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TB and COVID-19 co-infection: rationale and aims of a global study

Dear Editor,

The potential impact of COVID-19 on TB patients and services continues to generate significant attention.^{1–4} Although several concerns have been raised, scientific evidence remains modest. As COVID-19 is a new disease, more time is needed to collect quality-assured scientific data.^{3–5}

A recent study on the global impact of COVID-19 on TB services has highlighted a reduction in TB disease and infection diagnosis in different countries and settings.² A Chinese study (based on 10 cases) estimated a prevalence of TB in COVID-19 patients of 0.5% to 4.5%.⁶ A study from the Western Cape in South Africa showed that both current and previous TB were associated with COVID-19 deaths with an adjusted hazard ratio of 2.70 and 1.51, respectively.⁷ A modelling study from the Philippines showed that the risk of death in COVID-19 patients with TB was 2.17 times higher than in non-TB patients, and that the likelihood of recovery was 25% less with a longer time to recovery.⁸

The GTN (Global Tuberculosis Network) has described the first cohort of patients ($n=49$) with TB or previous TB and co-infected with SARS-CoV-2 from eight countries, including Belgium; Brazil (Rio Grande do Sul State); France; Italy; Russia (Moscow Region); Singapore; Spain; and Switzerland (Vaud Canton).⁹ This showed that COVID-19 is usually diagnosed after previous TB ($n = 26$, 53.0%), although 14 patients had COVID-19 diagnosed before TB ($n = 14$, 28.5%), and 9 (18.3%) within the same week; 42 (85.7%) patients were under treatment for active TB, while 7 (14.3%) were suffering from post-treatment TB sequelae.⁹ Combining the data from this cohort with those of a second cohort of young migrants admitted to a reference hospital in Northern Italy¹⁰ revealed an overall case fatality rate of 8/69 (11.6%), comprising a case-fatality rate of 14.7% (7/49) in Tadolini et al.'s study⁹ and 5% (1/20) in the study on young migrants without any comorbidities.¹¹ The available evidence raises many questions for TB and COVID-19 co-infection, including the following: 1) Does COVID-19 increase the risk of TB reactivation? 2) What risk on TB mortality can be attributed to COVID-19? 3) What are the other determinants of mortality in patients co-infected with TB and COVID-19? 4) Is BCG vaccination protective? 5)

Do patients co-infected with TB and COVID-19 require different management? If yes, what type of management? 6) What impact will COVID-19 have on TB services over the coming years? 7) Are patients with post-TB sequelae at a higher risk of acquiring COVID-19?^{11–14}

To address these questions, the GTN, in collaboration with partners and national TB programmes, and with support from the WHO, have launched a global study: “Clinical course and outcomes of people with COVID-19 and TB: a multi-centre cohort study”. The aim of this Letter is to present the aims, study design and expected results of the call for a global effort on this important topic. This project will describe the characteristics of and outcomes in COVID-19 patients with concurrent or past TB based on an anonymised, prospective, non-interventional study whose features are similar to those of previously published collaborative studies.^{9,11} The primary objective of the study is to describe the characteristics of patients with COVID-19 and TB (current or past), including diagnostic tests and prescribed therapies. Secondary objectives are 1) to examine the logistic and organisational feasibility of creating a global repository for patients with COVID-19 and TB; and 2) to describe the clinical outcomes (outcomes of COVID-19 disease, and interim and final treatment outcomes of TB patients and survivors).

The study population consists of all consecutively diagnosed and registered TB patients with COVID-19 (concomitant and non-concomitant), including paediatric cases, with no specific exclusion criteria. All clinical centres, organisations and/or national programmes willing and able to participate in this project will be included. We will collect basic demographic, epidemiological, microbiological and clinical information (including outcomes) on TB and COVID-19 patients during the study period (1 June 2020 onwards). The coordinating centre has received approval from an ethical committee to conduct an anonymised, non-interventional, multi-centre study on TB and COVID-19. Each participating centre has submitted a request for local ethical approval according to national/local regulations on personal data protection.

As of 13 October 2020, 132 centres from 36 countries/regions joined the global study (see Figure). Data covering 597 individual patients have already been provided by 27 countries/regions, and three

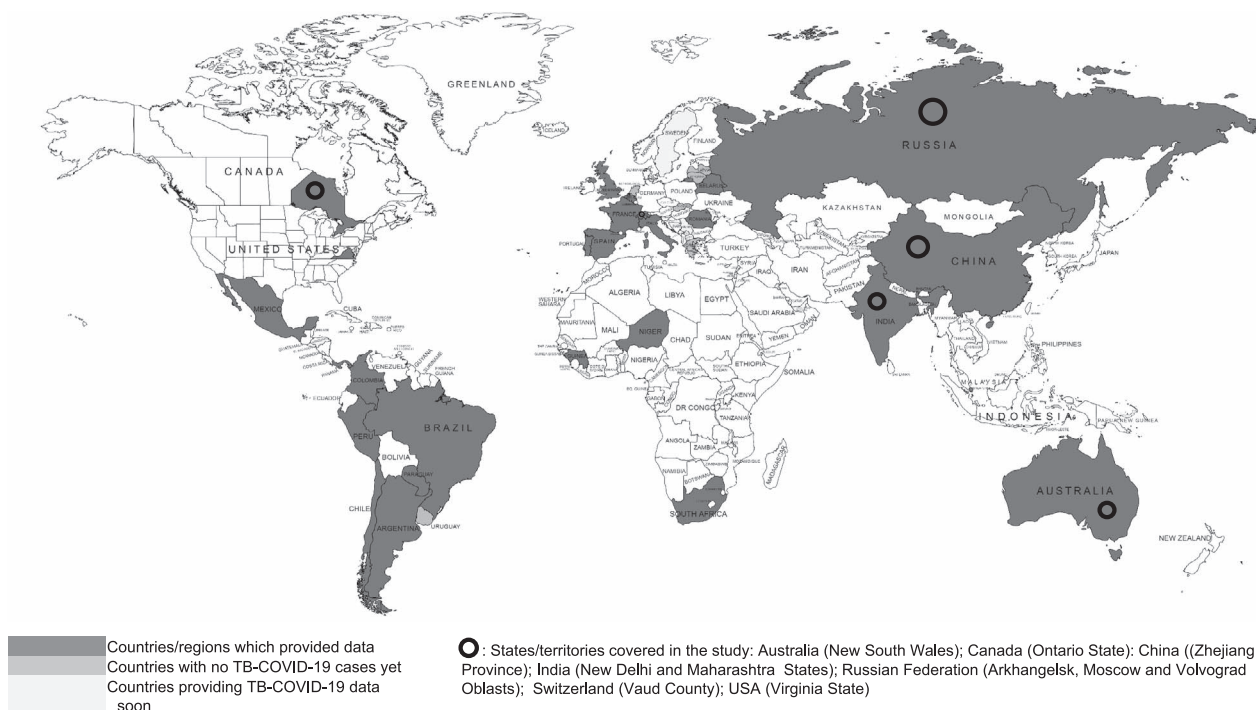


Figure Global distribution of the countries/regions participating in the study. Slate grey = countries/regions which provided data; dark grey = countries with no TB-COVID-19 cases yet; light grey = countries providing TB-COVID-19 data soon; O = states/territories covered in the study: Australia (New South Wales); Canada (Ontario State); China (Zhejiang Province); India (states of New Delhi and Maharashtra); Russian Federation (Arkhangelsk, Moscow and Volgograd Oblasts); Switzerland (Vaud Canton); USA (Virginia State).

countries have committed to provide data soon. To date, six countries have not reported any cases of TB and COVID-19 (Greece, Latvia, Lithuania, the Netherlands, Slovakia, Uruguay). The data verification process is ongoing. As the study is in progress, patient enrolment and analysis of follow-up data are planned at the end of the patients' TB treatment. We invite clinicians and programme officers interested in participating to contact the corresponding author and support our efforts in better understanding how to prevent and manage this double curse.

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Conflicts of interest: none declared.

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