



ELSEVIER

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

The WHO Global Tuberculosis 2021 Report – not so good news and turning the tide back to End TB

Jeremiah Chakaya^{1,*}, Eskild Petersen², Rebecca Nantanda³, Brenda N. Mungai⁴, Giovanni Battista Migliori⁵, Farhana Amanullah⁶, Patrick Lungu⁷, Francine Ntoumi⁸, Nagalingeswaran Kumarasamy⁹, Markus Maeurer¹⁰, Alimuddin Zumla¹¹

¹ Department of Medicine, Therapeutics, Dermatology and Psychiatry, Kenyatta University, Nairobi, Kenya and Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

² Institute for Clinical Medicine, Aarhus University, Denmark; European Travel Medicine Network, Méditerranée Infection Foundation, Marseille, France

³ Makerere University Lung Institute, College of Health Sciences, Makerere University, Kampala, Uganda

⁴ Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK

⁵ Servizio di Epidemiologia Clinica delle Malattie Respiratorie, Istituti Clinici Scientifici Maugeri IRCCS, Tradate, Italy

⁶ Department of Pediatrics, The Indus Hospital and Health Network and the Aga Khan University, Karachi, Pakistan

⁷ National TB and Leprosy Programme, Ministry Of Health, Lusaka, Zambia

⁸ Fondation Congolaise pour la Recherche Médicale (FCRM), Brazzaville, Republic of Congo; Faculty of Sciences and Technology, University Marien Ngouabi, Brazzaville, Republic of Congo; University of Tübingen, Tübingen, Germany

⁹ VHS-Infectious Diseases Medical Centre, VHS Hospital, Chennai, India

¹⁰ Champalimaud Centre for the Unknown, Lisbon, Portugal; Medizinische Klinik, Johannes Gutenberg University Mainz, Germany

¹¹ Division of Infection and Immunity, Center for Clinical Microbiology, University College London, and NIHR Biomedical Research Centre, UCL Hospitals NHS Foundation Trust, London, United Kingdom

ARTICLE INFO

Article history:

Received 10 February 2022

Revised 7 March 2022

Accepted 7 March 2022

Available online xxx

Keywords:

Tuberculosis

WHO 2021 Global TB Report

MDR/XDR-TB

New tools

COVID-19

END TB Strategy

ABSTRACT

Objective: To review the data presented in the 2021 WHO global TB report and discuss the current constraints in the global response.

Introduction and methods: The WHO global TB reports, consolidate TB data from countries and provide up to date assessment of the global TB epidemic. We reviewed the data presented in the 2021 report.

Results: We noted that the 2021 WHO global TB report presents a rather grim picture on the trajectory of the global epidemic of TB including a stagnation in the annual decline in TB incidence, a decline in TB notifications and an increase in estimated TB deaths. All the targets set at the 2018 United Nations High Level Meeting on TB were off track.

Interpretation and conclusion: The sub-optimal global performance on achieving TB control targets in 2020 is attributed to the on-going COVID-19 pandemic, however, TB programs were already off track well before the onset of the pandemic, suggesting that the pandemic amplified an already fragile global TB response. We emphasize that ending the global TB epidemic will require bold leadership, optimization of existing interventions, widespread coverage, addressing social determinants of TB and importantly mobilization of adequate funding required for TB care and prevention.

© 2022 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

On March 24, 2022, the world will commemorate the World TB Day in remembrance of the day in 1882, when the German scientist, Robert Koch, gave his famous lecture in which he announced the discovery of the pathogen that causes tuberculosis, *Mycobacterium tuberculosis* (Barberis, et al, 2017). It is a day for raising awareness about TB and to reflect on the status of this age-old global epidemic. This year's theme for World TB Day is 'Invest to

* Corresponding author.

E-mail addresses: chakaya.jm@gmail.com (J. Chakaya),

eskild.petersen@gmail.com (E. Petersen), r.nantanda@gmail.com (R. Nantanda),

brendanyambura2013@gmail.com (B.N. Mungai), giovannibattista.migliori@icsmaugeri.it

(G.B. Migliori), farhana.amanullah@tih.org.pk (F. Amanullah),

lungupatrick99@gmail.com (P. Lungu), ntoumi@fcrm-congo.com (F. Ntoumi),

kumarasamyn@gmail.com (N. Kumarasamy), [\[acaochampalimaud.pt\]\(mailto:acaochampalimaud.pt\) \(M. Maeurer\), \[a.zumla@ucl.ac.uk\]\(mailto:a.zumla@ucl.ac.uk\) \(A. Zumla\).](mailto:markus.maeurer@fund</p>
</div>
<div data-bbox=)

Table 1
End TB Strategy and UNHLM Targets and progress 2015–2022

Parameter	Target	Achieved
Incidence decline (compared with 2015 baseline)	20%	11%
Deaths decline (compared with 2015 baseline)	35%	9.2%
Catastrophic costs incurred by individuals with TB/their families	0	47%
People treated for TB, 2018–2022	40 million	19.8 million (50%)
Children treated for TB, 2018–2022	3.5 million	1.4 million (41%)
People with MDR TB treated, 2018–2022	1.5 million	483, 000 (32%)
Children with MDR TB treated, 2018–2022	115,000	12,200 (11%)
People treated for LTBI, 2018–2022	30 million	8.7 million (29%)
People living with HIV treated for LTBI, 2018–2022	6 million	7.2 million (>100%)
Household contacts <5 years treated for LTBI, 2018–2022	4 million	1.2 million (29%)
Household contacts >5 years treated for LTBI, 2018–2022	20 million	0.32 million (1.6%)
Annual funding needs	13 billion USD	5.3 billion USD
Annual Research funding for TB	2 billion USD	901 million USD

Sourced from the [WHO Global TB Report 2021](#).

End TB' and it comes at a time when global TB care and prevention efforts are being hampered by the pressures on health services due to the COVID-19 pandemic.

The World Health Organization (WHO) annual TB Reports consolidate TB data reported to the WHO by most countries of the world. They provide a comprehensive and up to date assessment of the global TB epidemic. The most recent WHO global TB report was produced in 2021 and provides data on the TB epidemic for the year 2020 ([WHO Report, 2021](#)). This report consolidates data submitted to WHO by 197 countries and territories covering more than 99% of the world population. While previous WHO global TB reports have, on the whole, provided uplifting news on the trajectory of the global burden of TB, the 2021 report is different, providing not so good news and makes grim reading.

In 2020, the world fell significantly off track on all the United Nations General Assembly (UNGA) targets ([Sahu, et al, 2021](#)). Thus, the small annual decline in TB incidence that had been witnessed over the previous years almost ground to a halt, notifications of people with TB declined by 18% when compared with the previous year. For the first time in 9 years the number of estimated TB deaths increased ([Table 1](#)). TB deaths increased because of restricted access to disrupted TB services in light of the COVID-19 pandemic, resulting in almost half of the estimated persons who fell ill due to TB not being diagnosed and treated. Furthermore, the number of people with drug-resistant TB and LTBI receiving treatment dropped significantly. The report also indicates that there was a reduction in funding for TB, and BCG coverage among children. This sad state of affairs is largely attributed to the on-going COVID-19 pandemic. As the COVID-19 pandemic established itself in 2020, it disrupted essential health services ([Migliori, et al, 2021](#)) including those for TB, in addition to imposing an additional health burden to people with TB who appear to be more vulnerable to suffering severer forms of this new infectious disease ([Visca et al., 2021](#); [The Globle TB Study group, 2021](#)). Indeed, the COVID-19 pandemic has highlighted the fragility of TB services globally, and the negative consequences especially among the poor and most disadvantaged populations. Since the COVID-19 pandemic is far from over and continues to burden health services since the 2021 TB Report was published in August 2021, it is to be anticipated that achieving Global TB control targets is becoming even more distant as TB services continue to be disrupted. However, on a brighter side, the COVID-19 pandemic has shown several potential access, diagnostic and follow-up innovations which can be leveraged for improvements in delivering TB services ([Odhiambo, et al, 2021](#)).

While it may be appropriate to accord the blame to the COVID-19 pandemic for retarding progress towards achieving the targets set by the World Health Assembly in 2014 and those set by world leaders at the first ever United Nations High Level Meeting on TB held in September 2018, it is important to note that even before

the COVID-19 appeared, some of the targets appeared already off track ([Sahu et al, 2021](#); [Zumla et al, 2021](#)). The COVID-19 pandemic storm has further aggravated the situation which calls for reflections on several important issues regarding a) the targets and ask if they remain relevant and feasible, b) recommended interventions and tools for TB care and prevention and ask if these interventions and tools are being applied at the right level in the settings where TB imposes its greatest toll, c) measures being taken to mitigate social determinants of TB and d) the funding landscape for TB and approaches in place to close TB financing gaps.

Targets

The End TB Strategy adopted by the World Health Assembly in 2014 and which has been implemented for about six years now has ambitious targets and was intended to end TB as a global public health threat by 2035. If TB care and prevention progresses as outlined in the End TB Strategy the world expects to see declines in TB incidence and mortality of 95% and 90% respectively by 2035 compared with 2015. Additionally, by now no person or family would be incurring catastrophic costs on account of TB. Had the world been on track to achieve these targets, by now TB incidence and mortality would have declined by at least 20% and 35% respectively compared to the rates in 2015. However, performance has been sub-optimal with only an 11% decline in TB incidence and a 9.2% decline in TB mortality by 2021. Additionally, while the UNHLM on TB set a target of 20 million people over the age of 5 years to receive TB preventive therapy by 2022, in 2020, only 16% of people who could have benefited from this treatment had received it. Considering the current trajectory of these epidemiological indicators, it is not unreasonable to pose a few questions: are these targets achievable? Do we lack the necessary tools to prevent and manage TB or are we slow in implementing them?

The interventions and tools

The epidemiological framework for the prevention and care of TB is based on what is currently known about its transmission, the risk of progression from infection to disease and the effect of various interventions on these processes. Interventions for the prevention and management of TB ideally should encompass measures to: reduce exposure to *Mycobacterium tuberculosis*, identify all infected persons and provide preventive therapy to limit progression to active TB disease, especially for those persons at risk for this outcome, identify early, people with active TB and provide effective treatment to ensure relapse free cure, reduced risk of acquired drug resistance and prevention of long term morbidity from TB ([Ozcaglar, et al, 2012](#); [Lönnroth, et al, 2015](#); [Carvalho, et al, 2018](#); [Mandal, et al, 2015](#)) These interventions need to be applied in the

context of the health care system, preferably under the umbrella of universal health coverage and with the right level of political commitment which then leads to the mobilization of adequate financial resources to support care and prevention of the disease. Pillar 1 and 2 of the End TB strategy are intended to support this epidemiological framework for TB care and prevention. Thus, the world appears to have an appropriate and well thought out strategy that if implemented to the full, should lead to the achievement of the ambitious targets of the End TB strategy.

Additionally, the fight against TB has been buoyed by the development and deployment of new tools. While a perfect situation is still far away, improvements have been made in the portfolio of TB diagnostics. In the last few years WHO has approved or endorsed new TB diagnostic tests (WHO Report, 2020), which offer the potential for targeted treatment of people with TB as a result of up-front knowledge of anti-TB drug susceptibility profiles. These advances together with the deeper understanding of host immune responses that can be used to design host directed therapies, ability to assess and monitor drug responses and progress with biomarker discoveries offers a real potential to provide precision medicine for TB (Lange C et al 2020). Treatment of TB and especially treatment of drug resistant forms of TB has also advanced with medicines that have a higher efficacy while also being safer becoming available (Mirzayev et al., 2021; WHO, 2021b). Even though progress is slow, national TB programs across the world are increasingly taking up TB prevention through better application of infection prevention measures at health facility level and the provision of TB preventive therapy. Advances in the development of TB vaccines is providing hope that an efficacious vaccine will become available in the period covered by the End TB Strategy (Gopaldaswamy, et al, 2022). Screening programs for active TB using highly sensitive tools is slowly gaining ground providing hope that the paradigm to find, treat and prevent TB will become a reality for a large proportion of people with TB across the world. We know that when interventions are applied consistently and widely to achieve a high population coverage, the burden of TB can be brought down (Comstock et al 1961; Corbett et al 2010, Marks et al 2019). The challenge seems to be related to sub-optimal application of effective interventions which may have multiple origins, with inadequate financing being a major driver of this situation.

Social determinants

It is well known that TB is a poverty driven disease and therefore addressing social determinants of the disease was included as a critical component of pillar 2 of the End TB Strategy. While it may be argued that addressing social determinants of TB is not a direct remit of TB care and prevention programs, these governmental agencies need to be linked with and if feasible drive processes for the development and implementation of multi-sectoral approaches that support TB prevention at the population level. The WHO has been working hard to push countries to develop multi-sectoral approaches to TB care and prevention including the development of appropriate accountability frameworks (WHO, MAF- TB). Whether effective TB multi-sectoral accountability frameworks in high TB burden settings are in place and the impact they are having on local TB responses is currently unclear. It is certain that TB care and prevention targets are unlikely to be achieved if large proportions of the populations of the world are allowed to continue languishing in poverty and at a high social risk of exposure to the TB bacillus and progression to active TB disease on account of under-nutrition, poor housing, socially driven substance abuse and poor access to health services. Unfortunately, this is the situation that the world finds itself today. Global poverty rates rose, with an estimated 119-124 people pushed back to extreme poverty in 2020, driven partly by the COVID-19 pandemic

but also by other factors that imposed a deceleration effect on the rate of decline in poverty long before COVID-19 came along, such as armed conflicts and environmental disasters linked to the effects of climate change (World Bank, 2020). If these poverty trends continue the prospects for achieving the global targets for ending TB are indeed grim.

Tuberculosis financing

The delivery of effective TB care and prevention interventions demands that adequate resources are mobilized to facilitate wide coverage of the population with these interventions in addition to identifying new tools (research to identify new diagnostics and treatment) and new ways of delivering existing interventions through operations and implementation research. The 2021 WHO global TB report (WHO,2021) highlights a major annual global funding gap. Of the annual need of about USD 13 billion, only 5.3 billion USD was available for TB care and prevention in 2020 and of the 2 billion USD required for TB research, only USD 901 million was available in 2020. With these huge funding gaps in TB care and prevention, it is not surprising that slow progress is being made towards the attainment of the ambitious End TB Strategy and UNHLM TB targets. What is the main reason for the chronic underfunding for TB? Is it that global TB advocates aren't doing enough or not doing the right thing? Why have targets of TB advocacy not responded appropriately?

We believe that the COVID-19 pandemic has important lessons for TB advocacy and TB financing. It appears fortuitous that many high TB burden settings have not experienced the full wrath of the COVID-19 pandemic. For example, by the end of January 2022, sub-Saharan Africa (SSA) had contributed only 1.5% of all confirmed SARS-COV 2 infections and about 3% of all COVID-19 deaths (WHO COVID-19 Dashboard) a situation that cannot be fully explained by non or under identification and reporting of SARS – COV2 infections and COVID-19 deaths in this continent. The COVID-19 pandemic has brought to the fore the inequities in global health: high income countries rapidly mobilized financial resources that led to the development of diagnostic tests, medicines and novel vaccines at such a speed that has never been seen before. While this is great for global public health and public good, the fact that most of these tools remain unavailable for large sections of the population in low resource settings is cause for concern (Bolcato, et al, 2021). The burden of TB is higher in low resource settings and within those settings the poor suffer even more. If the inequities being observed with COVID-19 diagnostics, treatment, and preventive tools (vaccines) is a reflection of human thinking and behavior, then we should resign to the fact TB will be with us for a long time to come, certainly it will not have ended by 2035. This would be shameful and should be stopped. We hope that TB advocates at all levels will use the lessons from the COVID-19 pandemic to craft new ways of telling the TB story to support mobilization of adequate resources to fight this disease. We need to end inequities in the TB response.

In conclusion while the data presented by 2021 WHO global TB report show a deteriorated scenario, we believe that the tide can be changed. We have reflected on the status of the global burden of TB, the strategies, and interventions in place for confronting TB and the progress being made with TB care and prevention targets as presented in the 2021 WHO global TB report. It is still feasible to achieve the ambitious End TB Strategy targets in the remaining time. This will require global solidarity with nations becoming each other's keeper, enhanced application of current interventions and tools and doubling of efforts to fund and support TB research and innovation. Improving the resilience of health systems will be key in achieving the set targets. The clock is ticking, and humanity

should tick even more to invest to End TB, save lives and make TB history (WHO 2022).

Transparency declaration

This article is part of a supplement entitled Commemorating World Tuberculosis Day March 24th, 2022: "Invest to End TB. Save Lives" published with support from an unrestricted educational grant from QIAGEN Sciences Inc.

Acknowledgments

Sir Alimuddin Zumla and Prof Francine Ntoumi acknowledge support from the EU-EDCTP funded PANDORA-ID-NET, CANTAM-3 and EACCR-3 programs. Sir Zumla is a Mahathir Foundation Science Award, and Pascoal Mocumbi Prize laureate. Eskild Petersen chairs the ESCMID Emerging Infections Task Force.

Conflicts of interest

All authors have an interest in TB. All authors declare no conflicts of interests.

Funding source

The development of this manuscript was not funded by any funding source.

Ethical Approval Statement

The development of this manuscript did not involve direct research on human subjects and therefore approval by an institutional review board was not required.

References

- Barberis I, Bragazzi NL, Galluzzo L, Martini M. The history of tuberculosis: from the first historical records to the isolation of Koch's bacillus. *J Prev Med Hyg* 2017;58(1):E9-E12 Mar PMID: 28515626; PMCID: PMC5432783.
- Bolcato M, Rodriguez D, Feola A, Di Mizio G, Bonsignore A, Ciliberti R. COVID-19 Pandemic and Equal Access to Vaccines. *Vaccines (Basel)* 2021;9(6):538 May 21 PMID: 34063863; PMCID: PMC8224034. doi:10.3390/vaccines9060538.
- Carvalho ACC, Cardoso CAA, Martire TM, Migliori GB, Sant'Anna CC. Epidemiological aspects, clinical manifestations, and prevention of pediatric tuberculosis from the perspective of the End TB Strategy. *J Bras Pneumol* 2018;44(2):134-44 Apr PMID: 29791553; PMCID: PMC6044667. doi:10.1590/s1806-37562017000000461.
- 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 Oct 9 PMID: 20923715; PMCID: PMC2956882. doi:10.1016/S0140-6736(10)61425-0.
- Comstock GW, Philip RN. Decline of the tuberculosis epidemic in Alaska. *Public Health Rep* 1961;76:19-24.

- Gopaldaswamy R, Subbian S. An Update on Tuberculosis Vaccines. *Methods Mol Biol* 2022;2410:387-409 PMID: 34914059. doi:10.1007/978-1-0716-1884-4_20.
- Lange C, Aarnoutse R, Chesov D, van Crevel R, Gillespie SH, Grobbel HP, et al. Perspective for Precision Medicine for Tuberculosis. *Front Immunol* 2020 Oct 8;11:566608. doi:10.3389/fimmu.2020.566608. PMID: 33117351; PMCID: PMC7578248.
- Lönnroth K, Migliori GB, Abubakar I, D'Ambrosio L, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. *Eur Respir J* 2015;45(4):928-52 Apr PMID: 25792630; PMCID: PMC4391660. doi:10.1183/09031936.00214014.
- Mandal S, Arinaminpathy N. Transmission modeling and health systems: the case of TB in India. *Int Health* 2015;7(2):114-20 Mar PMID: 25733561. doi:10.1093/inthealth/ihv004.
- Marks GB, Nguyen NV, Nguyen PTB, Nguyen TA, Nguyen HB, et al. Community-wide Screening for Tuberculosis in a High-Prevalence Setting. *N Engl J Med* 2019;381:1347-57.
- Migliori GB, Thong PM, Alffenaar JW, et al. Gauging the impact of the COVID-19 pandemic on tuberculosis services: A global study. *Eur Respir J* 2021;58. doi:10.1183/13993003.01786-2021.
- Mirzayev F, Viney K, Linh NN, Gonzalez-Angulo L, Gegia M, et al. World Health Organization recommendations on the treatment of drug-resistant tuberculosis, 2020 update. *Eur Respir J* 2021 Jun 4;57(6) PMID: 33243847; PMCID: PMC8176349. doi:10.1183/13993003.03300-2020.
- Odhiambo CO, Mataka A, Massinga Loembe M, Ondoa P. Maintaining routine HIV and tuberculosis testing services in sub-Saharan African countries in the context of COVID-19: Lessons learnt and opportunities for improvement. *Afr J Lab Med* 2021 Jun 17;10(1):1413 PMID: 34230879; PMCID: PMC8252131. doi:10.4102/ajlm.v10i1.1413.
- Ozcaglar C, Shabber A, Vandenberg SL, Yener B, Bennet KP. Epidemiological models of Mycobacterium tuberculosis complex infections. *Mathematic Biosciences* 2012;236(2):77-96.
- Sahu S, Ditiu L, Sachdeva KS, Zumla A. Recovering from the Impact of the Covid-19 Pandemic and Accelerating to Achieving the United Nations General Assembly Tuberculosis Targets. *Int J Infect Dis* 2021;113 Suppl 1:S100-3 DecEpub 2021 Mar 11 PMID: 33716198; PMCID: PMC7948527. doi:10.1016/j.ijid.2021.02.078.
- The TB/COVID-19 Global Study Group. Tuberculosis and COVID-19 co-infection: description of the global cohort. *Eur Respir J*. 2021 Nov 11. doi:10.1183/13993003.02538-2021.
- Visca D, Ong CWM, Tiberi S, Centis R, D'Ambrosio L, Chen B, et al. Tuberculosis and COVID-19 interaction: A review of biological, clinical and public health effects. *Pulmonology* 2021;27(2):151-65 Mar-AprEpub 2021 Jan 22 PMID: 33547029; PMCID: PMC7825946. doi:10.1016/j.pulmoe.2020.12.012.
- WHO Report 2020: WHO Multisectoral Accountability Framework for TB (MAF-TB) Baseline Assessment Checklist for country use in pursuing a national MAF-TB https://cdn.who.int/media/docs/default-source/documents/tuberculosis/multisectoral-accountability-framework-tb-tuberculosis-checklist96a80040-12bd-438d-b79e-428e4e770ebe.pdf?sfvrsn=6ba20074_1&download=true - accessed February 2nd 2022.
- WHO. Global tuberculosis report 2021. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO; 2021a <https://www.who.int/publications/i/item/9789240037021> -accessed January 31st, 2022.
- WHO. WHO consolidated guidelines on tuberculosis. Module 3: diagnosis - rapid diagnostics for tuberculosis detection, 2021 update. Geneva: World Health Organization; 2021b Licence: CC BY-NC-SA 3.0 IGO.
- WHO, 2022. COVID-19 Africa Dashboard. <https://covid19.who.int/region/afro/country/cf> -accessed February 6th, 2022.
- World Bank. Poverty and Shared Prosperity 2020: Reversals of Fortune. Washington, DC: World Bank; 2020 License: Creative Commons Attribution CC BY 3.0 IGO.
- Zumla A, Chakaya J, Khan M, Fatima R, Wejse C, Al-Abri S, et al. World Tuberculosis Day 2021 Theme - 'The Clock is Ticking' - and the world is running out of time to deliver the United Nations General Assembly commitments to End TB due to the COVID-19 pandemic. *Int J Infect Dis* 2021;113 Suppl 1:S1-6 DecEpub 2021 Mar 18. PMID: 33746094. doi:10.1016/j.ijid.2021.03.046.