Reassessingtuberculosis control in the Philippines considering COVID-19 impacts

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Australian Tuberculosis Modelling Network

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Abbreviations

CNR	Case Notification Rate
DOTS	Directly Observed Therapy Short-Course
Community-DOTS	Community-based Directly Observed Therapy Short Course
HIU	Health Information Unit, the Philippines Department of Health
ICER	Incremental cost-effectiveness ratio
IPT	Isoniazid based treatment of latent *M.tb* infection for prevention of tuberculosis
KAP	Key Affected Populations
MDR	Multi-drug resistant
M.tb	*Mycobacterium tuberculosis*
NSP	National Strategic Plan
NTP	The Philippines National Tuberculosis Programme
QMRL	Queensland Mycobacterial Reference Laboratory
TB	Tuberculosis
TBCU	Tuberculosis control unit
TST	Tuberculin skin test
WHO	World Health Organization

Executive summary

This report summarises findings from an epidemiological analysis conducted by the Australian Tuberculosis Modelling Network (AuTuMN) team, through the Global Fund, with contributions from partners in the National Tuberculosis Program and the Universities and Institutes associated with the AuTuMN Team (Australian Institute of Tropical Health and Medicine, James Cook University, Monash University). The mathematical model of tuberculosis (TB) transmission and disease progression used in this analysis can examine numerous TB intervention programmes and population types. The model allows for epidemic and economic scenario analyses, which can be used to maximise cost-effectiveness of various interventions and estimate total financial commitment.

Background and context

The coronavirus disease 2019 (COVID-19) pandemic has severely impacted most countries around the world and outbreak responses have disrupted many public health services such as TB surveillance. In the Philippines, active TB case notifications approximately halved when community quarantines began in late March 2020 (in response to COVD-19) and have not returned to pre-COVID levels. Additionally, many activities that the TB control unit conduct to improve long-term epidemiological control, such as contact tracing of households and workplaces, were conducted in a more limited capacity, or postponed throughout 2020. At the same time, COVID-19 may have had some positive impacts on the TB epidemic in the Philippines. Since the modes of transmission are similar for COVID-19 and TB, interventions to control COVID-19 should also limit the spread of TB. For instance, social contact patterns have been highly modified in response to COVID-19, which is predicted to also reduce TB transmission. Recently, several vaccines have shown high efficacy to reduce infection of COVID-19, but with limited vaccine doses available, COVID-19 will likely continue to spread and disrupt public health services through 2021.

The AuTuMN model accounted for COVID-19 related disruptions and TB prevalence data to project different scenarios of TB in the Philippines in the future. The prevalence survey results in 2016 showed higher TB prevalence than expected in Philippines, with approximately 1000 per 100,000 people over 15 years affected (or 1% of the population). As a result, new goals have been developed in the PhilStep report[1]. The AuTuMN model has been updated for this report (from the 2016 model), to account for COVID-19 and higher than expected prevalence estimates. The new features include:

(1) Recalibration of the model to prevalence surveys in 1997, 2007, and 2016
(2) Calibration of the model to MDR TB incidence and notifications
(3) Incorporation of age-structured mixing matrices, with COVID-19 associated adjustments based on Google mobility data
(4) Estimation of the impacts of COVID-19 on case detection rates and contact tracing, assumed to last through 2021
(5) Seven interventions developed with the TBU of the Philippines, reflecting PhilStep priorities

Epidemic trends in tuberculosis in the Philippines

The Philippines has the third highest prevalence of TB globally, with the most recent prevalence survey (from 2016) showing unexpectedly high incidence. About 1 million Filipinos are currently living with active TB and drug resistant TB is becoming more common (estimated at 5.7% in 2012). The World Health Organization identified the Philippines as one of the few countries where the number of people with TB continues to increase each year. The Philippines is committed to the ambitious goals set by the END TB program to eliminate TB by 2050 with interim goals to reduce TB incidence, prevalence, and mortality to specified levels by 2030 and 2035. COVID-19 has disrupted TB detection and overall public health services, raising the question of whether the interim 2030 TB reduction goals can be achieved.

Questions for the AuTuMN analysis

The AuTuMN analysis aims to help the Philippines assess potential TB interventions by modelling different scenarios of TB transmission and quantifying the estimated change in TB cases given each intervention. The following scenarios were selected:

Scenario	Description
Baseline	Modelled TB prevalence and incidence if pre-COVID conditions are resumed in 2022 and carried forward, providing a comparison for other scenarios.
1	Increased contact tracing of LTBI with co-prevalent cases and all TST positive householders offered IPT. This scenario was also extended to include workplace contacts.
2	Improved retention in care and treatment success.
3	Reduced effective contact rate through ongoing physical distancing (currently enforced due to COVID-19) in communities and hospitals.
4	Widespread use of short course treatment for drug-resistant tuberculosis (which the TB control unit fully adopted in January 2020) and counterfactual model with continued use of long course therapy.
5	Increased use of firstline diagnostic GeneXpert at 50% and 100%. Current (2019) GeneXpert use is approximately 30%.
6	Improved case detection rate

Conclusions

Movement restrictions due to COVID-19 response policies have likely helped reduce TB transmission in the Philippines while decreased case detection has likely increased TB. Increased TB transmission due to disruptions from COVID-19 are not expected to increase TB transmission in the long-term if programs resume by 2022. If pre-COVID conditions resume in 2022, TB is estimated to gradually decrease to 2035. However, the model results indicate that under this baseline scenario and all interventions considered, the END TB targets will not be achieved. Notwithstanding, several interventions could help substantially reduce TB incidence and prevalence in the Philippines.

Recommendations

Increasing GeneXpert use to 100%, active case finding in households and workplaces, and continuing to use short course MDR-TB therapy are estimated to be the most effective interventions while improving retention in care and treatment success is least likely to reduce TB.

Chapter 1 Introduction

Careful evaluation of costs and potential for success (e.g., achieving END TB targets) across public health programs can help optimise allocation of limited resources. Crises like the COVID-19 pandemic make already limited resources and finances for tackling public health problems even more scarce. Modelling provides a method to simulate disease transmission dynamics and assess impacts of different programs on current and future epidemic outcomes. Model results can therefore help identify programs where scarce resources and time can have the largest potential impact on reducing disease. The AuTuMN team and Philippines TBU selected several intervention scenarios based on PhilStep to assess potential impact on reducing TB. The Philippines TBU assisted modellers in interpreting the programs into parameters that could be modelled, as described below. These analyses aim to help the Philippines understand their TB epidemic, including the various stages of latency and active disease driving transmission dynamics now and into the future, to assess whether the country is likely to achieve specified goals (e.g., END TB goals), and to identify whether any changes are needed from the NTP to achieve the specified goals. This report includes modelling results for:

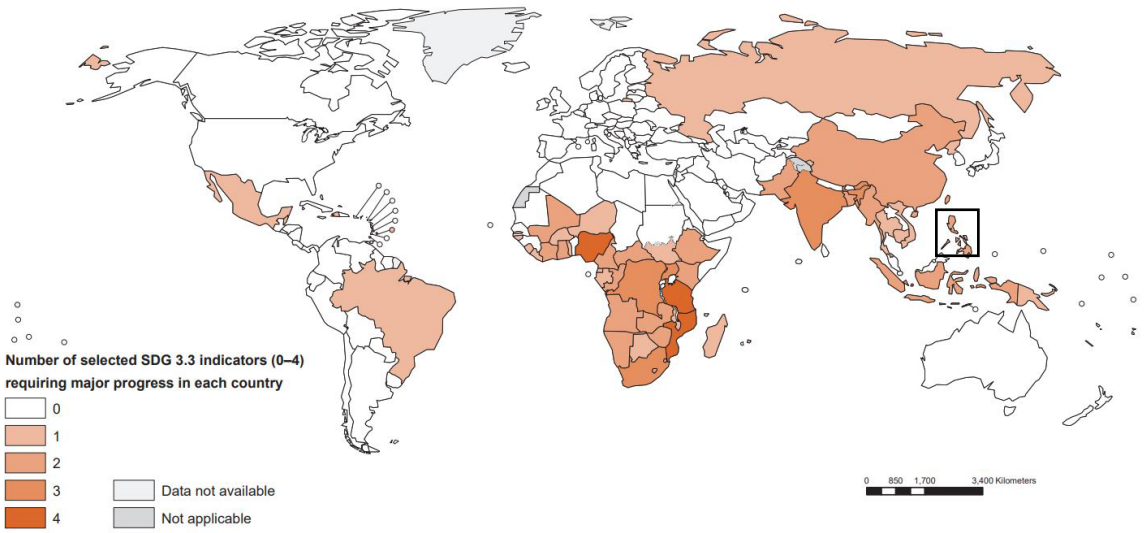
1. **Understanding the current TB epidemic and the impacts of COVID-19 on TB, both positive and negative**
2. **Predicting intervention outcomes and prioritising interventions and how these may change based on COVID-19 disruptions**
3. **Achieving NSP and END TB targets**
4. **Targeting areas of need**

Chapter 2 Background

2.1 Global setting

Tuberculosis is the number one infectious disease killer globally even though TB is curable and preventable. There were an estimated 10 million cases and 1.4 million deaths attributed to TB (including TB-HIV) in 2019 alone[2]. Tuberculosis primarily affects adults and people with impaired immune systems (particularly those living with HIV). TB control is hindered by drug resistant TB and weak health care services and surveillance systems. END TB targets, aimed at eliminating TB globally by 2050, are ambitious and will require renewed efforts to address TB.

The Philippines is the fourth highest burden country in the world for tuberculosis and is included in the Western Pacific Region (WPRO), which together with the South-East Asia Region (SEARO) make up over half the global burden of TB. The Philippines has an estimated incidence of 600 per 100,000 population[2], with increasing rates of drug resistance[2]. Philippines is committed to the END TB goals of elimination by 2050, but the country requires major progress to reach these and other Sustainable Development Goals (Fig. 1). This includes interim milestones including reduction in incidence of 5% by 2020, 80% by 2030, and 90% by 2035; reduction in mortality by 25% by 2020, 90% by 2030, and 95% by 2035 (compared with baseline 2014 WHO TB estimates); and maintaining treatment success rate above 85%.



Source: Global AIDS update 2019: communities at the centre. Geneva: Joint UN Programme on HIV/AIDS; 2019 *(15)*; Global tuberculosis report 2019. Geneva: World Health Organization; 2019 *(16)*; World Malaria Report 2019. Geneva: World Health Organization; 2019 *(17)*; Ending the neglect to attain the Sustainable Development Goals – A road map for neglected tropical diseases 2021–2030. Geneva: World Health Organization; 2020 *(18)*.

Figure 1. World map showing countries with potential to make progress against SDG 3.3 indicators, which include ending tuberculosis by 2030. This figure is from the WHO World Health Statistics 2020 Monitoring Health for the Sustainable Development Goals (SGDs). The Philippines (black box) requires major progress to reach these goals [2].

2.2 TB epidemiology in The Philippines

2.2.1 Prevalence

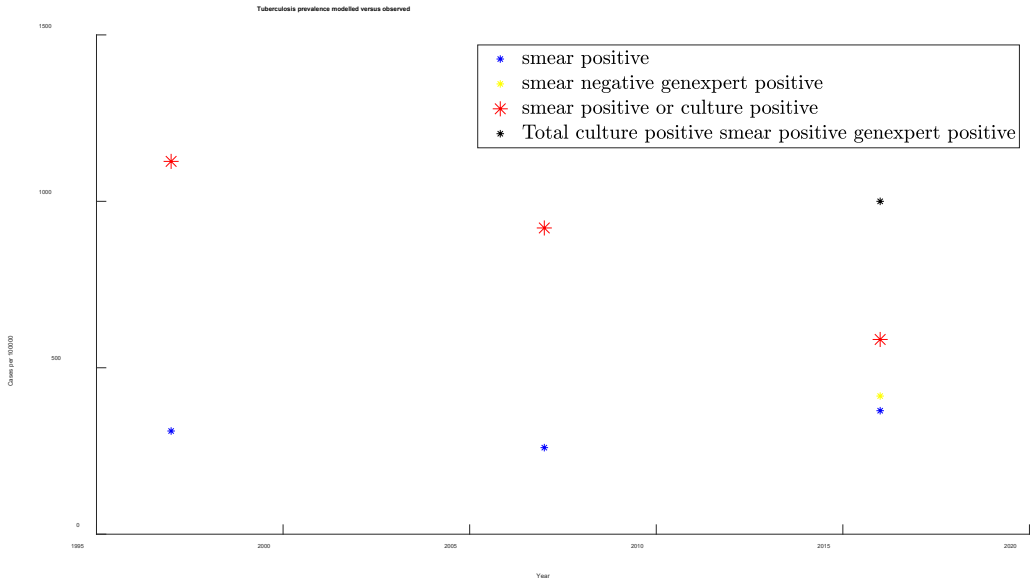


Figure 2. Prevalence survey results for tuberculosis. The surveys in 1997 and 2007 only reported smear and culture positive results, while the 2016 survey also reported smear negative, culture negative, and GeneXpert positive results.

2.2.2 Notifications and inferred incidence

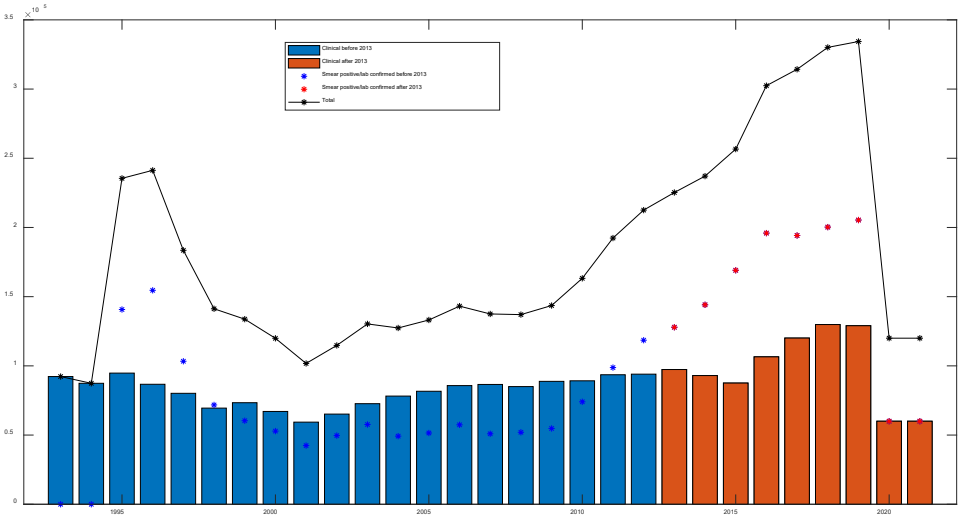


Figure 3. Notifications of Tuberculosis in the Philippines through time. Laboratory confirmed cases are shown in bars, while clinically diagnosed cases are shown as stars with the total shown as the black line. Diagnoses are distinguished between before or after 2012 as at this point, smear positive was replaced as laboratory confirmed –to incorporate smear geneXpert and culture results.

The WHO estimates that the incidence between years 2000 and 2018 were around 550 per 100,000 (see **Figure 8**). The absolute numbers given above, should be divided by 1000 to give the numbers per 100,000. This suggests that the case detection rate (proportion) was increasing from a low of around 20% in 2001 to a high of around 65% in 2019, prior to the onset of COVID, at which point it fell to levels of around 20%. The numbers for 2021 assume TB services and notifications continue to be impacted similar to 2020 for another 12 months.

2.3 Control programs under consideration

Table 1. PhilSTEP strategies to control TB that were considered for the AuTuMN model analysis.

RANK	TB control action	Modelling strategy	REMARKS
1	TB Preventive Treatment for household contacts (all ages)	Move people from Latent to Susceptible Move some people from Active undetected to Detected	PhilSTEP Strategy 13 (TPT) To be used for advocacy to Local Chief Executives
2	Establish TB Health Care PRovider Network per Local Government Unit (integrated DOTS strategy or delivery of full DRTB services in primary care facilities)	Improve TB success rates	PhilSTEP Strategy 9 (HCPN) Part of Universal Health Care
3	Community and home-based treatment (family DOT; digital adherence technologies/DAT)	Improve TB success rates	PhilSTEP Strategy 10 (PCC)
4	Infection Prevention and Control in Health Facilities, Congregate Settings and households (IPC)	Change in mixing matrix, which was developed during COVID-19 modelling and uses Google mobility results and contact matrices developed by Prem et al. 2017	PhilSTEP Strategy 14 Recommended by Health Secretary/ Minister
5	Engagement of private physicians (Mandatory Notification)	Reduce private fraction for all interventions from 30% in 2010 to 8% in 2020. Improve type of care	PhilSTEP Strategy 5 (MN) in Autumn List
6	Health promotion and communication (awareness campaign)	Improve case detection rate	One of the elements of UHC
7	Active Case Finding- community-based chest x-ray or in jails; Intensified Case Finding- facility-based chest x-ray, Enhance Case Finding- household visits with symptom screen; Contact investigation	Improve case detection rate	PhilSTEP Strategy 1-4 (ACF, ICF, ECF, CI)
8	Use of standardized shorter all oral regimen	Shorter course with improved success rates and reduce duration of treatment adopted from 2020.	PhilSTEP Strategy 10 (PCC)
9	Use of Xpert as primary diagnostic tool With Sputum transport system Include other RDTs: TruNAT, Xpert Ultra, Xpert XDR	Increase detection of both ds and mdr TB and fewer mis-categorised	PhilSTEP Strategy 6 (RDT) In Autumn List

Chapter 3 Modelling objectives and constraints

Priority modelling questions for the National Tuberculosis control Program, the Philippines[1]{, 2020 #96}:

1. What is the impact of COVID-19 on the tuberculosis epidemic in the Philippines?
2. Can the Philippines achieve the NSP and END TB targets for TB incidence and prevalence, and if so, how long might it take to reach these targets?
3. What should the annual targets for TB burden reduction be to achieve the END TB targets?
4. How will targeting national resources to special population groups affect outcomes?

3.1 Time horizons and goals of the NTP

The Philippines has set ambitious targets towards elimination of TB by 2050, aligning with the WHO Sustainable Development Goals and the END TB targets. The interim goals of the program aim to reduce incidence by 80% and mortality by 90% by 2035. To assist with these goals, the AuTuMN model analysis used 2030 as the time horizon and examined the impact of different interventions on TB prevalence and incidence. Additionally, The Philippines has developed a shorter-term action plan, the Phil-Step 1 updated for 2020 to 2023 with goals for interventions: screening, notifications, treatment of latent TB, and treatment of drug resistant TB, and for outcomes: deaths, incidence, catastrophic costs and patient satisfaction.

3.3 Approach and overview of methods

Here we present a brief description of the methods.

3.3.1 Epidemiology model

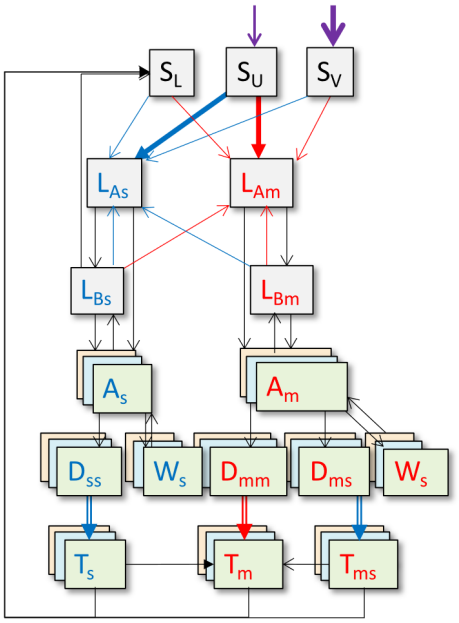
The AuTuMN model is a population- and age-structured compartmental model that allows individuals to transition from susceptible to various states of tuberculosis infection,

activation, diagnosis, and treatment. In the model, people can transition through TB states and age groups. Transition rates were guided by parameters, such as the rate of moving from latent to active TB, or the rate of aging from the 0-5 age group to the 5-15 age group. Parameters could vary through time, for example, treatment rate and success of treatment both improved in the 1960s and the model fluctuated these parameters from year-to-year to match observations. Data inputs into the epidemiology model include:

- **Demographics**: age strata and fertility from 1900 to 2020
- **Treatment**: historical commencement of treatments, such as DOTS
- **Prevalence, incidence, mortality, and case notification rates from TB:** WHO data from 1993 to 2020
- **Natural history of tuberculosis:** evidence from the literature
- **Intervention program impacts:** evidence from peer-reviewed literature

The main model outputs were projected TB incidence and prevalence. These outputs were stratified by age. Additional outputs that could be calculated include mortality, the number of people with latent TB (or in any other compartment), and the cumulative or current rate of flow between compartments. These outputs can also be used as inputs into an economic model.

AuTuMNtransmission dynamic model: states



Susceptible

Sl – Susceptible (previously infected)

Su – Susceptible unvaccinated

Sv – Susceptible vaccinated

Latent infection

Las – Early latent (drug-susceptible)

Lam – Early latent (drug-resistant)

Lbs – Late latent (drug-susceptible)

Lbm – Late latent (drug-resistant)

Active infection

As – Active (drug-susceptible)

Am – Active (drug-resistant)

Tms – Undergoing treatment (drug-resistant, incorrect)

Detected

Dss – Detected (drug-susceptible, correctly diagnosed)

Ws – Lost-to-follow-up

Dmm – Detected (drug-resistant, correctly diagnosed)

Dms – Detected (drug-resistant, incorrectly diagnosed)

Ws – Lost-to-follow-up

Treatment

Ts – Undergoing treatment (drug-susceptible, correct)

Tm – Undergoing treatment (drug-resistant, correct)

Figure 4. Diagram of AuTuMN epidemiological model. Compartments (boxes) represent states of TB infection (including susceptible), transition rates between compartments (arrows), and TB strain (box colours). Compartments were further stratified by age and comorbidity status. Compartments representing states of tuberculosis infection, activation, diagnosis, and treatment differ for drug resistant (red labels) and drug susceptible (blue labels) TB.

3.3.2 Scenarios

The AuTuMN model was used to simulate TB transmission dynamics to 2030 for a baseline scenario (pre-COVID-19 conditions carried forward starting in 2022) and six intervention scenarios. An initial set of nine interventions were considered (Table 2) and subsequently reduced to seven scenarios because of similarities in modelling approaches to simulate their impacts or because they are already widely used (and hence incorporated into baseline projections). For each intervention selected, a set of parameters were varied to reflect changes associated with an intervention. For example, to increase contact tracing, the detection rate of early and late latent TB would increase, thereby increasing transitions of individuals from those compartments back into susceptible compartments (e.g., bold arrows in **Figure 5**). Additional changes for other interventions are given in Appendix 2.

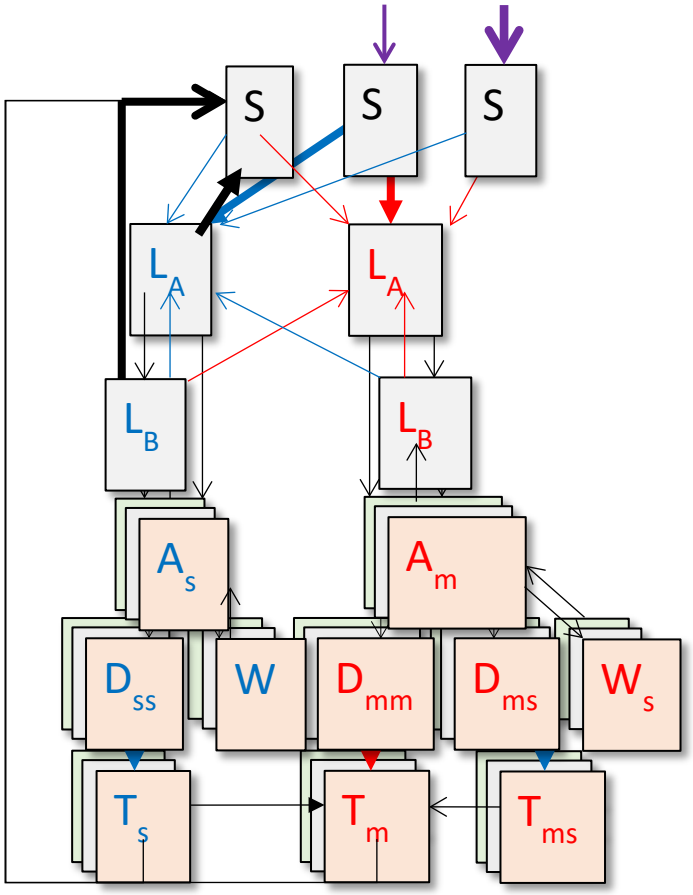


Figure 5. Example of parameter changes associated with scenario for increase in active case finding. The bold arrows show increased identification of TB and co-prevalent TB cases through increased detection of early (L_A) and late (L_B) latent drug susceptible (DS)-TB infected individuals, which would lead to an increase in individuals returning to a susceptible state.

Chapter 4 COVID and its impact on tuberculosis in The Philippines

4.1 COVID-19 Model

The AuTuMN COVID-19 model for the Philippines is an age-structured compartmental model (similar to the TB model) that incorporates time-varying changes in mobility, testing, and personal protective behaviours (to represent the Philippine's Minimum Health Standards). The model included six sequential compartments representing susceptible, non-infectious exposed, infectious exposed, early actively infectious, late actively infectious, and recovered/removed. The compartments were stratified based on detection status and disease severity as well as by age group using 5-year age bands from birth to >75 years old (Fig. 6). The proportion symptomatic, susceptibility to infection, infection fatality rate, and probability of hospitalisation differed by age group. Multiple epidemiological parameters were estimated in the model fitting process to better understand the epidemiology of COVID-19 in the Philippines. The model was calibrated to local daily confirmed COVID-19 cases, ICU occupancy, and cumulative deaths. The model outputs and scenarios are visualized on a Microsoft Power BI interface.

COVID-19 policy responses (e.g., community quarantines) have substantially impacted mobility in the Philippines, impacting COVID-19 transmission and likely TB transmission as well. The AuTuMN COVID-19 model introduced heterogeneous mixing by age through synthetic matrices developed by Prem et al. 2017. These dynamic mixing matrices were varied daily based on Google mobility data (https://www.google.com/covid19/mobility/). Google mobility data was used to scale the contribution of mixing from different locations to the overall mixing matrix based on changes in mobility in the household, work, and all other locations (e.g., transit, parks, retail). Changes in mobility have likely impacted TB transmission as well. Therefore, the AuTuMN TB model scenarios include COVID-19 adjustments to mobility based on Google mobility data lasting through 2020 and 2021.

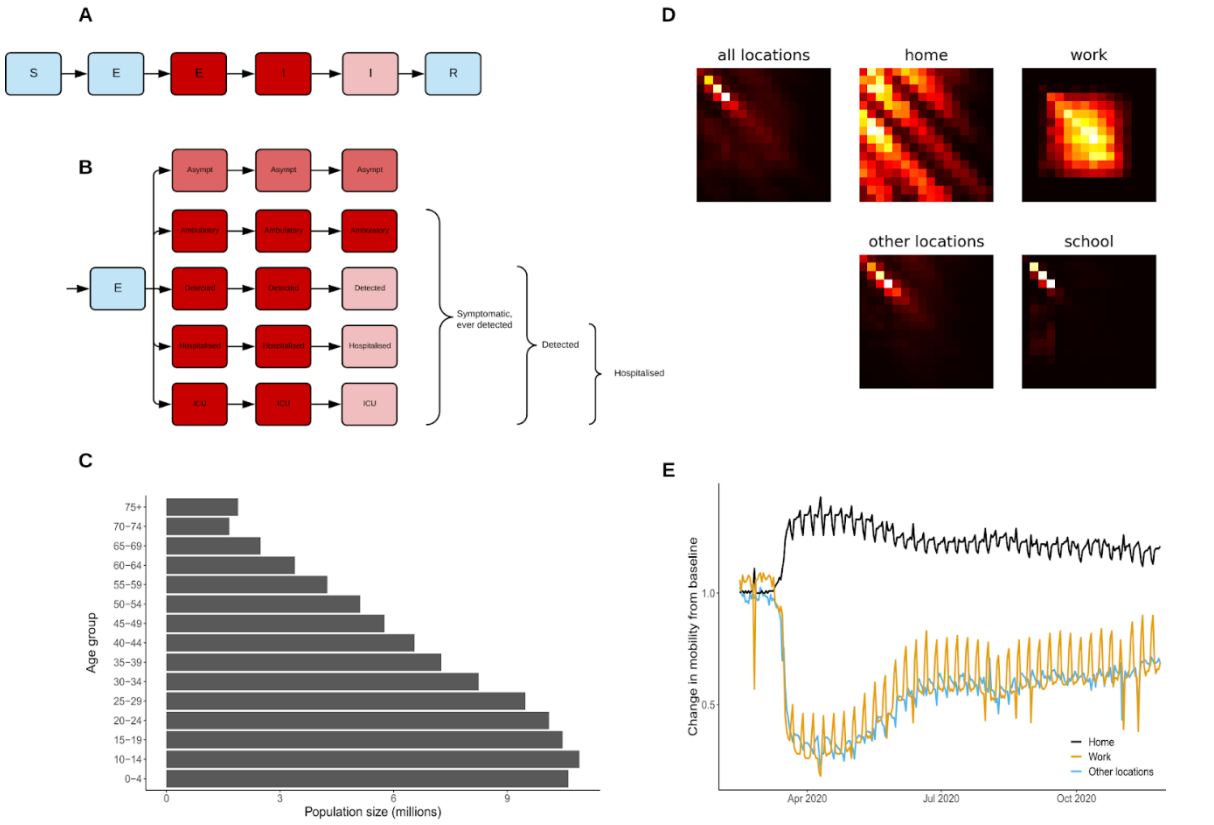


Figure 6. Age-structured COVID-19 model informed with population size, contact rates, and mobility from the Philippines. (A) Unstratified model structure. (B) Stratification by infection and detection status. (C) Age distribution of the population in the Philippines. (D) Heterogeneous mixing matrices by age in the absence of interventions. (E) Community quarantine driven mobility adjustments applied to the mixing matrices. Other locations include average from retail and recreation, supermarket and pharmacy, parks, and public transport.

4.2 Modelling COVID-19 impacts on TB

The impacts of COVID-19 on TB were incorporated into the AuTuMN TB model through changes in mobility, which occurred due to policy instated restrictions on movement and travel. Changes in mobility were incorporated into the AuTuMN TB model by multiplying the overall age-structured mixing matrix with the average change in mobility at work and all other locations (based on May 20, 2020) compared with pre-COVID mobility levels. These mobility adjustments were incorporated into the mixing matrix for 2020 and 2021 for all scenarios, except for the scenario where physical distancing continues indefinitely.

In addition to mobility adjustments, the AuTuMN TB model also accounted for reduced TB case detection rate for 9 months in 2020 and for all of 2021. This adjustment accounts for the decreased TB notification rate in the Philippines in 2020, likely due to several factors such as diverted TB resources and personnel to serve COVID-19 patients and changes in care-seeking behaviours due to reduced access to health care and/or perceived risk of

contracting COVID-19 when seeking care for TB. As shown in **Figure 3**, notifications in The Philippines in 2020 has been around 60,000 for each of smear positive and clinical diagnosis (from Department of Health Philippines dashboard: http://tbdashboard.doh.gov.ph/#!/layouts/dashboard-fullview.html). We assume for baseline estimates that this disruption continues until the end of 2021, whereas we assume that the changes in physical distancing continue until the end of 2020.

Chapter 5 Modelling the past to provide insights for the future

5.1 Calibration of AuTuMN to the Philippines TB epidemic data

For the period 1993 to 2019, incidence, estimated prevalence, and notified deaths were accessed from TB WHO reports [3-5]. The AuTuMN model was calibrated to align with TB prevalence by adjusting TB infectiousness, fitness cost of MDR-TB, and proportion smear positive. Additionally, the model was calibrated to mortality trends by adjusting the proportion of deaths from TB known to the TB program. TB incidence was used for cross validation in the fitting process (i.e., the model was not fitted to incidence data).

5.1.1 Prevalence

The AuTuMN model, calibrated to prevalence data, estimated decreasing TB prevalence between 1995 and 2020 for smear positive, smear negative culture positive, smear negative culture negative, and GeneXpert positive TB (Fig. 7). The model aligns well with data from the 1997 and 2007 well, and to a slighter lesser extent with the 2016 prevalence survey, likely because of the addition of highly sensitive GeneXpert diagnosis of pulmonary TB.

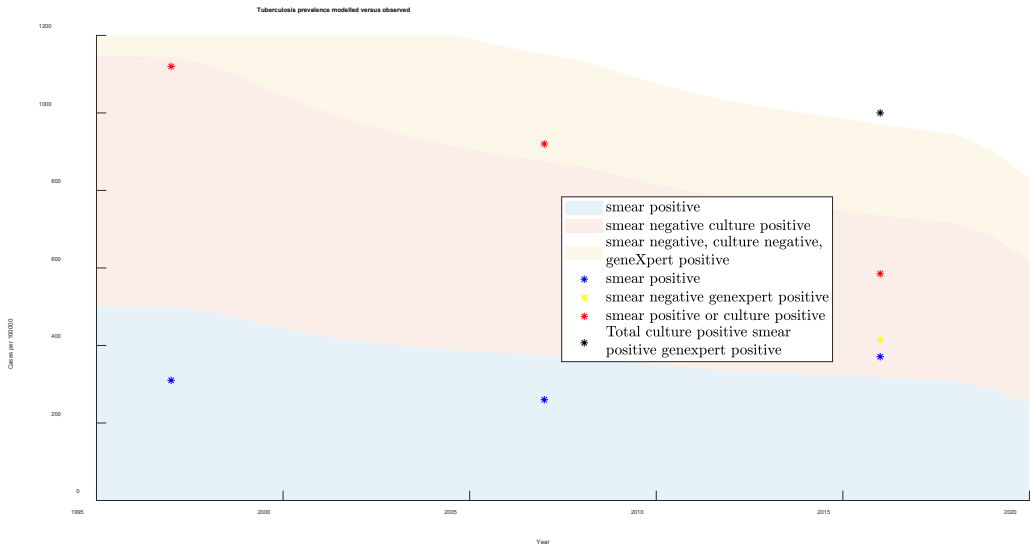


Figure 7. Model calibration to prevalence data. Model outputs (shaded regions based on diagnostic output) overlaid with data from the prevalence survey by diagnostic test (coloured points).

5.1.2 Incidence

The AuTuMN model results for incidence align well with WHO incidence estimates through 2008 and then diverge (Fig. 8). After 2008, the AuTuMN model estimates a gradual decline in TB incidence, continuing the pattern seen prior to 2008, while the WHO estimates gradually increasing TB incidence. The divergence in incidence estimates between the AuTuMN and WHO models is driven by interpretation of the unexpectedly high number of pulmonary TB cases in the 2016 prevalence survey. The WHO model interprets the high number of pulmonary TB cases from the prevalence survey as an overall increase in TB compared with previous years, whereas the AuTuMN model attributes the increase in pulmonary TB results to an increased detection rate because the survey included results from GeneXpert, a more sensitive test, which was not used in earlier surveys.

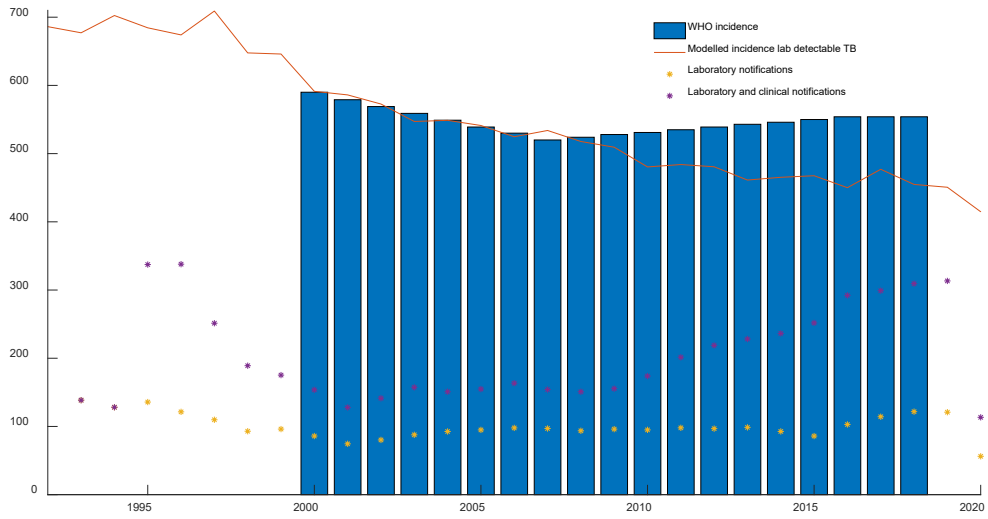


Figure 8. TB incidence in the Philippines through time. WHO model (blue bars), AuTuMN model (red line), and laboratory (yellow dots) and clinical (purple diamonds) notifications.

5.2 Base model parameters

The AuTuMN model included several time-varying and fixed parameters (Appendix). Key parameters in the model include:

Table 1. Core model baseline parameters

Parameter	Value and source
Case notification rate	The case notification rate (defined as the number of cases notified in 2015 divided by the number of incident cases) was 56% and was derived from both WHO data and the calibration process.
Treatment success rate	The treatment success rate was 92% and reflects the most recent three years of data from the Philippines NTP reports.
Treatment success rate for short course MDR-TB	The treatment success rate for short course MDR-TB was 88% based on the most recent three years of data from the Philippines NTP reports.
Frontline GeneXpert proportion	Frontline GeneXpert proportion was set to 30% based on data from 2019.
Proportion receiving BCG	The proportion receiving BCG was 99% based on the most recent three years of data from the Philippines NTP reports.

Chapter 6 Tuberculosis control programs and scenarios analysed

6.1 Baseline

The baseline scenario assumed current programs (as of 2015) continue until 2030 and provide a comparison to evaluate the impact of intervention scenarios. Outcomes for treatment programs were calculated as mean values from the most recent three years of data, as described in the NTP reports. These fixed treatment program values (from 2015) were carried forward in the baseline and intervention scenarios (unless specifically modified) and include success rates at 92% for DS TB, death rates at 2% and failure or default rates at 6%. Retention in care from point of presentation to commencement of treatment was assumed to be 80% and proportion of cases presenting to private facilities without mandatory notification was assumed to decline to zero from 2022. Case detection rate was assumed to remain at 56% for smear positive cases. BCG coverage was assumed to be 99% of the birth cohort. The full table is given in the appendix,

6.2 Scenarios analysed

Many different TB control actions can be simulated in the model by varying the same parameter values, therefore some of scenarios explored (Table 2) were modelled together. For example, there are many different efforts currently employed to improve case detection, including intensive case finding, active case finding, and enhanced case finding. The differences in the strategies are the degree to which they can find the missing cases, the efficiency in doing so (i.e., numbers of screened individuals needed to identify a case), and the cost of improving case detection. Therefore, TB control action 6 and 7 were modelled together. Similarly, community-based home care and healthcare provider networks are different strategies but both aimed at improving retention in care and successful outcomes, as well as reducing hospital inpatient costs. They were therefore modelled together as a single intervention of “improvement in care”. The scenarios in Table 2 were therefore reduced to:

Table 2. Interventions considered in the model

Scenario	Description
Baseline	Modelled TB prevalence and incidence if pre-COVID conditions are resumed in 2022 and carried forward, providing a comparison for other scenarios.
1	Increased contact tracing of LTBI with co-prevalent cases and all TST positive householders offered IPT. This scenario was also extended to include workplace contacts.
2	Improved retention in care and treatment success.
3	Reduced effective contact rate through ongoing physical distancing (currently enforced due to COVID-19) in communities and hospitals.
4	Widespread use of short course treatment for drug-resistant tuberculosis (which the TB control unit fully adopted in January 2020) and counterfactual model with continued use of long course therapy.
5	Increased use of firstline diagnostic GeneXpert at 50% and 100%. Current (2019) GeneXpert use is approximately 30%.
6	Improved case detection rate

6.3 Results

6.3.1 Baseline scenario – impact of current programs running from 2020 to 2030

If baseline conditions (e.g., pre-COVID conditions resuming in 2022) are carried forward, the AuTuMN model estimates TB incidence and prevalence will continue to decline by 2030. For both prevalence (Fig. 9) and incidence (Fig. 10), the AuTuMN model estimates a decline in TB incidence in 2020 resulting from the changes in physical distancing, followed by a rise in incidence in 2021 and 2022 as the reduction in activities of case notification and treatment dominates. This is followed by a sustained gradual decrease in both incidence and prevalence. In 2030 there is an uptick in incidence, reflecting the risk of MDR TB.

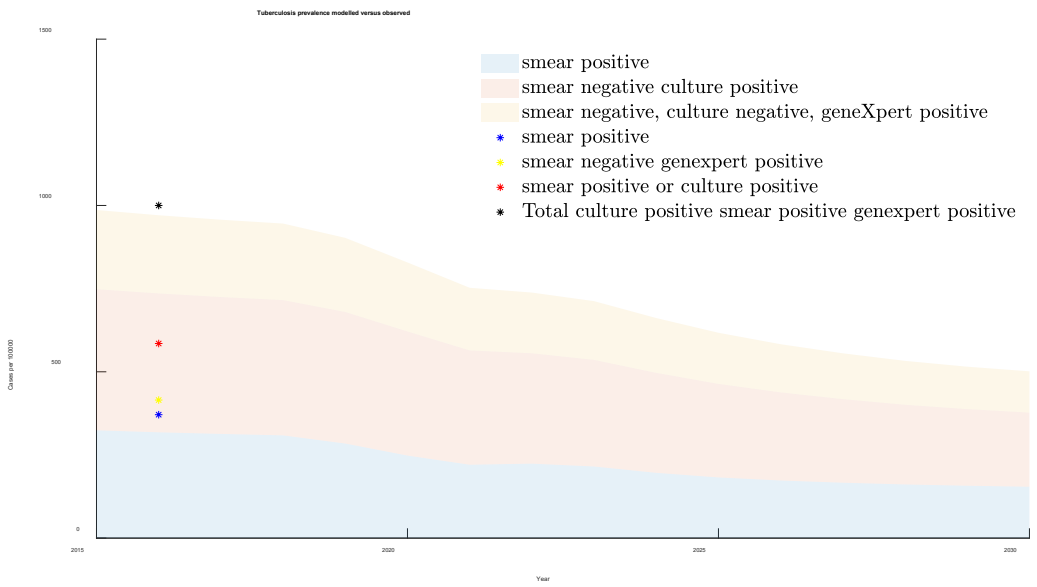


Figure 9. Modelled impact of continuing with the 2018 case notification and treatment program success rates (with reduced rates for 2020 and 2021 due to COVID-19) for TB prevalence.

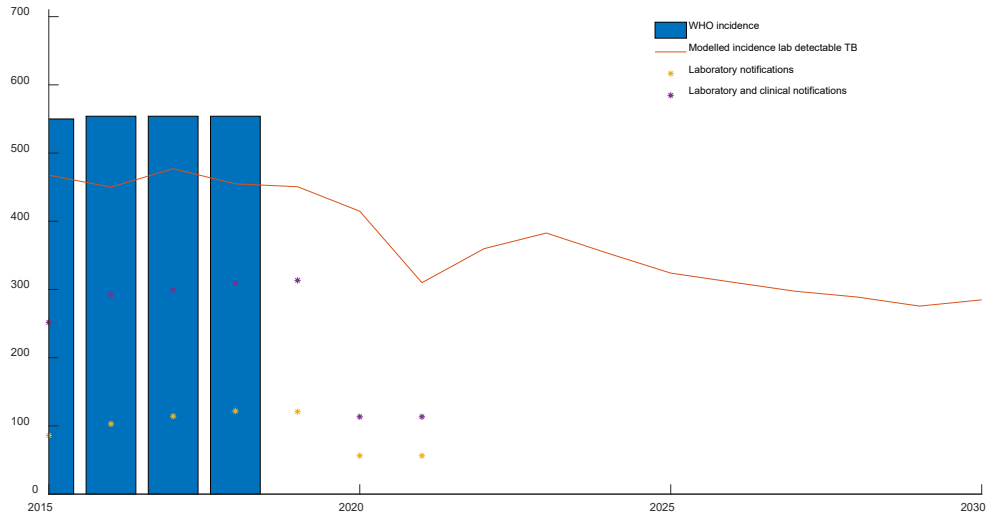
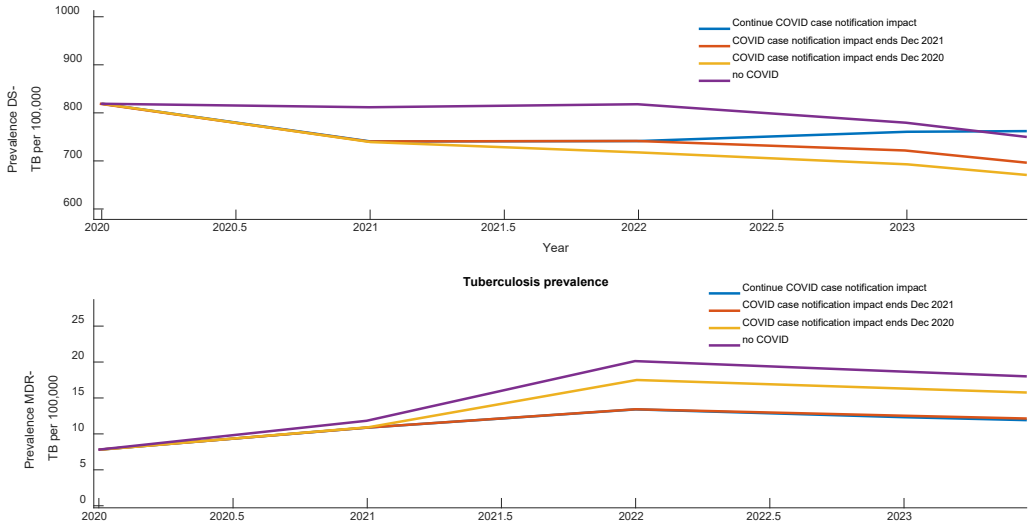


Figure 10. Modelled impact of continuing with the 2018 case notification and treatment program success rates (with differing rates for 2020 and 2021 due to COVID-19) on TB incidence.

Figure 11 shows the predicted impact of the COVID-19 pandemic on TB prevalence. This is assuming the change in physical distancing imposed by lockdown and COVID have a similar impact on TB as they did on COVID. COVID has a beneficial impact as a result of changes in contacts. However this trend reverses after 2021 and the reduced notification then determines the trajectory. If reduced notifications continue indefinitely, the TB epidemic is estimated to deteriorate compared with the “no covid” scenario in 2023. However, if pre-

COVID activities resume in 2021 or 2022, we estimate that there will be minimal impact on the TB epidemic in the Philippines.

Figure 11. Impact of COVID on the TB epidemic assuming baseline programs



6.3.2 Scenario 1 – Contact tracing

Household contact tracing of latent TB infection with co-prevalent cases and TST positive householders offered IPT is estimated to reduce DS-TB prevalence through time but not MDR-TB prevalence (Fig. 11). If contact tracing is extended to the workplace, the model estimates a more substantial decrease in DS-TB prevalence but a slight increase in MDR-TB prevalence (Fig. 12).

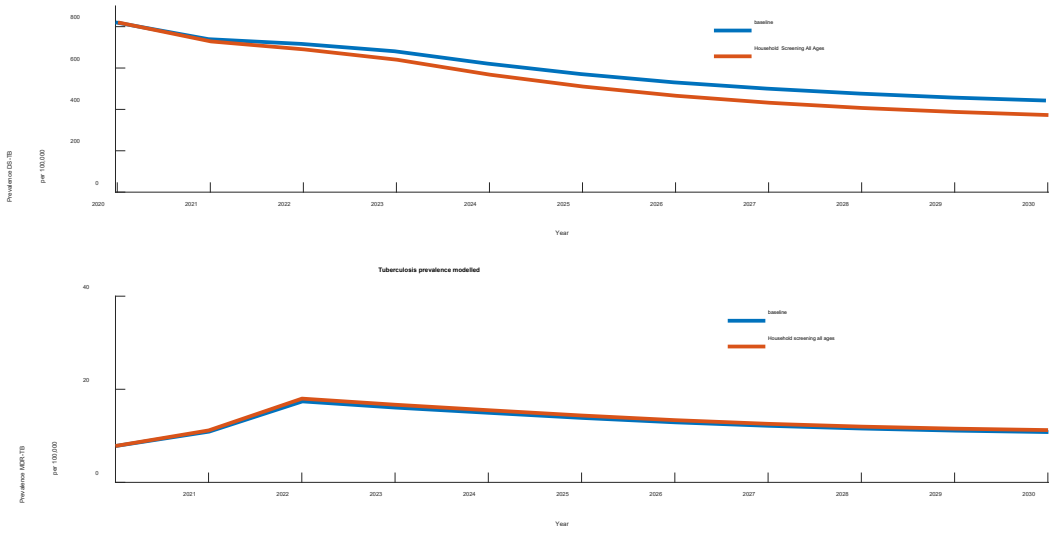


Figure 12. Scenario 1a results, DS-TB (top) and MDR-TB (bottom) prevalence through time with increased household contact tracing (red lines) compared with baseline scenario (blue lines).

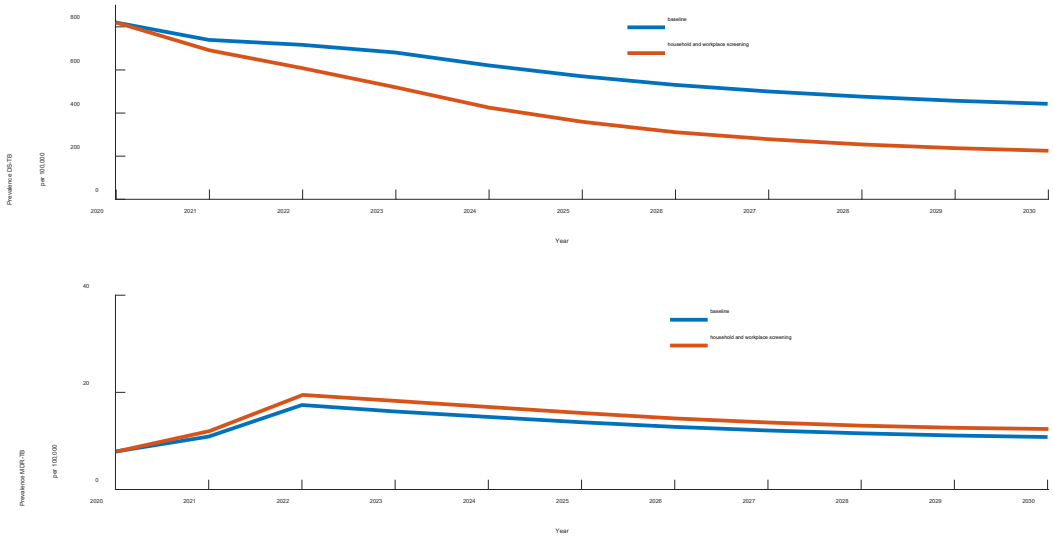


Figure 13. Scenario 1b results, DS-TB (top) and MDR-TB (bottom) prevalence through time with increased household and workplace contact tracing (red lines) compared with baseline scenario (blue lines).

6.3.3 Scenario 2 – Improving treatment success

Improving retention in care and treatment success is estimated to have almost no effect on reducing DS-TB prevalence and minimal effect on reducing MDR-TB prevalence (Fig. 13).

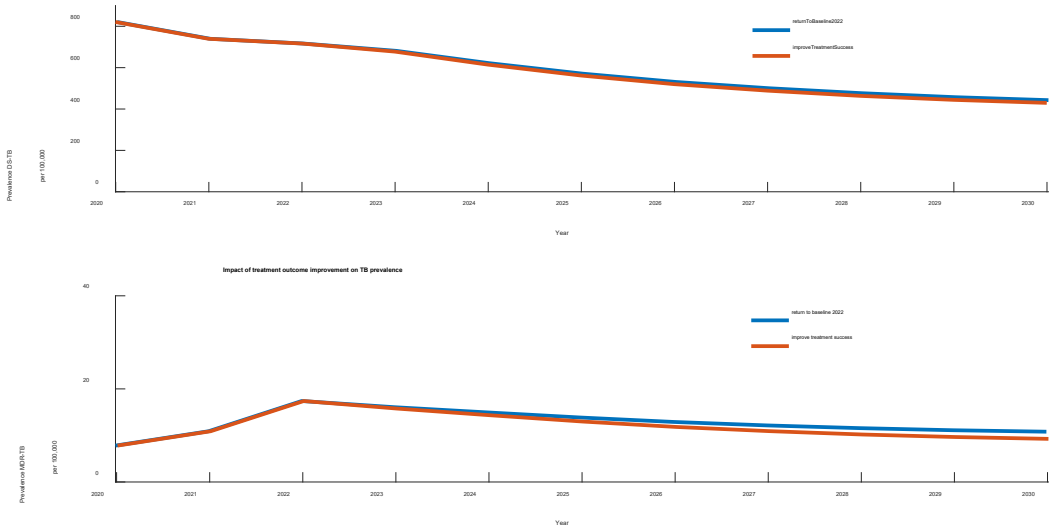


Figure 14. Scenario 2 results, DS-TB (top) and MDR-TB (bottom) prevalence through time with improved retention in care and treatment success (red lines) compared with baseline scenario (blue lines).

6.3.4 Scenario 3 – Reducing effective contact rate through physical distancing

If carried forward indefinitely, physical distancing and restricted movement, which have been enforced throughout the Philippines to reduce COVID-19 transmission, would reduce DS-TB prevalence by about 200 per 100,000 cases by 2030 and MDR-TB prevalence by about 5 per 100,000 cases by 2030 (Fig. 14).

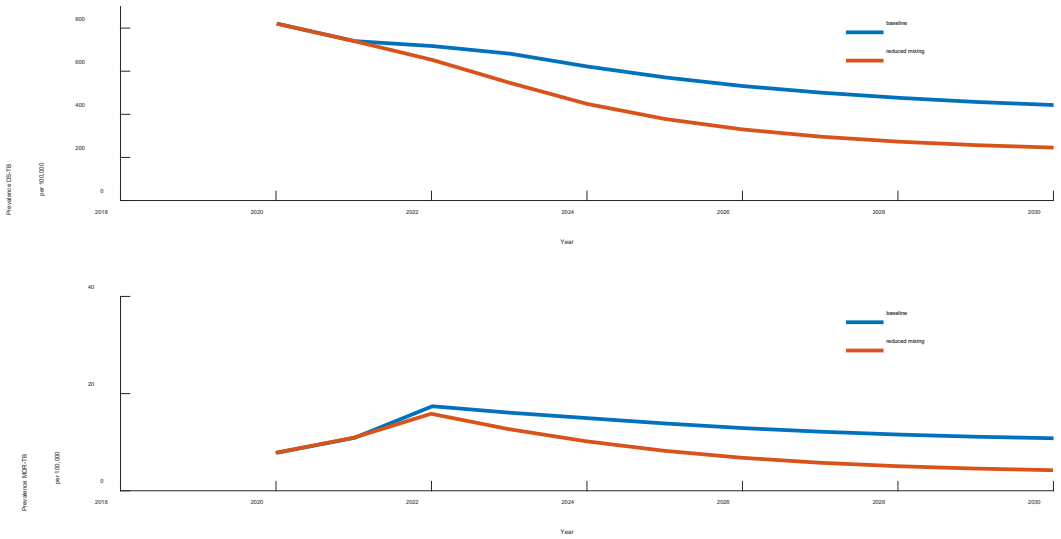


Figure 15. Scenario 3 results, DS-TB (top) and MDR-TB (bottom) prevalence through time with reduced effective contact through physical distancing (red lines) compared with baseline scenario (blue lines).

6.3.5 Scenario 4 - Short course versus long course MDR-TB therapy

The Philippines TB control unit fully adopted short-course treatment for MDR-TB in January 2020, therefore, in this scenario, short-course treatment was considered the new baseline ("return to baseline 2022") and compared with a counterfactual scenario where long-course therapy was used. The model results indicate no expected difference in DS-TB prevalence by 2030 but a reduction in MDR-TB starting around 2023 and increasing through time to 2035 (Fig. 15).

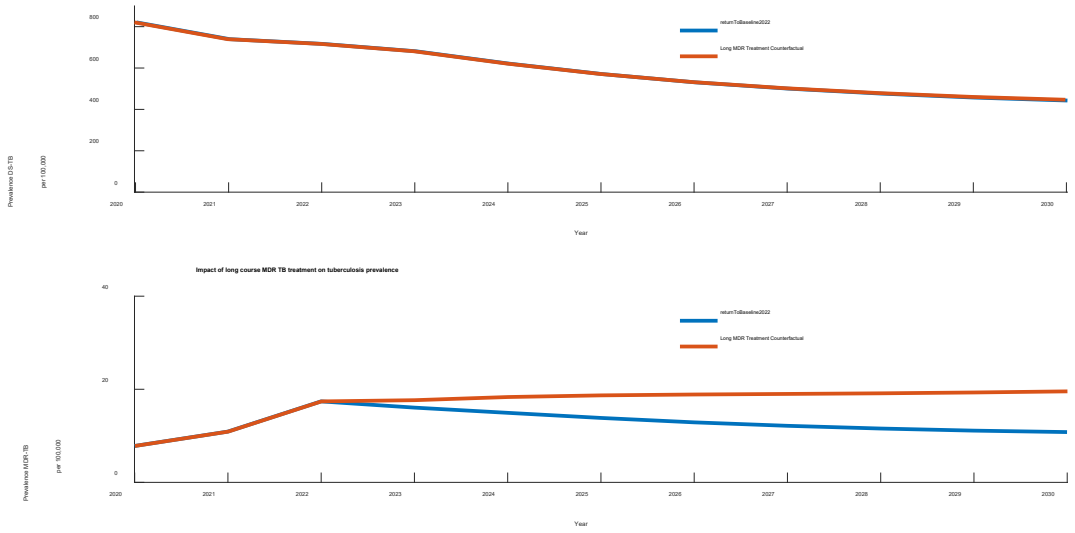


Figure 16. Scenario 4 results, DS-TB (top) and MDR-TB (bottom) prevalence through time with short course (blue lines) or long course (red lines) MDR-TB therapy.

6.3.6 Scenario 5 – GeneXpert increase as firstline testing

Increasing firstline diagnostic GeneXpert testing from 30% to 50% is estimated to slightly reduce DS-TB prevalence and gradually reduce MDR-TB prevalence to 2030 (Fig. 16). Increasing firstline diagnostic GeneXpert testing to 100% of firstline tests is predicted to lead to a gradual reduction in DS-TB and a more pronounced reduction in MDR-TB (Fig. 17).

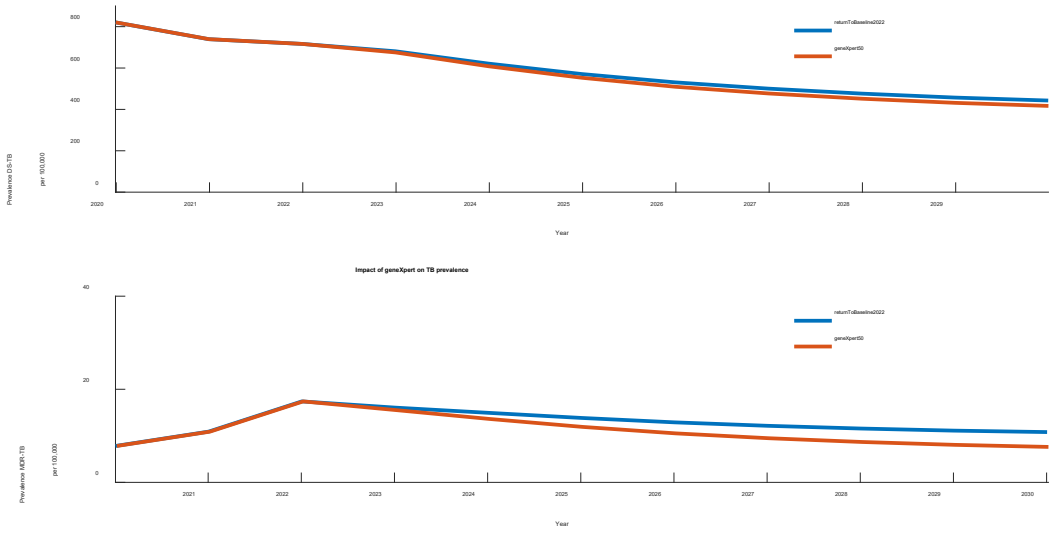


Figure 17. Scenario 5 results, DS-TB (top) and MDR-TB (bottom) prevalence through time with 50% increase in GeneXpert firstline diagnoses (red lines) compared with baseline (blue lines).

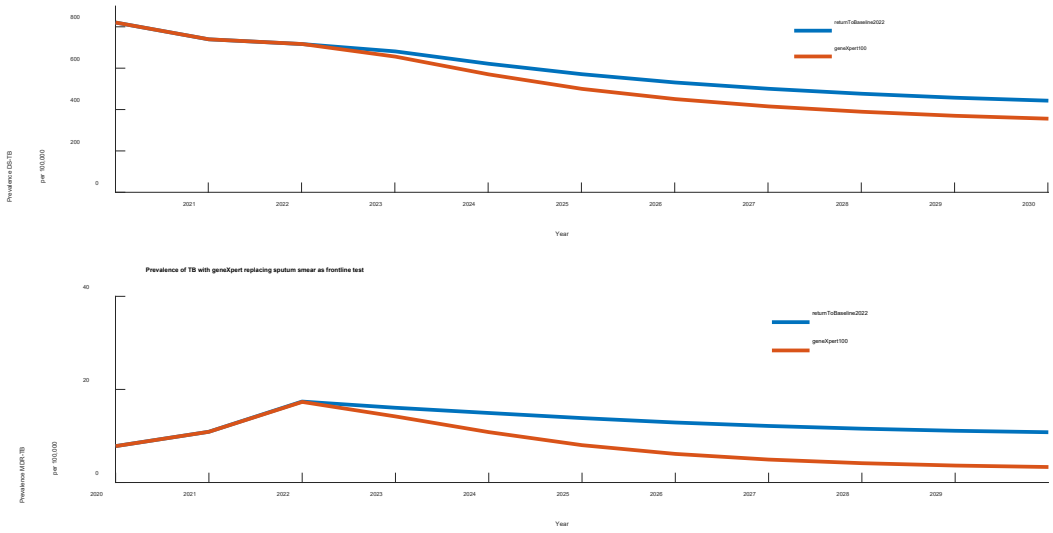


Figure 18. Scenario 5 results, DS-TB (top) and MDR-TB (bottom) prevalence through time with 100% increase in GeneXpert firstline diagnoses (red lines) compared with baseline (blue lines).

6.3.7 Scenario 6 – Improved case detection rate

As case detection rates increase from 56% to 95%, prevalence of DS-TB is estimated to decline while MDR-TB is not estimated to vary considerably (Fig. 18). Even with 95% case

detection rate of DS-TB, prevalence does not decrease to zero.

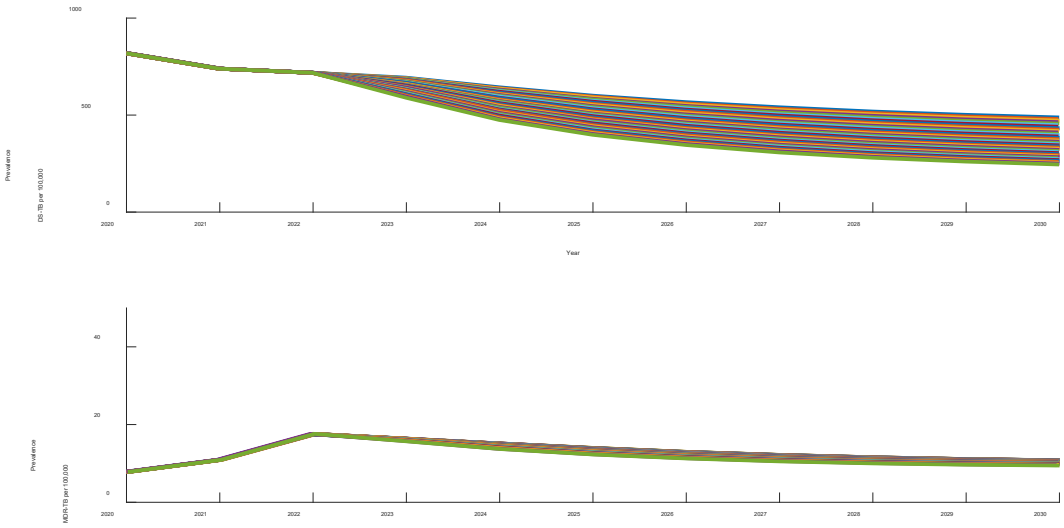
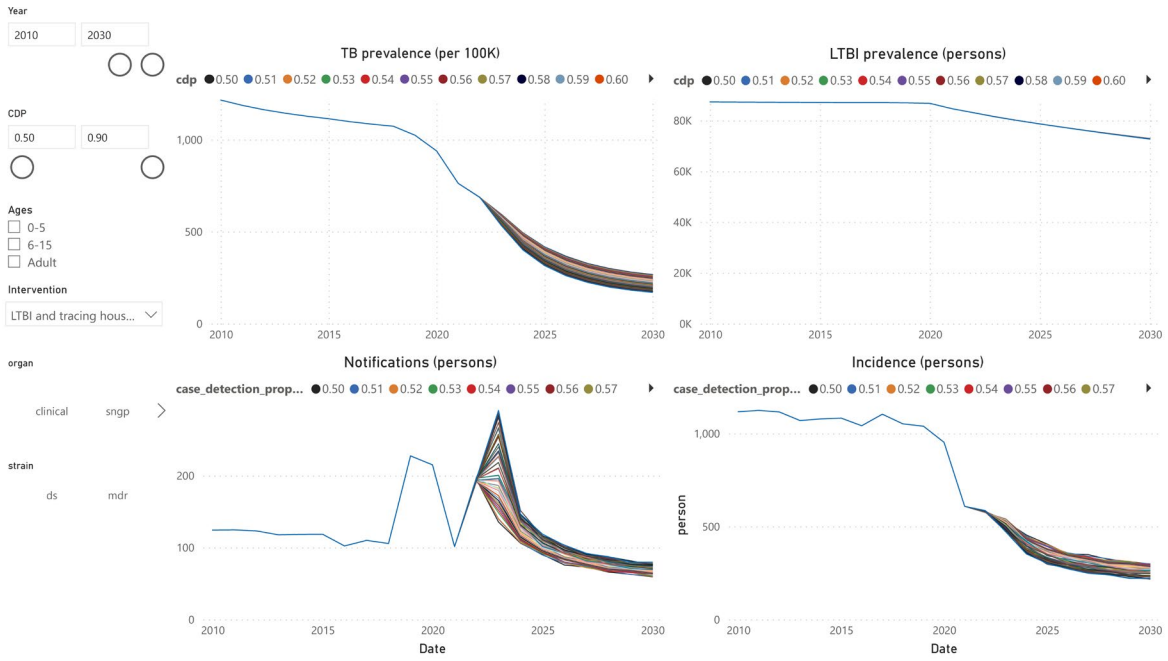


Figure 19. Scenario 6 results, DS-TB (top) and MDR-TB (bottom) prevalence through time with for overall case detection rates from 56-95% in 1% increments (coloured lines).

6.3.8 Interaction of more than one scenarios

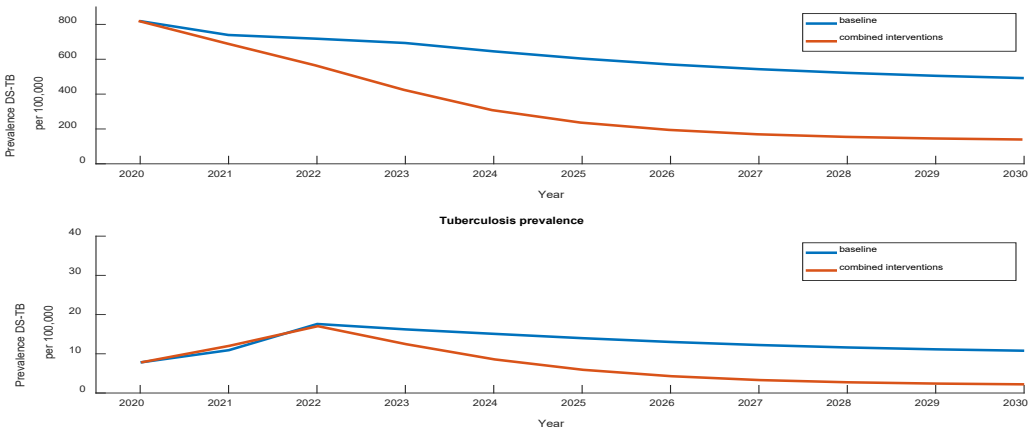
To examine the impact of differing case detection rates on the impact of other scenarios, we performed each of scenarios 1 to 5 across different case detection rates from 50% to 90% in increments of 10%. This is presented in the powerBI interactive output, an example is shown in Figure 20 in which the case detection proportion along with the impact of increase contact tracing is shown.

Figure 20. Screenshot of the interactive power BI tool with epidemiological consequences of two interacting interventions: contact tracing with household screening and treatment of latent TB, along with general increase in case detection.



The final model was that of the combination of all scenarios, shown in Figure 20.
Combination of all scenarios

Figure 21. Combination of all scenarios, DS-TB (top) and MDR-TB (bottom) prevalence through time



Chapter 7: Case detection impact tool

We developed a tool for estimating the impact of case detection activities for use by the TB control unit, found here.

It allows TB policy makers to calculate the change in case detection that could occur for a given program, and in turn the impact of that case detection would have on the epidemic more broadly, if it were implemented in 2021 and continued until 2030. The required information for the tool are the size of the target group, the prevalence or relative prevalence in the group of TB, the screening/detection method (in particular its sensitivity). Costs can be calculated for the program if unit costs per screened person and start-up and annual fixed costs are included.

An example is provided:

Key affected population: Urban poor

Size of key affected population: 5,037,800

Prevalence of tuberculosis in the key affected population: 12.4 per 1000 culture positive

Screening tool: chest Xray followed by Xpert TB ref (~92.4% sensitive for lab pulmonary confirmed TB).

This example and the output is used in the powerBI tool and the output in powerBI is shown below in Figure 21.

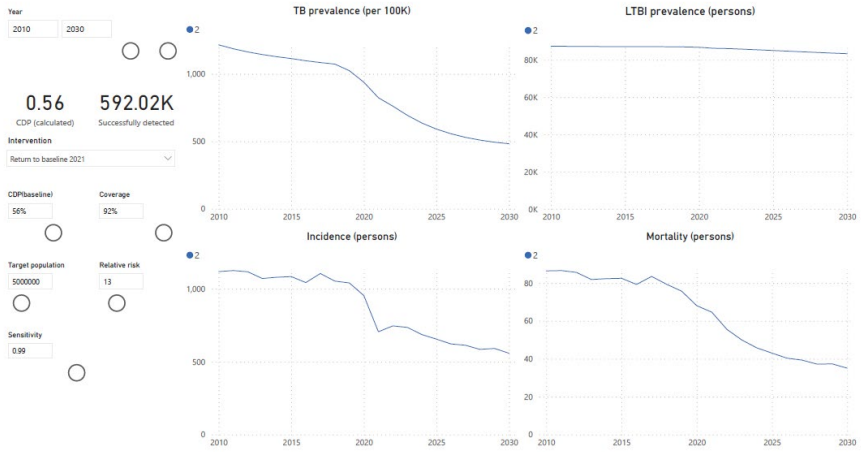


Figure 22 Impact of case detection regimen proposed above.

Chapter 8
Conclusions and recommendations

7.1 Conclusions

Policy responses to COVID-19 that increased physical distancing have likely helped reduce TB transmission in the Philippines. Based on the modelled scenarios, maintained physical distancing would offer the most effective TB intervention in the future, however, it is unlikely that people will voluntarily continue physical distancing and movement restrictions once COVID-19 is controlled. Thus, the conclusions below focus on other scenarios that are likely more achievable. Further, increases in TB due to COVID-19 related disruptions to public health services were not projected to affect long term TB trends.

Can the Philippines achieve the national strategic plan and END TB targets for TB incidence and prevalence, and if, so how long might it take to reach these targets?

The model results indicate that the Philippines cannot achieve the NSP or END TB targets for TB incidence and prevalence by 2030. However, the results indicate that under current (baseline) activities, incidence and prevalence should continue to decline in the future, falling from the WHO estimated incidence of approximately 550 cases per 100,000 population to approximately 300 per 100,000 population by 2025 and 280 per 100,000 population by 2035. Several interventions could further reduce incidence and prevalence.

Which interventions are the most impactful?

Increasing active case finding, GeneXpert use, and continued use of short course MDR-TB therapy are estimated to be highly effective at reducing TB prevalence given the scenarios considered. Simultaneously improving active case finding in the household and workplace is estimated to reduce DS-TB burden substantially, although it is unlikely to reduce MDR-TB and could even lead to a small increase in MDR-TB prevalence. Increasing firstline diagnosis with GeneXpert by 100% is estimated to effectively reduce both DS-TB and MDR-TB prevalence. Finally, carrying forward with short course MDR-TB therapy, which has already been widely adopted, is estimated to reduce MDR-TB prevalence considerably compared

with long course therapy. Therefore, the model results indicate this intervention is highly effective.

Which intervention is the least impactful?

Improving retention in care and treatment success is estimated to have almost no effect on reducing DS-TB prevalence and minimal effect on reducing MDR-TB prevalence, and therefore is considered the least impactful intervention considered. This is likely due to the already high success rates experienced for DS TB in the Philippines once a person is in care, and anticipated high success rate now that the NTP has transitioned to new short course and all oral management of MDR-TB.

7.2 Recommendations

The results of this analysis indicate that TB incidence and prevalence should gradually decrease over the next 15 years in the Philippines and any negative effects from COVID-19 will not last if program activities resume by 2022. Increasing firstline diagnosis testing with GeneXpert to 100% would be a highly effective intervention. Increasing active case finding in the household and workplace would further provide extensive reductions in TB. Finally, the newly adopted short course MDR-TB therapy should reduce MDR-TB considerably between now and 2030. The results also suggest that less emphasis should be placed on improving retention in care and treatment success as the potential gains from these programs are limited.

References

1. Updated Philippine Strategic TB Elimination Plan, Phase 1: 2020–2023. Manila: Department of Health, Philippines, 2020.
2. Global Tuberculosis Report. World Health Organisation. Geneva; 2020.
3. Global Tuberculosis Report. World Health Organisation. Geneva; 2016.
4. WHO. Global Tuberculosis Report. Geneva , Switzerland, 2015.
5. Global tuberculosis report 2020: , 2020.

Appendix A: Baseline parameters

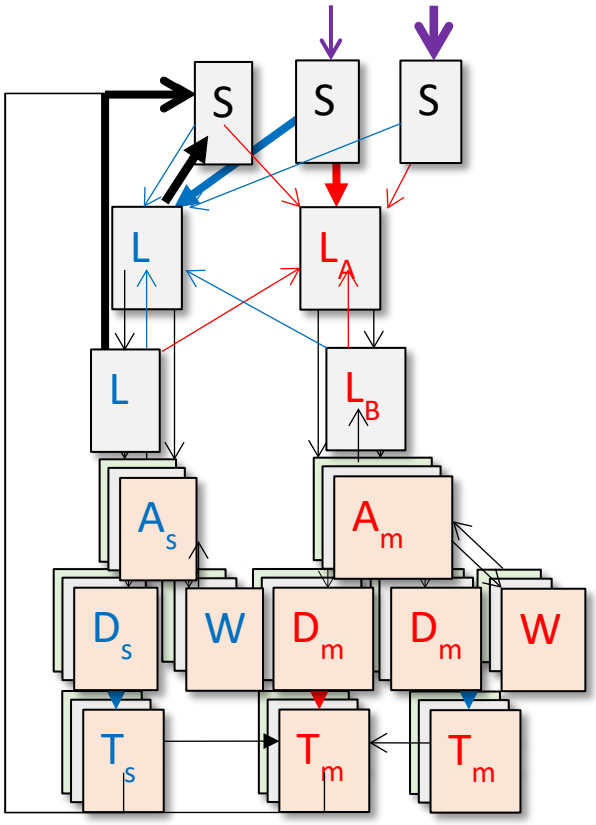
Parameter names and values used in the AuTuMN model. These parameter values reflect pre-COVID-19 conditions and were held constant in the scenarios starting in 2022 (unless specifically modified for intervention purposes). Time-varying values are coloured in orange while fixed values are shown in black.

Table 3 Baseline parameters from 2022 in the model.

Parameter name in model	Baseline value
detected	
case_detection_proportion	**0.56**
case_detection_proportion_sp	**0.56**
case_detection_proportion_clinical	**0.28**
retention_dx_rx	**0.80**
frontline_xpert_proportion	**0.30**
treatment	
treatment_success	**0.92**
treatment_success_mdr	**0.88**
mortality_on_treatment	*0.02*
mortality_on_treatment_mdr	**0.07**
default_failure	*0.06*
default_failure_mdr	*0.05*
proportion_mdr_misdiagnosed_as_ds_transition_to_fail_retreat	*0.40*
proportion_mdr_misdiagnosed_as_ds_transition_to_fail_lost	*0.10*
proportion_mdr_misdiagnosed_as_ds_transition_to_spont_recover	*0.10*
proportion_mdr_misdiagnosed_as_ds_transition_to_death	*0.30*
death	
treatment_success_under_short_course_mdr_tb_regimens	**0.88**
probability_of_treatment_success_of_mdr_incorrectly_diagnosed_as_ds	*0.20*
probability_of_death_on_treatment_for_short_course_mdr	*0.05*
natural_death_sp	*0.70*
natural_death_sngp	*0.29*
natural_death_clinical	*0.29*
natural_recovery_sp	*0.23*
natural_recovery_sngp	*0.13*
natural_recovery_clinical	*0.13*
natural_recovery_all	*0.20*
tb_prop_casefatality_untreated	*0.40*
life_expectancy	*70.00*
durations	
tb_timeperiod_early_latent	*0.16*
tb_timeperiod_activeuntreated	*3.00*
tb_timeperiod_ontreatment_ds	*0.50*

tb_timeperiod_ontreatment_mdr	**0.75**
tb_timeperiod_ontreatment_xdr	*2.00*
tb_timeperiod_infect_ontreatment_ds	*0.04*
tb_timeperiod_infect_ontreatment_mdr	*0.08*
tb_timeperiod_infect_ontreatment_xdr	*0.17*
testing	
diagnostic_sensitivity	*0.90*
mean_time_to_diagnosis_days	*16.00*
inverse_treatment_wait_time	*26.00*
inverse_treatment_wait_time_mdr	13.00
preventive_therapy_for_under5y_tstp_uptake	*0.14*
proportion_of_first_line_diagnostics_using_genexpert	*0.03*
force_of_infection	
tb_multiplier_force_smearneg	0.24
tb_multiplier_child_infectiousness	0.10
tb_multiplier_child_infectiousness_age0to10	0.10
tb_multiplier_child_infectiousness_age10up	1.00
tb_prop_amplification	0.07
mdr_fitness_cost	0.80
LTBI_intervention	
number_moved_LA_S3	0.00
number_moved_LB_S3	0.00
number_coprevalent_TB_found	0.00
sensitivity_of_ltbi_test	0.75
probability_of_contacts_becoming_infected	0.52
sensitivity_of_xpert_on_smear_negative_cases	0.67
chest_x_ray_sensitivity	0.90
tb_prop_infections_in_household	0.40
program_timeperiod_await_treatment_smearneg_xpert	0.02
program_timeperiod_community_ipt_round	1.00
average_household_size	4.60
cascade_of_care	
missed_to_active_rate	4.00
program_prop_child_reporting	0.40
proportional_reduction_in_adverse_outcomes_from_the_treatment_support_intervention	0.40
awareness_raising	
program_ratio_case_detection_with_raised_awareness	1.52
program_prop_population_screened	0.27
program_prop_population_screened_prison	0.80
vaccination	
proportion_receiving_bcg	0.99
immunity_wane_rate	0.03
proportion_private	0.00

Appendix A: Intervention parameters

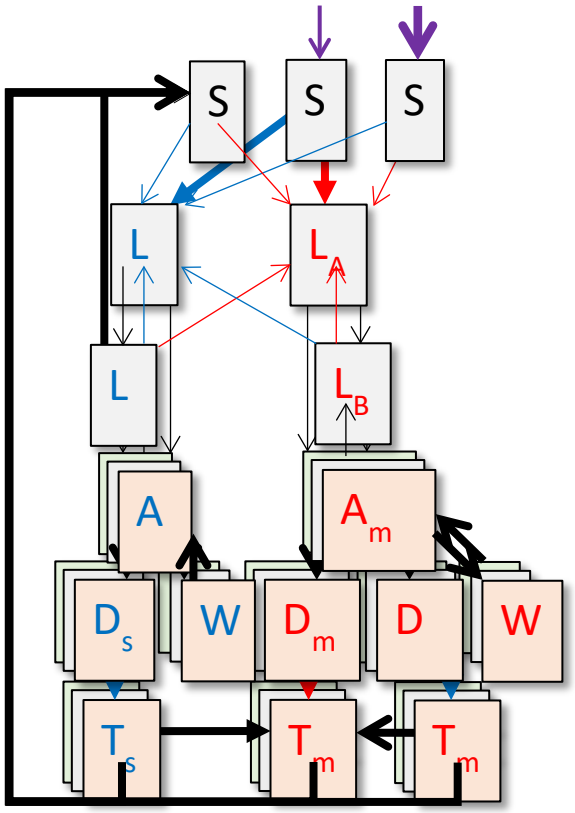


TB control action

1a Contact tracing with identification of co-prevalence cases and TB Preventive Treatment for household contacts

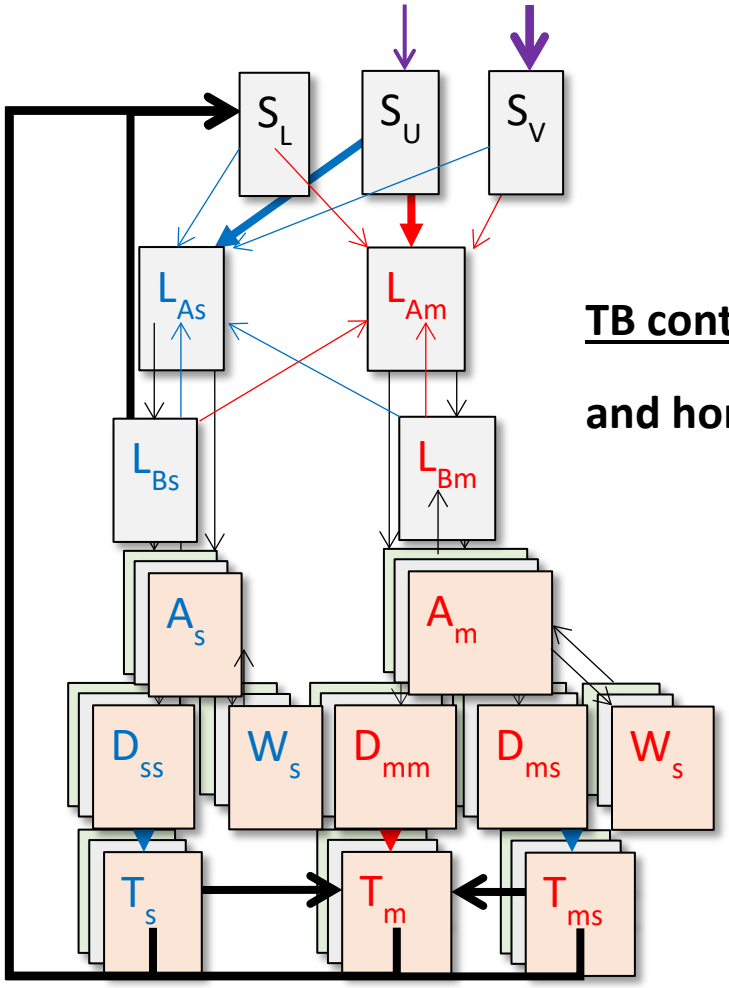
1b extends this to workplaces

Contact tracing of each notified pulmonary TB case, with assessment of all household contacts using TST to identify latent TB and co-prevalent TB. We estimate that this would lead to on average 0.55 people in the latent state to be moved to the susceptible state and 0.18 people found with co-prevalent TB and treated. With expansion of contact tracing to workplaces, this increases to 2.76 movements from latent TB to susceptible and 0.92 co-prevalent cases found.



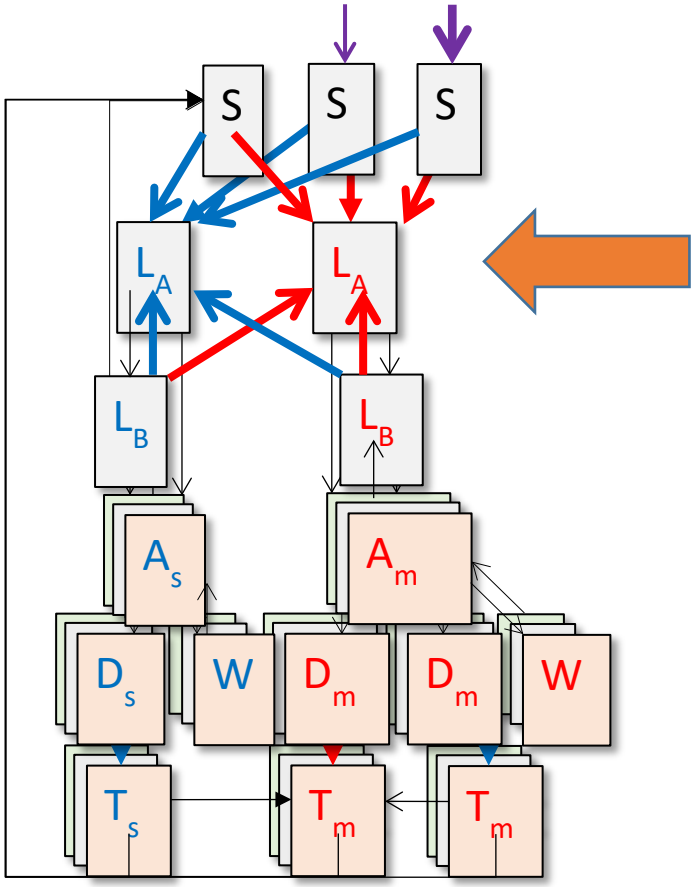
TB control action 2:

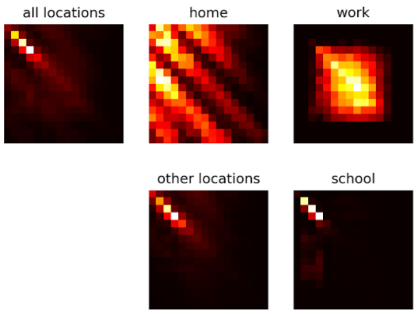
Establish TB Health Care Provider Network per Local Government Unit



<u>TB control action 3:</u> Community and home-based treatment

Both action 2 and action 3 are centred around improving the quality of care and treatment of TB cases once diagnosed, and were therefore regarded as one intervention in the model, with parameters indicated in Table 4.

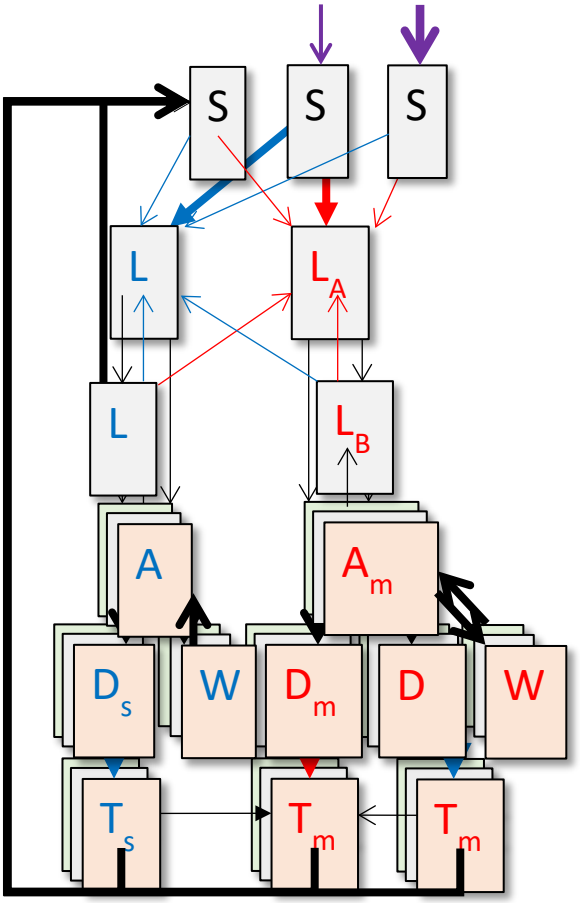




TB control action 4:

Infection prevention in control and health facilities

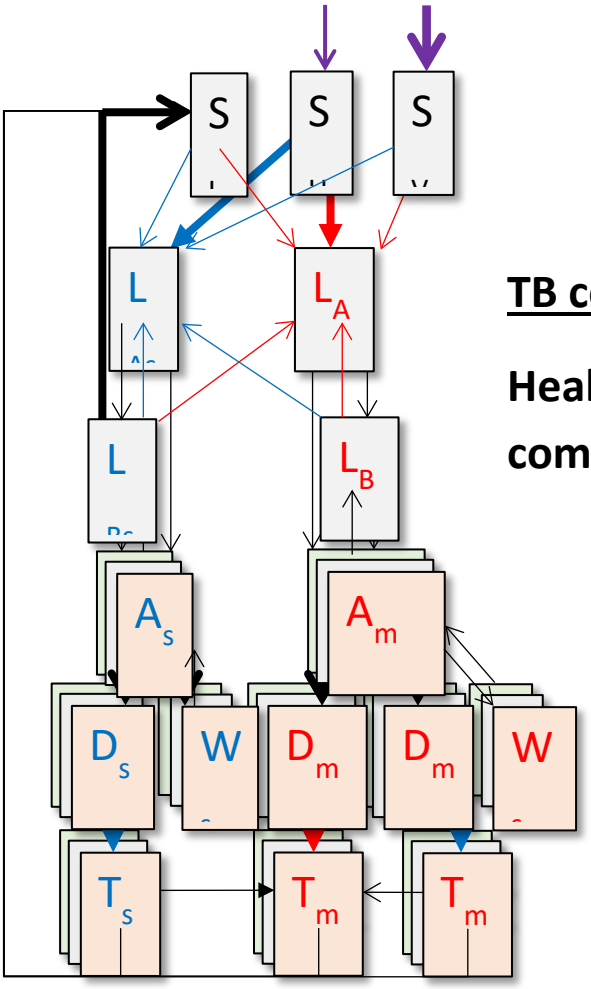
The mixing intervention considers the change in the contact matrix which occurred during the COVID epidemic lock-down in The Philippines in mid-2020. This has been shown to reduce transmission of COVID-19 and is also postulated to have a similar effect on TB transmission. This was modelled by having an age-dependent mixing matrix at baseline and another for 2020, representing the impact of COVID in reducing the number of effective contacts that people have during the lockdown.



TB control action 5:

Engagement of private physicians including compulsory notification

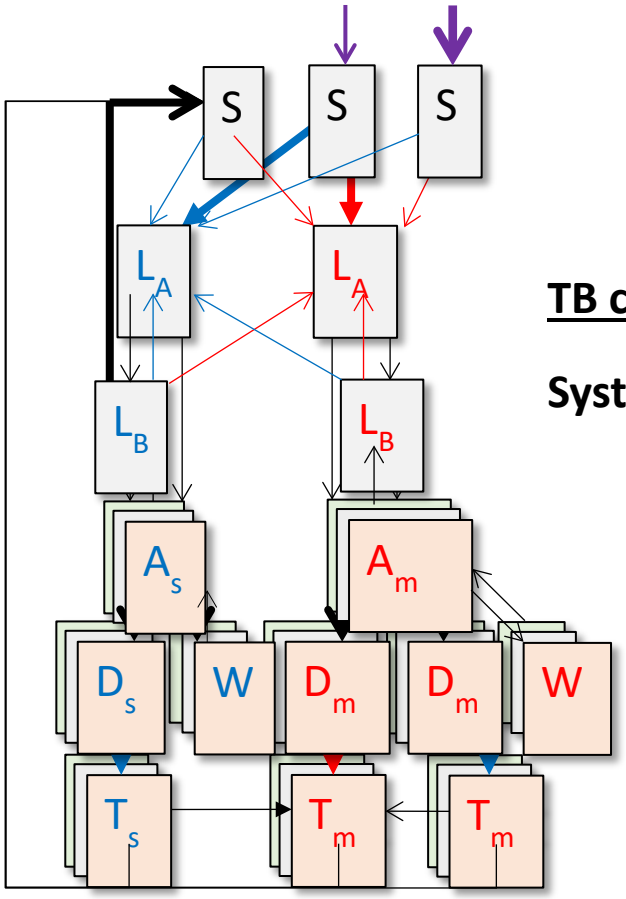
We model the engagement of private physicians by increasing the number of notified cases which are then placed into effective management according to WHO guidelines.



TB control action 6:

Health promotion and communication

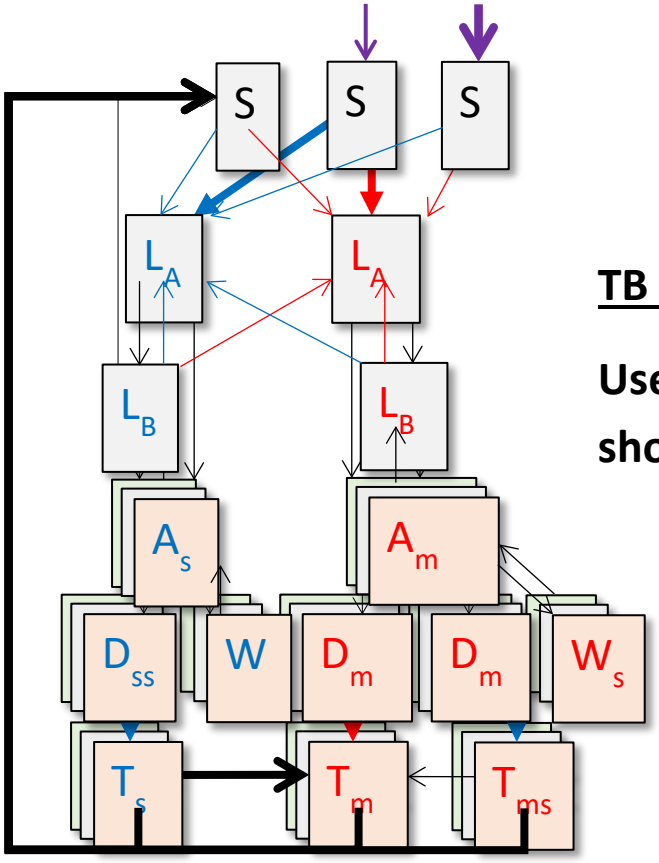
Health promotion is modelled by increasing the case detection rate of both MDR and DS TB, moving the active in the community undiagnosed (the A category) to the diagnosed (D category).



TB control action 7:

Systematic screening

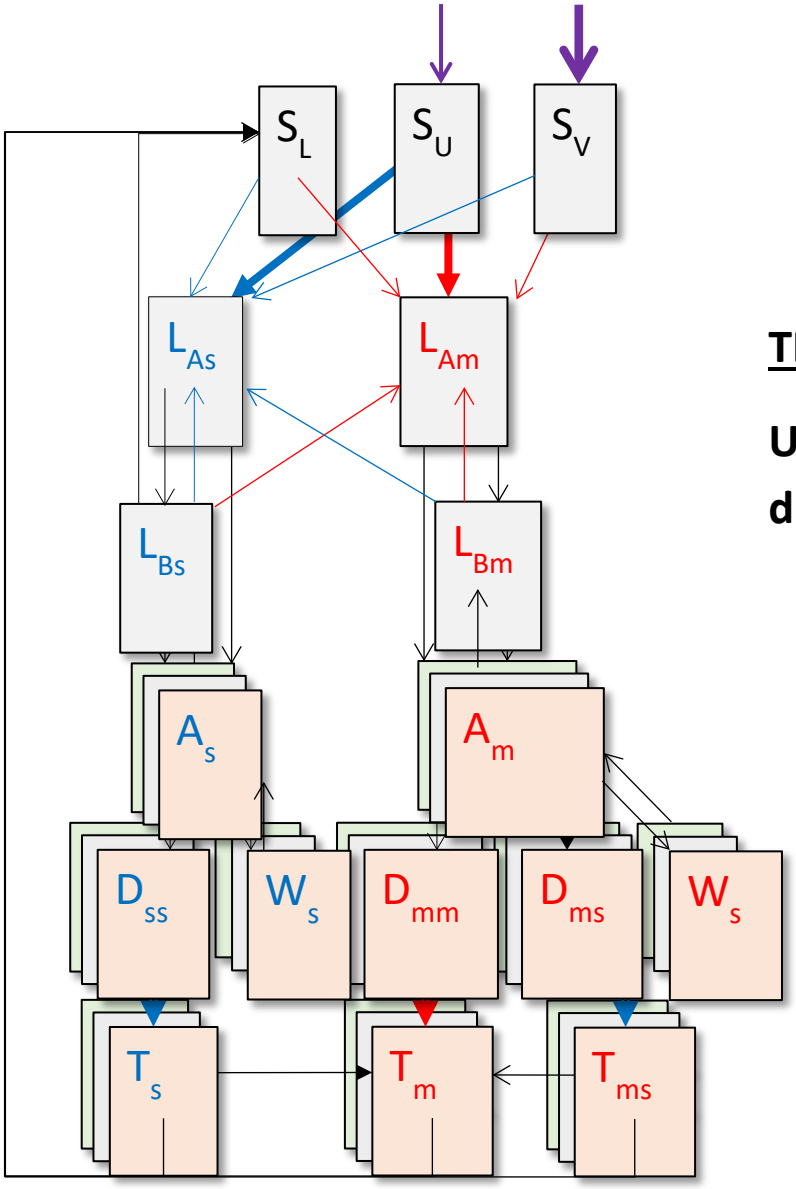
Systematic screening, like awareness raising, also acts by increasing diagnosis, so was modelled under the same intervention scenario.



TB control action 8:

Use of standardized shorter all oral regimen

Shorter course treatment was modelled as improved results for MDR TB, with reduced time under treatment and reduced failure/loss to follow-up for MDR TB.



TB control action 9:

Use of Xpert as primary diagnostic tool

Using GeneXpert as the primary frontline diagnostic impacted the DS tB by increasing the proportion of smear negative/geneSpert positive TB cases that are diagnosed, and in the case of MDR it also allowed for correct classification and treatment, improving success rates and reducing loss to follow-up rates.

param	return to baseline	LTBI household screening	LTBI household and workplace	improve treatment success	mixing	2020 long MDR treatment	geneXpert 50	geneXpert 100	all
susceptible									
effective_contact_rate	*6.50*	*6.50*	*6.50*	*6.50*	*6.50*	*6.50*	*6.50*	*6.50*	*6.50*
tb_multiplier_vac_protection	*0.50*	*0.50*	*0.50*	*0.50*	*0.50*	*0.50*	*0.50*	*0.50*	*0.50*
tb_multiplier_novelvac_protection	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*
latent									
la_active_early_progression	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*
la_active_early_progression_ageunder5	*2.41*	*2.41*	*2.41*	*2.41*	*2.41*	*2.41*	*2.41*	*2.41*	*2.41*
la_active_early_progression_age5to15	*0.99*	*0.99*	*0.99*	*0.99*	*0.99*	*0.99*	*0.99*	*0.99*	*0.99*
la_active_early_progression_ageover15	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*	*0.10*
la_lb_stabilisation_rate	*3.65*	*3.65*	*3.65*	*3.65*	*3.65*	*3.65*	*3.65*	*3.65*	*3.65*
la_lb_stabilisation_rate_ageunder5	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*
la_lb_stabilisation_rate_age5to15	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*	*4.38*
la_lb_stabilisation_rate_ageover15	*1.97*	*1.97*	*1.97*	*1.97*	*1.97*	*1.97*	*1.97*	*1.97*	*1.97*
lb_active_late_progression_rate	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
lb_active_late_progression_ageunder5	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
lb_active_late_progression_age5to15	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
lb_active_late_progression_ageover15	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*	*0.00*
active									
proportion_sp	*0.52*	*0.52*	*0.52*	*0.52*	*0.52*	*0.52*	*0.52*	*0.52*	*0.52*
proportion_sngp	*0.33*	*0.33*	*0.33*	*0.33*	*0.33*	*0.33*	*0.33*	*0.33*	*0.33*
proportion_clinical	*0.15*	*0.15*	*0.15*	*0.15*	*0.15*	*0.15*	*0.15*	*0.15*	*0.15*
genexpert_sensitivity_sn	*0.67*	*0.67*	*0.67*	*0.67*	*0.67*	*0.67*	*0.67*	*0.67*	*0.67*
rr_of_developing_active_tb_in_those_treated_with_ipt	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*
relative_risk_of_infection_in_those_already_latently_infected	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*	*0.40*

natural_death_rate	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
detected									
case_detection_proportion	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.90
case_detection_proportion_sp	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.56	0.90
case_detection_proportion_clinical	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.45
retention_dx_rx	0.80	0.80	0.80	0.80	0.80	0.80	0.80	0.80	0.80
frontline_xpert_proportion	0.30	0.30	0.30	0.30	0.30	0.30	0.50	1.00	1.00
treatment									
treatment_success	0.92	0.92	0.92	0.96	0.92	0.92	0.92	0.92	0.96
treatment_success_mdr	0.88	0.88	0.88	0.94	0.88	0.5	0.88	0.88	0.88
mortality_on_treatment	0.02	0.02	0.02	0.01	0.02	0.024	0.02	0.02	0.02
mortality_on_treatment_mdr	0.07	0.07	0.07	0.02	0.07	0.2	0.07	0.07	0.07
default_failure	0.06	0.06	0.06	0.03	0.06	0.056	0.06	0.06	0.06
default_failure_mdr	0.05	0.05	0.05	0.04	0.05	0.3	0.05	0.05	0.05
proportion_mdr_misdiagnosed_as_ds_transition_to_fail_retreat	0.40	0.40	0.40	0.40	0.40	0.4	0.40	0.40	0.40
proportion_mdr_misdiagnosed_as_ds_transition_to_fail_lost	0.10	0.10	0.10	0.10	0.10	0.1	0.10	0.10	0.10
proportion_mdr_misdiagnosed_as_ds_transition_to_spont_recover	0.10	0.10	0.10	0.10	0.10	0.1	0.10	0.10	0.10
proportion_mdr_misdiagnosed_as_ds_transition_to_death	0.30	0.30	0.30	0.30	0.30	0.3	0.30	0.30	0.30
death									
treatment_success_under_short_course_mdr_tb_regimens	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88	0.88
probability_of_treatment_success_of_mdr_incorrectly_diagnosed_as_ds	0.20	0.20	0.20	0.20	0.20	0.2	0.20	0.20	0.20
probability_of_death_on_treatment_for_short_course_mdr	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
natural_death_sp	0.70	0.70	0.70	0.70	0.70	0.7	0.70	0.70	0.70
natural_death_sngp	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29
natural_death_clinical	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29
natural_recovery_sp	0.23	0.23	0.23	0.23	0.23	0.231	0.23	0.23	0.23
natural_recovery_sngp	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13
natural_recovery_clinical	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13
natural_recovery_all	0.20	0.20	0.20	0.20	0.20	0.2	0.20	0.20	0.20

tb_prop_casefatality_untreated	0.40	0.40	0.40	0.40	0.40	0.4	0.40	0.40	0.40
life_expectancy	70.00	70.00	70.00	70.00	70.00	70	70.00	70.00	70.00
durations									
tb_timeperiod_early_latent	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16
tb_timeperiod_activeuntreated	3.00	3.00	3.00	3.00	3.00	3	3.00	3.00	3.00
tb_timeperiod_ontreatment_ds	0.50	0.50	0.50	0.50	0.50	0.5	0.50	0.50	0.50
tb_timeperiod_ontreatment_mdr	0.75	0.75	0.75	0.75	0.75	2	0.75	0.75	0.75
tb_timeperiod_ontreatment_xdr	2.00	2.00	2.00	2.00	2.00	2	2.00	2.00	2.00
tb_timeperiod_infect_ontreatment_ds	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
tb_timeperiod_infect_ontreatment_mdr	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
tb_timeperiod_infect_ontreatment_xdr	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17
testing									
diagnostic_sensitivity	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90
mean_time_to_diagnosis_days	16.0	16.00	16.00	16.00	16.0	16.00	16.00	16.00	16.00
inverse_treatment_wait_time	26.0	26.00	26.00	26.00	26.0	26.00	26.00	26.00	26.00
inverse_treatment_wait_time_mdr	13.0	13.00	13.00	13.00	13.0	13.00	13.00	13.00	13.00
preventive_therapy_for_under5y_tstp_uptake	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14
proportion_of_first_line_diagnostics_using_genexpert	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
force_of_infection									
tb_multiplier_force_smearneg	0.24	0.24	0.24	0.24	0.24	0.24	0.24	0.24	0.24
tb_multiplier_child_infectiousness	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
tb_multiplier_child_infectiousness_age0to10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
tb_multiplier_child_infectiousness_age10up	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
tb_prop_amplification	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07
mdr_fitness_cost	0.80	0.80	0.80	0.80	0.80	0.80	0.80	0.80	0.80
LTBI_intervention									
number_moved_LA_S3	0.00	0.55	2.76	0.00	0.00	0.00	0.00	0.00	2.76
number_moved_LB_S3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
number_coprevalent_TB_found	0.00	0.18	0.92	0.00	0.00	0.00	0.00	0.00	0.92
sensitivity_of_ltbi_test	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
probability_of_contacts_becoming_infected	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52

sensitivity_of_xpert_on_smear_negative_cases	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.67
chest_x_ray_sensitivity	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90
tb_prop_infections_in_household	0.40	0.40	0.40	0.40	0.40	0.40	0.40	0.40	0.40
program_timeperiod_await_treatment_smearneg_xpert	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
program_timeperiod_community_ipt_round	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
average_household_size	4.60	4.60	4.60	4.60	4.60	4.60	4.60	4.60	4.60
cascade_of_care									
missed_to_active_rate	4.00	4.00	4.00	4.00	4.00	4.00	4.00	4.00	4.00
program_prop_child_reporting	0.40	0.40	0.40	0.40	0.40	0.40	0.40	0.40	0.40
proportional_reduction_in_adverse_outcomes_from_the_treatment_support_intervention	0.40	0.40	0.40	0.40	0.40	0.40	0.40	0.40	0.40
awareness_raising									
program_ratio_case_detection_with_raised_awareness	1.52	1.52	1.52	1.52	1.52	1.52	1.52	1.52	1.52
program_prop_population_screened	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27
program_prop_population_screened_prison	0.80	0.80	0.80	0.80	0.80	0.80	0.80	0.80	0.80
vaccination									
proportion_receiving_bcg	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	25.00
immunity_wane_rate	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	3.11
proportion_private	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	36.70

Table 4. Intervention parameters.