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LETTER

How TB and COVID-19 compare: an opportunity to integrate both control programmes

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Dear Editor,

With attention focused on the COVID-19 response, there has been an impact on TB diagnosis and care.[1–3] The COVID-19 pandemic is threatening efforts to control TB, and as a direct consequence the WHO has estimated that (with a 3-month lockdown plus a 10-month recovery period) 6.3 million additional new TB cases and an additional 1.4 million TB deaths will be registered between 2020 and 2025.[1–3] In Ecuador, TB services have also been obstructed and personal communications with hospitals show a more than 90% reduction in the processing of clinical samples for TB diagnosis. Since the lockdown in March 2020, the Eugenio Espejo Hospital (in Quito, the capital city) is processing only 10 clinical samples per month, down from 250 samples per month. Other cities in Ecuador, hospitals in Azogues, Cuenca and El Oro, report a similar reduction of about 90% (personal communication NM, NG, MET, AA). This is not only a problem in Ecuador. In Venezuela, there is a >90% decrease in the number of samples processed for TB diagnosis in the second quarter of 2020 (personal communication, JHdW);

and in Sierra Leone, Africa, a drop of 75% in confirmed and suspected cases of TB was reported in April 2020 after lockdown was declared by the government.[4]

In our opinion, we have to address both COVID-19 and TB if we are to guarantee an effective response to COVID-19 while ensuring that TB services are maintained. Considering the many overlaps between TB and COVID-19 in disease presentation, transmission and control strategy, the integration of both programmes could be key to making this happen. Moreover, co-infection of both diseases has been reported; clinical experience with concomitant TB and COVID-19 is extremely limited,[5] and high case-fatality rates have been reported.[6]

Integration of both programmes should be relatively easy. The COVID-19 control programme is based on the same strategy as the TB control programme, i.e., early detection of an infectious case, infection prevention and contact tracing. Both diseases have many clinical and epidemiological characteristics in common.[7] Both primarily attack the lungs and diseased patients show similar clinical symptoms, such as a cough, fever and shortness of breath.[1,2,7] Both diseases are transmitted by respiratory aerosols or droplets and spread from person to person through the air via close contact. Both also share the same drivers for transmission: crowding and social mixing. Underlying conditions or risk factors for poor outcomes in either disease include diabetes, immune suppression, old age and COPD (see Table). COVID-19 and TB in Ecuador also affect more men than women (55% and 58%, respectively) and there is an important similarity in the geographical distribution of reported TB cases and COVID-19 cases (Figure). The coastal region—in particular Ecuador's largest city, Guayaquil—has registered the highest number of TB and COVID-19 cases (80% and 82% of the case load, respectively), followed by the Andean Region, including the capital Quito (16% and 17%, respectively).[8,9] In other words, where COVID-19 cases are diagnosed, we are also likely to find most of the TB cases (see Figure).

A serious problem for the integration of a control programme for both diseases is the diversion of health service funding solely towards COVID-19 diagnosis and control. Both financial and workforce resources should instead work together to provide services for both conditions. TB control already has an established infrastructure and a laboratory network in Ecuador that can be used to support the COVID-19 response, while also continuing to respond to TB. With regard to diagnosis, testing facilities can be shared and TB laboratory staff could participate in COVID-19 diagnosis. TB laboratories are used to working with a dangerous infectious disease and in general have safety measurements in place to avoid infection by aerosol-generating activities. In Ecuador, TB laboratories that culture *Mycobacterium tuberculosis* are Biosafety Level 2 laboratories equipped with a biosafety cabinet as

recommended by the WHO, which are also suitable for diagnosing COVID-19.[10,11] However, direct sputum smear microscopy for TB (the diagnostic technique used in type 1 hospitals in Ecuador) is considered a low-risk process and can be performed in a well-ventilated laboratory without a biosafety cabinet. However, as sputum samples of TB patients and COVID-19 patients may mix in the TB laboratory, such samples should be processed in a safety cabinet.[11] Therefore, future investment in safety features for laboratories equipped for COVID-19 diagnosis should also take into account these "ventilated" TB laboratories. Providing a safety cabinet will establish a safe working environment for COVID-19 samples, and also enable the future processing of sputum samples for the culture of *M. tuberculosis*. Also, equipment for the diagnosis of both diseases can be shared and investments in new equipment for COVID-19 diagnosis should be made in a way that ensures their continued usefulness for TB diagnosis. An example is GeneXpert (Cepheid, Sunnyvale, CA, USA), which provides real-time data collection for drug-resistant TB testing and which can be used to test for both TB and COVID-19.[12] Laboratories that will be equipped for COVID-19 diagnosis should consider this equipment instead of a real-time quantitative polymerase chain reaction (PCR) apparatus. Sample preparation is straight forward and GeneXpert can report a result within 30 minutes, without the need for a separate RNA isolation step. Real-time PCR diagnosis of COVID-19 requires the isolation of RNA from the patient sample, which is technically demanding and requires trained personnel (not readily available in a rural setting), and which adds additional cost to the diagnosis.

With regard to patient care, TB doctors and nurses should be trained in COVID-19 diagnosis and management and control as patients will mix.[3,7] TB specialists and health workers at the primary health care level may be points of reference for patients with pulmonary complications from COVID-19.[3,7] Doctors evaluating COVID-19 suspects should implement TB orientated testing algorithms, and COVID-19-negative patients with clinical manifestations and/or risk factors for TB should be followed up by TB testing. Chest X-rays used to distinguish pneumonia from COVID-19 should also be evaluated for the presence of lesions typical for TB. SARS-COV-2 infection may mask radiological manifestations of TB.

The community also has a role to play, and community-wide education may encourage TB testing in case of a negative COVID-19 result. The community should be made aware of the differences between the two diseases but also the similarities. Although the sample types being collected for TB and COVID-19 are different (sputum vs. nasal swabs), research has shown that both diseases can be tested for with one sample type. Saliva and sputum have been shown to be equivalent,[13] and in some studies superior,[14] to nasal swabs in the detection of

SARS-COV-2 and could thus be used for both TB and COVID-19 diagnosis. National reference laboratories and providers of commercial diagnostic tests should validate saliva and sputum samples and authorise the use of these samples for COVID-19 and TB diagnosis.

Last but not least, measles, pneumococcal disease and other respiratory pathogens can also present with similar symptoms and should be tested where relevant (and before de-isolation of patients) to avoid the risk transmission of these other communicable diseases.[15]

Integrating TB and COVID diagnosis can help to overcome the decrease in registered TB cases. The COVID-19 pandemic has created an opportunity for case finding for both diseases at the same time.[12,14] The integration of control programmes for HIV and TB have been successfully established and newly diagnosed TB patients in Ecuador are always tested for HIV before starting on TB treatment. The same integrated approach could be used for COVID-19 and TB. COVID-19 appears to be here to stay – at least for the near future. We should not forget TB is a major infectious and deadly disease in low- to middle-income countries. By integrating funding, the control programmes for both diseases and raising awareness at all levels of health care, we can contain both.

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Table Similarities and differences between COVID-19 and TB.

Similarities between COVID-19 and TB	Differences between COVID-19 and TB
• Both are respiratory infections • They share two important main symptoms: fever and a (dry) cough and attack the lung • They share the same transmission drivers: social mixing and indoor overcrowding • They share the same control strategy (see text) • Chest X-ray may be required to further refine the diagnosis • Wearing a mask provides a barrier to prevent the spread • Associated comorbidity, like diabetes, chronic obstructive pulmonary disease and immunosuppression • Diagnostic activities should be carried out in a biosafety cabinet under at least BSL-2 • More severe with higher age • Both predominantly affect males‡ • Both diseases share the same geographical regions‡ • Protection through BCG vaccination?§ • Disease associated stigma	• Viral versus bacterial infection • Transmission through droplets vs. aerosols?* • Acute versus chronic disease. • A short vs. long period of pre-incubation before disease development. • Temporary colonisation vs. life-long latent infection • Infection rate (R_0) 3–5 vs. 2–10 • Sample for diagnosis: nasopharyngeal swab vs. sputum sample • TB is treatable and curable; for COVID-19 treatment is under definition • In Ecuador, the mortality rate for COVID-19 is estimated at 8.3%† and TB is 3% (2018) • Biosafety: COVID-19 diagnosis and TB diagnosis by culture: a BSL-2 laboratory with a biosafety cabinet; direct sputum smear microscopy for TB is considered a low-risk process that can be done in a well-ventilated laboratory • The pace and intensity of the global response

*See discussion in Liu Y, Ning Z, Chen Y, et al. Aerodynamic analysis of COVID-19 in two Wuhan hospitals. Nature 2020; https://doi.org/10.1038/s41586-020-2271-3. †The mortality rate of COVID-19 depends on the attack rate of the virus, which is still unknown. Serology studies in the future will determine the real attack rate of COVID-19. The mortality rate for Ecuador is based on data for 16 May 2020 when 32,763 cases and 2,688 deaths were registered for COVID-19 infection. ‡In Ecuador. See the text of this report for details. §BCG protection for COVID-19 disease is still under investigation and clinical trials are underway. See: https://clinicaltrials.gov/ct2/show/NCT04327206. Moreover, BCG protection against TB varies considerable by country and by disease manifestation.

Figure. Distribution of the registered cases of COVID-19 (April and May 2020) vs. registered TB cases (in the year 2018) according to the main geographic regions of Ecuador.