



Published in final edited form as:

Int J Tuberc Lung Dis. 2021 March 01; 25(3): 167–170. doi:10.5588/ijtld.20.0830.

TB research amidst the COVID-19 pandemic

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The COVID-19 pandemic has led to catastrophic worldwide health consequences, with .56 million confirmed cases and .1.3 million deaths to date.¹ Essential public health interventions such as limitations on travel and the need for social distancing have disrupted research and public health activities related to other diseases including TB.^{2–4} From the beginning of the pandemic, the COVID-19 response has been recognized as both a challenge and an opportunity for TB control.⁵ Modeling studies suggest an additional 6.3 million cases and 1.4 million deaths due to TB through 2025.^{6,7} Indeed, data indicate that people are accessing services for TB less than usual, as case notifications, TB-related hospital discharges, active TB, and latent TB infection outpatient visits decreased substantially in early 2020, suggesting that cases and interventions are already being missed.^{8,9} As the response progresses, adapting TB research and clinical care to restrictions imposed by the pandemic presents opportunities for innovation globally. Our experience as members of a community advisory board, a patient treated for TB, clinicians, and investigators provides an example that may be relevant to other settings.

RESEARCH CHALLENGES

How should TB stakeholders approach ongoing research? The close relationship between research and programmatic management of TB highlights unique ethical issues as epidemics raise questions of justice related to distribution of resources and the burden of disease.^{10,11} Maintaining ethics board review is critical to ensure the protection of participants, which must be done if we are to move at a reasonable pace to advance both TB and COVID-19 research. Study designs which present minimal risk to participants, such as retrospective studies, have made use of existing research infrastructure to provide important early data.¹² The WHO guidance for managing these research challenges during public health emergencies such as COVID-19 includes maintaining a collaborative partnership of

stakeholders that incorporates community members, ensuring a reasonable risk-benefit ratio of studies, and considering the social value of research.^{13,14} A collaborative partnership between participants, clinicians, researchers, and the community should be equitable so that research is directed by the priorities of local partners, and should consider the safety of participants, researchers, and staff, with attention to minimizing the risk of exposure to COVID-19. The Nuffield Council on Bioethics (London, UK) suggests an “ethical compass” to guide decision making on research in global health emergencies informed by values of fairness, equal respect, and reduced suffering.¹⁵ Those involved in TB research can act from a position of understanding TB disease to investigate the convergence of COVID-19 and TB, supporting the values of fairness and respect to reduce suffering from both diseases.

National TB programs (NTPs) and their collaborators share this understanding and mission. In Georgia, the National Center for Tuberculosis and Lung Disease (NCTLD) is the main referral center for TB diagnosis and treatment and manages the national anti-TB network, including medical and scientific activities. The NCTLD has been recognized as a center of excellence for specialized TB services, and provides care to approximately one third of all notified TB cases and their contacts registered annually in the country. In addition to programmatic activities, the NCTLD includes a clinical research unit (CRU) with 43 ongoing studies, including five multicenter clinical trials. To address the COVID-19 pandemic, the Georgia Ministry of Health (Tbilisi, Georgia) created 40 triage centers at healthcare facilities including the NCTLD. During March–July 2020, NCTLD staff screened a total of 161 people for COVID-19, of whom five were confirmed (Table 1); in August 2020, the NCTLD became a treating facility for people with moderate COVID-19 disease. During this time period (March–August 2020), Georgia had a total of 1510 cases of COVID-19 and 19 reported deaths.¹⁶ NTPs benefitted from relevant respiratory infection prevention guidelines and expertise that enabled the Infection Control Committee (ICC) to transform one of the pediatric TB hospitals into a COVID-19 triage center.¹⁷ ICC members established COVID-19-specific requirements for administrative, engineering, and respiratory protection, and over a 6-month period there were no documented nosocomial cases of COVID-19 among the 539 NCTLD staff members, including 28 people fully dedicated to COVID-19 services. The safety of patients, staff, and the community is paramount while continuing TB and COVID-19 research.

An existing community advisory board (CAB) that was established in 2017 and includes representatives from nongovernmental organizations and former TB patients provided essential patient outreach by maintaining educational and supportive communication with TB patients via mobile devices. The CAB was consulted early in the COVID-19 pandemic for their recommendations, leading to the following adjustments to clinical and laboratory monitoring for study participants: providing a month supply of medication, video-observed therapy (VOT) instead of on-site directly observed therapy (DOT), arranging transportation for safety monitoring visits, making clinicians available for phone consultations or home-based visits in case of safety concerns, moving safety laboratory testing to local laboratories to avoid delays associated with flight restrictions, and rescheduling study visits within the protocol window period to improve physical distancing at the clinic. This highlights the critical importance of community engagement in research, particularly during unexpected

challenges such as outbreaks, for adapting research activities to the current situation in a context-appropriate manner.^{18,19}

OPPORTUNITIES FOR INNOVATION

As our experience illustrates, TB stakeholders have an opportunity to develop innovative approaches to their research and programmatic TB services while adding appropriate COVID-19 services. This is in line with the WHO guidance to “integrate research into broader outbreak response efforts”.¹³ NTPs have existing capabilities that can be leveraged for containment of the pandemic. Specifically, research and program staff are experienced in screening patients for respiratory symptoms and conducting contact investigations for TB, skills which translate to identifying and tracing potential cases of COVID-19. Combining case finding for COVID-19 and TB could reduce stigma and disparities associated with these diseases, as has been proposed for HIV.^{20,21} Existing and emerging technologies also play a role. The U.S. National Institutes of Health recommends considering limiting study visits to those needed for safety or clinical care, and to convert to virtual visits where possible.²² NCTLD staff have used technology to deliver care remotely with VOT since September 2016.²³ During the COVID-19 lockdown, VOT capabilities were extended to ongoing randomized controlled trials after training additional staff. This is consistent with the increased use of telemedicine services by TB programs in several countries early in 2020, underlining the growing role of technology in delivering care and the need for continued investment in these platforms.^{8,24} The Xpert system (Cepheid, Sunnyvale, CA, USA) utilized by many NTP laboratories may provide expanded SARS-CoV-2 diagnostic testing capability for the “test and trace” phase of the COVID-19 response using a sensitive and specific test with short turnaround time.^{25,26} The National Reference Laboratory, part of the NCTLD, used their existing Xpert testing capacity to implement dual screening for TB and SARS-CoV-2 rapidly and efficiently, testing an average of 100 people with TB per month for SARS-CoV-2 since May 2020, at a positive proportion of 0.3% (Table 1). In addition to the dedicated cohort studies addressing TB and COVID-19 coinfection, TB surveillance systems could be adapted to include COVID-19 surveillance and queried to answer important research questions about the intersection of these epidemics.¹² Global successes in capacity building for TB research and management provide important opportunities to address COVID-19 while continuing to improve the TB response.²⁷ Experience gained now will support the response to the current epidemic and improve preparedness for future public health emergencies.

CONCLUSION

The COVID-19 pandemic has required a focused response from nearly all sectors of society and disrupted clinical research, including in TB. Even when this pandemic eventually ends, others will follow, making it ever more important to innovate, adapt, and prepare research activities for the future. People affected by TB are particularly vulnerable in the short term due to possible underlying lung disease and new barriers to diagnosis and care, and in the long term due to slowed research progress toward ending the TB epidemic.⁷ Those involved in TB management and research must maintain a collaborative partnership so that the priorities of local partners inform next steps and protect participants as research activities

continue. Our experience at the NCTLD illustrates some of the ways in which community members, investigators, and clinicians can leverage existing research, diagnostic, and management capacity to find innovative solutions to the formidable challenges of COVID-19 and TB. The TB community is well-positioned to take advantage of this opportunity to ensure that research moves forward in the service of those affected by TB.

Acknowledgements

This editorial was supported in part by grants from the U.S. National Institutes of Health, Bethesda, MD, USA (UL1TR002378, TL1TR002382, and D43TW007124). The content is solely the responsibility of the authors and does not necessarily represent the views of the NIH.

References

1. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* 2020; 20(5): 533–534. [PubMed: 32087114]
2. McDermott MM, Newman AB. Preserving clinical trial integrity during the coronavirus pandemic. *JAMA* 2020; 323(21): 2135–2136. [PubMed: 32211830]
3. Collins LF. Persons with HIV and the COVID-19 pandemic: a viral synergy of biology and sociology. *Clin Infect Dis* doi: 10.1093/cid/ciaa1715.
4. Pang Y, et al. Impact of COVID-19 on tuberculosis control in China. *Int J Tuberc Lung Dis* 2020; 24(5): 545–547. [PubMed: 32398213]
5. Zumla A, et al. COVID-19 and tuberculosis-threats and opportunities. *Int J Tuberc Lung Dis* 2020; 24(8): 757–760. [PubMed: 32912377]
6. Kissler SM, et al. Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science* 2020;368: 860–868 [PubMed: 32291278]
7. Stop TB Partnership. The potential impact of the COVID-19 response on tuberculosis in high-burden countries: a modelling analysis. Geneva, Switzerland: Stop TB Partnership, 2020.
8. Migliori GB, et al. Worldwide effects of coronavirus disease pandemic on tuberculosis services, January–April 2020. *Emerg Infect Dis* 2020; 26(11): 2709–2712. [PubMed: 32917293]
9. Dookie N, Padayatchi N, Naidoo K. Tuberculosis elimination in the era of COVID-19: a moving target. *Clin Infect Dis* doi: 10.1093/cid/ciaa1400.
10. Selgelid MJ. Ethics and infectious disease. *Bioethics* 2005; 19(3): 272–289. [PubMed: 16167406]
11. Kazanjian P. Polio, AIDS, and ebola: a recurrent ethical dilemma. *Clin Infect Dis* 2020; 70(2): 334–337. [PubMed: 31339992]
12. Tadolini M, et al. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *Eur Respir J* 10.1183/13993003.01398-2020
13. World Health Organization. Guidance for managing ethical issues in infectious disease outbreaks. Geneva, Switzerland: WHO, 2016. <https://www.who.int/ethics/publications/infectious-disease-outbreaks/en/>. Accessed October 2020.
14. World Health Organization. Ethical standards for research during public health emergencies: distilling existing guidance to support COVID-19 R&D. Geneva, Switzerland: WHO, 2020. <https://www.who.int/blueprint/priority-diseases/key-action/liverecovery-save-of-ethical-standards-for-research-during-public-health-emergencies.pdf>. Accessed April 2020.
15. Nuffield Council on Bioethics. Research in global health emergencies: ethical issues. <https://www.nuffieldbioethics.org/publications/research-in-global-health-emergencies>. London, UK: Nuffield Council on Bioethics, 2020. Accessed October 2020.
16. World Health Organization. WHO coronavirus disease (COVID-19) dashboard. Geneva, Switzerland: WHO, 2020. <https://covid19.who.int/>. Accessed October 2020.
17. Houghton C, et al. Barriers and facilitators to healthcare workers' adherence with infection prevention and control (IPC) guidelines for respiratory infectious diseases: a rapid qualitative evidence synthesis. *Cochrane Database Syst Rev* 2020; 4: CD013582. [PubMed: 32315451]

18. Gilmore B, et al. Community engagement for COVID-19 prevention and control: a rapid evidence synthesis. *BMJ Glob Health* 2020; 5: e003188.
19. Anoko JN, et al. Community engagement for successful COVID-19 pandemic response: 10 lessons from Ebola outbreak responses in Africa. *BMJ Glob Health* 2020; 4:e003121.
20. Nguyen T-AC, et al. Adapting a TB contact tracing strategy for COVID-19. *Int J Tuberc Lung Dis* 2020; 24: 548–550 [PubMed: 32398215]
21. Nosyk B, Armstrong WS, Del Rio C. Contact tracing for COVID-19: an opportunity to reduce health disparities and end the HIV/AIDS epidemic in the US. *Clin Infect Dis* 2020; 19;71(16):2259–2261 [PubMed: 32339245]
22. National Institutes of Health. Guidance for NIH-funded clinical trials and human subjects studies affected by COVID-19. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-087.html>. Bethesda, MD, USA: NIH, 2020. Accessed April 2020.
23. Ravenscroft L, et al. Video-observed therapy and medication adherence for tuberculosis patients: randomised controlled trial in Moldova. *Eur Respir J* 2020; 56(2): 2000493. [PubMed: 32381495]
24. Koura KG, et al. COVID-19 in Africa: community and digital technologies for tuberculosis management. *Int J Tuberc Lung Dis* 2020; 24: 863–865. [PubMed: 32912396]
25. Homolka S, et al. Two pandemics, one challenge-leveraging molecular test capacity of tuberculosis laboratories for rapid COVID-19 case-finding. *Emerg Infect Dis* 2020; 26(11): 2549–2554. [PubMed: 32956612]
26. Loeffelholz MJ, et al. Multicenter evaluation of the Cepheid Xpert Xpress SARS-CoV-2 test. *J Clin Microbiol* 2020; 58(8): e00926–20. [PubMed: 32366669]
27. Reid MJA, et al. Building a tuberculosis-free world while responding to the COVID-19 pandemic. *Lancet* DOI:10.1016/S0140-6736(20)32138-3

Table 1

SARS-CoV-2 PCR testing at the National Center for TB and Lung Disease, Tbilisi, Georgia

	General screening (March–July 2020)	Screening people with confirmed TB (May–November 2020)
Positive tests	5	2
Total tests	161	619
Proportion positive, %	3.1	0.3

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, PCR = polymerase chain reaction.

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Table 2

Opportunities for innovation in TB-COVID-19 research and clinical care

Research phase	Opportunities
Design	Integrate research into COVID-19 response
	Community input on optimal responses to TB research and care via community advisory boards
	Expedited ethics review of minimal risk study designs, such as retrospective studies
	Mobile technology to enhance recruitment and retention
Implementation	TB and COVID-19 screening/contact tracing
	Combined TB-COVID-19 surveillance systems
	Remote clinical or research visits (VOT)
	Utilizing existing testing platforms and human resources to scale up SARS-CoV-2 testing (i.e., GeneXpert; Cepheid, Sunnyvale, CA, USA)
	Maintaining adaptable research programs

COVID-19 = coronavirus disease 2019; VOT = video-observed therapy; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.