

The Impacts of the COVID-19 Pandemic on Tuberculosis

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Introduction

Prior to the onset of the SARS-CoV-2 pandemic in 2020, *Mycobacterium tuberculosis* (Mtb) – the causative agent of tuberculosis – was the leading cause of death due to an infectious disease. In 2019, Mtb killed 1.4 million people and approximately 10 million people contracted the disease. Mtb is a bacteria primarily transmitted by aerosol or droplet, and like COVID-19, can be transmitted when a person with an active Mtb infection coughs. Several health conditions put an individual at higher risk of contracting Mtb, including malnutrition, HIV/AIDS, and diabetes. The disease exists in two forms: an active form capable of being transmitted to others, and a latent form in which the patient is asymptomatic and cannot spread Mtb. Between the two forms, it is estimated that nearly a quarter of the world's population is infected with Mtb. Most of those infections occur in low- to middle-income countries with limited resources.

SARS-CoV-2 has upended daily life globally and has impacted all aspects of tuberculosis. Supply chain disruptions and the diversion of healthcare resources to the COVID-19 response have made detection and diagnosis of Mtb more difficult. Similarly, SARS-CoV-2 has hampered the months-long treatment regimen of tuberculosis in patients as well as caused disruptions to critical clinical trials and research. These impacts have been witnessed first-hand via the National Institutes of Health (NIH-DAIDS) *Mycobacterium tuberculosis* Quality Assessment (TBQA) Program at MRIGlobal (contract number HHSN272201700001C). Here, we present a status update on tuberculosis in 2022 and discuss ongoing impacts on healthcare capacity, detection, treatment, antimicrobial resistance, and SARS-CoV-2 co-infection. The far-reaching effects of SARS-CoV-2 on Mtb mitigation efforts highlight the need for novel strategies to prevent future disruptions.

Progress against Mtb before COVID-19

Tuberculosis elimination is a top priority for the World Health Organization (WHO) and its partners. As the leading cause of death due to an infectious agent until 2020, Mtb has been heavily targeted by public health strategies. In the United States, the incidence of Mtb steadily declined from 1982 until the start of the COVID-19 pandemic (Figure 1).¹ Rates of infection for Mtb dropped dramatically in 2020, but the drop is attributed to multiple factors (service disruptions, failure to seek care, isolation from the community) and is not a true reduction in incidence.² This assumption is supported by Mtb mortality rates in 2020, which indicate an increase in deaths due to Mtb for the first time in 15 years.³

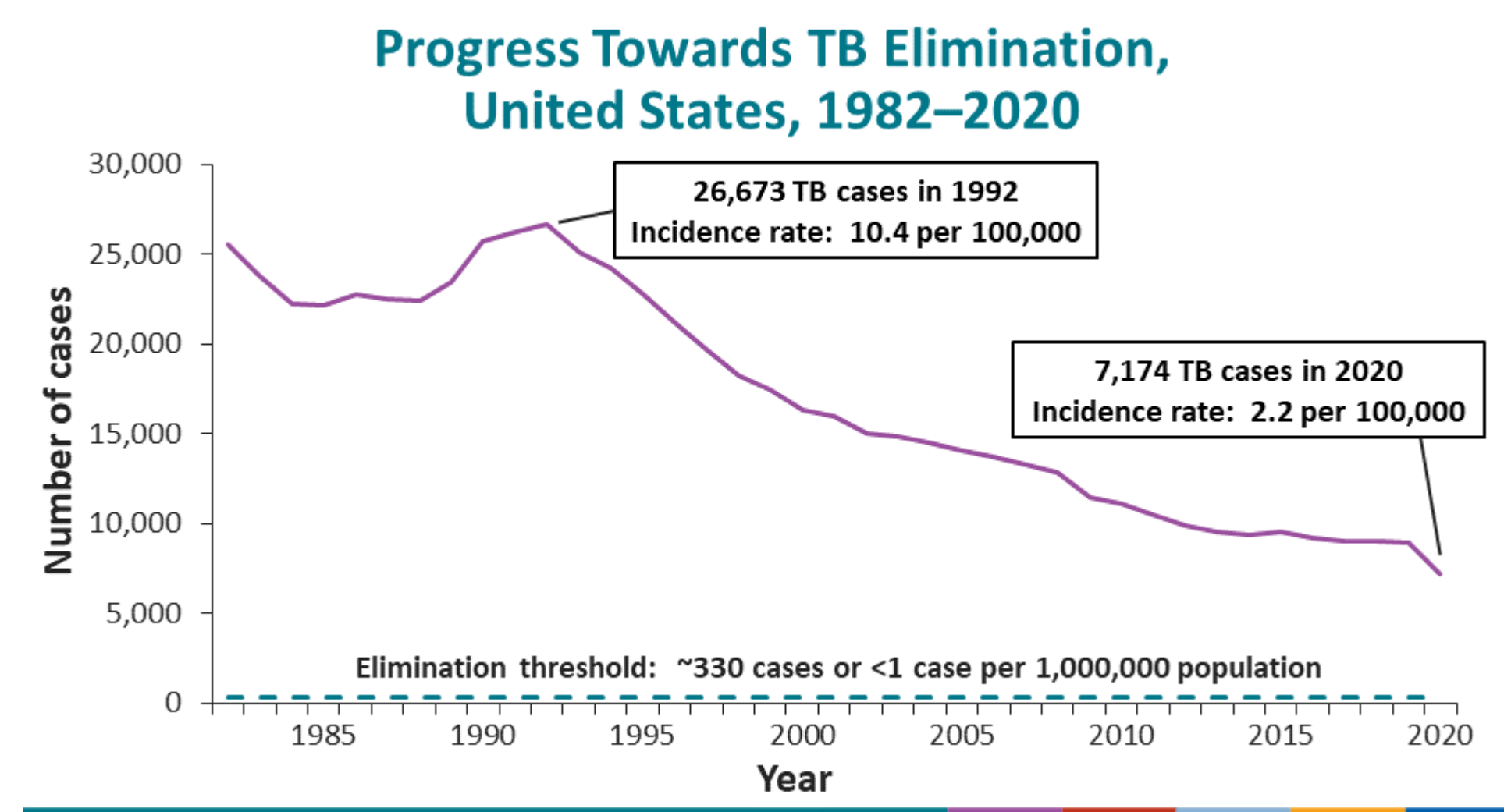


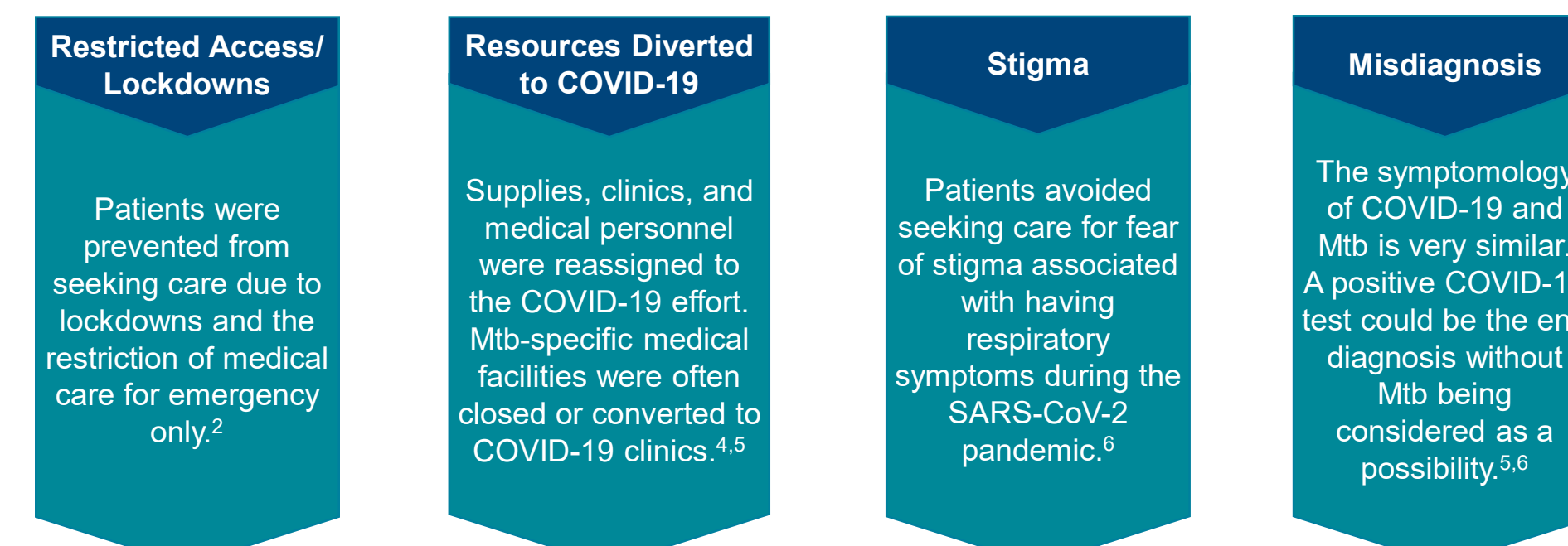
Figure 1: Mtb incidence rate over time in the US, from 1982-2020 (CDC.gov)¹

Key Components of Mtb Control Efforts

Early Diagnosis	Patient receives care before disease becomes more complicated
Contact Tracing	Close contacts are identified and tested to prevent further spread
Therapeutic Intervention	Combinations of multiple antibiotics are administered for a long duration (typically, 6-24 months) for active Mtb, often with side effects. Latent Mtb can be treated with a single antibiotic before developing into active Mtb
Mtb-Specific Resources	Support is provided through specialized medical staff and clinics. Directly-Observed-Therapy (DOT) monitors patients for medication compliance

Impact on Diagnosis of Mtb

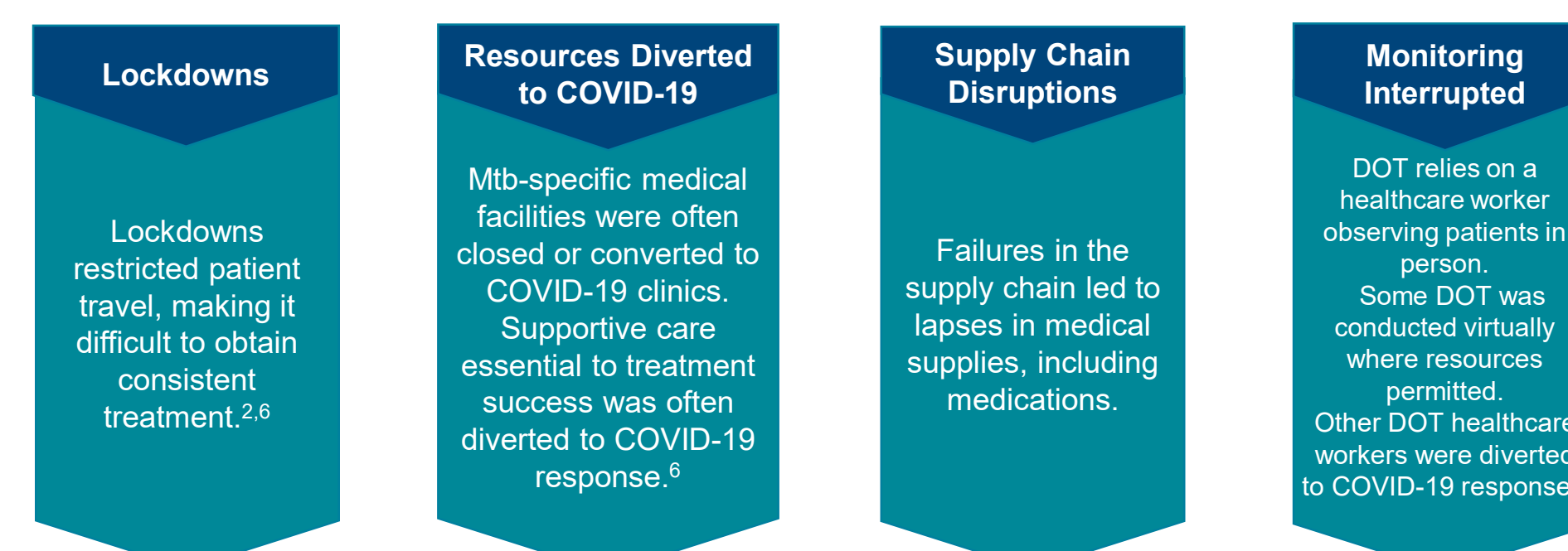
Mtb diagnosis is the crucial first step in eradicating tuberculosis. Ideally, patients are diagnosed soon after contracting Mtb but that's not often the case. Through contact tracing, other potential patients are identified, tested, and treated to prevent further spread. The fallout from the COVID-19 response efforts has posed many challenges to patients needing diagnosis.



Delayed or missed diagnosis results in more complicated and severe Mtb disease, and increases transmission.^{2,5}

Impact on Treatment of Mtb

Mtb treatment involves a long course of antibiotic therapy involving multiple drugs. Patient adherence is often monitored (DOT) and supportive care given to navigate the long and difficult treatment. Patients often suffer severe side effects, social isolation, and stigma. COVID-19 mitigation strategies and their subsequent effects have had a strong impact on Mtb treatment.



Interruptions in treatment can lead to the development of drug resistance, treatment failure, disease spread, and death.^{2,6}

Impact on Mtb Clinical Trials and Research

The execution of clinical trials has been negatively impacted by the pandemic. Lockdowns and travel restrictions have hindered studies in progress and have prevented new studies from being initiated. Supply chain disruptions have limited access to necessary study materials. STREAM (Evaluation of a Standardized Treatment Regimen of Anti-tuberculosis Drugs for Patients with Multidrug-resistant tuberculosis) is a large-scale, multi-country clinical trial funded initially by the USAID, and it, too, has been negatively impacted by the pandemic (Table 1).⁷ Other clinical trials, such as TB-PRACTECAL conducted by Médecins Sans Frontières (MSF), have experienced similar COVID-19 consequences.⁸

Country	Participants on Treatment	Participants in Follow up	Movement Restrictions Preventing Clinic Visits	Restrictions on Import/Export
Ethiopia	Yes	Yes	No	Yes
Georgia	No	Yes	No	No
India	Yes	Yes	Yes	Yes
Moldova	Yes	Yes	No	No
Mongolia	Yes	Yes	No	Yes
South Africa	No	Yes	Yes	Yes
Uganda	Yes	Yes	Yes	Yes

Table 1: STREAM stage 2 countries and current status of participants and restrictions on travel and import/export (as of 15 April 2020)⁷

General TB laboratory research has also been impeded as laboratory operations were reduced, in part due to limitations on the number of staff permitted in the lab. Reduced operations also resulted from SARS-CoV-2 infection among staff, forcing them to take some time away from the lab. Supply chain shortages added another layer of difficulty, as research facilities struggled to find the materials to conduct studies.

Impact on Transmission of Mtb

With the COVID-19 pandemic still in progress, it is too early to measure the full scope of its impacts on Mtb transmission. Most public health practitioners agree, however, that Mtb transmission has been worsened by the pandemic. Delayed diagnosis, for instance, has likely increased the opportunity for transmission.²

Some COVID-19 mitigation measures, such as mask-wearing and social distancing, may have prevented Mtb transmission as the diseases are similarly transmitted.^{2,4} Conversely, COVID-19 lockdowns may have promoted Mtb transmission within households that had to share living space for a long time.^{2,6}

Co-Infection of Mtb and COVID-19

Patients living with Mtb have diminished lung function, putting them at greater risk of secondary lung infections. COVID-19, which differentially affects the upper and lower respiratory tracts, is no exception. The most severe COVID-19 complications occur when lung capacity is severely weakened.⁹ Consequently, SARS-CoV-2 infection makes it more challenging for lungs of Mtb patients to quickly recover, even after the resolution of the viral infection.

A study in South Africa found that 50% of rifampicin-resistant Mtb patients that contracted COVID-19 died of the complications.¹⁰ The association of current Mtb infection and COVID-19 was furthermore reported in another study in the same country, resulting in poor outcomes.¹¹

Conclusions

The COVID-19 pandemic has undoubtedly disrupted years of effort to eradicate Mtb. Public health measures, such as lockdowns and the diversion of resources to the pandemic response, have directly and indirectly impacted all aspects of the Mtb fight. Patients lost access to healthcare support and have been more likely to suffer from complicated co-infection with COVID-19. Additionally, the long-term goal for fight against Mtb has been impacted by delays and interruptions to crucial clinical trials and research.

While there has been significant ground lost toward the goal of eradicating Mtb, there have been some valuable lessons learned. The pandemic helped identify gaps in the healthcare system. Strategies employed for COVID-19 response, including digital health, home delivery of medications, and data dashboards, could be leveraged in the efforts against Mtb.¹² Globally, laboratories scaled up their molecular testing capabilities, which could be utilized for Mtb testing. Finally, the rapid developments of mRNA vaccines, could serve as a model for developing a more efficacious vaccine against Mtb and help eradicate it going forward.

Without a plan in place, geopolitical instability, natural disasters, or a new pandemic could again derail the fight against Mtb. Consideration of Mtb should be included in all crisis preparedness planning for the future. The current war in Ukraine – a high burden drug-resistant Mtb country – highlights the serious challenge posed to the global community. Learning from COVID-19 responses in a coordinated and global way should be our priority to attain our common goal of eradicating tuberculosis.

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