Guidance for country-level TB modelling

Description of guidance and next steps

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TB Modelling and Analysis Consortium

WHO Global Task Force on TB Impact Measurement
Glion-Sur-Montreux, Switzerland
Wednesday May 2nd, 2018
What is mathematical modelling?

Simple functional relationships

Est. Incidence = Notifications × Adjustment Factor

Complicated simulation models

\[ \frac{dS}{dt} = -\frac{\beta SI}{N} \]
\[ \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \]
\[ \frac{dR}{dt} = \gamma I \]
Aim
– To increase the effectiveness and efficiency of TB control policy and practice at global and country level

Objectives
– Building stronger and more effective links between decision makers, modellers and economists
– Creating new high quality modelling resources, and making them available and accessible to decision makers
– Enabling better informed decision making communities and modellers, and ensuring TB decision makers are better equipped to integrate these modelling resources in their decision making
Motivation for modelling guidance

• Mathematical modelling becoming a commonly-applied tool to inform country-level TB program decisions
Growth of TB modelling

Country-level modelling guidance
Growth of TB modelling

Have used country-level modelling
Have not used country-level modelling

2013
Growth of TB modelling

Have used country-level modelling
Have not used country-level modelling

2014

Country-level modelling guidance
Growth of TB modelling

Have used country-level modelling
Have not used country-level modelling

2015
Growth of TB modelling

Country-level modelling guidance
Growth of TB modelling

2017

Have used country-level modelling
Have not used country-level modelling

Country-level modelling guidance
Growth of TB modelling

Number of Publications

Publication Year

Menzies et al 2018

Country-level modelling guidance
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• Mathematical modelling becoming a commonly-applied tool to inform country-level TB program decisions

• Recent evidence suggests that models can produce a wide range of results when investigating similar/identical policy questions
Variable results

TB Targets exercise

- Multi-model collaboration
- Same countries
- Same policies being evaluated
- Different results

Cost Effectiveness of Intensified TB Control Options (China)

- Expand access
- Introduce Xpert
- Improve treatment
- Combination

Menzies et al 2016
Houben et al 2016
Variable results

HIV guideline revision

- Multi-model collaboration
- Same countries
- Same policies being evaluated
- Different results

Incremental Cost of Expanded ART Access, 20 years (South Africa)

Individual model results

Eaton et al 2014

Country-level modelling guidance
Variable results

Review of published TB models

- Systematic review of 312 modelled analyses
- Rebuilt parts of models from infection to disease
- Compared TB incidence following infection
- Found wide variation between models

Model Estimates for Cumulative TB Incidence

Menzies et al 2018

Country-level modelling guidance
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• Mathematical modelling becoming a commonly-applied tool to inform country-level TB program decisions

• Recent evidence suggests that models can produce a wide range of results when investigating similar/identical policy questions

• Currently no domain-specific guidance about how modelling should be applied to support country decision making
Existing guidance
Existing guidance

⇒ Economic evaluation

Country-level modelling guidance

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5. Warwick Medical School, University of Warwick, Coventry, UK;
6. Centre for the Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine, London, UK;
7. Human papillomavirus vaccine introduction in LMICs.
8. The objective of this study was to provide recommendations to optimize the reporting of models and tools with which to improve HIV Program Planning and Resource Allocation.
9. Out of 44 candidate items, 24 items and accompanying explanations were selected: a user-friendly 24-item checklist.
10. The concept of a “reference case” and a set of standard methodological practices must be conveyed to allow scrutiny of study findings. Despite a goal to provide recommendations to improve the reporting of models and tools with which to improve HIV Program Planning and Resource Allocation, heterogeneity, sensitivity analysis, uncertainty, and adherence rates of intervention implementations are, indeed, more complex than necessary. This report describes a consensus report and guide for a country-level modelling guidance on the use of cost-effectiveness models.

Results:

Before and after vaccination of adolescent girls were compared in terms of HPV prevalence and cervical cancer incidence. A decision tree model for a given lifetime horizon was constructed to consider different vaccination and vaccine-specific assumptions. The model was iteratively validated using empirical data to develop and parameterize the model. The solution we mean the set of decision values that optimally meet the objective function, and their relationships, data sources, validation, and adherence rates of intervention implementations.

Constrained Optimization Model

E-mail: dave.eddy@archimedesmodel.com

© 2012, International Society for Pharmacoeconomics and Outcomes Research (ISPOR).
Existing guidance

→ Disease-specific
Scope of the modelling guidance

• Focus on the use of mathematical models to support national TB policy and planning (incl. Global Fund applications)

• Design and estimation of the mathematical models themselves, plus how modelling is integrated into the process of policy identification and comparison

• Covers both epi and econ aspects of modelling, to capture all considerations arising in typical decision support exercises
  ➞ e.g. Project future epi outcomes and budget for current programme approach
  ➞ e.g. Evaluate consequences of competing policy options
  ➞ e.g. Assess cost-effectiveness /allocative efficiency, identify optimal portfolio
Target audience

• Participants and stakeholders in country-level TB modelling efforts:
  – Modellers (individual who build models + individuals who apply models)
  – Country policy-makers
  – Country technical experts
  – International funding and technical partners
  – Other individuals engaged in supporting country decision-making
Process

• Guidance development led by TB MAC

• Supported by key global stakeholders incl. WHO-GTB, Global Fund, Gates Foundation, Stop TB Partnership, World Bank, and USAID
Process

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Outline developed by TB MAC and WHO-GTB

1. Review by expert stakeholders
2. Full draft developed by writing group
3. Review by TB MAC and WHO-GTB
4. Draft guidance revised
5. Review during TB MAC/Task Force 2017 Annual Meeting
6. Draft guidance revised
7. Review by expert stakeholders
8. Draft guidance revised
9. Review during Task Force 2018 May Meeting
10. Finalization, dissemination
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Format

- 10 principles
- 2-7 practices for implementing each principle
- Flow chart mapping to typical steps of a modelling exercise
- Suggested responsibilities for each stakeholder

<table>
<thead>
<tr>
<th>PRINCIPLE</th>
<th>GOOD PRACTICE</th>
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</table>
| 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  
1.2 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  
2.2 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  
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  
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  
4.2 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  
5.2 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, DALYs saved)  
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  
7.2 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 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  
7.7 Placing should be conducted to ensure that results can be provided when they are required, including review/revision of scenarios and assumptions  
8.1 The modelling process is curtailed in order to meet a deadline, drawbacks of this should be described |
| 8 Timeliness: Modelling should provide results in time for decisions to be made | 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  
9.2 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 Choice of modelling TA 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  
10.2 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 shows assumptions to be incorrect |

Country-level modelling guidance
Principles for developing principles

- Need to balance desire for specificity against desire for broad applicability
- Need to consider practical implications
- Higher-level principles:
  1. Model-based policy evaluation makes best use of available evidence
  2. Modelling is incorporated into policy-making in a way that clearly expresses strengths and weaknesses
  3. Modelling supports (rather than replaces) policy-making as a deliberative, country-led process
### Principles and good practices for modelling

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*Modelling should report results for a wide range of outcomes* |
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Future activities to operationalize the principles

1. Shorter syntheses interpreting guidance for particular audiences
   - Difficult to meet information needs for all parts of audience in larger guidance document (e.g. decision-makers with little experience with modelling)
   - Persistent message through external review, easier to address in tailored materials

2. Develop benchmarks for country-level TB modelling
   - Quantitative benchmarks describing features of TB natural history, epidemiology, health services, and costs
   - Assumptions /results of a modelling application compared to benchmarks to assess appropriateness for a given policy question and country context
Future activities to operationalize the principles

3. Develop standard reporting approach for modelling applications
   - Standard format for reporting modelling results for use in Nat. Strategic Plan development, country funding applications (template, reviewers checklist)
   - Ensure reporting on process & outcomes follows accepted standards, required to report on common areas of concern

4. Develop external review mechanism for modelling applications
   - TB MAC to administer a system to engage reviewers and link to requests for review of country modelling applications
   - Either during process of modelling, or after modelling completed
   - Reviewers represent themselves, not TB MAC. Reviews funded separately
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- Modelling guidance
- Benchmarking
- Reporting standards
- External review
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### Timeline of activities

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<td>Publication</td>
<td>Mid 2018</td>
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<td>Dissemination</td>
<td>Mid 2018 – Ongoing</td>
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<tr>
<td>Benchmarking, Reporting, Review</td>
<td>Development</td>
<td>March 2018 – Sept 2018</td>
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<td>Piloting</td>
<td>Oct 2018 – Early 2019</td>
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Discussion questions

1. Do the members of this Task Force endorse the county-level TB modelling guidance?

2. Are there suggestions about the planned activities to operationalize the guidance (short summaries, benchmarks, standardized reporting, external review)?

3. Are there suggestions for other activities that would be valuable, or blind spots in the plans that have been presented?