Guidance for country-level TB modelling

COVID-19 update

TB Modelling and Analysis Consortium

Outline

The COVID-19 pandemic has forced most countries to impose stringent control measures. However, these measures are also impacting negatively on access to health care services, with many countries reporting a drop in TB notifications, seeing delayed treatment initiations, reduced treatment adherence and in general a significant weakening of TB services. Mathematical modelling can help to anticipate the effects that these disruptions could have on TB incidence and mortality over the next few years, and aid in strategic planning to counteract these effects.

Existing WHO/TB MAC country-level TB modelling guidance[1] outlines principles and good practices to follow to ensure the quality and relevance of mathematical modelling used to inform policy-making. This document outlines a stand-alone temporary update to that guidance, identifying additional good practices to be considered during the COVID-19 pandemic. The document will be updated as new data become available or recommendations change.

The document was developed by the TB Modelling and Analysis Consortium (TB MAC) with input from leading TB modelling groups and technical experts. Preparation of this guidance was led by C Finn McQuaid and Richard G White, with input and review from Nimalan Arinaminpathy, Madeleine Clarkson, Kathy Fiekert, Rein Houben, Sherrie Kelly, Jens Levy, Rowan Martin-Hughes, Emma McBryde, Nicolas A Menzies, Puck Pelzer and Carel Pretorius.

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[1]Guidance for country-level TB modelling. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO

TABLE 1 ■ Summary of original and additional principles and good practices for country-level TB modelling

ORIGINAL PRINCIPLE	ORIGINAL GOOD PRACTICE	ADDITIONAL GOOD PRACTICE
1. Relevance: Modelling should assess relevant policies and outcomes	1.1 Decision-makers, policy questions, constraints, outcomes and perspective should be determined before modelling begins	1.3 In addition to those requested by country stakeholders, standardised scenarios* of the baseline current and future potential impact of COVID-19 should be considered, for global stakeholders 1.4 If relevant to the policy analysis, models should examine separate policy options for service prioritisation both during lockdowns and when lockdowns ease
	1.2 A clear description of policy scenarios should define all actions to be modelled	
2. Realism: Modelling should consider implementation challenges and examine requirements for policy success	2.1 Realistic assumptions should be made about policy costs and effectiveness	2.7 When specifying scenarios, modelling should consider the reduced health system capacity due to COVID-19, and the increased difficulty of implementing TB services 2.8 For analyses examining program costs and budgetary needs, the effect of capacity or budgetary constraints due to COVID-19 economic impacts should be appropriately considered, in addition to
	2.2 Analyses should consider the additional costs of service expansion as well as any effect on existing services	
	2.3 Where there is little prior experience of policies, sensitivity analyses should be conducted, and results appropriately labelled as speculative	
	2.4 The modelling process should remain objective	

	2.5 Assumptions and evidence for the pace and success of implementation should be documented	changes in prices and/or intervention unit costs
	2.6 Capacity limitations should be appropriately included in the analysis	
3. Appropriateness of model structure: Model design should be justified in terms of the policy questions being considered and avoid unnecessary complexity	3.1 The model used should represent major mechanisms generating TB outcomes in the given setting	No additions
	3.2 Major structural decisions in the model should be justified	
	3.3 Model choice should be based on the appropriateness to the setting, evidence, policies and outcomes in question	
4. Consideration of all evidence: Modelling should consider all available evidence relevant to the decision problem	4.1 A review of all pertinent evidence should be carried out	4.8 Standardised, prioritised approaches to filling key data gaps† should be used, or justification provided for alternative approaches
	4.2 Evidence should be checked for quality and appropriateness	
	4.3 Conflicting evidence should be investigated	
	4.4 Routine data should be checked for appropriate use	
	4.5 Decisions informed by expert opinion should be validated where possible	
	4.6 The implications of parameter uncertainty on results should be investigated	

	4.7 Model calibration should be reported in full	
5. Validation: Results should be compared to evidence not used for model parameterization or calibration	5.1 Models should avoid broad claims of validity and actively test performance	5.6 Approaches and results should be discussed with other technical assistance providers in the modelling space to share learnings and identify concerns
	5.2 Model results should be checked against local epidemiology and health service characteristics, as well as general TB epidemiology	
	5.3 Model sensitivity to assumptions should be checked	
	5.4 Results should be compared to other modelling results or empirical assessments where possible, or through consultation with stakeholders	
	5.5 Rates of decline in burden should be compared with historical evidence of limits in rates of decline	
6. Informativeness: Modelling should report results for a wide range of outcomes	6.1 Analyses should report summary measures of health benefit (e.g. DALYs averted, QALYs saved)	6.5 Standardised outputs‡ should be produced and made available to enable comparisons with other applications
	6.2 Models should additionally report policy consequences for a wide range of epidemiological and programmatic outcomes	
	6.3 Analyses should disaggregate total cost estimates into categories relevant for budgeting (e.g. by payer, cost category and year)	

	6.4 Analyses should investigate the impact of different time horizons	
7. Transparency: Reporting should include a description of supporting evidence, limitations, sensitivity analyses and conflicts of interest	7.1 Details of model structure and implementation should be made available in technical documentation	7.7 Models should highlight COVID-19-specific data gaps, and associated uncertainties and potential implications for results should be communicated to stakeholders 7.8 The primary purpose and audience of modelling (to aid decision-making or for advocacy) should be highlighted alongside key results
	7.2 Policy and baseline scenarios should be fully described	
	7.3 A non-technical description of uncertainties, limitations, evidence sources and validation should accompany results	
	7.4 In contentious contexts, additional efforts should be made to seek engagement and agreement on the modelling approach from all important stakeholders	
	7.5 Conflicts of interest should be identified, managed and explicitly stated	
	7.6 An external review of the modelling analysis should be conducted where possible	
8. Timeliness: Modelling should provide results in time for decisions to be made	8.1 Planning should be conducted to ensure that results can be provided when they are required, including review/revision of scenarios and assumptions	8.3 Initial modelling should provide rapid assessment to highlight the wide range of potential impacts, followed by continuous engagement to improve projections for critical decision-making
	8.2 If the modelling process is curtailed in order to meet a deadline, drawbacks	

	of this should be described	
9. Country ownership: Modelling should be conducted through participation with local stakeholders	9.1 Full engagement with local stakeholders should be gained	9.6 While maintaining this principle where possible, TA providers should be sensitive to the demands COVID-19 has made of local stakeholders in the TB sector
	9.2 Plans to increase country capacity should be implemented where possible	
	9.3 Country input at each stage of the modelling process should be enabled	
	9.4 Modelling should be planned in the light of existing efforts in research, evaluation and surveillance	
	9.5 Choice of modelling technical assistance provider should be determined by ability to meet decision-maker needs	
10. Iteration: Modelling should be an iterative process, and reconsidered given new evidence	10.1 Stakeholders should evaluate initial versions of the modelling approach, policy scenarios and results, and these should be revised if needed	10.4 Initial assessments should be updated as routine programmatic data become available and other key data gaps are filled
	10.2 The sensitivity of the model to new evidence should be described	
	10.3 The validity of model projections should be reconsidered if early programmatic data show assumptions to be incorrect	

*Good practice 1.3 – standardised scenarios

In order to ensure that modelling results are most useful to both in-country and global stakeholders, three different sets of COVID-19 scenarios (compared to a baseline "no COVID-19" scenario) should be used to consider current and future disruptions to TB during the COVID-19 epidemic. These scenarios include:

→ Scenarios requested by the National TB Programme, to ensure that the development of appropriate policy questions is led by country stakeholders,

→ The set of standard scenarios developed by the Global Fund[2], to ensure that international funders and stakeholders can more readily compare results,

→ Data-driven scenarios using available information about health service disruption. Where possible, these scenarios should be updated on a monthly basis until December 2020 as data become available, and should consider a "best", "most likely" and "worst" case scenario based on the available evidence

†Good practice 4.8 – data gaps

Data gaps exist in our understanding of the impact of COVID-19 on TB. Some areas, such as the impact on health service delivery, are highly country-specific and likely to be addressable if informed with (relatively) easily collated data, while others will be more difficult to inform and address. A list of data gaps to inform this impact, which will likely require assumptions to be made by modellers, is provided below. These include data gaps around the impact of COVID-19 on (a) health systems, (b) *M.tb* transmission, (c) comorbidity of COVID-19/TB, (d) emergence of TB drug resistance due to incomplete treatment, and (e) the costs of providing TB services and budgetary implications. Outlined below are approaches to take for modelling each area when conducting country-level TB modelling for decision-making.

As a common approach for when no, or very poor, data exist, where possible each data gap should be modelled with 3 scenarios; 'low', 'medium' (a 'most likely' estimate), and 'high'.

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[2] Hogan AB, Jewell BL, Sherrard-Smith E et al (2020). Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. Lancet Global Health. 2020; 8 (9): e1132-e1141

a) Health systems

While some TB health systems data on disruption (e.g. notifications) due to the COVID-19 pandemic may be relatively easily collated, data to allow us to understand why health systems are being disrupted (for example, supply of services vs. demand for services) is likely to be more difficult to collect. However, these data are essential to understand how to best mitigate these disruptions. Given this, the following data should be collated and used to calibrate/parameterize models, where available:

- TB testing (including positivity, bacteriological confirmation and extrapulmonary rates) and notification rates
- Drug susceptibility testing (including positivity rate) and treatment initiation
- HIV testing (including positivity rate) and ART initiation
- TB treatment outcomes and delays across the care cascade
- TB comorbidity-risk factor burden (e.g. diabetes)
- Constraints or disruptions with specific intervention inputs or logistics (e.g. staffing, drugs/reagents, personal protective equipment)
- BCG vaccination coverage

Where data are unavailable for each of the above, surveys of disruptions reported by healthcare providers and patients should be used where possible to inform estimates of the degree of disruptions.

If such surveys are not available, expert opinion should be used to identify a 'most likely' estimate, and low/medium/high scenarios modelled as described above. Regional/global default values from comparable settings could also be used to inform this, ideally as a starting point for further discussion and collating better data.

b) Transmission

It is not clear how interventions to reduce SARS-CoV-2 transmission will affect *M.tb* transmission, particularly as discussion around the importance of transmission within the household continues.

Lockdowns will also be highly context-specific, with very similar countries (in terms of TB epidemiology) taking very different approaches. In addition, changes to social interactions more broadly, as well as the introduction of masks, may have a major effect on *M.tb* transmission. Approaches to evaluate changes in transmission should use estimates of pre-COVID-19 household transmission as a proportion of all transmission in conjunction with, and in order of preference:

- Country-specific pre- and post-COVID-19 contact matrices,
- Expert opinion on change in *M.tb* transmission, as informed by mobility and mask-wearing data.

c) Comorbidity

There are multiple questions around the potential impact of COVID-19 and *M.tb* infection and TB disease (current or previous) comorbidity. Of particular interest are the impact of SARS-CoV-2 infection on TB infection progression or disease outcomes, and COVID-19 on TB infection progression or disease outcomes. Current data available on these is limited, if any, as research has focused on the impact of TB disease on COVID-19 outcomes instead. Given this lack of data, in addition to unknown (and rapidly changing) prevalence of SARS-CoV-2 or COVID-19, modelling should not include COVID-19 as a risk factor for TB.

d) Drug resistance

With potential ongoing reductions in supply (stockouts and reduced access to clinics) and demand for treatment (reluctance to attend clinics), initial evidence suggests that fewer people are completing courses of treatment for TB, or are more likely to have irregular adherence. This runs the risk of increased emergence of drug resistance. Forecasting the emergence of drug resistance, however, is complex, and risk will vary on an individual rather than population level. Acquisition of drug resistance is also likely greater amongst those with irregular adherence, as opposed to incomplete treatment.

Prior assumptions around rate of acquisition of TB drug resistance should therefore not be changed in the primary analysis, but a general statement on this limitation should be issued and discussed. If data on patient adherence to treatment and treatment interruption are available, this should at most be used in a sensitivity analysis due to current limitations in our understanding.

e) Intervention costs and budgeting

Several factors need to be considered for costing and budgeting TB services in light of the pandemic. Firstly, approaches to providing TB interventions may change, either through design (e.g. increased needs for personal protective equipment, additional staff time required to undertake infection control and physical distancing measures, revised clinic visit schedules to reduce exposure), or through shortages or constraints on some inputs. Second, demand for services may change rapidly, such that standard unit cost estimates may not apply. For example, a rapid reduction in demand may not result in significant cost savings if many cost inputs are fixed over the short term. Third, prices for different intervention inputs could change substantially. Fourth, the available budget for supporting TB services may be lower, with resources reprogrammed to coronavirus care or mitigation.

For many programs, concerns about costs and budgeting may be secondary concerns to questions about revised program strategy, but these questions will likely arise at some point. The following should be collected and used for cost calculations, where available:

- → Expectations from Ministries of Health and Finance about whether TB budgets will be expanded/stable/reduced over the past and coming year.
- → Resource utilization within current TB programmes, and cost data or estimates where available
- → Any changes in prices of TB programme inputs (using TB programme reporting and market research)

→ Any planned changes to TB intervention details that have important cost implications (e.g. adding personal protective equipment, reducing clinic visit frequency, shift to community and/or digital remote support).

‡Good practice 6.5 – standard outputs

In order to ensure that modelling results are easily comparable across countries and modelling groups, standardised outputs should be reported. For each of the standardised COVID scenarios and mitigation strategies used, the following table should be completed

TABLE 2 ■ Standardised output indicators for reporting

	OUTPUT MEASURE	CUMMULATIVE UP TO YEAR		IN THIS YEAR		
		2025	2030	2020	2025	2030
Difference in number compared to baseline	TB incidence					
	TB mortality					
	TB notifications					
% difference in number compared to baseline no COVID-19	TB incidence					
	TB mortality					
	TB notifications					

In addition, figures should be produced showing point estimates for all output rates over time for each scenario and the baseline.