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Impact of shelter-in-place orders on TB case notifications and mortality in the Philippines during the COVID-19 pandemic

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ABSTRACT

Background: Policies implemented to slow transmission of COVID-19 are expected to have disrupted delivery of routine health services, including tuberculosis (TB) care.
Methods: We analyzed daily counts of drug-susceptible (DS)-TB case notifications from all health facilities affiliated with the Philippines National TB Program (NTP) before and after implementation of community quarantine (January 1-December 31, 2020). Using an interrupted time series design, we assessed the immediate and sustained effects of community quarantine on TB case reporting. Using 2019 WHO estimates of national TB incidence, treatment, and mortality rates for the Philippines, we modeled excess mortality from TB, assuming a national decline in TB case reporting were extended for 12 months, followed by a return to pre-community quarantine trends.
Results: The analysis included 192,918 DS-TB case notifications from 2,986 facilities located in 113 provinces and highly urbanized cities across 17 regions and covered 49 observations days before and 174 days after community quarantine implementation. We found an significant drop and steeper decline in daily TB case notifications after the implementation of community quarantine, resulting in 44.6% (95% CI 38.3–50.1) fewer daily TB case notifications 60 days after implementation of community quarantine. During 2020, DS-TB case notifications never returned to pre-quarantine levels. Assuming a 12-month disruption of TB case reporting, we estimate there will be 56.3% increase in TB-related deaths in the Philippines.
Conclusion: Modified delivery of TB prevention and care should be prioritized alongside efforts to combat COVID-19.

1. Introduction

In response to the COVID-19 pandemic, countries around the world have implemented measures to prevent the spread of disease by limiting movement of the population through transportation restrictions, curfews, and shelter-in-place orders. While such measures have been shown to slow the transmission of COVID-19 [1], these policies may also disrupt the delivery of routine care. The consequences for tuberculosis (TB) prevention and care are expected to be large [2] but few studies have quantified the impact on a national scale.

2. Methods

2.1. Study design

We conducted an interrupted time-series analysis to evaluate the effect of community quarantine policies due to COVID-19 on case notifications for drug-susceptible tuberculosis (DS-TB) in the Philippines.

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2.2. Study setting and population

The first case of COVID-19 in the Philippines was reported on January 30, 2020 and the first confirmed case of local transmission on March 7, 2020 [3]. Shortly after, the Philippine President declared a state of calamity throughout the Philippines and imposed Enhanced Community Quarantine throughout Luzon, the largest island of the Philippines, on March 16, 2020 [4]. Under Enhanced Community Quarantine, the public was instructed to stay at home, only essential businesses were permitted to operate and public transport was suspended. Outside of Luzon, decisions to implement community quarantine policies were made by Local Government Units in each province or highly urbanized city (HUC).

We analyzed daily counts of DS-TB case notifications from all health facilities participating in the Philippines National TB Program (NTP) over the period spanning from January 1-December 31, 2020. Affiliated health facilities report TB case notification data quarterly using the Integrated Tuberculosis Information System (ITIS), an electronic case notification system. We excluded facilities from four provinces without a known community quarantine implementation date (Basilan, the City of Isabela, Maguindanao, and Western Samar). To address the possibility of lower reporting on non-working days, we excluded TB case notifications that occurred on Saturdays, Sundays, and holidays. Days of observation were numbered sequentially, with Mondays falling one day after the previous Friday.

2.3. Ethics statement

This project was reviewed by the University of California San Francisco Committee on Human Research and determined not to meet the criteria for human subjects research (IRB number 20–31202). The Philippines National Tuberculosis Program determined that analysis of routinely reported data for program planning does not require human subjects research approval per Philippines guidelines.

2.4. Definitions

The intervention studied was the implementation of community quarantine to prevent transmission of COVID-19. The date of community quarantine implementation was ascertained for each province/HUC through review of local guidance and news, then confirmed with regional TB coordinators (**Supplementary Table 1**). TB case notifications were categorized as occurring before, during, or after community quarantine implementation based on the date of implementation in the province where the treatment facility was located.

TB case notifications were then aggregated across all facilities by day, relative to the date of community quarantine implementation. We considered day 0 to be the day of community quarantine implementation (or the next weekday if implemented on a weekend); negative days to represent days before community quarantine implementation and positive days to represent days after community quarantine implementation. The number of pre- and post-intervention days varied across facilities due to differences in the date of community quarantine implementation in their province. We excluded pre- and post-intervention days when all included facilities were not represented.

2.5. Statistical analysis

Segmented negative binomial regression was used to model the change in number of DS-TB case notifications before and after implementation of community quarantine. Visual inspection of the data indicated volatile changes in TB case notifications over the first two months of community quarantine. To avoid over-interpreting the immediate drop in TB case notifications during this period, we used a spline term with three knots to model the trend during the first 59 days of community quarantine implementation and compared the linear trend pre-quarantine to the linear trend starting 60 days after implementation of community quarantine. A likelihood ratio test showed evidence of overdispersion ($p < 0.001$), supporting the use of a negative binomial model. In addition to the spline terms, the model included time (days), an indicator variable for the days before and after community quarantine implementation, and an interaction term to allow for a change in slope before vs. after community quarantine. We assessed the immediate effect (change in level) and sustained effect (change in slope) of community quarantine on TB case reporting between the pre-quarantine period and the period starting 60 days after community quarantine implementation. Visual inspection of autocorrelation plots and statistical testing showed evidence of autocorrelation in the data (Durbin Watson statistic = 0.86), which we adjusted for using heteroskedasticity and autocorrelation corrected standard errors using the Newy-West method.

Subgroup analyses were performed in the same manner for each of four geographic divisions or subgroups (the three most populated regions in the Philippines (all located in Luzon), the rest of Luzon Island, Visayas, and Mindanao) and for clinically diagnosed vs. bacteriologically confirmed TB case notifications. We compared the effect of community quarantine among subgroups by assessing the statistical significance of a subgroup-period interaction term when added to the non-stratified model with an indicator variable for the subgroup.

We used the results of the interrupted time series analysis to estimate the projected excess TB mortality due to community quarantine policies using a published conversion formula [5], assuming 12 months of interruption due to COVID-19 community quarantine policies, followed by a resumption of pre-quarantine trends. We used 2019 WHO estimates of national TB incidence, treated TB cases, and TB mortality [6,7].

All analyses were performed using STATA 15 [8].

3. Results

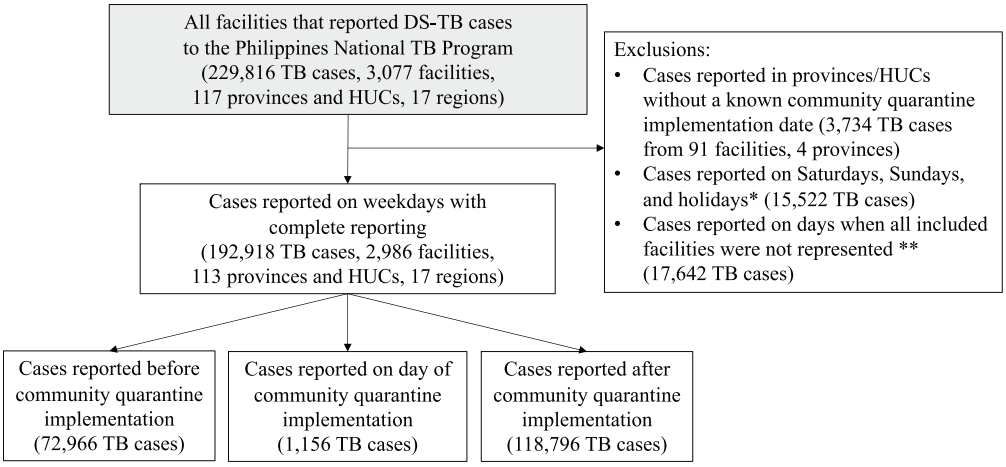
3.1. Study population

The analysis included 192,918 DS-TB case notifications from 2,986 facilities located in 113 provinces/HUCs across 17 regions and covered 49 observations days before and 174 days after community quarantine implementation (Fig. 1). We excluded TB cases notified on weekends, national holidays, and during the first week of the year (N = 15,522) or on pre- and post-intervention days when all health facilities were not represented (N = 17,642). The majority (85.7%) of facilities included were rural health units/health centers, and almost all (97.7%) were public facilities (Table 1).

3.2. Change in TB case notifications

Over the 49 days before community quarantine implementation, there was a statistically significant decline in daily TB case notifications (0.3% decline per day, 95% CI 0.1–0.4) (Fig. 2). This decline may reflect early impacts of pandemic-related fear, given the Philippines' proximity to China where the COVID-19 pandemic began; the first case of COVID-19 in the Philippines was reported January 30th, 2020. Following implementation of community quarantine, there was a sharp decline in TB case notifications until about 20 days following implementation, at which point TB case notifications began to increase again, retuning to a stable reporting rate about 2 months after implementation; however TB case notifications never returned to pre-pandemic levels. During the stable post-quarantine period, TB case reporting had dropped 44.6% (95% CI 38.3–50.1), with no significant change over time from day 60–174 following community quarantine implementation ($p = 0.20$). On the lowest reporting day, 18 days after community quarantine implementation, TB case notifications had dropped 74.8% from pre-quarantine levels.

Assuming the national TB incidence, treatment, and mortality rates for the Philippines from 2019 are similar to those of 2020 and that TB



HUC: Highly Urbanized Cities
* New Year's week, Chinese New Year, People Power Revolution, Day of Valor, Good Friday, Labor Day, Eid al Fitr, Independence Day, Eidul Adha, Ninoy Aquino Day, National Heroes Day, All Saints Day, Bonifacio Day, Feast of the Conception of Mary, Christmas Eve, Christmas, Rizal Day
** This depends on date of community quarantine implementation. The earliest date of implementation was March 14, 2020, which allowed for 49 days of pre-quarantine time. The latest date of implementation was April 15, 2020, which allowed for 174 days of post-quarantine time

Fig. 1. Study population.

Table 1
Facility Characteristics.

Characteristic	Facilities (N = 2,986) n (%)
Type of facility	
Hospital/hospital-based	298 (10.0%)
Stand-alone clinic	93 (3.1%)
Rural health unit/health center	2,559 (85.7%)
Jail/Prison	36 (1.2%)
Facility ownership	
Public	2,917 (97.7%)
Private	69 (2.3%)

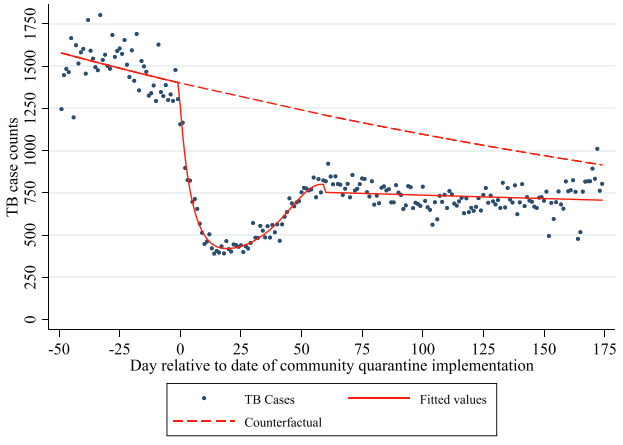


Fig. 2. Daily DS-TB case notifications at 2,986 DS-TB treatment facilities in the Philippines, January-December 2020.CQ: community quarantine, DS-TB: drug-susceptible tuberculosis.

case notifications were disrupted for 12 months followed by an immediate restoration to baseline [6,7], the interruption in TB treatment will significantly increase TB-related mortality. Specifically, the 44.6% decline in TB case notifications observed 60 days after community quarantine implementation would result in a 56.3% increase (95% CI 48.3–63.2) in TB-related deaths in the Philippines over a 12-month period, amounting to 43,459 additional deaths (95% CI 41,259–45,389).

3.3. Subgroup analyses

The immediate decline in TB case notifications was larger for clinically diagnosed (48.9%, 95% CI 43.6–53.7) than bacteriologically confirmed cases, (38.2%, 95% CI 30.7–44.9), but the difference was not statistically significant (p = 0.12) (Table 2, Fig. 3).

Across geographic areas of the Philippines, all regions saw a similar pattern in the decline of TB case notifications following implementation of community quarantine. A steep immediate decline in the first month of community quarantine was followed by a moderate increase and leveling off by around two months after implementation. In the three most populated regions of the Philippines (National Capital Region, Region III, Region IV), the pre-quarantine trend in TB case notifications was stable (slope 1.00, p = 0.01). In the other island groups (all other regions of Luzon, the Visayas, and Mindanao), TB case notifications

Table 2
Impact of community quarantine by disease type and island group.

	Percentage decrease in TB case notifications compared to expected reporting (95% CI) following community quarantine implementation
Disease type	
Bacteriologically confirmed	38.2% (95% CI 30.7–44.9)
Clinically diagnosed	48.9% (95% CI 43.6–53.7)
Island Group	
Most populous 3 regions	62.9% (95% CI 57.8–67.4)
Rest of Luzon Island	38.5% (95% CI 30.8–45.4)
Visayas	46.1% (95% CI 37.4–53.6)
Mindanao	12.8% (95% CI 4.5–20.5)
All	**44.6% (95% CI 38.3–50.1)**

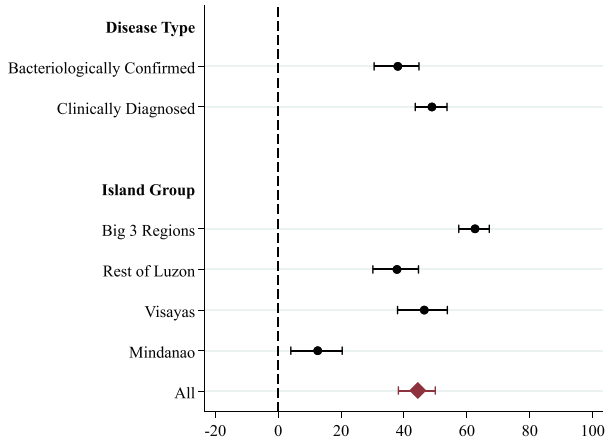


Fig. 3. Percent decrease in daily TB case notifications after community quarantine by disease type and island group.

were decreasing during the pre-quarantine period. Compared to the other island groups, the three most populated regions of the Philippines experienced the largest decrease in TB case notifications following community quarantine implementation ($p < 0.001$ vs. the rest of Luzon, Visayas and Mindanao) (Table 2, Fig. 3).

4. Discussion

Following the implementation of community quarantine policies to prevent the spread of COVID-19 in the Philippines, there was an immediate large decline in TB case notifications. Despite a slight increase in daily reporting about a month later, TB case notifications never returned to pre-pandemic levels, resulting in a 45% decline observed for the remainder of the year (about 9 months). While declines were observed across all regions and island groups in the Philippines, the largest 3 regions, which includes the National Capital Region, saw the largest percent decrease in TB case reporting. We project that this drastic reduction in TB case notifications would lead to a 56% increase in TB mortality over a 12-month period.

4.1. Limitations and strengths

It is possible that this model overestimates the increase in TB mortality if TB case notifications were to return to pre-quarantine levels before 12 months, or if TB transmission were simultaneously reduced during the community quarantine period. However, this could be an underestimate of the impact on TB mortality if the disruption to TB care lasts longer than 12 months, a realistic possibility given the Philippines remains under community quarantine as of October 2021, or if TB transmission were to increase during this period due to non-treated cases.

Strengths of this study include complete case reporting of drug-susceptible TB in the Philippines, a long follow-up period with 174 days of post-quarantine observation time, as well as province-specific implementation dates to allow for geographic variation in implementation.

4.2. Conclusion

Given the increased projected mortality due to TB following the implementation of community quarantine, we conclude that enhanced delivery of TB diagnosis and care services should be prioritized alongside efforts to combat COVID-19.

The observed reduction in TB case notifications during this period has major implications for TB program planning and may be used independently or in conjunction with further modeling. As health workers are vaccinated against COVID-19, and community quarantine restrictions are lifted, it will be imperative to increase active case finding efforts to compensate for the high number of missed TB diagnoses.

CRediT authorship contribution statement

Rebecca Crowder: Methodology, Data curation, Formal analysis, Visualization, Writing - original draft. **Donna Mae Geocaniga-Gaviola:** Conceptualization, Project administration, Writing - review & editing. **Ronald Allan Fabella:** Conceptualization. **Alexander Lim:** Data curation. **Evanisa Lopez:** Data curation. **Jillian L. Kadota:** Methodology, Formal analysis, Visualization. **Tania F. Reza:** Methodology, Formal analysis, Visualization. **Adithya Cattamanchi:** Methodology, Supervision, Writing - review & editing. **Anna Marie Celina Garfin:** Conceptualization, Resources, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jctube.2021.100282.

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