



Editorial

Impact of COVID-19 on Tuberculosis Control

Impacto de la COVID-19 en el control de la tuberculosis



The onset of the COVID-19 pandemic came through a World Health Organization (WHO) statement declaring an outbreak of pneumonia, similar to severe acute respiratory syndrome (SARS), in a population in central China.¹ What appeared to be a common outbreak of a zoonotic virus in Southeast Asia, where most outbreaks of respiratory disease originate, turned into an epidemic that triggered chaos in hospitals and primary care services until they collapsed in a matter of weeks. On March 11, the WHO declared COVID-19 as a global pandemic.² Since then, the irruption of COVID-19 has led to the suspension of routine health care services in almost every country.³ Low- and middle-income countries (LMICs) experienced substantial difficulties with interruptions in services for the three of the main health priorities, specifically HIV/AIDS, tuberculosis (TB), and malaria.⁴

TB is the most deadly infectious disease worldwide (above HIV/AIDS), with an estimated 10 million new cases and 1.5 million deaths per year.⁵ TB and COVID-19 are airborne infectious diseases that primarily attack the lungs. Both diseases have similar symptoms such as cough, fever and shortness of breath. However, testing for COVID-19 or TB should be conducted according to the clinical characteristics, history, and local burden of TB to ensure that TB patients' diagnostic needs are not neglected while testing for COVID-19.⁶ In LMICs where the burden of TB is highest, the differential diagnosis of COVID-19 and TB is key to detect the co-infection and prevent a bad evolution and even death.^{7,8} COVID-19 pandemic response, particularly containment measures, reassignment of health care personnel and equipment are affecting TB prevention and care programs.^{9–12} After the first three months of the pandemic, a survey was sent to 165 countries, of which 42% reported partial disruptions in TB case detection and treatment.³ A study conducted in 33 centres in 16 countries on five continents reported that during confinement 82% of centres showed reductions in TB-associated hospital discharges, 84% of centres reported a decrease in newly diagnosed active TB cases, 95% showed a decrease newly LTBI outpatient visits, and 75% and 81% of centres showed reductions in TB and LTBI outpatient visits, respectively.¹³ Estimates of the impact of the COVID-19 pandemic on the TB response suggest that a 3-month lockdown and a 10-month protracted recovery could result in 6.3 million additional TB cases between 2020 and 2025, and 1.4 million additional TB deaths during this time. These numbers would imply a regression of at least 5–8 years in the fight against TB.⁶ Over the last few months, an impressive number of molecular assays ($n = 378$) and immunoassays ($n = 444$) have

emerged for the diagnosis of COVID-19.¹⁴ Most of them have taken advantage of existing technologies to develop COVID-19 diagnostics. Among which is the Xpert® Xpress SARS-CoV-2 test for use in GeneXpert® devices.⁶ Due to the health emergency, countries with fewer resources have experienced the shared use of GeneXpert for COVID-19 and TB.¹⁵ The diversion of attention and resources away from TB could have a devastating effect on the diagnosis and treatment of the disease, especially in LMICs.⁵ A 25% reduction in global TB detection over three months is predicted to lead to a 13% increase in TB deaths, bringing us back to the TB mortality figures reported in 2015.

Pulmonology, infectious medicine, and microbiology services have been overwhelmed by the pandemic. All resources have been devoted to the fight against COVID-19, leading to the paralysis of most of the TB screening programs in public dining rooms, shelters, and drug cessation centres. This fact, associated with the difficulty of patients to access primary care, has reduced the number of TB cases diagnosed since the beginning of the pandemic. Economic and social problems arising from the pandemic suggest an increase in the delay of diagnosis and the severity of cases being diagnosed. However, containment and the use of personal protective equipment could have had a positive impact on TB control by helping to mitigate community transmission of the disease. Thus, the reduction of mass gatherings in spaces such as buses, trains, cinemas, or sports events, as well as the intensive use of masks, may have contributed to reducing the risk of TB transmission during the pandemic and after confinement. It would be interesting to include these variables in predictive analyses in order to know the long-term effect these measures could have on TB control.

COVID-19 could have a severe impact on case detection and treatment success.¹¹ However, TB may contribute to the control of COVID-19 with lessons learned and possible direction for future COVID-19 preventive treatment strategies. Thus, public health strategies employed in TB programs could serve as examples to identify and mitigate potential risks of SARS-CoV-2 infection.¹⁵ Taking TB as precedent, contact studies developed by TB prevention and control services have been applied to identify contacts of patients infected with SARS-CoV-2.¹⁶ *Bacille de Calmette et Guérin* (BCG) has been the vaccine against TB for almost one hundred years. However, BCG has also demonstrated a protective effect on the immune system that reduces overall mortality during the first few years of life by improving responses to other respiratory infections such as respiratory viruses.¹⁷ This evidence has led to clinical tri-

als to assess whether BCG would be able to provide non-specific protection to mitigate the outbreak before a specific COVID-19 vaccine is developed.¹⁸ However, until these trials are completed, continued routine use of the vaccine exclusively for TB is strongly recommended so as not to jeopardise the necessary supply of BCG to protect children against TB in high-incidence areas.¹⁹

The pandemic has altered sustainable development goals into a challenge for humanity in the coming years. Global support should be provided to enable the countries and communities most affected by TB to respond to the pandemic while ensuring the maintenance of TB services. The pandemic response should be integrated into existing disease workflows to create synergies and strengthen health systems in a transversal approach. Over the next few years, we must promote bi-directional screening, multi-pathogen tests, and work using connectivity solutions for TB/COVID-19 surveillance.

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References

1. Wang R, Zhang X, Irwin DM, Shen Y. Emergence of SARS-like coronavirus poses new challenge in China. *J Infect.* 2020;80:350–71, <http://dx.doi.org/10.1016/j.jinf.2020.01.014>.
2. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19-11; 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020> [accessed 8.10.20].
3. World Health Organization. Pulse survey on continuity of essential health services during the COVID-19 pandemic: interim report, 27 August 2020; 2020. <https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS-continuity-survey-2020.1> [accessed 8.10.20].
4. The Global Fund. Mitigating the Impact of Covid-19 on Countries Affected by HIV Tuberculosis, and Malaria; 2020. https://www.theglobalfund.org/media/9819/covid19_mitigatingimpact_report_en.pdf [accessed 8.10.20].
5. World Health Organization. Global tuberculosis report; 2019. <https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf> [accessed 8.10.20].
6. World Health Organization. Tuberculosis and COVID-19: Considerations for tuberculosis care; 2020. <https://www.who.int/docs/default-source/documents/tuberculosis/infonote-tb-covid-19.pdf> [accessed 8.10.20].
7. Motta I, Centis R, D'Ambrosio L, García-García JM, Goletti D, Gualano G, et al. Tuberculosis COVID-19 and migrants: Preliminary analysis of deaths occurring in 69 patients from two cohorts. *Pulmonology.* 2020;26:233–40, <http://dx.doi.org/10.1016/j.pulmoe.2020.05.002>.
8. Tadolini M, Codecasa LR, García-García JM, Blanc FX, Borisov S, Alffenaar JW, et al. Active tuberculosis, sequelae and COVID-19 co-infection: First cohort of 49 cases. *Eur Respir J.* 2020;56:2001398, <http://dx.doi.org/10.1183/13993003.01398-2020>.
9. Buonsenso D, Iodice F, Sorba Biala J, Goletti D. COVID-19 effects on tuberculosis care in Sierra Leone. *Pulmonology.* 2020, <http://dx.doi.org/10.1016/j.pulmoe.2020.05.013>.
10. Magro P, Formenti B, Marchese V, Gulletta M, Tomasoni LR, Caligaris S, et al. Impact of the SARS Coronavirus 2 epidemic on tuberculosis treatment outcome, Northern Italy. *Eur Respir J.* 2020;56:2002665, <http://dx.doi.org/10.1183/13993003.02665-2020>.
11. Finn McQuaid C, McCreesh N, Read JM, Sumner T, Houben RMGJ, White RG, et al. The potential impact of COVID-19-related disruption on tuberculosis burden. *Eur Respir J.* 2020;56:2001718, <http://dx.doi.org/10.1183/13993003.01718-2020>.
12. Cronin AM, Railey S, Fortune D, Wegener DH, Davis JB. Notes from the field: effects of the COVID-19 response on tuberculosis prevention and control efforts—United States March–April 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:971–2, <http://dx.doi.org/10.15585/mmwr.mm6929a4>.
13. Migliori GB, Thong PM, Akkerman O, Alffenaar JW, Álvarez-Navascués F, Assao-Neino MM, et al. Worldwide effects of coronavirus disease pandemic on tuberculosis services January–April 2020. *Emerg Infect Dis.* 2020;26:2709–12.
14. FIND. SARS-CoV-2 diagnostic pipeline; 2020. <https://www.finddx.org/covid-19/pipeline/?section=show-all#diag-tab> [accessed 8.10.20].
15. 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;19:1–6, <http://dx.doi.org/10.1186/s12941-020-00363-1>.
16. Bellmunt JM, Caylà JA, Millet JP. Contact tracing in patients infected with SARS-CoV-2 The fundamental role of Primary Health Care and Public Health. *Semerger.* 2020;46:55–64, <http://dx.doi.org/10.1016/j.semerg.2020.06.001>.
17. Kandasamy R, Voysey M, McQuaid F, De Nie K, Ryan R, Orr O, et al. Non-specific immunological effects of selected routine childhood immunisations: systematic review. *BMJ.* 2016;355:i5225, <http://dx.doi.org/10.1136/bmj.i5225>.
18. Curtis N, Sparrow A, Ghebreyesus TA, Netea MG. Considering BCG vaccination to reduce the impact of COVID-19. *Lancet.* 2020;395:1545–6, [http://dx.doi.org/10.1016/S0140-6736\(20\)31025-4](http://dx.doi.org/10.1016/S0140-6736(20)31025-4).
19. World Health Organization. Bacille Calmette-Guérin (BCG) vaccination and COVID-19; 2020. [https://www.who.int/publications/i/item/bacille-calmette-gu%C3%A9rin-\(bcg\)-vaccination-and-covid-19](https://www.who.int/publications/i/item/bacille-calmette-gu%C3%A9rin-(bcg)-vaccination-and-covid-19) [accessed 8.10.20].

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