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subsequently progress to tuberculosis disease.[3] In another publication, we used Bayesian latent class analysis of the combination test results to estimate performance characteristics of the three different tests for latent tuberculosis infection.[3] We used published data on contacts with known tuberculosis exposure, test results, and subsequent progression to disease as initial estimates and refined them with the Bayesian analysis. Among those born outside the USA with a history of BCG vaccination, the TST had the lowest modelled specificity of 70% for latent tuberculosis infection. The TST modelled specificity for latent tuberculosis infection was 92% among US-born individuals who did not have HIV infection. Thus, the interpretation of test results needs to account for test sensitivity and specificity as affected by an individual's previous exposure to tuberculosis cross-reacting antigens and the strength of their underlying immune response. In people who are not contacts with known tuberculosis exposure but originate from countries with high tuberculosis rates and high BCG vaccination, IFNγ release assays offer a distinct advantage over TST.

Moreover, we agree with Arend and Uzorka's statement that the risk of progression to tuberculosis is very low among those with negative IFNγ release assay results if they are immunocompetent.

We declare no competing interests.

Published by Elsevier Ltd.

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Has the COVID-19 pandemic increased tuberculosis mortality?

In October, 2021, WHO estimated that—because of the COVID-19 pandemic—global deaths from tuberculosis had increased for the first time in a decade.[1] This estimate of increased mortality has been widely interpreted as an objective fact.[2] But it is important to point out a footnote published with these estimates: "To estimate the impact [of COVID-19 on tuberculosis]…models were developed for…16 countries…and a statistical model was used to extrapolate results to other low- and middle-income countries. The most important assumption was that reductions in notifications of people diagnosed with tuberculosis reflected real reductions in the number of people with tuberculosis who accessed treatment".

In other words, if reductions in tuberculosis notifications were fully driven by reduced health-care access, then tuberculosis mortality has increased during the pandemic. But if lower notifications also (even partly) reflect reductions in transmission of *Mycobacterium tuberculosis*, it is possible that the effect of the pandemic on tuberculosis mortality has been overestimated. A separate model found that if lockdowns and other measures substantially reduced *M tuberculosis* transmission, overall tuberculosis incidence (if not mortality) could fall as a result of the pandemic.[3] Furthermore, although pandemic-related restrictions are unlikely to have reduced household transmission, most *M tuberculosis* transmission in high-burden settings probably occurs outside the household.[4] Additionally, there is indirect evidence that pandemic measures reduced respiratory contact rates, as the incidence of influenza[5] and other respiratory viral illnesses plummeted in 2020. Thus, it is at least a reasonable possibility that measures taken in response to the COVID-19 pandemic—through policy or behaviour change—had a salutary effect on transmission of *M tuberculosis*.

In summary, there can be no question that the COVID-19 pandemic has devastated global systems for tuberculosis control. But in doing so, it is possible that the pandemic has also dealt a blow to transmission of the pathogen. As such, although it is likely (if not proven) that the COVID-19 pandemic has substantially increased tuberculosis mortality, it is also possible that tuberculosis incidence has genuinely declined. If we can move urgently to strengthen systems for finding, treating, and preventing tuberculosis, it is possible that global targets for ending tuberculosis are more achievable than ever before. But if we fail to act on tuberculosis in 2022, it seems almost certain that increases in mortality will be transformed from modelled estimates to reality.

I declare no competing interests. This letter was written with support from a Catalyst Award from Johns Hopkins University.

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Implications of bedaquiline-resistant tuberculosis

Nazir Ahmed Ismail and colleagues[1] have published their groundbreaking research on the epidemiological and genetic aspects of bedaquiline resistance and the clinical outcomes in patients with rifampicin-resistant tuberculosis. Ismail and colleagues concluded that bedaquiline resistance was associated with poorer treatment outcomes. The authors also identified the *Rv0678* mutation as related to bedaquiline resistance and linked with possible bedaquiline and clofazimine cross-resistance.[1]

The WHO classification of drugs used to treat multidrug-resistant and rifampicin-resistant tuberculosis lists bedaquiline as a group A drug and clofazimine as a group B drug. Additionally, WHO has recently redefined extensively drug-resistant tuberculosis as tuberculosis caused by a *Mycobacterium tuberculosis* strain that fulfils the definition of multidrug-resistant or rifampicin-resistant tuberculosis (ie, strains that are resistant to both rifampicin and isoniazid or rifampicin alone) and that is also resistant to any fluoroquinolone and at least one additional group A drug.[2] Thus, bedaquiline resistance or clofazimine resistance (increasing the risk of bedaquiline resistance through cross-resistance) places patients with tuberculosis at a higher risk of developing extensively drug-resistant tuberculosis. As per the current WHO recommendations, bedaquiline and clofazimine are essential components of all the shorter and longer regimens for treating multidrug-resistant and rifampicin-resistant tuberculosis.[3] The novel and shorter bedaquiline, pretomanid, and linezolid regimen has been shown to have more favourable treatment outcomes in patients with drug-resistant tuberculosis in the Nix-TB and ZeNix trials than the second-line injectable-based shorter regimen for treating multidrug-resistant and rifampicin-resistant tuberculosis that was previously recommended by WHO.[4]

However, the speed with which national programmes, including the Indian national tuberculosis elimination programme, are implementing bedaquiline-based or clofazimine-based regimens is not reflected in the pace of capacity building for rapid diagnostic tools for detecting drug resistance. This capacity building process is important since none of the regimens has a 100% success rate in treating patients with drug-resistant tuberculosis, and some patients are expected to have unfavourable treatment outcomes due to factors such as extensive disease, adverse drug reactions, and loss to follow-up. With the increased exposure of these medications to patients in all prescribed multidrug-resistant and rifampicin-resistant tuberculosis treatment regimens, resistance might increase in the population. In the absence of the availability of rapid tools to diagnose resistance to important second-line drugs, such resistance would be catastrophic, especially for the programmatic management of drug-resistant tuberculosis that is difficult to treat. For drug sensitivity testing, WHO currently recommends the traditional and time-consuming culture-based phenotypic bedaquiline drug sensitivity testing, which is not commonly available in the field. The development of rapid molecular diagnostic methods that can detect resistance to at least all medicines from group A (ie, levofloxacin, moxifloxacin, bedaquiline, and linezolid) is urgently needed. At the start of treatment, the availability of whole-genome sequencing for all patients with confirmed tuberculosis would be ideal. The *Rv0678* mutation seems to be an appealing target for developing rapid diagnostic tools for bedaquiline resistance.

National tuberculosis programmes across the globe need to develop and scale-up facilities for rapid diagnostic techniques for detecting drug resistance to important second-line anti-tuberculosis drugs, including bedaquiline, in a similar manner in which they are accepting the WHO-recommended bedaquiline-based treatment regimens for multidrug-resistant tuberculosis.

We declare no competing interests.

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Nazir Ahmed Ismail and colleagues show a 3·8% baseline resistance to bedaquiline in patients with rifampicin-resistant tuberculosis and 2·3% prevalence of acquired resistance to bedaquiline during treatment with the currently recommended all-oral treatment regimen.[1] Treatment