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Learning from COVID-19 to reimagine tuberculosis diagnosis



The ongoing COVID-19 mass testing and vaccination campaigns are the result of unprecedented financial investments, rapid research and development, collaborative science, and innovation in delivery systems. It would be a shame to not leverage these systems for other priorities in global health.

Before COVID-19, tuberculosis was the leading infectious killer of humans, affecting 10 million people in 2019 and causing 1.4 million deaths. Now, COVID-19 and tuberculosis pose a deadly, dual threat—a syndemic that feeds on social inequities and poverty.¹ The tuberculosis epidemic is worsening because of the COVID-19 pandemic, and most countries have seen big reductions in tuberculosis notifications. Given the massive setback to progress in reaching tuberculosis targets, it is crucial to leverage COVID-19 innovations and systems to improve tuberculosis care and control.

Because over 1 million people have found it difficult to get tuberculosis diagnosed during the pandemic, we believe the most urgent priority is case finding. We see many opportunities to use the lessons of COVID-19 to reimagine tuberculosis diagnosis.

First, we advocate for sustained use of digital tools for education about tuberculosis. The need for mass dissemination of COVID-19 information and disrupted health services brought on by lockdowns sparked wide uptake of smartphone apps and chatbots for interactive education, risk assessment, referrals, and contact tracing.² For example, HealthConnect, a set of interconnected information dissemination, case detection, and case-management services using WhatsApp enabled the Government of South Africa to reach more than 6 million people and health-care workers within the first 7 weeks of deployment. These tools are made freely available and have been customised for WHO and other countries, including Mozambique, Bangladesh, and Australia. Such digital solutions developed for COVID-19 need to be repurposed for tuberculosis. Since tuberculosis and COVID-19 will coexist, there is a huge opportunity for tuberculosis programmes and health-care providers to use these tools for information sharing and patient centred care.

Second, we advocate making tuberculosis sample collection easier and simpler. Currently, diagnosis of tuberculosis remains highly reliant on sputum, which

is difficult to collect, process, and transport, particularly from children, people living with HIV, and patients with early stage and extrapulmonary disease. COVID-19 demanded rapid and simpler testing options that led to innovation in new sample types and sample collection methods. For example, improved and affordable polyester swabs and new approaches to sampling using saliva, mouthwash, oral swabs, and absorbent strips in face masks have shown promise for COVID-19 sample collection and are now being tried for tuberculosis.^{3,4} An easy to obtain sample that also could be used to detect other pathogens (such as SARS-CoV-2) would be revolutionary for tuberculosis.

Third, we need to take tuberculosis diagnosis closer to homes. Currently, many tests are available only at the district level or higher, and this forces patients into complex, tedious pathways, with long diagnostic delays. By contrast, every country has improved access to COVID-19 testing. Decentralised testing with drive-through facilities, mobile testing sites, community health-care workers, pharmacies, schools, and workplaces have been effective and well adapted for self-sampling. Within the past 3 months, COVID-19 self-testing kits detecting SARS-CoV-2 antigen and even a single-use PCR test have obtained Emergency Use Authorisation, and other technologies, such as CRISPR, present new opportunities for rapid diagnostics.⁵ The investments in infrastructure and innovation suggest a promising future for next generation point-of-care tuberculosis tests. Although urine lipoarabinomannan antigen detection tests are rapidly evolving (with more sensitive products),⁶ tuberculosis diagnosis could be revolutionised by even simpler sampling options, such as oral swabs.

Fourth, we call for adoption of artificial intelligence imaging systems for tuberculosis and other respiratory infections. COVID-19 has sparked several innovations in artificial intelligence. For example, systems for automated interpretation of chest x-ray images with computer-aided design software. These systems have been under development for tuberculosis for a decade and were quickly reconfigured for COVID-19 within the first months of the pandemic.⁷ When combined with improved battery operated, ultra-portable, digital x-ray systems, this technology can be used throughout

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the health-care system and offer promise for high-throughput screening and integrated COVID-19 and tuberculosis testing. Cough analysers using artificial intelligence and digital stethoscopes with ambient noise cancelling are in early in development but COVID-19 has accelerated innovation that could be re-engineered for tuberculosis and other respiratory diseases.

Fifth, we propose exploiting multi-disease molecular technologies.⁸ To control COVID-19, countries have needed to scale-up their capacity to run molecular tests. In many settings, this capacity was enabled from pre-existing HIV and tuberculosis programmes that had centralised multi-disease molecular platforms (eg, HIV viral load assays) and could be expanded to meet demand.⁹ Similarly, several countries have leveraged automated, cartridge-based molecular technologies (eg, GeneXpert and TrueNAT) for tuberculosis and COVID-19. This wide use of molecular technologies and bi-directional testing will be good for tuberculosis diagnosis and will reduce the reliance on suboptimal tools, such as smear microscopy.

Finally, we believe that making data visible can benefit all disease care programmes. COVID-19 is a digitalised disease with real time data aggregation and analysis being used to visualise the pandemic and direct the public health response. By contrast, tuberculosis remains an analogue disease relying on paper-based systems and annual summary reporting. Investments in data systems, connected diagnostics, and use of crowd sourced data offers the opportunity to rethink tuberculosis surveillance and case notification. For example, location history and self-assessment data collected through the Government of India's Aarogya Setu app has been used to accurately forecast COVID-19 hotspots across the country. Vulnerability indices further offers the opportunity to deploy precise and tailored responses. Although these tools come with privacy and data security concerns that must be addressed,¹⁰ the opportunities brought on by COVID-19 big data aggregators should be applied to tuberculosis.

In conclusion, COVID-19 proves that tools and solutions can be found when there is investment and collaboration. We hope such efforts will also be made to find products and solutions for tuberculosis, an ancient disease that has caused millions of deaths. The time has come to reimagine tuberculosis care, and COVID-19 can be the blueprint.

MR and SC are employees of Foundation of Innovative New Diagnostics (FIND). MP is an advisor to FIND. FIND is a not-for-profit foundation that supports the development, evaluation, and implementation of several diagnostics, including tuberculosis and COVID-19. FIND has product evaluation agreements with several private sector companies that design diagnostics for global health. These agreements strictly define FIND's independence and neutrality regarding the companies whose products get evaluated and describe roles and responsibilities. FIND is co-convener of the Access to COVID-19 Tools Accelerator, a partnership to accelerate access to the diagnostics tools needed in the COVID-19 response.

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- 1 Pai, M. Tuberculosis and COVID-19: fighting a deadly syndemic. Sept 26, 2020. <https://www.forbes.com/sites/madhukarpai/2020/09/26/tuberculosis-and-covid-19-fighting-a-deadly-syndemic/> (accessed March 5, 2021).
- 2 Budd J, Miller BS, Manning EM, et al. Digital technologies in the public-health response to COVID-19. *Nat Med* 2020; **26**: 1183–92.
- 3 Wyllie A, Fournier J, Casanovas-Massana A, et al. Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2. *N Engl J Med* 2020; **383**: 1283–86.
- 4 Williams C, D Pan D, Decker J, et al. COVID-19: exhaled virus detected by face-mask sampling provides new links to disease severity and potential infectivity. *medRxiv* 2020; published online Aug 21. <https://www.medrxiv.org/content/10.1101/2020.08.18.20176693v1> (preprint).
- 5 Sheridan C. Coronavirus testing finally gathers speed. *Nat Biotechnol* 2020; published online Nov 5. <https://doi.org/10.1038/d41587-020-00021-z>.
- 6 Broger T, Nicol MP, Sigal GB, et al. Diagnostic accuracy of 3 urine lipoarabinomannan tuberculosis assays in HIV-negative outpatients. *J Clin Invest* 2020; **130**: 5756–64.
- 7 Qin ZZ, Naheyant T, Ruhwald M, et al. A new resource on artificial intelligence powered computer automated detection software products for tuberculosis programmes and implementers. *Tuberculosis* 2021; **127**: 102049.
- 8 MacLean E, Kohli M, Weber SF, et al. Advances in molecular diagnosis of tuberculosis. *J Clin Microbiol* 2020; **58**: e01582–19.
- 9 Venkatesan, P. COVID-19 diagnostics—not at the expense of other diseases. *Lancet Microbe* 2020; **1**: e64.
- 10 Gasser U, Ienca M, Scheibner J, Sleight J, Vayena E. Digital tools against COVID-19: taxonomy, ethical challenges, and navigation aid. *Lancet Digit Health* 2020; **2**: e425–34.

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