




COVID-19-related healthcare impacts: an uncontrolled, segmented time-series analysis of tuberculosis diagnosis services in Mozambique, 2017–2020

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ABSTRACT

Introduction Currently, COVID-19 dominates the public health agenda and poses a permanent threat, leading to health systems' exhaustion and unprecedented service disruption. Primary healthcare services, including tuberculosis services, are at increased risk of facing severe disruptions, particularly in low-income and middle-income countries. Indeed, corroborating model-based forecasts, there is increasing evidence of the COVID-19 pandemic's negative impact on tuberculosis case detection.

Methods Applying a segmented time-series analysis, we assessed the effects of COVID-19-related measures on tuberculosis diagnosis service across districts in Mozambique. Ministry health information system data were used from the first quarter of 2017 to the end of 2020. The model, performed under the Bayesian premises, was estimated as a negative binomial with random effects for districts and provinces.

Results A total of 154 districts were followed for 16 consecutive quarters. Together, these districts reported 96 182 cases of all forms of tuberculosis in 2020. At baseline (first quarter of 2017), Mozambique had an estimated incidence rate of 283 (95% CI 200 to 406) tuberculosis cases per 100 000 people and this increased at a 5% annual rate through the end of 2019. We estimated that 17 147 new tuberculosis cases were potentially missed 9 months after COVID-19 onset, resulting in a 15.1% (95% CI 5.9 to 24.0) relative loss in 2020. The greatest impact was observed in the southern region at 40.0% (95% CI 30.1 to 49.0) and among men at 15% (95% CI 4.0 to 25.0). The incidence of pulmonary tuberculosis increased at an average rate of 6.6% annually; however, an abrupt drop (15%) was also observed immediately after COVID-19 onset in March 2020.

Conclusion The most significant impact of the state of emergency was observed between April and June 2020, the quarter after COVID-19 onset. Encouragingly, by the end of 2020, clear signs of health system recovery were visible despite the initial shock.

INTRODUCTION

SARS-CoV-2, which emerged at the end of 2019, and its resulting COVID-19, has brought

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Important primary healthcare service disruptions due to the COVID-19 pandemic have been reported in almost all regions, particularly in low-income and middle-income countries.
- ⇒ Little is known about the magnitude of the effects of COVID-19 on tuberculosis services at the sub-national level.

WHAT THIS STUDY ADDS

- ⇒ Before COVID-19 onset, Mozambique witnessed consistent and substantial improvements in tuberculosis case detection rate.
- ⇒ Significant cutbacks in case detection rate were observed in the quarter after COVID-19 onset, particularly in the southern region and among men.
- ⇒ Signs of gradual recovery to the levels prior to COVID-19 onset were observed 6 months after.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

- ⇒ Failure to detect over 17 000 new tuberculosis cases in a year in Mozambique is dramatic and can delay the country's goal of tuberculosis elimination.
- ⇒ Additional efforts are needed to ensure active case detection in health facilities and in the community.

serious and unprecedented public health concerns globally.^{1–4} As the world struggles to mitigate the direct impact of COVID-19 on people's lives—in the first quarter of 2022, many countries are still dealing with the third, fourth or fifth waves and many low-income countries have less than 15% of the population completely vaccinated—there is emerging evidence that the indirect effects of the COVID-19 pandemic will tremendously affect other health outcomes, primarily in low-income and middle-income countries.^{5 6} Indeed, as has been seen already, no health

system, including those in high-income countries, is immune to the adverse effects of COVID-19. A WHO survey on continuity of essential services underscored the relevance of indirect effects of COVID-19: 90% of surveyed countries reported some degree of service disruption.⁷

Mathematical models forecast a worrisome scenario despite the limited knowledge about the magnitude of COVID-19's indirect effects. A dramatic yet indirect impact is anticipated on HIV, tuberculosis (TB) and malaria, with 5-year forecasting indicating a magnitude similar to that of COVID-19's direct effects.⁸ Where COVID-19 hits areas with a high infectious disease burden, increases in HIV-related, TB-related and malaria-related deaths of 10%, 20% and 36%, respectively, are expected.^{8,9} For example, the countries with the largest TB burden may report on average about 23% (16%–41%) reduction in TB notifications in 2020, leading back to reporting levels last seen in 2008.^{10,11} A recent modelling analysis that aimed to assess the potential impact of COVID-19-related disruptions on TB incidence and mortality in India and Kenya predicted a 3-month suspension of TB services, 1.2 million additional TB cases and over 360 000 deaths in India, as well as over 24 700 new TB cases and 12 500 deaths in Kenya, the main driver in both countries being the number of undetected TB cases during the COVID-19 lockdown period.¹²

The negative impacts of COVID-19 are also anticipated in areas beyond infectious diseases.¹³ Approximately 253 000 additional child deaths and 12 000 maternal deaths are estimated to occur in 6 months of the pandemic globally should maternal and child health services coverage be reduced by 10%–19%.¹⁴ One critical driver of the negative impact on children's health outcomes is service disruption to immunisation programmes.¹⁵ To minimise the risk of important disruptions, countries' health systems will need to urgently adjust and innovate their current strategies to deliver healthcare services. They will also need to implement systematic changes to address chronic inefficiencies in service delivery practices.^{16,17}

Like many other countries, Mozambique was affected by COVID-19 in early 2020 (the first case was reported on 22 March 2020). At the time of writing, in December 2021, the country was dealing with its fourth Omicron-dominated wave, after struggling to respond to a third and most deadly wave that ended in early October 2021. From COVID-19 onset through 1 December 2021, the country cumulatively tested 979 501 samples, of which 151 594 were positive for COVID-19, resulting in a positivity rate of 15.5%.¹⁸ As new and more transmissible virus variants emerge (Beta, Delta and Omicron variants have already been confirmed), concerns over indirect effects increase. There are particular concerns over the effects to the routine healthcare service delivery system, which might lead to cutbacks in the progress made so far on TB case detection.¹⁹

TB is a significant public health concern that remains among the top 10 causes of premature death worldwide.

Globally, around 10 million people develop active TB disease and 1.45 million die yearly.²⁰ Southeast Asia (44%) and Africa (24%) together largely account for the worldwide TB burden. Mozambique is among the 20 countries with the highest TB burden, with an estimated 110 000 new TB cases in 2019, for an incidence of 361 per 100 000 people.²¹ Despite the improvement in the notified cases, efforts are needed to increase new case detection and treatment coverage (estimated at 88% in 2020) to break the disease transmission successfully.^{21,22} A recently conducted rapid assessment of a TB programme in Mozambique suggested that there had been an approximately 30% decrease in TB outpatient visits during the second quarter of 2020 (when COVID-19 spread began), although with substantial heterogeneity across provinces.⁴

As data become available, evidence on the COVID-19 pandemic's impact on the uptake of TB services is growing. However, to our best knowledge, no study has assessed the district-level impact on TB diagnosis services in Mozambique. This study aimed to understand COVID-19 disruptions to TB diagnosis services in Mozambique by comprehensively estimating the effects of COVID-19 state of emergency (SoE) measures on the total number of new cases of all forms of TB at the district level, including between-district variability. The goal is to inform decision-making and efficiently mitigate the adverse impacts of COVID-19 in Mozambique and other similar settings.

METHODS

Study design

A segmented time-series analysis was performed to quantify the effect of COVID-19-related measures on TB case detection indicators at the district level.^{23–25} A total of 154 administrative areas (the total number of districts in Mozambique) with available data were analysed. The results were aggregated at the province and region level (north, central and south). Given their unique characteristics, Maputo City and Maputo Province were treated as a single province. District-aggregated data consisted of over 1600 existing public health facilities country-wide.²⁶

Setting

Mozambique, a Southern African country, has around 31 million people (2017 census projections). Currently, the country has 11 provinces and 154 districts. TB services are integrated into primary healthcare, and services are offered down to the community level. Around 72% of the 1643 public health facilities offer TB services and 22% perform rapid molecular tests (GeneXpert MTB/RIF). The public sector is by far the main health provider and offers TB services free of charge. The private sector, concentrated in major cities, covers less than 10% of the population.

At the community level, community health workers provide a package of services including community

education, TB active screening of high-risk groups, screening of household and close community contacts, sputum sample collection and transportation, community referrals, community directly observed therapy and treatment adherence support, psychosocial assistance, TB counselling, nutritional education supplementation, and legal aid to patients with TB.

SoE and SoPC measures and potential effects on TB services

After recording its first COVID-19 case, Mozambique adopted preventive measures to delay the epidemic peak and prepare the national health system to respond efficiently to the shock. On 30 March 2020, the president, for the first time in the country's history, decreed a national SoE throughout the national territory.²⁷ This SoE lasted 30 days, subsequently underwent extensions, and on 4 September 2020 transitioned to a state of public calamity (SoPC). Unlike in some neighbouring countries, no full lockdown was ever observed. Several measures were enacted, including social or physical distancing (minimum of 1.5 metres), mask-wearing and hand sanitising, in full alignment with the WHO guidelines.

After the SoE was issued, substantial efforts were directed to preventing COVID-19 from spreading within the health facilities, which negatively impacted routine services availability. Several TB services were discontinued, including home visits, screening of household contacts, community collection and transport of sputum specimens, and provision of directly observed TB treatment. About 6% of the GeneXpert devices used for TB diagnosis were allocated exclusively for COVID-19 diagnosis. Under regular situations, all these supply-side activities contribute to 25%–30% of the total TB cases diagnosed in Mozambique. From the demand-side perspective, the

stay-home policy and its associated awareness messages led to misunderstandings, uncertainty, fear and stigmatisation, which ultimately reduced care-seeking. Activists conducting TB screening 'door to door' have had a much harder time convincing parents to send their children to health centres for TB evaluations due to parents' fear of exposing their children to COVID-19 at the health centres. Furthermore, in contexts such as Mozambique, with high unemployment and poverty rates, policies such as the stay-home could aggravate old problems, including access to transportation, therefore limiting healthcare access.

To minimise the anticipated COVID-19-related indirect effects, the national TB programme gradually implemented strategic operational changes and issued recommendations, with particular emphasis on facility-based and home-based care. These measures fell into three categories: (1) actions to ensure continued TB screening and diagnosis (with integrated screening and testing for COVID-19 whenever appropriate); (2) actions to protect the continuity and quality of healthcare; and (3) actions to provide continuity of care and promote follow-up at the community level through regular home-based visits (figure 1).

Data sources, data processing and variables of interest

Quarterly data from the first quarter of 2017 through the end of 2020 were extracted from the health information system database (based on DHIS2 - District Health Information Software 2). This study's primary outcome was the total number of new cases of all forms of TB, diagnosed clinically or via laboratory samples. Three secondary outcomes were constructed from the primary outcome: namely, new pulmonary TB cases, new cases

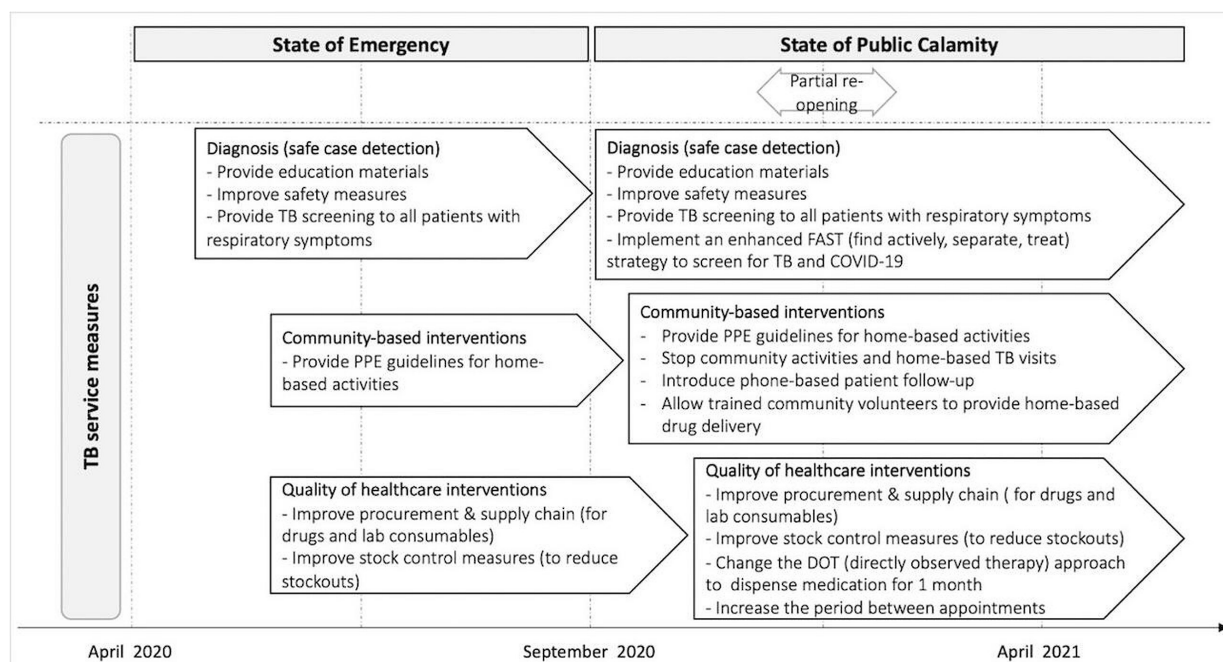


Figure 1 Summary of Mozambique's TB programme measures to mitigate the indirect impacts of COVID-19. TB, tuberculosis; PPE, personal protective equipment.

of all forms of TB among women and new cases of all forms of TB among men. TB incidence is defined as the number of new cases in the quarter divided by the quarter's projected population (to make this comparable with the yearly incidence of TB cases) and then multiplied by 100 000 habitants.²⁸ The same approach and denominator were used for every outcome.

Data analysis

To guide model parametrisation, the data were first explored through tables and plots to assess for completion, outliers, inconsistencies and residual distribution for every variable and district. We used a segmented time-series analysis for the ratio of counts of TB diagnosed cases per population, placing the interruption at the end of 2019. Each quarter of 2020 was then represented as a dummy to allow the model to capture specific 2020 quarterly changes. The second quarter of 2020 is when the SoE was issued at full force. The following is the estimated equation:

$$\begin{aligned} \log(\text{count}_{dt}) = & (\beta_0 + b_0^{*d} + b_0^{*p}) + (\beta_{time} + b_{time}^{*d} + b_{time}^{*p}) \cdot \text{time} \\ & + (\gamma_1 + g_1^{*d} + g_1^{*p}) \cdot I(\text{year} = 2020) \\ & + (\gamma_2 + g_2^{*d} + g_2^{*p}) \cdot I(\text{year} = 2020 \& \text{Quarter} = 2) \\ & + (\gamma_3 + g_3^{*d} + g_3^{*p}) \cdot I(\text{year} = 2020 \& \text{Quarter} = 3) \\ & + (\gamma_4 + g_4^{*d} + g_4^{*p}) \cdot I(\text{year} = 2020 \& \text{Quarter} = 4) \\ & + 1 \cdot \log(\text{Population}_{dt}) \end{aligned}$$

where *time* stands for time in years since January 2017; $I(\text{year} = 2020)$ is an indicator variable (0/1) for the year 2020; and $I(\text{year} = 2020 \& \text{Quarter} = 2)$, $I(\text{year} = 2020 \& \text{Quarter} = 3)$ and $I(\text{year} = 2020 \& \text{Quarter} = 4)$ are indicator variables for the second quarter of 2020, third quarter of 2020 and fourth quarter of 2020, respectively. γ_1 is the coefficient capturing the overall change in the level relative to the end of 2019. γ_2 , γ_3 and γ_4 are coefficients capturing changes in the second, third and fourth quarters of 2020 relative to a previous quarter, respectively. The coefficients are exponentiated to be interpreted as multiplicative (relative) changes of ratios of TB diagnoses per population (incidence rate).

The model was estimated as a negative binomial with random effects (the *b* and *g* terms) for districts (^d) and provinces (^p). We chose to use a Bayesian approach due to the many random-effects and complex convergence issues under the maximum likelihood.²⁹ The random-effects model was chosen, first, because it makes it easier to approach the hierarchical nature of the data set (national and province data are upper level compared with district data at the lower level), and second to efficiently deal with the potential for missing data being confused with under-reporting of zero counts. The models were estimated under Stan through brms library in R version 3.6.3.^{30 31} Markov Chain Monte Carlo (MCMC) was run for 15 000 iterations with 3000 burn-in replications, 6 chains and a thin of 10. This resulted in 14 400 posterior distribution samples. Convergence was assessed through trace plots

and autocorrelation evaluation. The default priors in the package were unchanged.

Relative losses for 2020 are computed as the ratio between the observed counts and the expected counts. The expected are computed for each quarter and district using the above-described model. In order to compute for the upper level (province, region and national) or time (year), the counts are first aggregated and then the ratios are computed.

Patient and public involvement

There was no patient or public involvement in this research.

RESULTS

Overall, 154 districts were followed between the first quarter of 2017 and the end of 2020. We present the findings for each outcome in the tables, figures and online supplemental appendix, and summarise the findings in the main text. Until onset of the COVID-19 pandemic, Mozambique's national TB notifications (all forms) had been increasing gradually since the first quarter of 2017; however, there was substantial heterogeneity between districts and provinces, with Maputo showing the widest range (from less than 200 to more than 1400 notified TB cases per 100 000 habitants) and Niassa exhibiting the smallest within-province variation (figure 2). Mozambique's northern region consistently reported the lowest TB notification rates across time and the lowest variability across districts (figure 2). Across provinces, Gaza, followed by Manica, had the highest TB notification rates in 2020, at 537 and 425 TB cases per 100 000 habitants, respectively (table 1).

The average national TB incidence in the first quarter of 2017 was 283 (95% CI 200 to 406) cases per 100 000 habitants; this was increasing annually by 5.0% until the end of 2019 (table 2). If this trend had continued, there should have been about 113 329 TB cases reported in 2020, on average (model-based estimate). However, only 96 182 cases were, in fact, observed in 2020. Therefore, potentially 17 147 new cases of all forms of TB were not identified, representing a 15.1% (95% CI 5.9 to 24.0) statistically significant relative loss. The scenario was even worse in the southern region, where a 40.0% (95% CI 30.1 to 49.0) relative loss was estimated. Maputo (province and city combined), which had accumulated 63.5% of the country's total COVID-19 cases, had the highest and statistically significant relative loss in notified TB cases, estimated at 56.6% (95% CI 46.7 to 65.3). On average, northern provinces had a relative loss of 9.6% (95% CI 1.1 to 17.8), with Niassa reporting the highest loss (12.4%). It is noticeable that three of the four provinces in Mozambique's central region (Zambézia, Tete and Sofala, but not Manica) had a net, although not significant, increase in notified TB cases compared with what was expected (table 2).

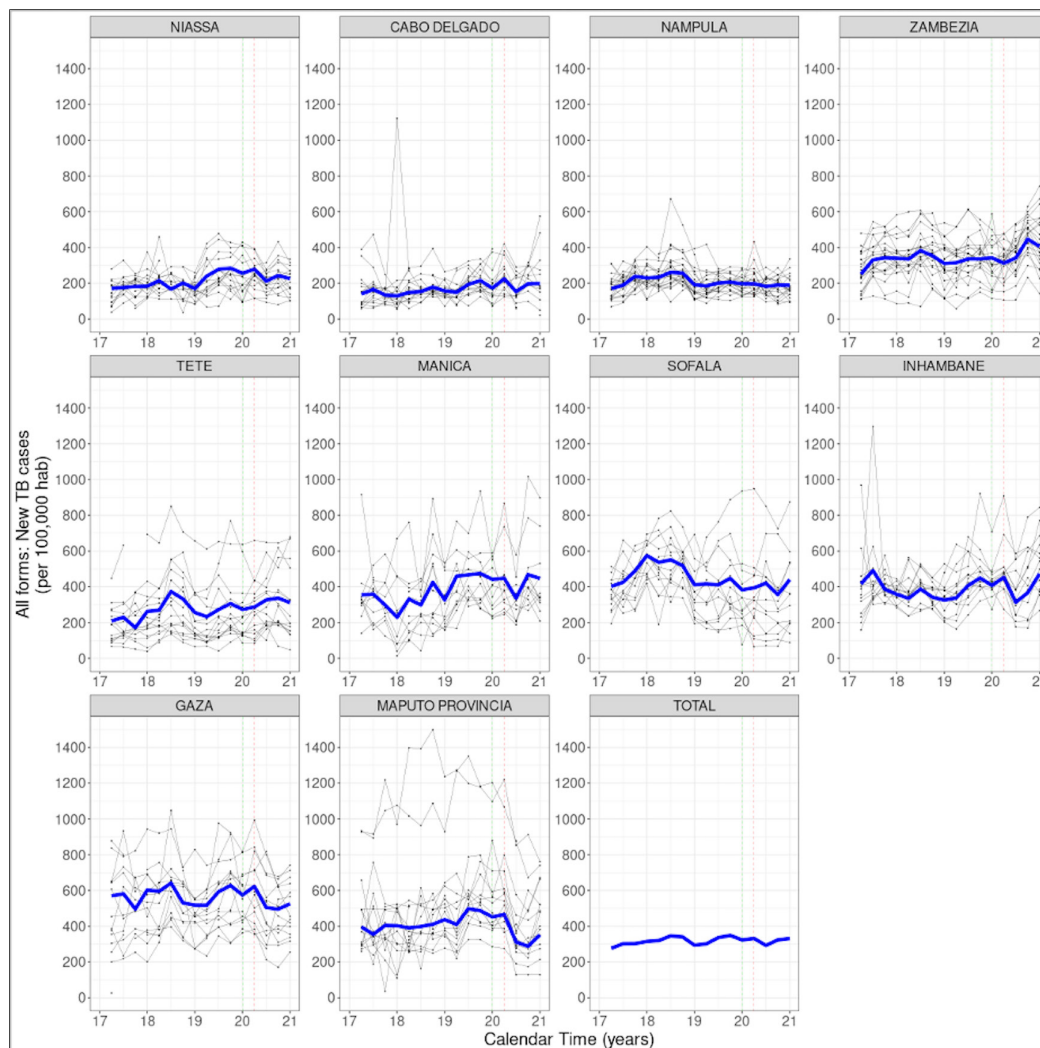


Figure 2 Notifications of all forms of tuberculosis (TB) per 100 000 habitants (hab) per province and district. The blue line shows the province's geometric mean. The grey lines represent district means. Data for Maputo City and Maputo Province were merged and presented as Maputo Provincia. The plot labelled 'total' shows the national incidence per 100 000 habitants.

The disruptions to healthcare delivery signalled by TB notification levels appeared much more prominent among men than among women across the three quarters following the first COVID-19 case. Among women, on average, the incidence of new cases of all forms of TB in the first quarter of 2017 was 260 per 100 000 habitants, with an annual non-significant relative increase estimated at 5% (Incidence Rate Ratio, IRR: 1.05; 95% CI 0.98 to 1.12) until the end of 2019. Compared with the fourth quarter of 2019, the first quarter of 2020 had a non-significant 2% (IRR: 0.98; 95% CI 0.91 to 1.05) decline in incidence among women; however, this scenario deteriorated in the second quarter of 2020, when there was a 12% (IRR: 0.88; 95% CI 0.78 to 1.00) lower incidence of all forms of TB among women compared with the first quarter of 2020 (table 3). Likewise, TB incidence among men had a positive trend before 2020, with an annual non-significant increase estimated at 4.2% (IRR: 1.04; 95% CI 0.99 to 1.09) until the end of 2019. This trend was interrupted after COVID-19, as the incidence of all forms of TB among men declined significantly by 15% (95%

CI 4.0% to 25.0%) in the second quarter compared with the first quarter of 2020 (table 3). Online supplemental figure 1 illustrates that across provinces the incidence of new cases of all forms of TB has been consistently greater among men than among women.

The pattern of new pulmonary TB cases is similar to that of new cases of all forms of TB. In the first quarter of 2017, on average nationally, there were 245 new pulmonary TB cases per 100 000 habitants, and from then to the beginning of 2020 pulmonary TB incidence was increasing at an average annual rate of 6.6% (95% CI 0.2% to 44%; see online supplemental table 2). From April to June 2020, there was a 15% (95% CI 2.0% to 26%) significant relative decrease in pulmonary TB incidence compared with the first quarter of 2020. Overall, during 2020, only 87 289 of the expected 103 103 pulmonary TB cases were observed, representing a 15.3% (95% CI 5.9% to 24.3%) decline. Of note is the 58.6% (95% CI 48.3% to 67.7%) fewer cases in 2020 in Maputo compared with what was expected (online supplemental figure 2). The southern region lost the most, with 41.1% (95% CI 31.0%

Table 1 Notifications of all forms of tuberculosis in Mozambique and incidence rates per 100 000 habitants, 2020

Region/province	Cases observed					Cases per 100 000 habitants (annualised)				
	Q1	Q2	Q3	Q4	Total	Q1	Q2	Q3	Q4	Total
North	5853	4856	5392	5304	21 405	218.6	181.4	201.4	198.1	199.9
Niassa	1391	1058	1216	1127	4792	278.4	211.8	243.4	225.6	239.8
Cabo Delgado	1416	971	1242	1260	4889	224.3	153.8	196.7	199.6	193.6
Nampula	3046	2827	2934	2917	11 724	197.0	182.9	189.8	188.7	189.6
Central	11 215	11 496	13 325	12 987	49 023	344.0	352.6	408.7	398.4	375.9
Zambézia	4341	4757	6212	5656	20 966	311.9	341.8	446.3	406.4	376.6
Tete	2081	2371	2445	2261	9158	287.0	327.0	337.2	311.8	315.8
Manica	2370	1782	2477	2362	8991	448.3	337.1	468.6	446.8	425.2
Sofala	2423	2586	2191	2708	9908	394.3	420.9	356.6	440.7	403.1
South	7875	5631	5600	6648	25 754	423.1	302.6	300.9	357.2	346.0
Inhambane	1735	1204	1404	1812	6155	453.0	314.4	366.6	473.1	401.8
Gaza	2251	1823	1791	1900	7765	622.7	504.3	495.5	525.6	537.0
Maputo Provincia	3889	2604	2405	2936	11 834	348.3	233.2	215.4	262.9	265.0
Total	24 943	21 983	24 317	24 939	96 182	319.9	281.9	311.8	319.8	308.4

Maputo City and Maputo Province data were merged and presented as Maputo Provincia.
Q, quarter.

to 50.4%) fewer pulmonary TB cases than expected in 2020, compared with 9% in the northern region (online supplemental tables 1 and 2).

DISCUSSION

This is the first robust evaluation of the effects of COVID-19 on TB case detection since the beginning of the pandemic, using the most granular data available in Mozambique. While the country’s COVID-19-related emergency measures were necessary, we demonstrate

Table 2 Expected number of 2020 notifications for all forms of tuberculosis in Mozambique using multilevel model and absolute differences between the observed and expected counts

Region/province	Model expected					Absolute differences					% loss from expected	
	Q1	Q2	Q3	Q4	Total	Q1	Q2	Q3	Q4	Total	%	95% CI
North	5798	5874	5955	6042	23 668	55	-1018	-563	-738	-2263	-9.6	-17.8 to -1.1
Niassa	1292	1341	1391	1445	5469	99	-283	-175	-318	-677	-12.4	-21.3 to -2.1
Cabo Delgado	1312	1351	1393	1436	5493	104	-380	-151	-176	-604	-11.0	-19.8 to -1.1
Nampula	3194	3182	3171	3161	12 707	-148	-355	-237	-244	-983	-7.7	-15.5 to -0.6
Central	11 487	11 616	11 755	11 904	46 763	-272	-120	1570	1083	2260	4.8	-4.2 to 13.8
Zambézia	4796	4835	4875	4917	19 423	-455	-78	1337	739	1543	7.9	0.5 to 15.6
Tete	2040	2088	2140	2195	8463	41	283	305	66	695	8.2	-1.5 to 18.4
Manica	2302	2372	2445	2521	9640	68	-590	32	-159	-649	-6.7	-16.0 to 3.2
Sofala	2350	2321	2295	2271	9237	73	265	-104	437	671	7.3	-4.1 to 16.9
South	10 334	10 587	10 850	11 126	42 898	-2459	-4956	-5250	-4478	-17 144	-40.0	-49.0 to -30.1
Inhambane	1686	1709	1734	1759	6888	49	-505	-330	53	-733	-10.6	-19.6 to -1.2
Gaza	2150	2171	2194	2218	8733	101	-348	-403	-318	-968	-11.1	-21.0 to 1.2
Maputo Provincia	6499	6706	6923	7149	27 277	-2610	-4102	-4518	-4213	-15 443	-56.6	-65.3 to -46.7
Total	27 619	28 076	28 561	29 073	113 329	-2676	-6093	-4244	-4134	-17 147	-15.1	-24.0 to -5.9

Maputo City and Maputo Province data were merged and presented as Maputo Provincia.
Q, quarter.

Table 3 Exponentiated coefficients and 95% CI of the negative binomial regression

Outcome	2017–2019		2020			
	Intercept	Preslope	Q1	Q2	Q3	Q4
All forms of TB, total	282.65 (199.99 to 405.64)	1.05 (0.99 to 1.11)	1.02 (0.94 to 1.10)	0.86 (0.76 to 0.98)	0.95 (0.80 to 1.13)	0.97 (0.86 to 1.08)
All forms of TB, female	259.73 (183.23 to 374.33)	1.05 (0.98 to 1.12)	0.98 (0.91 to 1.05)	0.88 (0.78 to 1.00)	0.99 (0.82 to 1.20)	1.02 (0.89 to 1.15)
All forms of TB, male	307.58 (214.38 to 438.47)	1.04 (0.99 to 1.09)	1.06 (0.96 to 1.16)	0.85 (0.75 to 0.96)	0.93 (0.79 to 1.08)	0.94 (0.85 to 1.05)
Pulmonary TB	244.65 (177.21 to 341.37)	1.06 (1.002 to 1.44)	1.02 (0.94 to 1.11)	0.85 (0.74 to 0.98)	0.96 (0.81 to 1.14)	0.97 (0.86 to 1.09)

Q, quarter; TB, tuberculosis.

their potential negative impact on the total number of new cases of all forms of TB. Not surprisingly, the most significant impact was observed between April and June 2020, the first 3 months of the SoE, where a 14% decrease in the incidence of all forms of TB was observed nationally compared with the prior quarter. These results corroborate previous modelling exercises that predicted substantial COVID-19-related disruptions on TB services.^{12 32}

Overall, previous studies in other settings have suggested a wide effect size on TB case detection, ranging from a little below 10% to over 75%,^{10 33–35} making findings from this study within the expected range. Encouragingly, as reported in other settings, by the end of 2020, a moderate recovery to the levels prior to COVID-19 was noted.³⁶ While in the second quarter of 2020 (during the SoE) about 5700 new pulmonary TB cases were lost, in the fourth quarter of 2020 (during the SoPC) this number shrank to 3800, providing hope about the effectiveness of the programmatic measures adopted to mitigate the impact of COVID-19 on TB case detection. To ensure gradual and sustained recovery, a close follow-up of the implementation of these programmatic measures is suggested since the results could support continued efforts to mitigate COVID-19-related service disruptions.

However, failure to detect over 15 800 new pulmonary TB cases in 2020 (corresponding to the estimated 15% loss) is tragic. It represents a tremendous setback to the overall effort to address the TB burden in Mozambique. With this number of potential undetected cases, a worse scenario is likely still to come, including the potential spread of multidrug-resistant forms and delays in achieving Mozambique's elimination targets.³⁷ To minimise this risk, the TB programme will need to innovate and implement additional programmatic changes to ensure continuity of service delivery and particularly active case detection and psychosocial support to strengthen treatment adherence.^{37–39} As shown in figure 1, changes such as phone-based follow-up (to monitor medication adherence and side effects and

provide counselling), long-term prescriptions for TB drugs and spacing inperson appointments to reduce outpatient visits were introduced to improve patient satisfaction and healthcare quality during the pandemic.^{17 35}

Indeed, such measures can reduce catastrophic costs for patients, minimise crowdedness within healthcare facilities, reduce unnecessary contact between health workers and patients, and minimise wait times.¹⁶ Yet these measures might be effective at improving the quality of healthcare for patients already diagnosed with TB and on treatment; they will likely be less effective in improving case detection, which ultimately is a major concern. For example, our findings that men were mostly affected may reflect privileges to women and children embedded into the primary healthcare structure and addressing this issue may require critical system reforms and not only focal programmatic interventions.

Understanding how COVID-19-related measures collectively affect TB case detection is challenging since each measure may act using a different mechanism. For example, wearing surgical and N95 masks has been documented to reduce TB transmission; however, the long-term effect of such measure is unclear since socio-economic barriers to access and use, fatigue and misuse undermine its effectiveness.^{40–42} On the other side, the stay-home policy may reduce healthcare-seeking, therefore decreasing TB case detection but not disease transmission. Therefore, as countries return to normal, this particular moment represents a critical opportunity to implement structural reforms and innovations and addressing chronic and systemic healthcare delivery inefficiencies, including studying the long-term benefits of masks and other measures on other health outcomes.⁴³

Hidden behind the 'big picture' (country level), where most provinces struggled in the first wave of the pandemic (ie, in the second and third quarters of 2020) and reported substantial healthcare disruptions, the province of Zambézia had the opposite trend, detecting almost 1500 more new cases of all forms of TB than was

expected for 2020. Two other provinces, Tete and Sofala, had a similar trend. We learnt that in these three provinces, plus Nampula, a new TB project had begun, close to the time of the SoE, which could justify this unexpected pattern. This new TB project supports community-based TB contact tracing and case finding and covers 50 of the 73 districts in Zambézia, Nampula, Tete and Sofala. However, given the characteristics of the SoE, the limitations imposed and the stepped-wedge approach of the project (in which districts were introduced gradually and sequentially, with around 20 districts in the initial cohort), it seems unlikely that a single project, which requires time for full maturation, would lead to substantial gains. Moreover, there are other factors to consider. In Tete, for example, we understood that donor-driven support hired additional health workers for COVID-19 treatment centres, which allowed existing staff to maintain routine services, and this could also justify the observed pattern. Further qualitative studies to document lessons from these provinces might be relevant to generate evidence, particularly if these gains are proven to be realistic and not anecdotal or an artefact of the data.

This study has several limitations. First, we trusted the district-level aggregated data, which may have quality issues. Indeed, some degree of missing data existed, which we assumed to be missing at random. Furthermore, COVID-19-related measures could have negatively impacted data completeness due to lack of registration books, therefore inflating the number of TB cases undetected. However, we anticipate this to be a delayed impact given the 3-month secure stock policy in place. Second, we could not incorporate some critical covariates at the district level due to a lack of data. Third, while several measures were adopted to mitigate the impact of COVID-19-related measures on TB case detection, the methodology applied does not allow us to understand which specific measures had the greatest impact on TB diagnosis continuity or disruptions. Despite these limitations, the analytic strategy (including the sensitivity analysis performed) provides our results with substantial robustness. It has several other strengths, including the use of routine data and the focus given to critical issues that policymakers need to address to improve Mozambique's COVID-19 response.

CONCLUSION

The results of this study provide relevant evidence to inform decision-making in Mozambique. It serves as a foundation for critical programmatic follow-up actions to mitigate the negative impacts of COVID-19 on health-care continuity. The methodology used sets an excellent example of applying routine health information system data to robust evaluations that drive decision-making during public health shocks. Overall, our finding of immediate significant disruptions to TB case notifications at the district and province level was not surprising. However, it is encouraging that at the end of 2020,

after the initial shock, there were signs of health system recovery. Further studies are suggested to identify specific drivers of disruptions, the most protective interventions and the high-risk groups.

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