The impact of COVID-19 on global tuberculosis control

Marc Lipman MD¹

C Finn McQuaid PhD²

Ibrahim Abubakar PhD³

Mishal Khan PhD⁴

Katharina Kranzer PhD⁵

Timothy D McHugh PhD⁶

Chandrasekaran Padmapriyadarsini PhD⁷

Molebogeng X. Rangaka PhD⁸

Neil Stoker PhD⁹

¹Professor of Medicine, UCL Respiratory, Royal Free Campus University College London, Rowland Hill Street, London, NW3 2PF; Royal Free London NHS Foundation Trust, Pond Street, London NW3 2QG UK

²Assistant Professor in Infectious Disease Epidemiology, TB Modelling Group, TB Centre and Centre for Mathematical Modelling of Infectious Diseases, Department of Infectious Disease Epidemiology, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT UK

³Professor of Infectious Disease Epidemiology & Director, Institute for Global Health, University College London, Room 305, 3rd floor Mortimer Market Centre, Capper Street, London WC1E 6JB UK

⁴Associate Professor of Health Policy and Systems, TB Centre and Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT UK

⁵Professor, Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT UK; Biomedical Research and Training Institute, Harare, Zimbabwe; Division of Infectious and Tropical Medicine, Medical Centre of the University of Munich, Munich, Germany

⁶Professor of Medical Microbiology, University College London Centre for Clinical Microbiology, Division of Infection & Immunity, Royal Free Hospital Campus, Rowland Hill Street, London NW3 2PF UK

⁷Director, ICMR-National Institute for Research in Tuberculosis No.1, Mayor Ramanatihan Road, Chetput, Chennai, India

⁸Clinical Associate Professor, Institute for Global Health, University College London, Room 305, 3rd floor Mortimer Market Centre, Capper Street, London WC1E 6JB UK; School of Public Health, and CIDRI-AFRICA, University of Cape Town, South Africa

⁹Clinical Trial Data Manager, University College London Centre for Clinical Microbiology, Division of Infection & Immunity, Royal Free Hospital Campus, Rowland Hill Street, London NW3 2PF UK

Keywords

COVID-19 - Economic - Impact - India - Modelling - Mycobacteria - Recovery - WHO

March 24 is World Tuberculosis (TB) Day. In many countries, events marking World TB Day in 2020 were cancelled as national lockdowns began. This was not due to TB, but the "other pandemic" - and the year will be remembered as one where the virus SARS-CoV-2 and its disease COVID-19 dominated global health and disrupted national economies. Its direct effect has been felt in every country; and its secondary impact has played out on other global diseases such as TB.

The United Nations Secretary General's 2020 progress report on TB¹ recognised the potential for a loss of focus on the persisting crisis of TB; and included as one of the ten priority recommendations for actions needed to accelerate progress towards global TB targets, "to ensure that TB prevention and care are safeguarded in the context of COVID-19 and other emerging threats". This was reinforced in the WHO Global TB Report 2020².

These international political statements are important, but for genuine impact they need to be enacted at regional, national and sub-national levels. This is vital given that the global TB targets set within the UN Sustainable Development Goals and the WHO End TB Strategy were not being met prior to the disruption brought about by COVID-19² – and are now therefore likely to be even further from their intended trajectory.

Here we discuss the short and long-term impact of COVID-19 on TB patients and services, using examples and information from around the world, with a focus on India.

The immediate effect of COVID-19 was a significant disruption to global health care. This included the redeployment of staff and reallocation of resource from TB to other/COVID-support services and a loss of staff due to sickness/quarantining. Further, a reduction in public transportation and the introduction of movement restrictions made it harder for staff to travel to work³.

The staff shortages affected preventive therapy programmes including BCG vaccination, with for example a million fewer Indian children than usual receiving BCG in April 2020⁴. It also became increasingly difficult for staff to reach TB patients on treatment. This was compounded by disruption to supply chains: meaning that medication and diagnostic reagents began to run-out.

COVID-19 and TB symptoms are similar⁵; and poor levels of public knowledge about COVID-19 combined with stigma (for both diseases)⁶ encouraged symptomatic people to isolate from communities yet continue to mix with close friends and family. New cases of TB were often too frightened to attend health care services (which they perceived as places where they could catch COVID-19)⁶. This was not helped by the precautionary messages that health care facilities put out, discouraging people from attending without good cause, and so avoid healthcare-related SARS-CoV-2 transmission⁷.

The net result of symptomatic TB patients not using health care services, which themselves were severely stretched, was a global fall in the number of reported TB notifications. India, which accounts for over one-quarter of the world's TB cases at an estimated 2.64 million in 2019, reported a 25% reduction in notifications for the first half of 2020 compared to the same period in 2019².

Much of the contribution to COVID-19 by TB and other services was informed by infection prevention and control considerations⁸. This included the prompt identification and management of possible infectious cases of COVID-19 through the use of robust clinical diagnostic criteria; the strengthening of infection prevention and control for airborne, droplet and contact transmission (both for patients and staff) and the avoidance of unnecessary visits to health facilities. The latter utilised where possible remote phone consultations and digital technology, which themselves required an up-scaling of relevant platforms. This had the potential to promote improved data collection by using simpler methodologies, though also the risk of information failure. The private sector was encouraged to work with public health services⁹.

Specific patient groups such as older people, those with diabetes, and the malnourished were recognised as being at particular risk during the twin pandemics, and extra support was provided to pregnant & breastfeeding woman and children, people with drug resistant TB, and those with HIV/TB co-infection. Effort was made in some settings to ensure that migrants and disadvantaged groups were reached and also supported.

Public statements emphasised the need to ensure that funding continued for TB services, and that on-going TB research programmes were continued. We will have more of an idea how this plays out over the next 1-2 years, though there are already reports of significant disruption⁶.

The not-for-profit private sector & non-governmental organisations supported TB services in a variety of ways¹⁰. This included: the production of guidance documentation (Mercy Corps, Pakistan, https://www.mercycorps.org/sites/default/files/2021-01/Addressing-the-Second-Order-Impacts-of-COVID-19-2021.pdf) and the detection of TB and COVID-19 using mobile facilities (BRAC, Bangladesh, https://www.who.int/bangladesh/news/detail/26-11-2020-protecting-tb-progresses-in-coxs-bazar-ensuring-that-tb-prevention-care-face-no-setbacks-during-covid-19-pandemic; KNCV, https://www.kncvtbc.org/en/2020/10/02/wow-trucks-revolutionary-tb-and-covid-19-testing-in-Nigeria, nigeria/), as well as artificial Intelligence methodology (Qure-ai, India, https://qure.ai/news.html). Diagnostics and treatment were supported using e-Pharmacies (SHOPS Plus, India, https://www.shopsplusproject.org/article/using-e-pharmacy-model-deliver-tb-medication-patientsduring-covid-19-pandemic) and home-delivery approaches (Innovators in Health, India; MSF, India, https://www.msfindia.in/covid-19-in-india-tackling-tuberculosis-in-the-middle-of-coronaviruspandemic/). Private general practitioners' clinics also helped distribute medication (Community Health Solutions, Pakistan, https://twitter.com/chs_health_care?lang=en). In several countries, telephonemonitoring (Innovators in Health, India, https://www.innovatorsinhealth.org/tuberculosis.html) and digital technology focused on maintaining treatment adherence (IRD, South Africa, https://www.usaid.gov/global-health/health-areas/tuberculosis/resources/news-and-updates/globalaccelerator-end-tb/stories/ird-south-africa-access-tb-services; UnitAid ASCENT KNCV, and Philippines, https://www.digitaladherence.org/), though their effectiveness has not been evaluated.

Financial support and solutions for TB services included the COVID-19 Response Mechanism (from the Global Fund to Fight AIDS, TB and Malaria, <u>https://www.theglobalfund.org/en/covid-19/response-mechanism/</u>) and cash payments for patients (Innovators in Health, India, <u>https://www.innovatorsinhealth.org/tuberculosis.html</u>). Advocacy for restoration of the following year's TB budget was also reported (PhilCAT, Philippines, <u>https://philcat.org/</u>).

All of this activity was crucial as modelling studies suggest that under-notification of TB in 2020 had a profound impact on the number of TB-related deaths. For example if COVID-19 led to a decrease in reported global TB cases of 25-50% for 3 months during 2020, there would be an estimated extra 200,000 – 400,000 future TB deaths worldwide² due to TB patients not accessing health services to get appropriate care.

Further modelling indicated that between 2020 and 2025 COVID-19 may cause an additional 6.3 million cases of TB globally. The (now optimistic) projection of starting with a single 3 months of lockdown could lead to an extra 1.4 million deaths¹¹. Our work suggested that over the same timeframe India will have around 100,000 excess deaths if there were a moderate reduction in transmission events in 2020 due to lockdown and a 50% reduction in health services for 6 months¹². We now know that a single lockdown was not adequate, and so the impact will likely be greater than described – and will most affect the vulnerable and disadvantaged at highest risk of TB¹³.

Driven by the collapse of many countries' economies, there will be an increase in population undernutrition - a major potential issue for TB in India¹⁴, continuing disruption of health services and sustained difficulty in diagnosing and treating TB patients. Countries whose battered economies are struggling to reset themselves will be a bad place for people with TB; and the catastrophic costs of TB (defined as the direct and indirect total costs due to TB exceeding 20% of annual household income¹⁵) will rise for them and their families.

Although SARS-CoV-2 vaccines appear to offer considerable promise, the issues of COVID-19 are likely to have on-going negative effects with unexpected twists for several years. A recent example is the identification of highly-transmissible SARS-CoV-2 strains that appear to have no reduction in pathogenicity, with the latest evidence suggesting that some do and some do not reduce current vaccine efficacy¹⁶.

Getting global TB control back on track

Against this background, how can we ensure that TB services rebuild as needed, in particular when there are so many competing demands on health and economic resource? The answer lies in political will and leadership. The WHO Multisectoral Accountability Framework TB to Accelerate Progress to end TB by 2030 (MAF-TB) was initiated at the first WHO Global Ministerial Conference on Ending TB (November 2017). Over the following two years, including discussion at the 71st World Health Assembly (May 2018), and the UN General Assembly High-Level Meeting on the fight against TB (September 2018), the final document was developed (with involvement from WHO Member States, and partners, including civil society), and released in May 2019¹⁷.

MAF-TB calls for multisectoral engagement and accountability at global, regional and national (including local) levels. It is hoped that the MAF-TB has enough weight and global recognition for Member States to continue to support and engage with its aims, and not avoid the costs associated with TB service re-development. In high TB burden settings the short-term gain of failing to honour the pledges made will be more than offset by the longer negative impact of uncontrolled TB. Political support for a further MAF-TB summit addressing the issue of COVID-19-related disruption on TB control, and what to do about it, would help retain international focus.

What can TB services and researchers do that will complement and enhance the desired political will encouraged by the MAF-TB? We suggest that they recognise their considerable value to patients and communities, and do what they do well. Namely, maintain disease prevention and management services (including testing and triaging for COVID-19), whilst learning from COVID-19 by for example advocating the routine use of masks by staff and patients to prevent infection transmission.

Public health services need to connect community members with TB health resources that can be adapted to local circumstances. Engagement with organizations trusted by the community will enable the public to receive clear messages about TB symptoms, when and how to seek help, and the availability of free treatment that needs to be taken as a full course and not discontinued early for maximal impact. This also requires there to be a consistent supply of medication available.

Measures such as the isolation of symptomatic TB patients, when possible, to reduce infection transmission within households should be promoted through community education. The same applies to household contact management, which is likely to be starting from a very low base across the world due to its near-abandonment in 2020, though is now even more important given the increased risk of transmission during COVID-19 lockdown.

New and innovative models of TB care need to be evaluated (including through the collection of operational data). Rapid molecular diagnostics (in place of older, less sensitive methods); as well as tele-health options for patients and carers to improve access need to be expanded and also

evaluated. Without evidence of benefits or harms of these different service adaptations, it will be difficult to make recommendations to health care planners going-forward.

There are also synergies for TB and other healthcare services, such as the importance of ensuring that poverty and malnutrition are managed (for example by cash transfer programs, and nutritional support). We also must understand how we can make TB control services less vulnerable to future external threats, in particular those such as COVID-19 which require a rapid response. This again has value beyond TB as the people most affected are those at greatest risk of other diseases.

Through all of this there is the need to support TB services' vital staff resource, who may have encountered both professional and personal loss themselves over this time. This could include include ensuring that healthcare workers receive prioritised SARS-CoV-2 vaccination¹⁸.

In conclusion, the COVID-19 pandemic has changed global society. We should take this opportunity to work together to end the old scourge of TB, whilst providing hope for a better future where the ravages of emergent diseases can be avoided.

References:

- Report of the Secretary-General. Progress towards the achievement of global tuberculosis targets and implementation of the political declaration of the high-level meeting of the General Assembly on the fight against tuberculosis. United Nations General Assembly 16 September 2020. Available from: <u>https://mailchi.mp/who/un-secretary-general-outlines-priority-</u> recommendations?e=5b995e9d69 accessed on 27 January 2021
- Global tuberculosis report 2020. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO Available from: <u>https://www.who.int/publications/i/item/9789240013131</u> accessed on 27 January 2021
- Khan MS, Rego S, Rajal JB, Bond V, Fatima RK, Isani AK *et al*. Mitigating the impact of COVID-19 on tuberculosis and HIV services: a cross-sectional survey of 669 health professionals in 64 low and middle-income countries. 2020. Available from: <u>https://www.medrxiv.org/content/10.1101/2020.10.08.20207969v1</u> accessed on 27 January 2021
- 4. Rukmini S. COVID-19 Disrupted India's Routine Health Services. IndiaSpend 27 August 2020. Available from: <u>https://www.indiaspend.com/covid-19-disrupted-indias-routine-health-services/</u> accessed on 27 January 2021
- 5. Udwadia ZF, Vora A, Tripathi AR, Malu KN, Lange C, Sara Raju R. COVID-19 -Tuberculosis interactions: When dark forces collide. Indian J Tuberc. 2020;67:S155-S162.
- 6. STOP TB Partnership. The impact of COVID-19 on the TB epidemic: A community perspective, 2020. Available from: <u>http://www.stoptb.org/assets/documents/resources/publications/acsm/Civil%20Society%20Report%20on%20TB%20and%20COVID.pdf?fbclid=IwAR3SOY4kyBs5a_35HIeUhcvwRIWspeP A4vVHESqcQxio7G4irivJ90cSU8k accessed on 27 January 2021</u>
- 7. Shrinivasan R, Rane S, Pai M. India's syndemic of tuberculosis and COVID-19. BMJ Global Health 2020; 5: e003979.
- 8. Meneguim AC, Rebello L, Das M, Ravi S, Mathur T, Mankar S, *et al.* Adapting TB services during the COVID-19 pandemic in Mumbai, India. Int J Tuberc Lung Dis. 2020;24:1119-1121
- Statement on Tuberculosis in Migrants during the COVID-19 Pandemic Migration across the globe. The Union. Available from: <u>https://theunion.org/sites/default/files/2020-12/TB Migr COVID Statement November2020.pdf</u>, accessed on June 12, 2021.
- 10. TB PPM Learning Network. Research Institute of the McGill University Health Centre. Available from: <u>https://www.tbppm.org</u> accessed on 27 January 2021
- 11. Cilloni L, Fu H, Vesga JF, Dowdy D, Pretorius C, Ahmedov S, *et al.* The potential impact of the COVID-19 pandemic on the tuberculosis epidemic a modelling analysis. EClinicalMedicine 2020 Oct 24;28:100603.
- McQuaid CF, McCreesh N, Read JM, Sumner T, CMMID COVID-19 Working Group; Houben RMGJ, et al. The potential impact of COVID-19-related disruption on tuberculosis burden. Eur Respir J. 2020;56:2001718.
- 13. Togun T, Kampmann B, Stoker NG, Lipman M. Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes. Ann Clin Microbiol Antimicrob. 2020;19:21.
- 14. Xu, K., Evans, D.B., G. Carrin, A.M. Aguilar-Rivera, P. Musgrove, T.G. Evans. Protecting households from catastrophic health spending. Health Affairs 2007; 26:972-983.
- 15. Bhargava A, Shewade HD. The potential impact of the COVID-19 response related lockdown on TB incidence and mortality in India. Indian J Tuberc. 2020;67:S139-S146.
- Abu-Raddad LJ, Chemaitelly H, Butt AA for the National Study Group for COVID-19 Vaccination. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants. New England Journal of Medicine 2021, May 5 <u>https://www.nejm.org/doi/full/10.1056/NEJMc2104974</u>, accessed on 12 June 2021.
- Multisectoral accountability framework to accelerate progress to end tuberculosis by 2030. Geneva: World Health Organization; 2019 License: CC BY-NC-SA 3.0 IGO; Available from: <u>https://www.who.int/tb/publications/MultisectoralAccountability/en/</u> accessed on 27 January 2021
- Centers for Disease Control and Prevention. What we can do; 2020. Available from: <u>https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/what-we-can-do.html</u> accessed on 27 January 2021