



Translating scientific discoveries during pandemics: ensuring equity for people affected by COVID-19 and tuberculosis

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The #COVID19 pandemic has emphasised major global health inequities: this editorial argues lessons learnt from TB must remind us of the gaps in the research agenda that must be addressed to ensure that scientific advances are equitably disseminated <https://bit.ly/3bTZHS3>

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The coronavirus SARS-CoV-2 has reached almost every corner of the globe. Trillions of dollars are being invested in the COVID-19 pandemic response to support frontline clinical and public health efforts and spur rapid advances in scientific research. Concurrently, we are in the grip of a pandemic of greater longevity that receives scant public attention despite causing 4000 deaths each day [1]. It strikes disproportionately at the poor, treatment is unsatisfactory, and there is no effective vaccine with lasting immunity. This is tuberculosis (TB), another respiratory pathogen that has much in common with COVID-19. In contrast to COVID-19, citizens of rich countries do not feel threatened by TB, which has long been associated with poverty and is therefore not a strategic priority. The rise in isolationism, nationalism, xenophobia, and racism has had negative impacts on health policy that have impaired global and national responses to TB [2]. It is against these barriers that the global response to COVID-19 has also been struggling. Worryingly, early models predict that the COVID-19 pandemic may drive an additional 6.3 million TB cases and 1.3 million deaths by 2025 [3] and early data indicate interactions between these diseases [4, 5]. Despite the political rhetoric suggesting that “we are all in this together” when it comes to COVID-19, closer inspection through the lens of TB reminds us that when it comes to benefitting from scientific advances to improve health, we are not all equal.

Rapid expansion and dissemination of COVID-19 clinical research

The number of clinical trials investigating COVID-19 registered with the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) had reached over 4800 as of 5 August, 2020 [6]. Collaboration between institutions is encouraged over competition, and ethical approval processes are taking days rather than months. Many publishing companies have made articles on COVID-19 open-access or free of charge, and the use of preprints can further improve transparency and encourage discourse between scientists and the public. These efforts prove that the research community can respond quickly and that the layers of bureaucracy normally shrouding clinical research can be reduced. Yet, there has been limited discourse about ensuring equity of access to future advances.

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Currently much of the focus of COVID-19 research is on treatment for hospitalised patients, often those in intensive care, not in the community where most COVID-19 patients are found. Exceptions include the UK PRINCIPLE (Platform randomised trial of interventions against COVID-19 in older people) trial, which seeks to evaluate treatments that could prevent hospitalisation in people over 50 years of age [7]. Lessons can be learned from the decentralisation of TB care, which seeks to promote earlier diagnosis and treatment to decrease transmission and reduce the need for hospital-based care [8]. Research focused on the development and implementation of community-based strategies, including social distancing and the use of facemasks [9], for COVID-19 prevention and mitigation is urgently needed, given that health systems in many countries have become overwhelmed to the point of collapse.

Diagnostics

In contrast to TB, there has been rapid progress to develop and obtain emergency use authorisations for COVID-19 tests. Yet, similarly to the challenges of interpreting immunological assays for latent TB infection or understanding the negative predictive value of tests such as smear microscopy or urine lipoarabinomannan for TB disease [10], COVID-19 testing has raised questions regarding the sensitivity and duration of positivity of molecular tests and the relationship between positive serological testing and lasting immunity [11]. New concepts have been proposed including “immunity passports”, which may be issued to those with detectable antibodies; however, this could negatively impact equity by creating a tiered society, and thus recommendations for serological test interpretation must be clear. While the ability to perform COVID-19 testing using the Gene Xpert platform may facilitate scale-up of COVID-19 testing in high TB incidence countries, challenges encountered during the widespread implementation of Xpert MTB/RIF including gaps in linkage to care, monopolisation by a single diagnostic platform, and reliance on donor support should inform COVID-19 testing strategies [12].

New drugs

Drug regulatory agencies such as the US Food and Drug Administration, European Medicines Agency, and UK Medicines and Healthcare products Regulatory Agency have set up COVID-19 treatment acceleration programmes to facilitate the navigation of administrative requirements and expedite review. In contrast, years of TB research underfunding have stifled TB drug development. More than 50 years elapsed between the development of the core drug regimen in the 1950s and the introduction of bedaquiline, the first new antibiotic developed to treat TB in the 21st century [13]. TB treatment has remained lengthy, complex, and toxic, particularly for people with drug-resistant TB [1].

Although regimens including new and repurposed drugs such as bedaquiline and linezolid are now recommended by the WHO, most patients who would benefit from new TB treatments are not receiving them due to prohibitive costs and delays in regulatory approvals [1, 14, 15]. Early indications that remdesivir may be effective in COVID-19 immediately highlighted similar equity concerns regarding treatment scale-up [16, 17], despite the substantial contribution of patients from low-resource settings to the clinical trials that were vital to drug development and evaluation [18]. While efforts to ramp up production were underway, Gilead donated its entire supply of remdesivir to the US government. However, the lack of transparency regarding the initial distribution of the drug within the USA received widespread criticism, particularly given its conspicuous absence in major safety net hospitals [19]. This is an important reminder that the global impact of effective new drugs will depend heavily on the speed and approach to scale-up drug production, as well as principles underpinning distribution, in the shifting landscape of heavily affected countries. Voluntary licences with generic drug manufacturers in countries like India may help. In contrast, data from the UK RECOVERY (Randomised Evaluation of COVID-19 Therapy) study indicate that a cheap and widely available drug, dexamethasone, decreases mortality in COVID-19 patients requiring respiratory support [20]. This highlights the important benefit that well-designed, timely clinical trials can provide to patients in both high- and low-income settings, if scale-up is rapid.

Vaccines

Promising early data suggest that recently developed vaccines may induce protection against SARS-CoV-2 [21]. Oxford University has formed a collaboration with AstraZeneca for global development and distribution of the University’s potential recombinant adenovirus vaccine, with both partners agreeing to operate on a not-for-profit basis during the pandemic [22]. It remains to be seen how accelerated plans for vaccine testing will be scaled up in low- and middle-income countries. We compare this to TB where there is just one vaccine in clinical use, the bacille Calmette–Guérin (BCG) vaccine, developed in the 1920s and which is of limited effectiveness, compared to the over 150 SARS-CoV-2 vaccines currently in development including 21 in clinical evaluation [23]. Shortages of the BCG vaccine continue to occur [24] and, ironically, media attention surrounding its potential role to prevent COVID-19 may further compromise

TABLE 1 Gaps in the COVID-19 research agenda informed by lessons learned from tuberculosis (TB)

Challenges shared by TB and COVID-19	Potential solutions informed by lessons learned from TB
Need for community-based strategies	Research on interventions such as social distancing and mask use
Implementation of rapid diagnostic tests Interpretation of diagnostic tests	Integrated use of test platforms such as Gene Xpert Clear communication regarding test sensitivity and interpretation of negative predictive value (for molecular tests) and positive predictive value (for serological tests)
Slow drug development, including testing in combination with other drugs Inequitable access to new drugs	Use of adaptive trial designs Principles of equity should be explicitly used to guide drug distribution
Vaccine hesitancy	Outreach to affected communities, cultural adaptation of communication strategies

supplies [25]. Vaccine implementation efforts will also need to address the vaccine hesitancy lobby, which remains resolute despite the universal risks of COVID-19 [26].

Developing an explicit agenda to address research equity

Analyses from UK data demonstrate that COVID-19 mortality is disproportionately higher in Black, Asian and Minority Ethnic groups, which is likely driven by unequal social determinants of health, including the occupational risks of serving as essential workers [27]. While urgent efforts are needed to tackle structural racism as a health issue, researchers must simultaneously ensure representation of affected communities in study populations. We know that those living near university-affiliated hospitals are more likely to be enrolled into clinical trials, leaving minorities, rural communities, and countries without links to established academic institutions at risk of being left behind [28]. The WHO has taken positive action through launching the SOLIDARITY trial which has over 90 countries participating, but more active steps to include marginalised populations are needed [29]. Successful interventions should be produced at scale and distributed according to need, not wealth.

Conclusions

The WHO's Alma-Ata declaration in 1978 stated that gross health inequalities are unacceptable. The COVID-19 pandemic emphasises the disproportionate burden of emerging threats faced by communities already suffering from major health inequities. Despite efforts by the USA to withdraw funding from the WHO, the need for a coordinated global public health response is more apparent than ever. Although COVID-19 has captured public and political attention in a way that TB has consistently failed to achieve, our experience with TB serves to remind us of the gaps in the research agenda that must be addressed to ensure that scientific advances are equitably disseminated (table 1). Unfortunately, as in TB, mistrust of governments and health systems is likely to compromise the COVID-19 response [30]. Consistent and clear scientific and political communication with the public can help to ensure the success of public health efforts. Interventions should not be executed in a one-size-fits-all manner, but should be adapted based on community needs and seek to mitigate social injustices. The response to COVID-19 has shown us that fast-track research, collaboration, data sharing, and rapid increases in funding to address global health crises are possible. We argue that these innovations must also be made available to those working to defeat TB and other public health threats, as part of long-term, sustainable strategies to ensure that all members of the global community benefit from scientific advances. This will require strong political leadership, and a commitment to the WHO's stated goal of Health for All.

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References

- 1 World Health Organization. Global Tuberculosis Report 2019. https://www.who.int/tb/publications/global_report/en/

- 2 Potter JL, Burman M, Tweed CD, *et al.* The NHS visitor and migrant cost recovery programme – a threat to health? *BMC Public Health* 2020; 20: 407.
- 3 Adams ER, Augustin Y, Byrne RL, *et al.* Rapid development of COVID-19 rapid diagnostics for low resource settings: accelerating delivery through transparency, responsiveness, and open collaboration. *medRxiv* 2020; preprint [https://doi.org/10.1101/2020.04.29.20082099].
- 4 Tadolini M, Codecasa LR, García-García J-M, *et al.* Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *Eur Respir J* 2020; 56: 2001398.
- 5 Motta I, Centis R, D'Ambrosio L, *et al.* Tuberculosis, COVID-19 and migrants: Preliminary analysis of deaths occurring in 69 patients from two cohorts. *Pulmonology* 2020; 26: 233–240.
- 6 World Health Organization. International Clinical Trials Registry Platform (ICTRP). www.who.int/ictpr/en/ Date last accessed 8 August 2020.
- 7 PRINCIPLE. PRINCIPLE trial rolled out across UK homes and communities. www.phctrials.ox.ac.uk/news/principle-trial-rolled-out-across-uk-homes-and-communities Date last accessed: 11 June 2020; date last updated: 12 May 2020.
- 8 Ndjeka N, Conradie F, Meintjes G, *et al.* Responding to SARS-CoV-2 in South Africa: What can we learn from drug-resistant tuberculosis? *Eur Respir J* 2020; 56: 2001369.
- 9 Chan TK. Universal masking for COVID-19: evidence, ethics and recommendations. *BMJ Glob Health* 2020; 5: e002819.
- 10 Huddart S, Nash M, Pai M. Tuberculosis diagnosis: Challenges and solutions. *J Health Specialties* 2016; 4: 230–237.
- 11 Weissleder R, Lee H, Ko J, *et al.* COVID-19 diagnostics in context. *Sci Transl Med* 2020; 12: eabc1931.
- 12 Albert H, Nathavitharana RR, Isaacs C, *et al.* Development, roll-out and impact of Xpert MTB/RIF for tuberculosis: what lessons have we learnt and how can we do better? *Eur Respir J* 2016; 48: 516–525.
- 13 Diacon AH, Pym A, Grobusch MP, *et al.* Multidrug-resistant tuberculosis and culture conversion with bedaquiline. *N Engl J Med* 2014; 371: 723–732.
- 14 World Health Organization. WHO consolidated guidelines on drug-resistant tuberculosis treatment 2019. www.who.int/tb/publications/2019/consolidated-guidelines-drug-resistant-TB-treatment/en/
- 15 Pai M, Furin J. Tuberculosis innovations mean little if they cannot save lives. *Elife* 2017; 6: e25956.
- 16 Grein J, Ohmagari N, Shin D, *et al.* Compassionate use of remdesivir for patients with severe Covid-19. *N Engl J Med* 2020; 382: 2327–2336.
- 17 Beigel JH, Tomashek KM, Dodd LE, *et al.* Remdesivir for the treatment of Covid-19 — Preliminary Report. *N Engl J Med* 2020; in press [https://doi.org/10.1056/NEJMoa2007764].
- 18 Mulangu S, Dodd LE, Davey RT, *et al.* A randomized, controlled trial of ebola virus disease therapeutics. *N Engl J Med* 2019; 381: 2293–2303.
- 19 Ison MG, Wolfe C, Boucher HW. Emergency use authorization of remdesivir: the need for a transparent distribution process. *JAMA* 2020; 323: 2365–2366.
- 20 Dexamethasone in hospitalized patients with Covid-19 — Preliminary Report. *N Engl J Med* 2020; in press [https://doi.org/10.1056/NEJMoa2021436].
- 21 Zhu F-C, Li Y-H, Guan X-H, *et al.* Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. *Lancet* 2020; 395: 1845–1854.
- 22 Oxford University. Oxford University announces landmark partnership with AstraZeneca for the development and potential large-scale distribution of COVID-19 vaccine candidate. www.ox.ac.uk/news/2020-04-30-oxford-university-announces-landmark-partnership-astrazeneca-development-and# Date last accessed: 3 June 2020; date last updated: 30 April 2020.
- 23 World Health Organization. Draft landscape of COVID-19 candidate vaccines. www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccine. Date last accessed: 4 August 2020; date last updated: 17 September 2020.
- 24 du Preez K, Seddon JA, Schaaf HS, *et al.* Global shortages of BCG vaccine and tuberculous meningitis in children. *Lancet Glob Health* 2019; 7: e28–e29.
- 25 Curtis N, Sparrow A, Ghebreyesus TA, *et al.* Considering BCG vaccination to reduce the impact of COVID-19. *Lancet* 2020; 395: 1545–1546.
- 26 Peretti-Watel P, Seror V, Cortaredona S, *et al.* A future vaccination campaign against COVID-19 at risk of vaccine hesitancy and politicisation. *Lancet Infect Dis* 2020; 20: 769–770.
- 27 Aldridge RW, Lewer D, Vittal Katikireddi S, *et al.* Black, Asian and Minority Ethnic groups in England are at increased risk of death from COVID-19: indirect standardisation of NHS mortality data [version 1; peer review: awaiting peer review]. *Wellcome Open Res* 2020; 5: 88 [https://doi.org/10.12688/wellcomeopenres.15922.2].
- 28 Kavanagh MM, Erondu NA, Tomori O, *et al.* Access to lifesaving medical resources for African countries: COVID-19 testing and response, ethics, and politics. *Lancet* 2020; 395: 1735–1738.
- 29 World Health Organisation. “Solidarity” clinical trial for COVID-19 treatments. www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments. Date last accessed: 5 May 2020; date last updated: 6 July 2020.
- 30 Law S, Daftary A, Mitnick CD, *et al.* Disrupting a cycle of mistrust: A constructivist grounded theory study on patient-provider trust in TB care. *Soc Sci Med* 2019; 240: 112578.