herbert, N., Sharma, V., Masham, B. S., Sheehan, B. S., Hauser, J., & Zumla, A. (2018b). Concrete action now: UN High-Level Meeting on Tuberculosis. *Lancet Infect Dis, 18*(7), 709-710. doi:10.1016/S1473-3099(18)30171-3

Horton, K. C., MacPherson, P., Houben, R. M., White, R. G., & Corbett, E. L. (2016). Sex Differences in Tuberculosis Burden and Notifications in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis. *PLoS Med, 13*(9), e1002119. doi:10.1371/journal.pmed.1002119

Houben, R., Menzies, N. A., Sumner, T., Huynh, G. H., Arinaminpathy, N., Goldhaber-Fiebert, J. D., . . . White, R. G. (2016). Feasibility of achieving the 2025 WHO global tuberculosis targets in South Africa, China, and India: a combined analysis of 11 mathematical models. *Lancet Glob Health, 4*(11), e806-e815. doi:10.1016/S2214-109X(16)30199-1

Houben, R. M., & Dodd, P. J. (2016). The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. *PLoS Med, 13*(10), e1002152. doi:10.1371/journal.pmed.1002152

House of Commons (2018, June 7). *Tuberculosis debate* (vol 642 col 524). Retrieved from https://hansard.parliament.uk/commons/2018-06-07/debates/9BF50C2B-C9AF-47C5-9000-F306378A3821/Tuberculosis

Hudson, M., Rutherford, G. W., Weiser, S., & Fair, E. (2018). Linking private, for-profit providers to public sector services for HIV and tuberculosis co-infected patients: A systematic review. *PLoS One, 13*(4), e0194960. doi:10.1371/journal.pone.0194960

TB CARE I. (2014). *International standards for tuberculosis care*. Retrieved from The Hague: http://www.who.int/tb/publications/ISTC_3rdEd.pdf

Jaramillo, E., Sahu, S., & Van Weezenbeek, C. (2017). Ending TB-related stigma and discrimination. *Int J Tuberc Lung Dis, 21*(11), 2-3. doi:10.5588/ijtld.17.0229

Jenkins, H. E., Tolman, A. W., Yuen, C. M., Parr, J. B., Keshavjee, S., Perez-Velez, C. M., . . . Cohen, T. (2014). Incidence of multidrug-resistant tuberculosis disease in children: systematic review and global estimates. *Lancet, 383*(9928), 1572-1579. doi:10.1016/S0140-6736(14)60195-1

Kemp, J. R., Mann, G., Simwaka, B. N., Salaniponi, F. M., & Squire, S. B. (2007). Can Malawi's poor afford free tuberculosis services? Patient and household costs associated with a tuberculosis diagnosis in Lilongwe. *Bull World Health Organ, 85*(8), 580-585.

Khan, A. J., Khowaja, S., Khan, F. S., Qazi, F., Lotia, I., Habib, A., . . . Keshavjee, S. (2012). Engaging the private sector to increase tuberculosis case detection: an impact evaluation study. *Lancet Infect Dis, 12*(8), 608-616. doi:10.1016/S1473-3099(12)70116-0

Khan, B. J., Kumar, A. M. V., Stewart, A., Khan, N. M., Selvaraj, K., Fatima, R., & Samad, Z. (2017). Alarming rates of attrition among tuberculosis patients in public-private facilities in Lahore, Pakistan. *Public Health Action, 7*(2), 127-133. doi:10.5588/pha.17.0001

Khan, M. S., Salve, S., & Porter, J. D. (2015). Engaging for-profit providers in TB control: lessons learnt from initiatives in South Asia. *Health Policy Plan, 30*(10), 1289-1295. doi:10.1093/heapol/czu137

Langley, I., Lin H-H., Egwaga, S., Doulla, B., Ku, C-C., Murray, M., Cohen, T., Squire S.B. (2014). Assessment of the patient, health system, and population effects of Xpert MTB/RIF and alternative diagnostics for tubeculosis in Tanzania: an integrated modelling approach. *The Lancet Global Health*, 2(10), e581-e591. doi: 10.1016/S2214-109X(14)70291-8

Lei, X., Liu, Q., Escobar, E., Philogene, J., Zhu, H., Wang, Y., & Tang, S. (2015). Public-private mix for tuberculosis care and control: a systematic review. *Int J Infect Dis, 34*, 20-32. doi:10.1016/j.ijid.2015.02.015

Lienhardt, C., Zumla, A., Gebreselassie, N., Frick, M., Gray, G., Kasaeva, T., & Raviglione, M. (2018). Tuberculosis research and development: seeding the future. *Lancet Respir Med, 6*(4), 242-244. doi:10.1016/S2213-2600(18)30050-X

Long, N. H., Johansson, E., Lonnroth, K., Eriksson, B., Winkvist, A., & Diwan, V. K. (1999). Longer delays in tuberculosis diagnosis among women in Vietnam. *Int J Tuberc Lung Dis, 3*(5), 388-393.

Lonnroth, K., Castro, K. G., Chakaya, J. M., Chauhan, L. S., Floyd, K., Glaziou, P., & Raviglione, M. C. (2010). Tuberculosis control and elimination 2010-50: cure, care, and social development. *Lancet, 375*(9728), 1814-1829. doi:10.1016/S0140-6736(10)60483-7

Macintyre, K., Bakker, M. I., Bergson, S., Bhavaraju, R., Bond, V., Chikovore, J., . . . Mitchell, E. M. H. (2017). Defining the research agenda to measure and reduce tuberculosis stigmas. *Int J Tuberc Lung Dis, 21*(11), 87-96. doi:10.5588/ijtld.17.0151

MacPherson, P., Houben, R. M., Glynn, J. R., Corbett, E. L., & Kranzer, K. (2014). Pre-treatment loss to follow-up in tuberculosis patients in low- and lower-middle-income countries and high-burden countries: a systematic review and meta-analysis. *Bull World Health Organ, 92*(2), 126-138. doi:10.2471/BLT.13.124800

Maleche, A., Citro, B., Tisile, P., & Abdullaev, T. (2017). Measuring TB-related stigma. *Int J Tuberc Lung Dis, 21*(11), 4-5. doi:10.5588/ijtld.17.0581

Mandalakas, A. M., Hesseling, A. C., Gie, R. P., Schaaf, H. S., Marais, B. J., & Sinanovic, E. (2013). Modelling the cost-effectiveness of strategies to prevent tuberculosis in child contacts in a high-burden setting. *Thorax, 68*(3), 247-255. doi:10.1136/thoraxjnl-2011-200933

Menzies, N. A., Cohen, T., Lin, H. H., Murray, M., & Salomon, J. A. (2012). Population health impact and cost-effectiveness of tuberculosis diagnosis with Xpert MTB/RIF: a dynamic simulation and economic evaluation. *PLoS Med, 9*(11), e1001347. doi:10.1371/journal.pmed.1001347

Menzies, N. A., Gomez, G. B., Bozzani, F., Chatterjee, S., Foster, N., Baena, I. G., . . . Vassall, A. (2016). Cost-effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa: a combined analysis of nine models. *Lancet Glob Health, 4*(11), e816-e826. doi:10.1016/S2214-109X(16)30265-0

Mhimbira, F. A., Cuevas, L. E., Dacombe, R., Mkopi, A., & Sinclair, D. (2017). Interventions to increase tuberculosis case detection at primary healthcare or community-level services. *Cochrane Database Syst Rev, 11*, CD011432. doi:10.1002/14651858.CD011432.pub2

Ministry of Health of the Russian Federation, W. (2017). *Moscow declaration to end TB*. Retrieved from Geneva: http://www.who.int/tb/features_archive/Moscow_Declaration_to_End_TB_final_ENGLISH.pdf?ua=1

Modi, N. (2018, March 13). PM Modi launches the TB Free India Movement to work towards eliminating TB by 2025. *Narendra Modi*. Retrieved from https://www.narendramodi.in/social-media-corner-13-march-2018-539309

Oxlade, O., & Murray, M. (2012). Tuberculosis and poverty: why are the poor at greater risk in India? *PLoS One, 7*(11), e47533. doi:10.1371/journal.pone.0047533

Pai, M. (2018). India's tuberculosis research contributions get international recognition. Retrieved from https://naturemicrobiologycommunity.nature.com/users/20892-madhukar-pai/posts/31180-india-s-tuberculosis-research-contributions-get-international-recognition

Pai, M., Bhaumik, S., & Bhuyan, S. S. (2016). India's plan to eliminate tuberculosis by 2025: converting rhetoric into reality. *BMJ Glob Health, 2*(2), e000326. doi:10.1136/bmjgh-2017-000326

Pantoja, A., Floyd, K., Unnikrishnan, K. P., Jitendra, R., Padma, M. R., Lal, S. S., . . . Lonnroth, K. (2009a). Economic evaluation of public-private mix for tuberculosis care and control, India. Part I. Socio-economic profile and costs among tuberculosis patients. *Int J Tuberc Lung Dis, 13*(6), 698-704.

Pantoja, A., Lonnroth, K., Lal, S. S., Chauhan, L. S., Uplekar, M., Padma, M. R., . . . Floyd, K. (2009b). Economic evaluation of public-private mix for tuberculosis care and control, India. Part II. Cost and cost-effectiveness. *Int J Tuberc Lung Dis, 13*(6), 705-712.

Press Information Bureau, G.o.I., Prime Minsiter's Office. (2017). *BRICS Leaders Xiamen Declaration*. Retrieved from http://pibphoto.nic.in/documents/rlink/2017/sep/p20179401.pdf

Rood, E. J. J., Mergenthaler, C., Bakker, M. I., Redwood, L., & Mitchell, E. M. H. (2017). Using 15 DHS surveys to study epidemiological correlates of TB courtesy stigma and health-seeking behaviour. *Int J Tuberc Lung Dis, 21*(11), 60-68. doi:10.5588/ijtld.16.0909

Siroka, A., Law, I., Macinko, J., Floyd, K., Banda, R. P., Hoa, N. B., . . . Ponce, N. A. (2016). The effect of household poverty on tuberculosis. *Int J Tuberc Lung Dis, 20*(12), 1603-1608.

Sommerland, N., Wouters, E., Masquillier, C., Engelbrecht, M., Kigozi, G., Uebel, K., . . . Rau, A. (2017). Stigma as a barrier to the use of occupational health units for tuberculosis services in South Africa. *Int J Tuberc Lung Dis, 21*(11), 75-80. doi:10.5588/ijtld.17.0030

Sreeramareddy, C. T., Qin, Z. Z., Satyanarayana, S., Subbaraman, R., & Pai, M. (2014). Delays in diagnosis and treatment of pulmonary tuberculosis in India: a systematic review. *Int J Tuberc Lung Dis, 18*(3), 255-266. doi:10.5588/ijtld.13.0585

Stenberg, K., Hanssen, O., Edejer, T. T., Bertram, M., Brindley, C., Meshreky, A., . . . Soucat, A. (2017). Financing transformative health systems towards achievement of the health Sustainable Development Goals: a model for projected resource needs in 67 low-income and middle-income countries. *Lancet Glob Health, 5*(9), e875-e887. doi:10.1016/S2214-109X(17)30263-2

Stop TB Partnership. (2018, June 14). Re: USD 31 million saved by Stop TB Partnership's Global Drug Facility through newly-reduced prices for TB medicines [Electronic mailing list]. Retrieved from https://mailchi.mp/stoptb.org/a-message-for-the-entire-tb-community-2018-the-year-when-we-make-it-or-break-it-830041?e=7f346d0e72

Stop TB Partnership. (2018, July 23). Re: South Africa ensures reduction of prices for Bedaquiline to benefit the world [Electronic mailing list]. Retrieved from https://mailchi.mp/stoptb.org/a-message-for-the-entire-tb-community-2018-the-year-when-we-make-it-or-break-it-830113?e=8971559302

Stop TB Partnership & UNOPS. (2015). *The Global Plan to End TB, 2016-2020*. Retrieved from Geneva: http://www.stoptb.org/global/plan/plan2/

Tanimura, T., Jaramillo, E., Weil, D., Raviglione, M., & Lonnroth, K. (2014). Financial burden for tuberculosis patients in low- and middle-income countries: a systematic review. *Eur Respir J, 43*(6), 1763-1775. doi:10.1183/09031936.00193413

TB Alliance. (2018) *Inadequate Treatment*. Retrieved from https://www.tballiance.org/why-new-tb-drugs/inadequate-treatment

The Union. (2018). *Silent Epidemic: A call to action against child tuberculosis*. Retrieved from https://childtb.theunion.org/wp-content/uploads/2018/08/Silent-Epidemic.pdf

Trajman, A., Durovni, B., Saraceni, V., Menezes, A., Cordeiro-Santos, M., Cobelens, F., & Van den Hof, S. (2015). Impact on Patients' Treatment Outcomes of XpertMTB/RIF Implementation for the Diagnosis of Tuberculosis: Follow-Up of a Stepped-Wedge Randomized Clinical Trial. *PLoS One, 10*(4), e0123252. doi:10.1371/journal.pone.0123252

Treatment Action Group. (2017). *2017 TAG Annual Report: Progress in the Fight for Better Treatment, Prevention, a Vaccine and a Cure for HIV, Tuberculosis and Hepatitis C Virus*. Retrieved from http://www.treatmentactiongroup.org/sites/default/files/tag_2017_annual_report_web2.pdf

UNDP. (2015). *Discussion Paper: Gender and Tuberculosis*. Retrieved from http://www.undp.org/content/dam/undp/library/HIV-AIDS/Gender%20HIV%20and%20Health/Gender%20and%20TB%20UNDP%20Discussion%20Paper%20(1).pdf

UN General Assembly. (1948). *Universal declaration of human rights* (217 [III] A). Paris. Retrievied from http://www.un.org/en/universal-declaration-human-rights

UN General Assembly. (1996). *International Covenant on Economic, Social and Cultural Rights* (2200A [XXI]). Paris. Retrieved from https://www.ohchr.org/en/professionalinterest/pages/cescr.aspx

Uplekar, M., Weil, D., Lonnroth, K., Jaramillo, E., Lienhardt, C., Dias, H. M., . . . , W. s. G. T. B. P. (2015). WHO's new end TB strategy. *Lancet, 385*(9979), 1799-1801. doi:10.1016/S0140-6736(15)60570-0

Vassall, A., van Kampen, S., Sohn, H., Michael, J. S., John, K. R., den Boon, S., . . . Cobelens, F. (2011). Rapid diagnosis of tuberculosis with the Xpert MTB/RIF assay in high burden countries: a cost-effectiveness analysis. *PLoS Med, 8*(11), e1001120. doi:10.1371/journal.pmed.1001120

Vassall, A. (2014). *Tuberculosis perspective paper: Benefits and Costs of the Tuberculosis Targets for the Post-2015 Development Agenda, Post-2015 Consensus*. Retrieved from https://www.copenhagenconsensus.com/sites/default/files/health_perspective_tb_-_vassall.pdf

Vassall, A., & Mustapha, G. (2015). *Post-2015 Development Agenda: Nigeria Perspectives Tuberculosis*. Retrieved from https://www.copenhagenconsensus.com/sites/default/files/nigeria_tb_resource_packet_0.pdf

Vassall, A., Mangham-Jefferies, L., Gomez, G. B., Pitt, C., & Foster, N. (2016). Incorporating Demand and Supply Constraints into Economic Evaluations in Low-Income and Middle-Income Countries. *Health Econ, 25 Suppl 1*, 95-115. doi:10.1002/hec.3306

Vassall, A., Siapka, M., Foster, N., Cunnama, L., Ramma, L., Fielding, K., . . . Sinanovic, E. (2017). Cost-effectiveness of Xpert MTB/RIF for tuberculosis diagnosis in South Africa: a real-world cost analysis and economic evaluation. *Lancet Glob Health, 5*(7), e710-e719. doi:10.1016/S2214-109X(17)30205-X

Verguet, S., Riumallo-Herl, C., Gomez, G. B., Menzies, N. A., Houben, R., Sumner, T., . . . Vassall, A. (2017). Catastrophic costs potentially averted by tuberculosis control in India and South Africa: a modelling study. *Lancet Glob Health, 5*(11), e1123-e1132. doi:10.1016/S2214-109X(17)30341-8

Voss, G., Casimiro, D., Neyrolles, O., Williams, A., Kaufmann, S. H. E., McShane, H., . . . Fletcher, H. A. (2018). Progress and challenges in TB vaccine development. *F1000Res, 7*, 199. doi:10.12688/f1000research.13588.1

Vynnycky, E., & Fine, P. E. (2000). Lifetime risks, incubation period, and serial interval of tuberculosis. *Am J Epidemiol, 152*(3), 247-263.

Weiss, M. G., Auer, C., Somma, D. B., Abouihia, A., Kemp, J., Jawahar, M. S., . . . Arias, N. L. (2006). *Gender and tuberculosis: Cross-site analysis and implications of a multi-country study in Bangladesh, India, Malawi, and Colombia*. Retrieved from Geneva: http://www.who.int/tdr/publications/documents/sebrep3.pdf

Wells, W. A., Uplekar, M., & Pai, M. (2015). Achieving Systemic and Scalable Private Sector Engagement in Tuberculosis Care and Prevention in Asia. *PLoS Med, 12*(6), e1001842. doi:10.1371/journal.pmed.1001842

WHO. (2010). *Tuberculosis diagnostics: Xpert MTB/RIF endorsement*. Retrieved from Geneva: http://www.who.int/tb/features_archive/new_rapid_test/en/

WHO. (2015a). *Global action plan on antimicrobial resistance*. Retrieved from Geneva: http://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1

WHO. (2015b). *A guide to monitoring and evaluation for collaborative TB/HIV activities: 2015 revision*. Retrieved from Geneva: http://apps.who.int/iris/bitstream/handle/10665/150627/9789241508278_eng.pdf;jsessionid=4EC1390FF642B8CED667F64446551DCB?sequence=1

WHO. (2015c). *Implementing the end TB strategy: the essentials*. Retrieved from Geneva: http://www.who.int/tb/publications/2015/end_tb_essential.pdf?ua=1

WHO. (2015d). *WHO End TB strategy: Global targets for tuberculosis prevention, care and control after 2015*. Retrieved from Geneva: http://www.who.int/tb/post2015_strategy/en

WHO. (2017a). *Global investments in Tuberculosis research and development: past, present and future. A policy paper prepared for the first WHO global ministerial conference in ending tuberculosis in the sustainable development era: a multisectoral response.* Retrieved from Geneva: http://www.who.int/tb/publications/2017/Global_Investments_in_Tuberculosis_Research_Investment/en/

WHO. (2017b). *Global investments in Tuberculosis research and development: past, present and future. A policy paper prepared for the first WHO global ministerial conference on ending tuberculosis in the sustainable development era: a multisectoral response*. Retrieved from Geneva: http://apps.who.int/iris/bitstream/handle/10665/259412/9789241513326-eng.pdf;jsessionid=0D64ADC8581BE68ACB28BF9F991F4C28?sequence=1

WHO. (2017c). *Global tuberculosis report 2017*. Retrieved from Geneva: http://www.who.int/tb/publications/global_report/en/

WHO. (2017d). *Tuberculosis patient cost surveys: a handbook*. Retrieved from Geneva: http://apps.who.int/iris/bitstream/handle/10665/259701/9789241513524-eng.pdf;jsessionid=B184EACFC56E1A886DDD8F25BAF2D7F8?sequence=1

WHO. (2018a, Septmeber). Tuberculosis (TB). UN General Assembly high-level meeting on ending TB. Retrieved from http://www.who.int/tb/features_archive/UNGA_HLM_ending_TB/en/

WHO. (2018b). *Latent tuberculosis infection: updated and consolidated guidelines for programmatic management*. Retrieved from Geneva: http://apps.who.int/iris/bitstream/handle/10665/260233/9789241550239-eng.pdf;jsessionid=779D52667B1104C08361C204B23F293C?sequence=1

WHO. (2018c). *Preparation for a high-level meeting of the General Assembly on ending tuberculosis: Draft multisectoral accountability framework to accelerate progress to end tuberculosis. Report by the Director-General* Retrieved from http://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_16Add1-en.pdf

Wouters, E., Masquillier, C., Sommerland, N., Engelbrecht, M., Van Rensburg, A. J., Kigozi, G., & Rau, A. (2017). Measuring HIV- and TB-related stigma among health care workers in South Africa: a validation and reliability study. *Int J Tuberc Lung Dis, 21*(11), 19-25. doi:10.5588/ijtld.16.0749

Zepeda-Teng, E. (2018, June 4). *A step change TB research: why TB research is critical and how to respond* [Panel presentation]. Retrieved from http://www.heart-resources.org/mmedia/tuberculosis-tb-research-briefing-un-missions-vital-role-research-tb-elimination/

Zwerling, A., Dowdy, D., von Delft, A., Taylor, H., & Merritt, M. W. (2017). Incorporating social justice and stigma in cost-effectiveness analysis: drug-resistant tuberculosis treatment. *Int J Tuberc Lung Dis, 21*(11), 69-74. doi:10.5588/ijtld.16.0839