Stop TB Partnership

Developed by Stop TB Partnership in collaboration with
Imperial College, Avenir Health, Johns Hopkins University and USAID.

THE POTENTIAL IMPACT OF THE COVID-19 RESPONSE ON TUBERCULOSIS IN HIGH-BURDEN COUNTRIES: A MODELLING ANALYSIS

BACKGROUND AND AIM

The global response to COVID-19 has slowed the spread of the virus for now but is continuing to cause serious, short and longer term, disruptions to the programmes for other major diseases. For tuberculosis (TB) in particular, lockdowns on society are already showing signs of severely curtailing diagnosis and notifications (1) and potentially the availability of drugs (2). A modelling study was therefore developed, to address the following questions:

- What is the potential impact of short-term lockdowns on TB incidence and mortality over the next 5 years, in high-burden countries?

- Following the lockdown, how can countries best accelerate the restoration of their TB control, to bring TB burden back under control?

Building on work for the 2019 Lancet Commission on TB (3), the modelling focuses on three high burden settings: **India**, **the Republic of Kenya** and **Ukraine**. Estimates from these countries were also extrapolated to create global estimates, for the impact of COVID-19 on TB.

APPROACH

The modelling approach involves deterministic, compartmental models capturing the dynamics of TB transmission, as described previously in ref. (4), and calibrated separately to each of the three countries. In consultation with experts from the Stop TB Partnership and USAID, a set of scenarios was prepared, to reflect the potential effects of a lockdown on different stages of the TB care cascade (Additional Table 1). It was assumed that these disruptions would be in effect over the course of a 2-month lockdown, after which there would be a gradual recovery to normal TB services, over a given 2-month 'restoration period'. A worst-case scenario was also modelled, of a 3-month lockdown followed by a 10-month restoration period. Model projections were performed, for the cumulative incidence

and mortality over the period from 2020 to 2025. Sensitivity analyses were conducted, to the durations of the lockdown and the restoration period.

While the modelling analysis principally focuses on India, Kenya and Ukraine, findings from these countries were extrapolated to the global level in the following way. The India model informed projections for countries with high TB burden and private sector involvement; the Kenya model informed projections for countries where HIV is a driver of the TB epidemic; and the Ukraine model informed projections for countries with a high proportion of drug-resistant TB, and hospital-based care delivery systems. Countries not in these groups were assigned the average impact of the three country models. Impact estimates were applied to cubic spline projections of TB cases and deaths reported by WHO.

Although there are several uncertainties involved in these projections, modelled impacts for the three focal countries may be underestimates for the following reasons. First, it is assumed that in the absence of the lockdown, current TB services would continue without change. Therefore, the model does not take account of major expansions in service delivery – e.g. private sector engagement in India – that could have occurred unhindered in the absence of the lockdown, as part of country plans to end TB and achieve the UNGA 2018 targets (5). Second, in Kenya the model captures the role of HIV trends in TB epidemiology, but not the potential implications of the COVID response, for HIV. Therefore, it does not capture the combined impact that is likely to be seen in such settings, as a result of disruptions in both HIV and TB services.

This analysis does not address direct interactions between TB and the SARS-CoV-2, although early evidence suggests that pre-existing TB infection may be a strong risk factor for severe outcomes (6). Moreover, those with previous TB history may – through resulting lung injury (7) – be prone to more severe outcomes upon infection with the SARS-CoV-2. Further studies would be invaluable in addressing these potential pathogen-pathogen interactions, and their implications for TB disease and mortality. The model also does not include potential increases in TB burden due to socioeconomic changes, for example increasing impoverishment arising from economic disruption. However, the model does allow for the potential impact of physical distancing measures on TB transmission.

FINDINGS

What is the potential impact of short-term lockdowns on TB incidence and mortality over the next 5 years?

For illustration, Figure 1 shows the dynamics of TB incidence and mortality resulting from a two-month lockdown followed by a two-month restoration period (red curve), and the worst-case scenario of a 3-month lockdown followed by ten-month restoration. Table 1 shows estimates for the excess TB burden, in each of the country settings. These results illustrate that it can take years for TB burden to return to pre-lockdown levels: the resulting excess TB cases and deaths can represent substantial setbacks in ending TB control in each country.

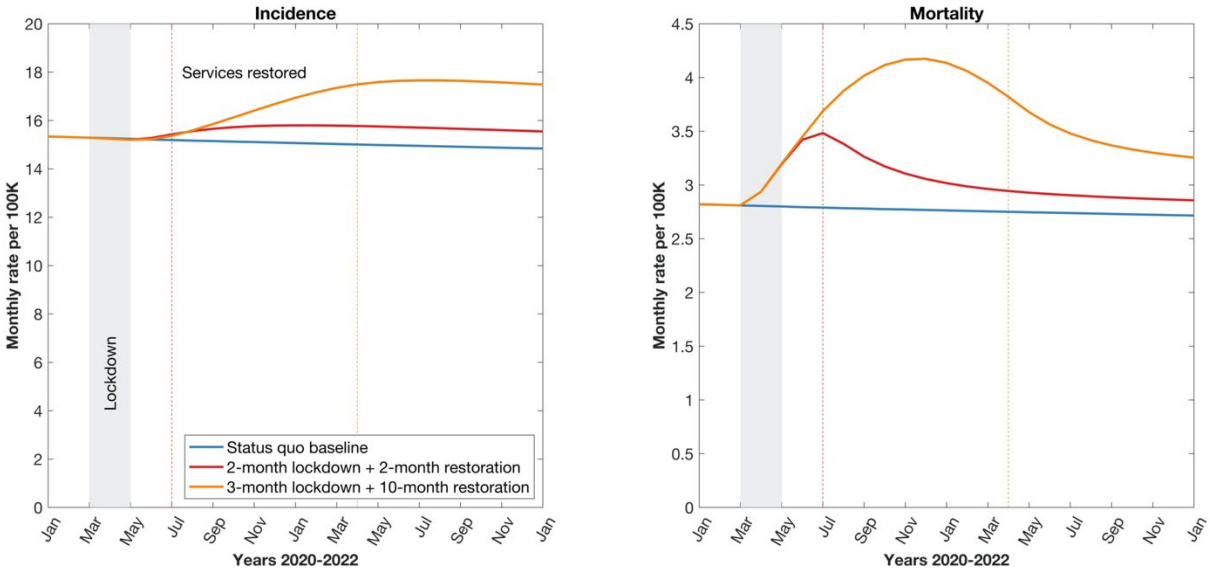

Figure 1. Dynamics of TB incidence and mortality following a COVID-19 lockdown, in the illustrative example of India. The grey shaded area shows the duration of the lockdown, while the vertical dashed line shows the point at which normal TB services are restored. Overall impacts in cumulative TB burden, from 2020 to 2025, are summarised in table 1 for each country.

Country	Excess cases between 2020-2025 (% increase)		Excess deaths between 2020-2025 (% increase)	
	2-month lockdown + 2-month recovery	3-month lockdown + 10-month recovery	2-month lockdown + 2-month recovery	3-month lockdown + 10-month recovery
India	514,370 (3.55%)	1,788,100 (12.32%)	151,120 (5.70%)	511,930 (19.31%)
Kenya	12,154 (1.51%)	40,992 (5.08%)	4,873 (2.15%)	15,800 (6.99%)
Ukraine	2,348 (1.19%)	7,589 (3.86%)	455 (2.40%)	1,578 (8.31%)
Global	**1,826,400 (3.1%)**	**6,331,100 (10.7%)**	**342,500 (4.0%)**	**1,367,300 (16.0%)**

Table 1. Model-estimated impact for the excess TB cases and deaths that would occur in each country, as a result of the COVID-19 response. As noted in the text, estimates are relative to a 'status quo' comparator, assuming that TB services continue indefinitely at pre-lockdown levels. Note that even though the global impact estimates fall within the range of country estimates, they are based on country-specific and different status quo trends than the ones used in the modelled countries (i.e. statistical projections of status quo as opposed to projections via a dynamic compartmental model).

Moreover, the pace of restoration has important consequences for TB burden in the medium term (i.e. between 2020 and 2025). Table 2 provides estimates for the medium-term implications of each month of lockdown, and for each month of restoration. The table emphasises the point that any excess TB burden that is allowed to accumulate during the COVID-19 response can hinder TB control over at least the next five years: rapid restoration of TB services is critical for minimising these adverse impacts.

Country	Excess TB cases from 2020 - 2025		Excess TB deaths from 2020 - 2025	
	For every month of lockdown	For every month of restoration	For every month of lockdown	For every month of restoration
India	232,665	144,795	71,290	40,685
Kenya	3,980	3,133	1,747	1,157
Ukraine	1,058	625	270	137
Global	**608,400**	**420,400**	**126,100**	**83,200**

Table 2. Estimates for incremental impact on TB burden by each additional month of lockdown or restoration

Following the lockdown, how can countries best accelerate the restoration of their TB services, to bring TB burden back under control?

Figure 2A illustrates the underlying reason that TB burden is affected so adversely by service disruptions: during the lockdown period, missed opportunities for diagnosis and treatment initiation give rise to a rapidly growing pool of undetected and unreported TB. Because normal TB services cannot reduce this expanded pool rapidly to pre-lockdown levels, they continue to contribute to transmission for years to come.

Therefore, in addition to the restoration of normal TB services, supplementary measures are required, with a focus on reducing the prevalent pool of TB. Such measures may involve a combination of intensive community engagement, maintaining awareness of the importance of TB services while emerging from the COVID-19 response, and ramped-up active case-finding, including rapid scale-up of contact tracing to compensate for missed diagnoses during the lockdown period.

We refer to a combined strategy, of restoring normal TB services (over a given duration) alongside supplementary measures (over a period of two months) as ‘enhanced restoration’. Figure 2B shows some illustrative examples of enhanced restoration, in the case of India. The figure illustrates the peak notifications that would arise, under these supplementary measures. Such indicators may offer helpful performance targets for enhanced restoration. For example, under a scenario where normal TB services take 2 months to be restored, a combination between these efforts and supplementary measures should aim to reach peak monthly notifications of 18 per 100,000 population.

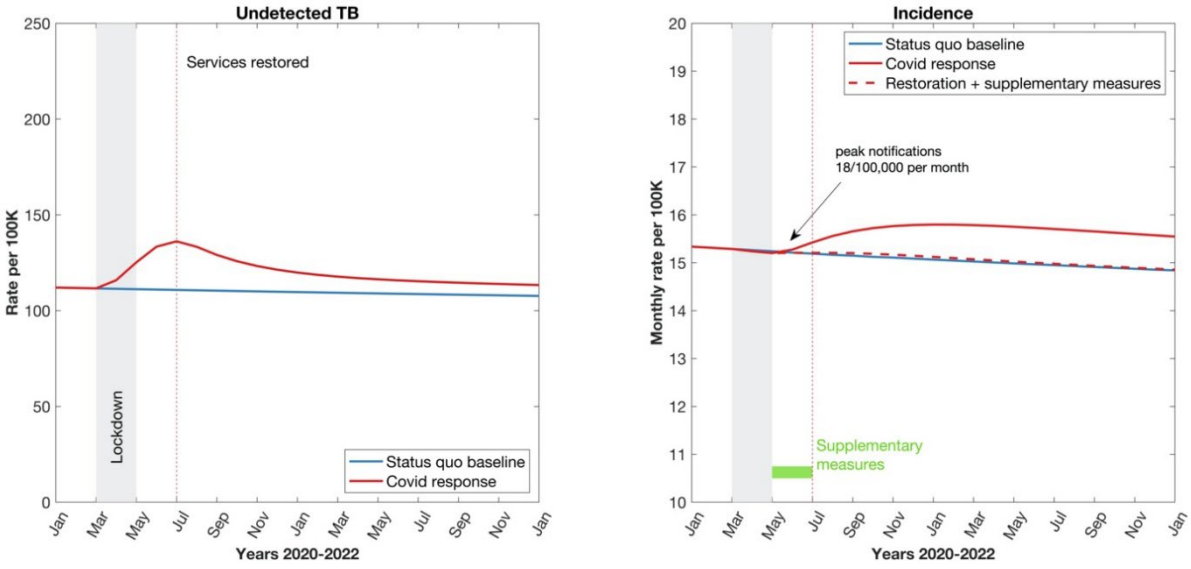

Figure 2. Accelerating the recovery from lockdown-induced setbacks to TB control. The left-hand panel illustrates a mechanism for the long-term impact of lockdown and restoration, on TB burden: missed opportunities for diagnosis give rise to a growing pool of undetected, infectious TB. Supplementary measures are needed, focused on addressing this challenge, alongside the restoration of normal TB services. The right-hand panel shows the potential impact of such measures (dashed line), illustrating their potential value in rapidly restoring TB incidence to pre-lockdown levels, and potentially further.

SUMMARY

- While stringent COVID-19 responses may only last months, they would have a lasting impact on TB in high-burden settings, through their effect mainly on TB diagnosis and treatment.

- Globally, a 3-month lockdown and a protracted 10-month restoration could lead to an **additional 6.3 million cases of TB between 2020 and 2025**, and an **additional 1.4 million TB deaths** during this time.

- As such, global TB incidence and deaths in 2021 would increase to levels last seen in between 2013 and 2016 respectively – **implying a setback of at least 5 to 8 years in the fight against TB**, due to the COVID-19 pandemic.

- Long-term outcomes can be strongly influenced by the pace of short-term recovery.

- Each month taken to return to normal TB services would incur, in India, an additional 40,685 deaths between 2020 and 2025; in Kenya, an additional 1,157 deaths; and in Ukraine, an additional 137 deaths over this period

- To recover the gains made over last years through increased efforts and investments in TB, it is important to have supplementary measures and resources to reduce the accumulated pool of undetected people with TB. Such measures may include ramped-up active case-finding, alongside intensive community engagement and contact tracing to maintain awareness of the importance of recognizing and responding to symptoms suggestive of TB, using digital technology and other tools. Securing access to an uninterrupted supply of quality assured treatment and care for every single person with TB will be essential. Notifications will provide a helpful approach for monitoring the progress of such supplementary efforts.

Indicator	Reason for effect	India	Kenya	Ukraine
From initiation of lockdown				
Reduction in transmission (DS- and DR-TB)	Physical distancing	Drops by 10%	Drops by 10%	Drops by 10%
Initial (pre-careseeking) patient delay	Restriction on movements	Increase by 50%	Increase by 50%	Increase by 30%
Probability of diagnosis per visit to a provider	Reduced lab capacity and availability of healthcare staff	Drops by 70%	Drops by 70%	Drops by 50%
First-line treatment completion rate, public sector and any engaged private	Healthcare staff unable to monitor and support treatment as usual	Drops to 70%	Drops to 70%	Drops to 50%
Second-line treatment completion rate, public sector and any engaged private		Drops to 25%	Drops to 25%	Drops to 25%
From a month into lockdown				
Proportion TB diagnoses having DST result	Xpert machines and other lab facilities used for COVID response	Drops to 5%	Drops to 5%	Drops to 25%
Treatment initiation	Stockouts and supply interruptions	Drops to 25%	Drops to 25%	Drops to 50%
Proportion PLHIV receiving IPT	Disruptions in HIV care	--	Drops to 10%	--

Additional Table 1: Summary of assumptions for the effect of lockdown, for each country. As described in the main text, it assumed that these disruptions are in full effect for 2 months of a lockdown in each country, and that TB services gradually resume to normal levels over a subsequent, 2-month 'restoration period'. In the worst-case scenario, we assume a 3-month lockdown followed by a 10-month restoration.

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