Published in final edited form as:

Int J Infect Dis. 2021 December ; 113(Suppl 1): S7–S12. doi:10.1016/j.ijid.2021.02.107.

Global Tuberculosis Report 2020 – Reflections on the Global TB burden, treatment and prevention efforts

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Conflicts of interest

All authors declare no conflicts of interest

All authors have a specialist interest in TB. All authors declare no conflicts of interest.

The development of this manuscript did not require ethical approval.

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Abstract

The October 2020 Global TB report reviews TB control strategies and United Nations (UN) targets set in the political declaration at the September 2018 UN General Assembly high-level meeting on TB held in New York. Progress in TB care and prevention has been very slow. In 2019, TB remained the most common cause of death from a single infectious pathogen. Globally, an estimated 10.0 million people developed TB disease in 2019, and there were an estimated 1.2 million TB deaths among HIV-negative people and an additional 208, 000 deaths among people living with HIV. Adults accounted for 88% and children for 12% of people with TB. The WHO regions of South-East Asia (44%), Africa (25%), and the Western Pacific (18%) had the most people with TB. Eight countries accounted for two thirds of the global total: India (26%), Indonesia (8.5%), China (8.4%), the Philippines (6.0%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%) and South Africa (3.6%). Only 30% of the 3.5 million five-year target for children treated for TB was met. Major advances have been development of new all oral regimens for MDRTB and new regimens for preventive therapy. In 2020, the COVID-19 pandemic dislodged TB from the top infectious disease cause of mortality globally. Notably, global TB control efforts were not on track even before the advent of the COVID-19 pandemic. Many challenges remain to improve sub-optimal TB treatment and prevention services. Tuberculosis screening and diagnostic test services need to be ramped up. The major drivers of TB remain

undernutrition, poverty, diabetes, tobacco smoking, and household air pollution and these need be addressed to achieve the WHO 2035 TB care and prevention targets. National programs need to include interventions for post-tuberculosis holistic wellbeing. From first detection of COVID-19 global coordination and political will with huge financial investments have led to the development of effective vaccines against SARS-CoV2 infection. The world now needs to similarly focus on development of new vaccines for TB utilizing new technological methods.

Keywords

Tuberculosis; Global TB Report 2020; Treatment; Prevention

Introduction

Every year since 1997, the World Health Organization (WHO) has published a Global Tuberculosis (TB) report, which provides an up-to-date assessment of the Global TB situation, and summarizes progress and efforts in prevention, diagnosis, and treatment of the disease, at country, regional and global levels. The 2020 Global TB report was released on 14 October 2020 and was compiled in the context of global TB control strategies and United Nations (UN) targets set in the political declaration at the September 2018 UN General Assembly high-level meeting on TB held in New York. The data accounted for over 99% of the world's population and reported data from 198 countries. The 2020 Global TB Report has two additional features of note: it complements and elaborates on the United Nations (UN) Secretary-General's 2020 progress report on TB, which was requested in the political declaration at the high-level meeting on TB. The report also includes preliminary assessments of how the unprecedented corona virus disease-2019 (COVID-19) pandemic may affect TB health services, treatment and prevention efforts. However, it is important to note that global TB control efforts were not on track even before the advent of the COVID-19 pandemic, and the numerical gap between the estimated number of people with TB globally and the numbers reported to public health authorities remains wide. If all the missing people with TB, including those from the private sector, could be identified, the shortfall in reaching all the targets might be greater; thus, the failure to reach the targets cannot be assumed to be because of the gap between reported and estimated numbers of people with TB.

In 2019, TB remained the most common cause of death from a single infectious pathogen. Globally, an estimated 10.0 million people developed TB disease in 2019, and there were an estimated 1.2 million TB deaths among HIV-negative people and an additional 208, 000 deaths among people living with HIV. Adults accounted for 88% and children, aged <15 years, for 12% of all people with TB. Most people who developed TB in 2019 were in the WHO regions of South-East Asia (44%), Africa (25%), and the Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8.2%), the Americas (2.9%) and Europe (2.5%). Eight countries accounted for two thirds of the global total: India (26%), Indonesia (8.5%), China (8.4%), the Philippines (6.0%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%) and South Africa (3.6%).

While progress is being made, it has been very slow, and it is anticipated that the world will not end TB as a global public health threat by 2035 as envisioned in the End TB Strategy. For example, while the target was to reduce TB incidence by 20% between 2015 and 2020, the 2020 global TB report indicates that there was a reduction of only 9% in TB incidence in this period, with an annual reduction of only about 2%. Similarly, mortality reduction targets, set at 35%, were not reached, with only a 14% change in death rates achieved between 2015 and 2020. The major constraints are related to inadequacies in the identification of people-including children-with TB, for all TB and drug resistant TB in particular, prevention of TB and financing of the TB response including of essential TB research. In this paper we highlight the status of TB care and prevention as presented in the 2020 WHO Global TB report, outline the persisting constraints, summarize the efforts that are being made to address these constraints and offer suggestions on how these efforts can be ramped up.

The gap in finding people with Tuberculosis

Of the 10 million people estimated to have developed TB in 2019, 7.1 million (71%) were identified and reported to national TB programs around the world, leaving a gap of 2.9 million people (29%). These missing people with TB include those who were diagnosed with TB, but were not reported to public health authorities, (including those not reported from the private sector) and those who were not diagnosed and therefore not treated. This pool also includes patients with drug-susceptible or drug-resistant TB, using current definitions. However, a greater proportion of people with drug resistant TB are missing: of the estimated 500,000 people with rifampicin resistant/multidrug-resistant TB (RR/MDR-TB), only 206, 030 (41%) were identified, as a result of inadequate testing for drug susceptibility especially among new people with TB. In 2019, only 57% of people identified to have pulmonary TB were bacteriologically confirmed, and of those who were bacteriologically confirmed, only 61% were tested for RR/MDR-TB, comprising 59% of people not previously treated for TB and 81% of those who had previously been treated for the disease. Whilst 206, 030 people with MDR/RR-TB were detected and notified in 2019, (a 10% increase from 186, 883 in 2018), only 177,099 people were enrolled in treatment, comprising only 38% of the estimated number of people who developed RR/MDR-TB in 2019.

Another important sub-group of the missing people with TB are children under 15 years of age. Tuberculosis diagnosis and treatment gaps are wider among children than adults.

There needs to be a sustained, concerted effort and universal focus on identifying and treating missing people with TB. WHO reports that a 50% drop in the number of people with TB detected could result in up to 400,000 additional TB deaths in a year. Governments of high TB endemic countries need to ensure there are rapid TB diagnostic services available in every health facility, so all people with TB can be reached. With COVID-19 causing disruption of health services, many countries have been reported to be using GeneXpert machines for COVID-19 testing, and others have reassigned TB programme staff to COVID-19, causing further shortages of the already meagre TB diagnostic and treatment resources. Innovative plans are needed to maintain TB diagnostic services in the wake of

the COVID-19 pandemic (Zumla et al., 2020). Innovations to adapt TB diagnostic platforms to screen for both TB and COVID-19, rolling out additional machines, and investing in development of low-cost rapid diagnostic tests for both infections are important and urgently needed.

The methods used by the WHO to estimate the global burden of TB includes the use of data from national prevalence surveys; notification data adjusted by a standard factor to account for under-reporting, over - and under diagnosis; inventory studies that measure under-reporting; and expert opinion on TB detection gaps. Prevalence surveys, more commonly than not, have shown that country estimates of prevalence have been lower than what was observed, consequently, the incidence estimates upon which the global estimates are based may be lower than what actually exists. While the methods used to estimate the burden of TB are continuously being improved, imperfections remain which may explain the relatively wide uncertainty intervals especially with country level estimates. Differences in methodological approaches for the estimation of the burden of TB have in the past led to significant differences in the estimates of the global burden of TB provided by the WHO and the Institute for Health Metrics and Evaluation that undertakes the Global Burden of Disease project (Garcıa-Basteiro et al., 2018). These methodological challenges in the estimates of the global burden of TB may have significant consequences at the programmatic level in countries. National TB programs may set unrealistically high targets or appear to be setting unambitious targets if national targets are based on trends of TB notifications as has been proposed by some experts (Trébucq and Schwoebel, 2016). We urge the global TB community under the leadership of the WHO Global Task Force on TB Impact measurement (WHO, 2019) to continue to address this challenge and to harmonize approaches for the estimation of the burden of TB so that disease burden estimates become more robust with a more precise estimate of the size of the TB incidence -detection gap. It is also equally important to develop robust approaches and tools for the estimation of the burden of TB at sub-national level where efforts to identify people with TB are focused as has been proposed by some countries e.g., Indonesia (Parwati et al., 2020).

Several interventions, many of which have been implemented to a variable degree in various settings are in place to narrow the TB incidence-detection gap and excellent reviews have been published on this subject (Reid et al., 2019). Some of the major steps that need to be taken to address the challenge of missing people with TB at the national and sub-national level in countries include the identification of TB at risk populations to be targeted to actively find people with TB, the use of highly sensitive methods for TB screening and specific TB diagnostic tests (e.g. Xpert MTB/RIF), linkage to care and treatment of all people identified to have active TB, measures to ensure retention in care and adherence to treatment, engagement with communities, development of strong partnerships with the non-state health sector and ensuring that TB is an integral component of evolving universal health care programs. Cascade analysis at all levels of the national TB program is an effective way of identifying bottlenecks in the pathway to care, treatment and cure of TB (Subbaraman et al., 2019). The misalignment of TB services with the places where people seek health care may be a significant impediment to detection of people with TB. Alignment of health services would be useful, not only for TB but for more efficient provision of health care services in general. Ensuring that a large proportion of the targeted population is

reached with TB screening and diagnostic test services that is sustained over time has been documented to reduce the incidence of TB in diverse settings (Corbett et al., 2010; Kaplan et al., 1972; Marks et al., 2019). Such approaches need to be adopted and scaled up in each country to ramp up TB detection efforts and to narrow the TB incidence- notification gap.

The challenge of sub-optimal TB treatment outcomes

The 2020 WHO global TB report contains data on the treatment outcomes of people treated for drug susceptible TB in 2018 and those initiated on treatment for drug resistant TB in 2017. Globally 85%, 76% and 57% of people with new and relapse TB, HIV-associated TB and RR/MDR-TB, respectively, were treated successfully. These figures represent a sub-optimal performance. The poor treatment outcomes are driven mainly by lack of evaluation, poor linkage to treatment, death and high loss to follow-up. The underlying causes of poor treatment outcomes include un-identified or additional drug resistance (Cegielski et al., 2014), inadequate support provided to people with TB to ensure high level of adherence, weak recording and reporting systems and inadequate prevention and management of advanced HIV disease including the provision of anti-retroviral treatment. For children specifically, challenges include under-identification, inadequate recording and reporting, poor drug formulation options, poor caregiver availability/capacity for treatment, and persistent issues with stock out of the few drug options appropriate for this population. By 2019, only 30% of the 3.5 million five-year target for children treated for TB had been achieved, including only 8% of the 115,000 target for treatment of children with RR/MDR -TB. Lapses in data collection and proper and consistent disaggregation continue to negatively affect identification and treatment as well as programming and resource-allocation for children under 15 years and adolescents 10–19 years of age.

Based on observational studies in Bangladesh and sub-Saharan Africa (Bulabula et al., 2019; Trebucq et al., 2018), which were confirmed by results of the standardised treatment regimen of anti-TB drugs for people with MDR-TB (STREAM) Stage 1 trial, WHO now recommends that the shorter 9-month MDR-TB regimens be preferred as it achieves treatment success in roughly 80% of participants (Nunn et al., 2019). Furthermore, second-line injectable drugs, if possible, should be replaced by a fully oral, bedaquiline (BDQ)-containing regimen, one of the new (along with delamanid and pretomanid) potent MDR-TB drugs that are now being increasingly prescribed globally. Such regimens should be urgently scaled-up to improve outcomes, minimize side effects and improve adherence along with point-of-care molecular drug susceptibility testing of second line MDR-TB drugs (Bisimwa et al., 2020; Cox et al., 2018; Diacon et al., 2014; Gler et al., 2012).

Furthermore, attempts have been made in the recent past to reduce the duration of treatment in drug susceptible TB focused on the use of fluoroquinolones, however, the large clinical trials that were undertaken for this purpose failed to demonstrate efficacy for relapse free cure (Grace et al., 2019). The 2020 Global TB report includes a comprehensive description of new medicines and regimens that are at various stages of clinical development and the reader is urged to consult this document. It is anticipated that medicines that are currently reserved for the treatment of drug-resistant TB will soon be available for the treatment of all TB including TB that is caused by pathogens currently considered to be drug-susceptible

and which have the potential to significantly shorten treatment. This is exciting and we urge that efforts to develop new medicines and treatment regimens be ramped up in line with the ambition that came out of the first ever United Nations High Level meeting on TB. This will require additional funding and more robust partnerships between research funders and research groups. It is particularly important that the global south where TB is endemic be deeply engaged in all the processes required for the development of new medicines and regimens for TB. Nations need to live up to the commitments that they have made, such as the pledge by the nations in the African Union made in 2006 to commit at least 1% of their Gross Domestic Product to research and development (African Union, 2007).

To ensure that TB treatment is taken as prescribed, directly observed of treatment (DOT), has been a pillar of TB care and prevention athough its efficacy compared with self-administered treatment has been questioned (Volmink and Garner, 2007). However, direct observation of TB treatment ingestion may be disempowering to the person being treated in addition to imposing demands on that person and the health care system that can be difficult to cope with. An approach that is based on providing comprehensive and individualized support to people being treated for TB is more likely to be acceptable to people with TB and their families and has been associated with better treatment completion rates (Alipanah et al., 2018). Furthermore, in the current digital world, new ways of supporting people on treatment, including interactive two-way mobile phone text message reminders and video assisted DOT have also been associated with good levels of treatment adherence while providing psychological support through remote counselling (Ngwatu et al., 2018).

Addressing sub-optimal TB prevention

Recent estimates of the global burden of latently infected persons with *Mycobacterium tuberculosis* suggests that 23% (95% uncertainty interval 20–4%–26.4%) of the global population or about 1.7 billion people harbor this infection. This large pool of latently infected persons is the seedbed of future TB. It has been estimated that by 2030 and 2050, this pool of latently infected persons will generate 16.3 and 8.3 people with active TB per 100,000 population respectively (Houben and Dodd, 2016). However, with current and hopefully future diagnostic and treatment tools most if not all these episodes of TB can be prevented. A major challenge for TB prevention currently is that there are no easily deployable tools that can identify the subset of latently infected persons who are likely to progress to active TB. While some bio-signatures offer this potential (Sumner et al., 2019) none has been developed to a state that can be used to support programs intended to deliver targeted TB preventive therapy. We urge that this area of research also receives due attention, especially funding, to help refine the targeting of TB preventive therapy as programmatic management of TB preventive therapy is advanced.

It is noteworthy that progress is being made in the provision of TB preventive therapy even though by 2019, the world was far off target. The small successes that are being made, however, need to be celebrated. For example, in 2019, TB preventive therapy was provided to 4.1 million people, which was nearly double the number that received this treatment in 2018. For HIV-infected individuals, 85% of those eligible to receive TB preventive therapy received this intervention, which is commendable. While provision of TB preventive therapy

to household contacts of people with active TB remained low, it seems TB programs across the world have begun to push forward with this intervention as evidenced by the increase in the number of household contacts who were provided with TB preventive therapy in 2019 (538, 396) compared to 2018 (423, 607).

The development of new regimens that are shorter and equally effective such as a weekly dose of rifapentine and isoniazid for 3 months (3HP), a daily dose of rifampicin plus isoniazid for 3 months (3HR), a daily dose of rifapentine plus isoniazid for 1 month (1HP), a daily dose of rifampicin for 4 months (4R) (Sterling et al., 2011; Swindells et al., 2019; WHO, 2020) appeared to have helped to advance implementation of TB preventive therapy at the country level. We believe that combination therapies such as 3HP, 3HR and 1HP have been a truly major advance in that they may have allayed the fears held by some TB program managers and opinion leaders at the national level, that TB preventive therapy, using isoniazid preventive therapy could promote the development of resistance paving the way for acceleration of TB preventive therapy. Our view is that this moment should be seized to ensure TB preventive therapy services are rapidly scaled-up. By doing this TB preventive therapy, will contribute to the global desire to accelerate declines in TB incidence.

Preventing future TB must not just be focused on finding and treating people with TB but should also include efforts to address social and other determinants of the disease. While efforts are being made to actively find people with TB and to provide TB preventive therapy, governments must ensure that the expansion of economies continues in this COVID-19 era (WHO, 2020) and percolate to all segments of the populations in every nation. The major drivers of TB – undernutrition, poverty, diabetes, tobacco smoking, and household air pollution (Dooley and Chaisson, 2009; Lee et al., 2020; Noubiap et al., 2019; Reid et al., 2019) must be addressed if the world is to expect to end TB as a public health threat by 2035. Moreover, Since the year 2000, WHO has projected that 54 million people have survived tuberculosis (including a large proportion of children and adolescents) (Allwood et al., 2020), however, these people are more likely to develop residual lung damage and recurrent tuberculosis (Allwood et al., 2019, 2020) and are at increased risk for all cause-mortality (standardized mortality ratios: 2.91 (95% CI 2.21–3.84) (Romanowski et al., 2019) compared with the general population or matched controls. We urge national TB programs to incorporate post-tuberculosis health and wellbeing interventions in the package of services provided to people with TB (Chakaya et al., 2016) and encourage the research community to undertake research intended to unravel the biomedical and social determinants impacting TB survivals' long-term prognosis (Romanowski et al., 2019).

It has been over two years since global leaders signed the UN general assembly high level meeting on TB declaration. It is disappointing and disheartening that we are not on track to reach the testing and treatment goals. While global political and public health systems have been severely shaken by the COVID-19 pandemic, which undoubtedly has dislodged TB from the number one slot in the year 2020 the expectation is that with the rollout of COVID-19 vaccines and public health measures, COVID-19 may be brought under control (Forni and Mantovani, 2021). The long-term socio-economic effects of the COVID-19 pandemic will further drive poverty, malnutrition and poor living conditions, which are risk

factors associated with TB prevalence. Thus, TB will likely quickly re-occupy the number one spot as the most common infectious cause of mortality worldwide. From first detection of COVID-19 as a new human pathogen, global coordination and political will with huge financial investments have led to the development of effective vaccines against SARS-CoV2 infection within 11 months. The world now needs to similarly focus on development of new vaccines for TB utilizing new technological methods.

We urge the WHO, other UN agencies and partners to develop mechanisms that strongly push countries to ensure TB multi-sectoral accountability frameworks are not just developed but are pursued with vigour. Holistic programs for human development need to be developed and leaders made to account for their implementation. Global health inequities driving TB epidemiology, including the environment and climate control, gender, age, socio-economic status, and wealth as well as resource distribution, should also be addressed by multiple approaches and sectors. It is not yet too late to do this and on the World TB Day 2021, we expect that every leader and person of influence will get the message that it is time to reduce inequities as we work towards a TB free world. While there is a continued need to develop new prevention and treatment tools for TB, we strongly believe that the effective and efficient application of current tools can significantly dent the burden of TB and advance the push to end TB as a global public health threat. The time to do this is now.

The world's TB control programs were already failing to meet the ambitious goals during the past 2–3 years, largely because of systemic weaknesses. The COVID-19 pandmic and its rapid global spread, highlights the intrinsic weaknesses of health care systems. The ultimate generic issue for all communicable diseases of public health importance is that of creating a systemically strong healthcare base upon which to build disease-specific programs such as for TB.

Acknowledgements

Professors Zumla, Francine Ntoumi, Peter Mwaba, Dorothy Yeboah-Manu, Sayoki Mfinanga,Timothy D McHugh, Ibrahim Abubakar, and Dr Kapata are members of the European and Developing Countries Clinical Trials Partnership the EU Horizon 2020 Framework Program, projects a) Pan-African Network on Emerging and Re-Emerging Infections (PANDORA-ID-NET, Grant Agreement RIA2016E-1609, (https://www.pandora-id.net/) and CANTAM-2 (EDCTP Grant No. RegNet2015-1045). Sir Prof Zumla is an AFREhealth Member and is in receipt of a UK-National Institutes of Health Research senior investigator award and is a 2020 Mahathir Science Award Laureate. Dr. Nachega is an infectious disease internist and epidemiologist supported by the NIH/Fogarty International Center (FIC) grant numbers 1R25TW011217-01 (African Association for Health Professions Education and Research); 1D43TW010937-01A1 (the University of Pittsburgh HIV-Comorbidities Research Training Program in South Africa—Pitt-HRTP-SA); and 1R21TW011706-01.

Dr. Sam-Agudu is supported by NIH/National Institute of Child Health and Human Development (NICHD) grant R01HD089866, and by an NIH/FIC award through the Adolescent HIV Prevention and Treatment Implementation Science Alliance (AHISA), for (CAWISA). Dr. P.D.M.C Katoto is supported by Pitt-HRTP-SA and is a CAWISA Fellow.

No funding source was used in the development of this manuscript.

References

African Union. Assembly of the African Union 8th Ordinary Session. . p. 164.

Alipanah N, Jarlsberg L, Miller C, Linh NN, Falzon D, Jaramillo E, et al. Adherence interventions and outcomes of tuberculosis treatment: A systematic review and meta-analysis of trials

and observational studies. PLoS Med 2018;15(7): e1002595, doi:10.1371/journal.pmed.1002595. [PubMed: 29969463]

Allwood B, van der Zalm M, Makanda G, Mortimer K, Andre FSA, Uzochukwu E, et al. The long shadow post-tuberculosis. Lancet Infect Dis 2019;9(11):1170–1, doi: 10.1016/S1473-3099(19)30564-X.

Allwood BW, Van Der Zalm MM, Amaral AFS, Byrne A, Datta S, Egere U, et al. Post-tuberculosis lung health: Perspectives from the First International Symposium. Int J Tuberc Lung Dis 2020;24(8):820–8, doi:10.5588/ijtld.20.0067. [PubMed: 32912387]

Bisimwa BC, Nachega JB, Warren RM, Theron G, Metcalfe JZ, Shah M, et al. Xpert Mycobacterium tuberculosis/Rifampicin–Detected Rifampicin Resistance is a Suboptimal Surrogate for Multidrug-resistant Tuberculosis in Eastern Democratic Republic of the Congo: Diagnostic and Clinical Implications. Clin Infect Dis 2020;26:ciaa873, doi:10.1093/cid/ciaa873.

Bulabula ANH, Nelson JA, Musafiri EM, Machekano R, Sam-Agudu NA, Diacon AH, et al. Prevalence, Predictors, and Successful Treatment Outcomes of Xpert MTB/RIF–identified Rifampicin-resistant Tuberculosis in Post-conflict Eastern Democratic Republic of the Congo, 2012–2017: A Retrospective Province-Wide Cohort Study. Clin Infect Dis 2019;69(8):1278–87, doi:10.1093/cid/ciy1105. [PubMed: 30759187]

Cegielski JP, Dalton T, Yagui M, Wattanaamornkiet W, Volchenkov GV, Via LE, et al. Extensive drug resistance acquired during treatment of multidrug-resistant tuberculosis. Clin Infect Dis 2014;59(8):1049–63, doi:10.1093/cid/ciu572. [PubMed: 25057101]

Chakaya J, Kirenga B, Getahun H. Long term complications after completion of pulmonary tuberculosis treatment: A quest for a public health approach. J Clin Tuberc Other Mycobact Dis 2016;3:10–2, doi:10.1016/j.jctube.2016.03.001.

Corbett EL, Bandason T, Duong T, Dauya E, Makamure B, Churchyard GJ, et al. Comparison of two active case-finding strategies for community-based diagnosis of symptomatic smear-positive tuberculosis and control of infectious tuberculosis in Harare, Zimbabwe (DETECTB): A cluster-randomised trial. Lancet 2010;376(9748):1244–53, doi:10.1016/S0140-6736(10)61425-0. [PubMed: 20923715]

Cox V, Brigden G, Crespo RH, Lessem E, Lynch S, Rich ML, et al. Global programmatic use of bedaquiline and delamanid for the treatment of multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2018;22(4):407–12, doi:10.5588/ijtld.17.0706. [PubMed: 29562988]

Diacon AH, Pym A, Grobusch MP, de Los Rios JM, Gotuzzo E, Vasilyeva I, et al. Multidrug-Resistant Tuberculosis and Culture Conversion with Bedaquiline. N Engl J Med 2014;371:723–32, doi:10.1056/NEJMoa1313865. [PubMed: 25140958]

Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. Lancet Infect Dis 2009;9(12):737–46, doi:10.1016/S1473-3099(09)70282-8. [PubMed: 19926034]

Forni G, Mantovani A. COVID-19 vaccines: where we stand and challenges ahead. Cell Death Differ 2021;, doi:10.1038/s41418-020-00720-9.

Garcıa-Basteiro AL, Brew J, Williams B, Borgdorff M, Cobelens F. What is the true tuberculosis mortality burden? Differences in estimates by the World Health Organization and the Global Burden of Disease study. Int J Epidemiol 2018;47 (5):1549–60, doi:10.1093/ije/dyy144. [PubMed: 30010785]

Gler MT, Skripconoka V, Sanchez-Garavito E, Xiao H, Cabrera-Rivero JL, Vargas-Vasquez DE, et al. Delamanid for multidrug-resistant pulmonary tuberculosis. N Engl J Med 2012;366:2151–60, doi:10.1056/NEJMoa1112433. [PubMed: 22670901]

Grace AG, Mittal A, Jain S, Tripathy JP, Satyanarayana S, Tharyan P, et al. Shortened treatment regimens versus the standard regimen for drug-sensitive pulmonary tuberculosis. Cochrane Database Syst Rev 2019;12:, doi:10.1002/14651858.CD012918.pub2CD012918.

Houben RMGJ, Dodd PJ. The Global Burden of Latent Tuberculosis Infection: A Re-estimation Using Mathematical Modelling. PLoS Med 2016;13(10):e1002152, doi:10.1371/journal.pmed.1002152. [PubMed: 27780211]

Kaplan GJ, Fraser RI, Comstock GW. Tuberculosis in Alaska, 1970. The continued decline of the tuberculosis epidemic. Am Rev Respir Dis 1972;105(6):920–6, doi:10.1164/arrd.1972.105.6.920. [PubMed: 5032713]

Lee KK, Bing R, Kiang J, Bashir S, Spath N, Stelzle D, et al. Adverse health effects associated with household air pollution: a systematic review, meta-analysis, and burden estimation study. Lancet Glob Heal 2020;8(11):E1427–34, doi: 10.1016/S2214-109X(20)30343-0.

Marks GB, Nguyen NV, Nguyen PTB, Nguyen T-A, Nguyen HB, Tran KH, et al. Community-wide screening for Tuberculosis in a high-prevalence setting. N Engl J Med 2019;381:1347–57, doi:10.1056/nejmoa1902129. [PubMed: 31577876]

Ngwatu BK, Placide Nsengiyumva Ntwali, Olivia Oxlade, Benjamin Mappin-Kasirer, Linh Nguyen Nhat, Ernesto Jaramillo, et al. The impact of digital health technologies on tuberculosis treatment: A systematic review. Eur Respir J 2018;51:, doi:10.1183/13993003.01596-20171701596.

Noubiap JJ, Nansseu JR, Nyaga UF, Nkeck JR, Endomba FT, Kaze AD, et al. Global prevalence of diabetes in active tuberculosis: a systematic review and meta-analysis of data from 2·3 million patients with tuberculosis. Lancet Glob Heal 2019;7(4):e448–60, doi:10.1016/S2214-109X(18)30487-X.

Nunn AJ, Phillips PPJ, Meredith SK, Chiang C-Y, Conradie F, Dalai D, et al. A trial of a shorter regimen for Rifampin-resistant tuberculosis. N Engl J Med 2019;380:1201–13, doi:10.1056/nejmoa1811867. [PubMed: 30865791]

Parwati CG, Farid MN, Nasution HS, Sulisty, Basri C, Lolong D, et al. Estimation of subnational tuberculosis burden: Generation and application of a new tool in Indonesia. Int J Tuberc Lung Dis 2020;24(2):250–7, doi:10.5588/ijtld.19.0139. [PubMed: 32127111]

Reid MJA, Arinaminpathy N, Bloom A, Bloom BR, Boehme C, Chaisson R, et al. Building a tuberculosis-free world: The Lancet Commission on tuberculosis. Lancet 2019;, doi:10.1016/S0140-6736(19)30024-8.

Romanowski K, Baumann B, Basham CA, Ahmad Khan F, Fox GJ, Johnston JC. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. Lancet Infect Dis 2019;19(10):1129–37, doi:10.1016/S1473-3099(19)30309-3. [PubMed: 31324519]

Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, et al. Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection. N Engl J Med 2011;365:2155–66, doi:10.1056/nejmoa1104875. [PubMed: 22150035]

Subbaraman R, Nathavitharana RR, Mayer KH, Satyanarayana S, Chadha VK, Arinaminpathy N, et al. Constructing care cascades for active tuberculosis: A strategy for program monitoring and identifying gaps in quality of care. PLoS Med 2019;16(2):e1002754, doi:10.1371/journal.pmed.1002754. [PubMed: 30811385]

Sumner T, Scriba TJ, Penn-Nicholson A, Hatherill M, White RG. Potential population level impact on tuberculosis incidence of using an mRNA expression signature correlate-of-risk test to target tuberculosis preventive therapy. Sci Rep 2019;9:11126, doi:10.1038/s41598-019-47645-z. [PubMed: 31366947]

Swindells S, Ramchandani R, Gupta A, Benson CA, Leon-Cruz J, Mwelase N, et al. One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis. N Engl J Med 2019;380:1001–11, doi:10.1056/nejmoa1806808. [PubMed: 30865794]

Trébucq A, Schwoebel V. Numbers of tuberculosis cases: Dreams and reality. Int J Tuberc Lung Dis 2016;20(10):1288–92, doi:10.5588/ijtld.15.0873. [PubMed: 27725036]

Trebucq A, Schwoebel V, Kashongwe Z, Bakayoko A, Kuaban C, Noeske J, et al. Treatment outcome with a short multidrug-resistant tuberculosis regimen in nine African countries. Int J Tuberc Lung Dis 2018;22(1):17–25, doi:10.5588/ijtld.17.0498. [PubMed: 29149917]

Volmink J, Garner P. Directly observed therapy for treating tuberculosis. Cochrane Database Syst Rev 2007;, doi:10.1002/14651858.CD003343.pub3.

WHO. Global Tuberculosis Report 2020. 2020.

WHO. Global Task Force on TB Impact Measurement. World Heal Organ. 2019. https://www.who.int/tb/areas-of-work/monitoring-evaluation/impact_measurement_taskforce/en/.

Zumla Alimuddin, Marais BJ, McHugh TD, Maeurer M, Zumla Adam, Kapata N, et al. COVID-19 and tuberculosis-threats and opportunities. Int J Tuberc Lung Dis 2020;24(8):757–60, doi:10.5588/ijtld.20.0387. [PubMed: 32912377]