TB Modelling and Analysis Consortium

Country-level TB Modelling

benchmarks, reporting & review

Overview of BRR initiative

→ Motivation

→ Efforts to date

→ Session objectives

Motivation

- Mathematical modelling increasingly used to understand the implications of TB policy and funding decisions

  → Supported by funders and technical orgs to facilitate objective decision-making

  → Utilized by countries to suggest priority interventions, allocate budgets, and support funding applications

  → Increasing professionalization of country-support modelling

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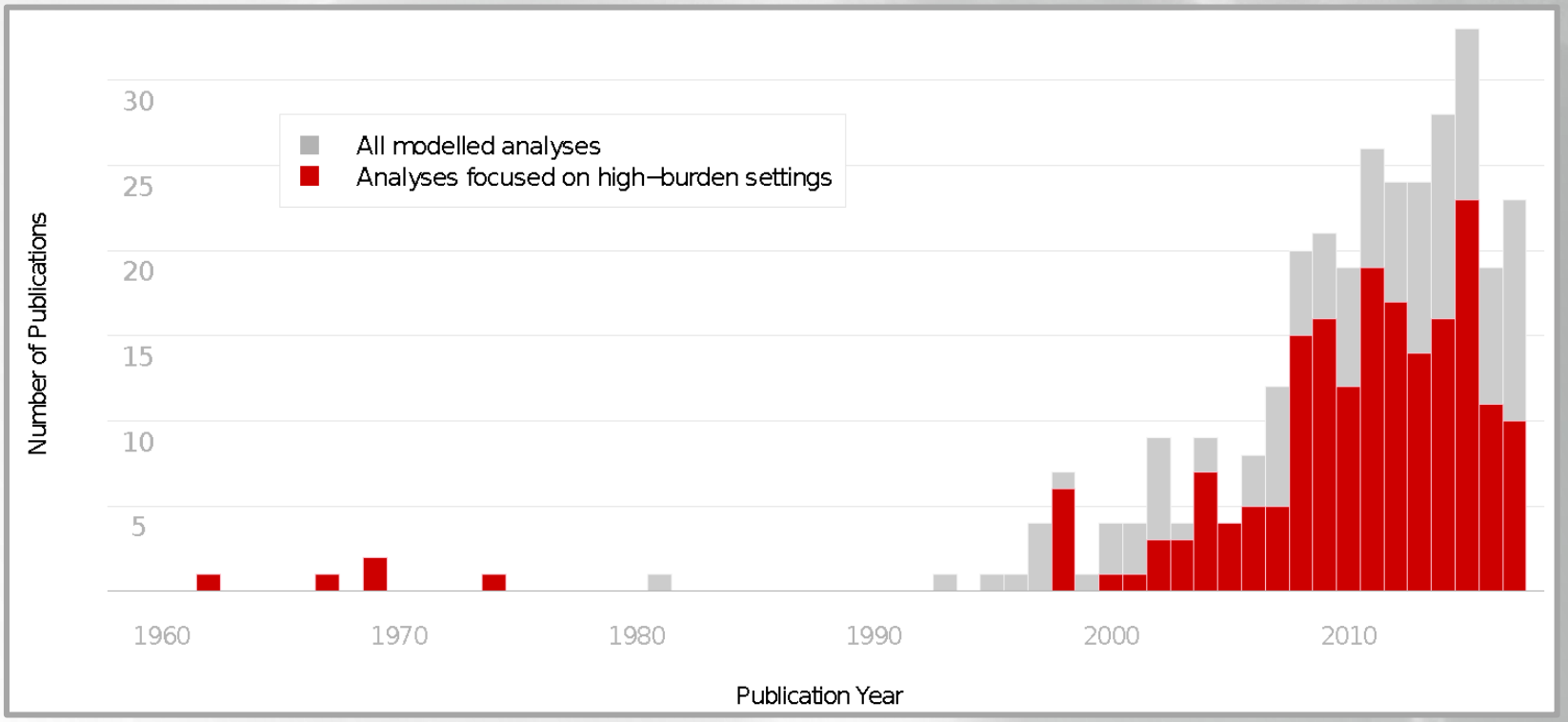
TB modelling in the scientific literature



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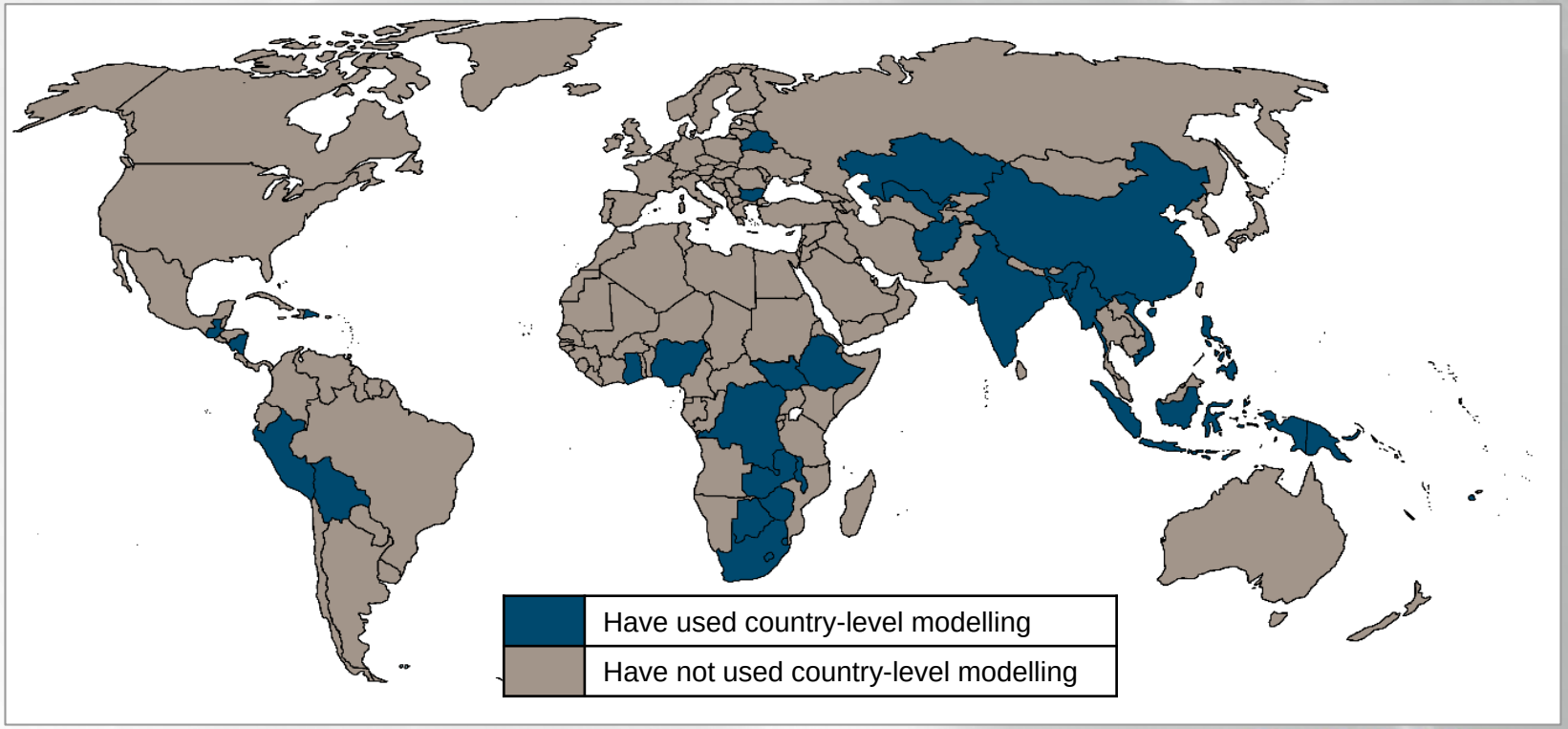
Menzies et al Lancet ID 2018

Country-level TB modelling applications, to 2017



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Modelling decision-support workforce

The past

- Small number of individuals involved
- Each application ad hoc, models developed for application
- Models simpler, constrained by computing power
- Same individuals filling multiple roles
  - Model developer also provides country-support
  - Country modelling closely tied to academic research

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Modelling decision-support workforce

The present

- Multiple modeling teams involved
- Investment in developing detailed models & codebases
  - Models universally more complicated
  - Models more durable, same model adapted to new settings
- Separation of functions:
  - Model development and country support by different individuals
  - Separation from traditional academic research

Analysis Consortium

Motivation

- Mathematical modelling increasingly used for understand the implications of TB policy and funding decisions
- Recent experience raises questions about the accuracy and reproducibility of model-based policy evaluation

  → When tuned to the same setting and policy question, different models giving different answers

  → When empirical evidence available to verify model projections, results don't always line up

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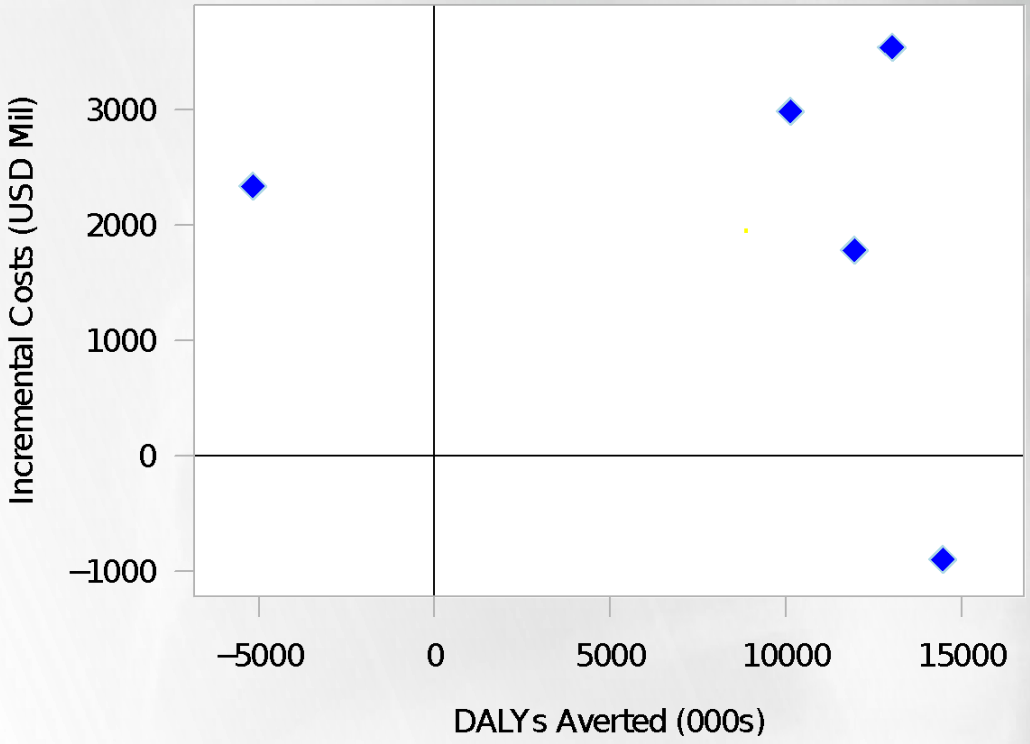
What is the cost-effectiveness of efforts to improve TB treatment in India?



- Inc cost and Inc DALYs from 5 models averaged to generate summary finding

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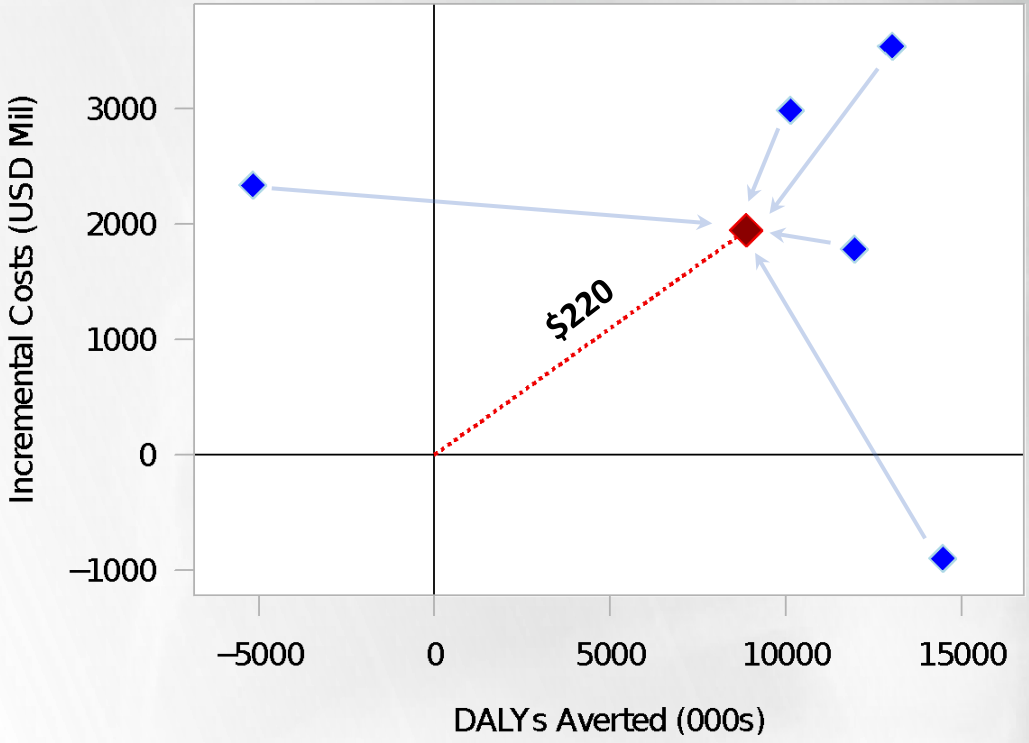
Menzies et al Lancet GH 2016

What is the cost-effectiveness of efforts to improve TB treatment in India?



- Inc cost and Inc DALYs from 5 models averaged to generate summary finding:

→ ***ICER = $220 per DALY averted***

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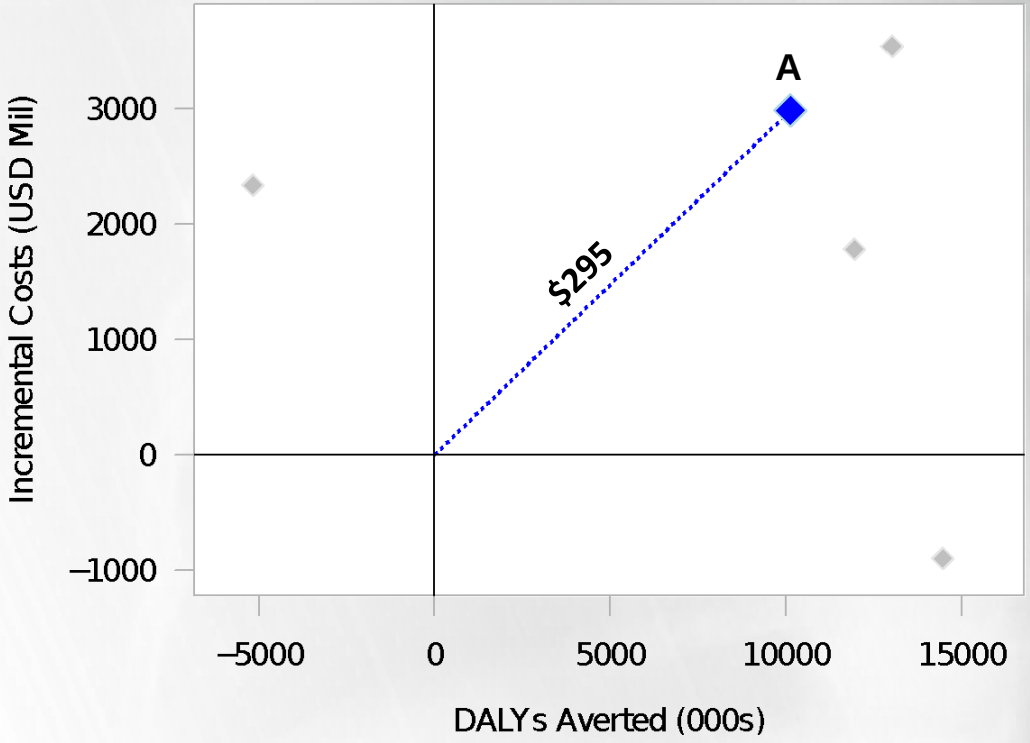
Menzies et al Lancet GH 2016

What is the cost-effectiveness of efforts to improve TB treatment in India?



- **What if only Model A?**

→ ***ICER = $295 per DALY averted***

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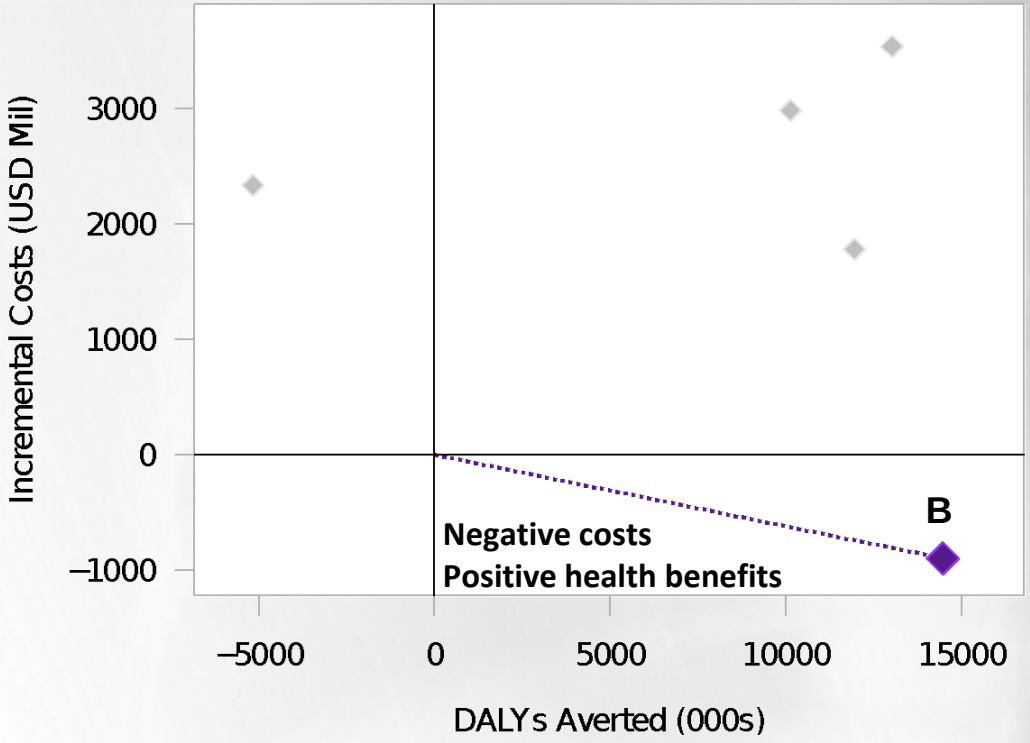
Menzies et al Lancet GH 2016

What is the cost-effectiveness of efforts to improve TB treatment in India?



- **What if only Model B?**

→ ***Policy dominates status quo***

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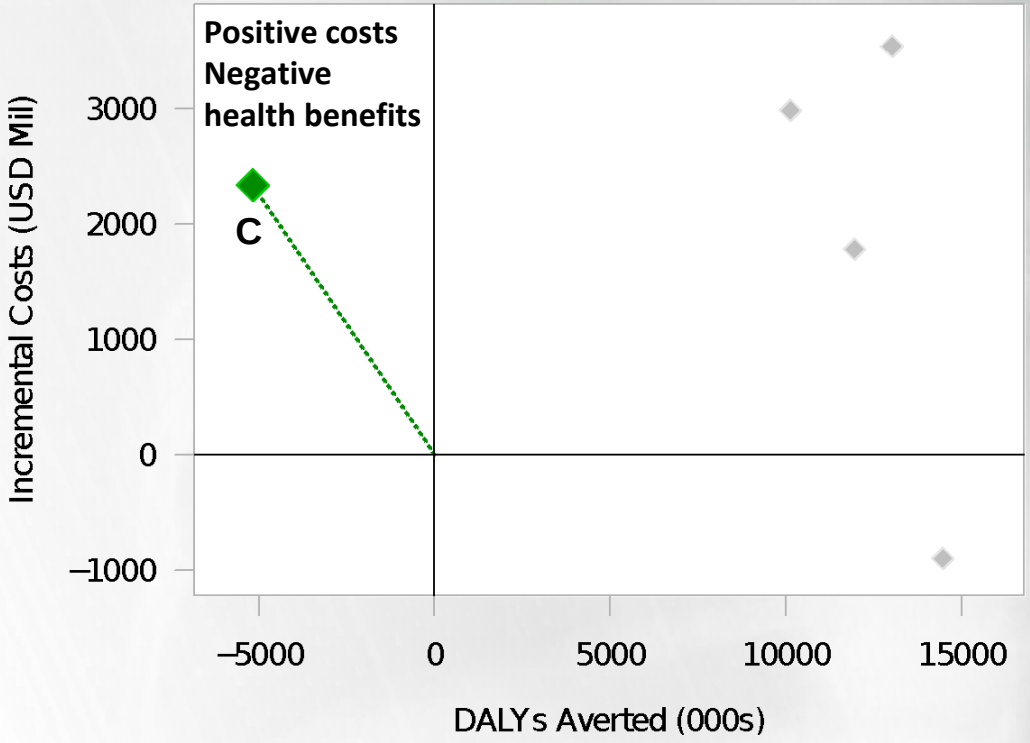
What is the cost-effectiveness of efforts to improve TB treatment in India?



- **What if only Model C?**

→ ***Policy dominated by status quo***

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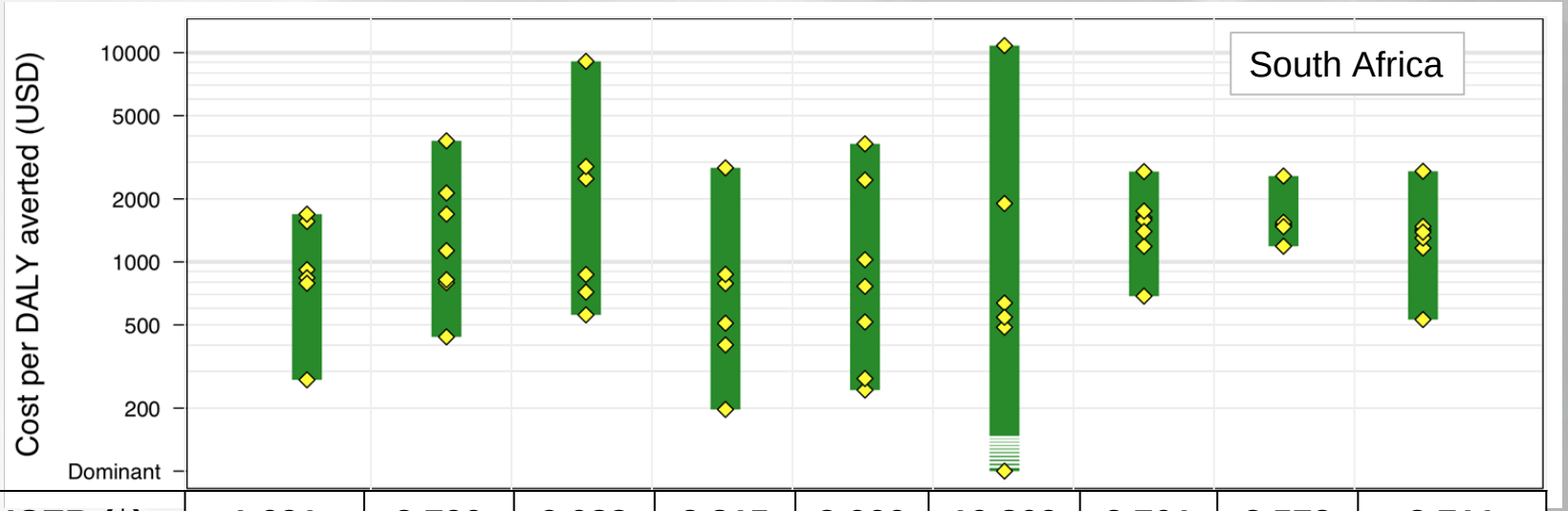
Menzies et al Lancet GH 2016

What is the cost-effectiveness of expanding coverage and eligibility for HIV treatment ?



Max ICER ($) :	**1,691**	**3,790**	**9,088**	**2,815**	**3,666**	**10,809**	**2,701**	**2,572**	**2,711**
Min ICER ($) :	**273**	**438**	**558**	**197**	**244**	**Dom***	**686**	**1,188**	**530**
Max / Min :	**6.2**	**8.6**	**16.3**	**14.3**	**15.0**	**---**	**3.9**	**2.2**	**5.1**

* ‘Dom’ = Dominant (negative costs, positive health benefits)

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Eaton et al Lancet GH 2014

Motivation

- Mathematical modelling increasingly used for understand the implications of TB policy and funding decisions
- Recent experience raises questions about the accuracy and reproducibility of model-based policy evaluation

→ *Demand for activities to improve the quality and reproducibility of modelling, confirm when models adequate for purpose*

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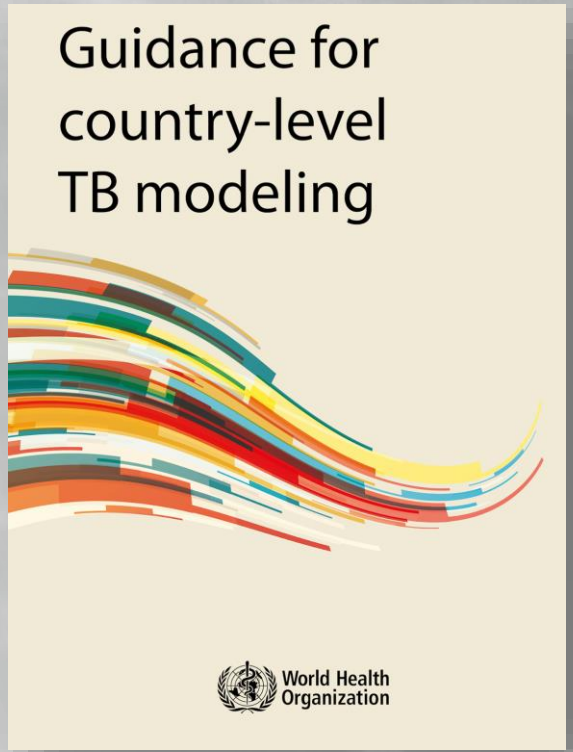
Response

1. Development of Country-level TB Modelling Guidance
   - Collaboration of TB MAC, WHO TB Dept, funders, modellers, country experts, other stakeholders
   - Developed 2017 to mid-2018
   - Published by WHO Global Taskforce on TB Impact Measurement



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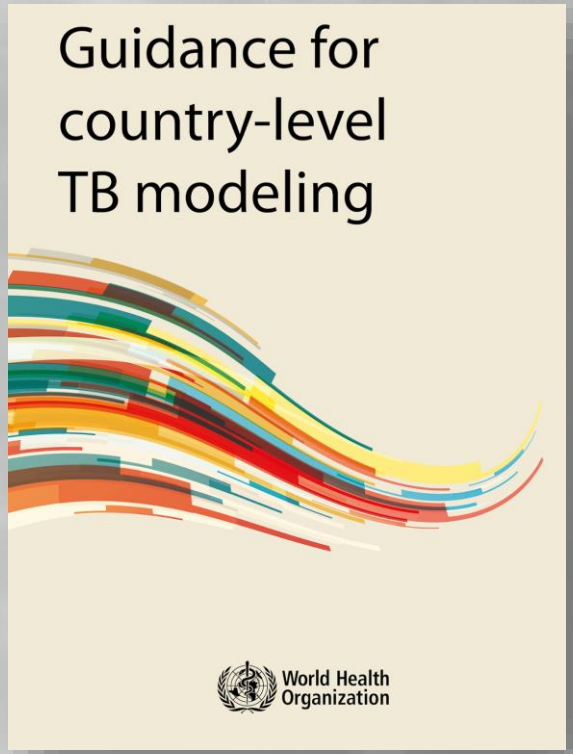
Response

1. Development of Country-level TB Modelling Guidance
   - Describes 10 principles for country decision support modelling
   - Examples and good practices for implementing principles
   - Concerned with the use of models, rather than just the models themselves



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Remaining gaps?

- Modeling guidance provides broad direction
- Does not provide mechanism to confirm that models are fit for purpose
- Countries looking for guidance on what model to use
- Funders looking for confirmation that models are valid for use

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BRR Initiative

- BRR = Benchmarking, reporting, external review
- Undertaken by TB MAC at the request of TB Roadmap Steering Committee and international funders

GOALS	
	Reveal where a modelling application is inconsistent with existing evidence or modelling best-practice
	Provide standard reporting template for describing modelling approaches and model performance
	Create a system for independent evaluation of modeling approach and results

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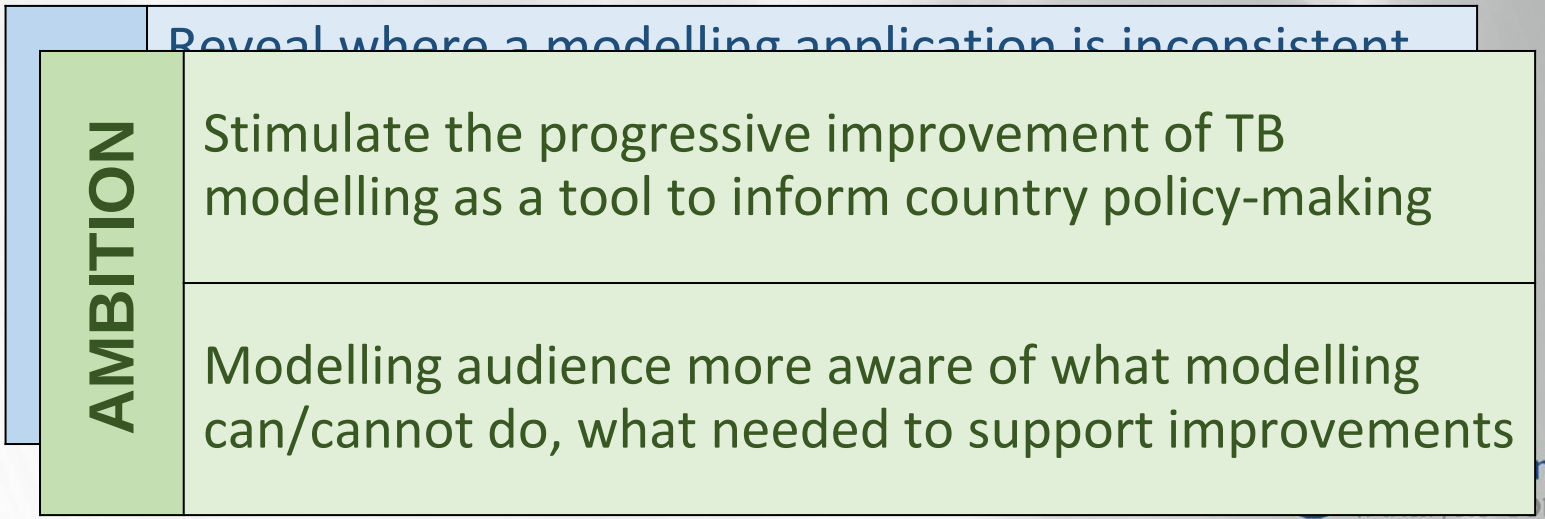
BRR Initiative

- BRR = Benchmarking, reporting, external review
- Undertaken by TB MAC at the request of TB Roadmap Steering Committee and international funders



BRR: to do list

1. Develop benchmarks for country-level TB modelling applications
2. Develop a standard reporting approach, template, and checklist
3. Develop a mechanism for external review of modelling applications
4. Pilot these new initiatives with modelling teams
5. Conduct annual review to this approach, to suggest revisions and improvements

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1. Develop benchmarks for country-level TB modelling applications

- Quantitative benchmarks describing features of TB natural history, epidemiology, health services, and costs
- Modelling assumptions & results compared to benchmarks to assess appropriateness for given policy question and context
- Not enforced dogmatically: modelling application would be asked to compare their assumptions and results to the benchmarks relevant to their work, and justify/discuss major deviations

2. Develop a standard reporting approach, template, and checklist

- Standard format for reporting modelling questions, approaches, and results, + checklist to assess completeness
- Include quantitative indicators (benchmarks) and process indicators of modelling good practice
- Final format will need to be adopted by the agencies that commission and fund modelling work
- General trends can inform evidence gaps, future activities

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3. Develop a mechanism for external review of modelling applications

- Mechanism to allow expert assessment of modelling approach, for a particular application
- TB MAC role: develop the system to link reviewing supply and demand, and approaches for how this should occur
- Expert reviewers represent themselves, not TB MAC
- When review needed: a decision for funder / country / modelling group

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BRR: activities to date

- Small working group formed to develop initial proposal for BRR components
- Draft approach developed for benchmarks, reporting template, review process
- Approach shared for comment from a range of experts, modellers, funders

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BRR: activities to date

- Small working group formed to develop initial proposal for BRR components
- Dra
tem
- App
modellers, funders

Thank you!

Ted Cohen, David Dowdy, Philippe Glaziou, Gaby Gomez, Finn McQuaid, Andrew Siroka, John Stover, Anna Vassall, Richard White

TB Modelling and Analysis Consortium

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TB Modelling and Analysis Consortium

BRR: activities to date

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- Draft ap
  templat
- Approach shared for comment from a range of experts, modellers, funders

More thank you!

Sevim Ahmedov, Meghan Bellerose, Anna Bershteyn, Stewart Chang, Madeleine Clarkson. Frank Cobelens, Katherine Floyd, Lara Gosce, Hassan Haghparast, Rein Houben, Michael Kimberling , Marek Lalli, Emma McBryde, Nim Pathy, Carel Pretorius, Romain Ragonnet, Anna Roberts, Jamie Rudman, Nabila Shaikh, Jolene Skordis-Worrall, Karyn Sutton, James Trauer, Bradley Wagner, Shufang Zhang

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BRR: activities today and tomorrow

- Discussion of approaches with modelling groups, stakeholders, & experts

Today (now to mid-afternoon)

- Brief description of one aspect of initiative (B → R → R)
- Summary of feedback received
- Issues to be resolved
- Open discussion

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BRR: activities today and tomorrow

- Discussion of approaches with modelling groups, stakeholders, & experts

Today (late afternoon)

- Something else (evidence gaps for country-level modelling)

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BRR: activities today and tomorrow

- Discussion of approaches with modelling groups, stakeholders, & experts

Tomorrow (until lunchtime)

- Review feedback and progress so far
- Small group work to propose how to move forward with feedback provided
- Summaries back to whole group
- Finish

Stakeholder perspective

- The need for these activities
- The wider context

Daniel Chin (BMGF)
Shufang Zhang (the Global Fund)

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Benchmarks 1

General epidemiological benchmarks

Rationale: General epidemiological benchmarks

- These benchmarks describe **general features of TB epidemiology**, and are assumed to apply to most settings in which TB is being modelled to evaluate policy/intervention options
- Broad ranges allow for local variation, inconsistency of the empirical evidence, and different health state definitions used by models

Current benchmarks

	Description	Benchmark
B1.1	**Cumulative incidence** of active TB (all forms) over the **first 5 years** following *M. tb* infection, no reinfection (%)	4-15%
B1.2	**Annual incidence** of active TB (all forms) for individuals **>5 years** after *M. tb* infection, no reinfection (%).	<0.2%
B1.3	**Case fatality** (probability of death before self-cure) for active TB, in the absence of treatment	40-70%
B1.4	**Duration of active TB** in the absence of treatment (years)	1.5-4.0 years
B1.5	**Reduction in the risk** of primary TB afforded by **prior *M. tb* infection** (percent)	40-85%

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Possible additional benchmarks

	Description	Benchmark
	Effect of HIV on TB natural history (only in high HIV settings, or where HIV-TB interventions modelled)	
	Effect of age on TB natural history (only where age-based interventions modelled)	

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Feedback from initial review

- Describe how stringently benchmarks will be assessed
- State when will benchmarks be assessed
- Clarify how benchmarks apply to stochastic models, models with parameter uncertainty, and stratified health states
- Clarify requested metrics, and standardize with WHO definitions
- Addition of benchmarks for risk groups (HIV) mostly supported, but concerns these could be hard to define

Ease of reporting responses

Benchmark Description	Model already produces this value	Model doesn't currently produce		
		Easy to add	Difficult to add	Impossible to add
Cumulative incidence of active TB (all forms) over the **first 5 years** following *M. tb* infection, no reinfection (%)	XXX	XX		
Annual incidence of active TB (all forms) for individuals **>5 years** after *M. tb* infection, no reinfection (%).	XXXX	X		
Case fatality (probability of death before self-cure) for active TB, in the absence of treatment	XXXX	X		
Duration of active TB in absence of treatment (yrs)	XXXX		X	
Reduction in the risk of primary TB afforded by **prior *M. tb* infection** (percent)	XXXXX			

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Discussion points

- *How stringently benchmarks to be assessed?*
  - Current approach: if model results fall outside of range, warrants discussion and justification.
- *Are wide ranges sufficient to allow variation between settings, and different state definitions by models?*
- *Should benchmarks be added for HIV and potentially other subgroups, and when would they apply?*

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Benchmarks 2

Country-specific epidemiological benchmarks

Rationale: Country-specific epidemiological benchmarks

- These benchmarks describe **country-specific features of TB epidemiology**
- There are multiple sources of country-level burden estimates. A given modelling application may be required to be consistent with a particular source, so need to allow flexibility on which source provides benchmarks

Current benchmarks

	Description
B2.1	General population **TB incidence rate** (all forms) in the most recent available year (per 100,000)
B2.2	**Change in** general population TB **incidence rate** (all forms) over most recent available year (%)
B2.3	General population **TB mortality rate** (all forms, including TB-HIV) in the most recent available year (per 100,000)
B2.4	**Change in** general population **TB mortality rate** (all forms, including TB-HIV) over most recent available year (%)
B2.5	**Change in** general population **TB case fatality** (ratio of TB mortality to incidence) over most recent available year (%)
B2.6	General population **TB prevalence** (per 100,000), in years for which a nationally-representative TB prevalence survey is available
B2.7	**Prevalence of MDR-TB among treatment-naive** notified TB cases, in the most recent available year (%)
B2.8	**Prevalence of MDR-TB among treatment-experienced** notified TB cases, in the most recent available year (%)

	Description	
B2.1	General population **TB incidence rate** (all forms) in the most recent available year (per 100,000)	554 (311- 866)
B2.2	**Change in** general population TB **incidence rate** (all forms) over most recent available year (%)	+ 0.73%
B2.3	General population **TB mortality rate** (all forms, including TB-HIV) in the most recent available year (per 100,000)	26 (22-29)
B2.4	**Change in** general population **TB mortality rate** (all forms, including TB-HIV) over most recent available year (%)	- 3.7%
B2.5	**Change in** general population **TB case fatality** (ratio of TB mortality to incidence) over most recent available year (%)	-2.3%
B2.6	General population **TB prevalence** (per 100,000), in years for which a nationally-representative TB prevalence survey is available	N/A
B2.7	**Prevalence of MDR-TB among treatment-naive** notified TB cases, in the most recent available year (%)	2.6% (1.8% - 3.3%)
B2.8	**Prevalence of MDR-TB among treatment-experienced** notified TB cases, in the most recent available year (%)	29% (20% - 38%)

Country: Philippines
Source: WHO

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Possible additional benchmarks

	Description
	Percentage of **incident TB cases** (or TB deaths) arising among **HIV positive** individuals, for high HIV settings
	HIV prevalence, for high HIV settings

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Feedback from initial review

- The addition of HIV benchmarks would be useful (multiple respondents)
- Consider removing case fatality (redundant given inclusion of TB incidence and mortality benchmarks)

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Ease of reporting responses

Benchmark Description	Model already produces this value	Model doesn't currently produce		
		Easy to add	Difficult to add	Impossible to add
General population **TB incidence rate** (all forms) in the most recent available year (per 100,000)	XXXXX			
Change in general population **TB incidence rate** (all forms) over most recent available year (%)	XXX	XX		
General population **TB mortality rate** (all forms, including TB-HIV) in the most recent available year (per 100,000)	XXXXX			
Change in general population **TB mortality rate** (all forms, including TB-HIV) over most recent available year (%)	XXX	XX		

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Ease of reporting responses (cont.)

Benchmark Description	Model already produces this value	Model doesn't currently produce		
		Easy to add	Difficult to add	Impossible to add
Change in general population **TB case fatality** (ratio of TB mortality to incidence) over most recent available year (%)	XX	XXX		
General population **TB prevalence** (per 100,000), in years for which a nationally-representative TB prevalence survey is available	XXXXX			
Prevalence of MDR-TB among treatment-naive notified TB cases, in the most recent available year (%)	XXXXX			
Prevalence of MDR-TB among treatment-experienced notified TB cases, in the most recent available year (%)	XXXXX			

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Discussion points

- *Should we include HIV benchmarks?*
- *How should we specify ranges for each benchmark?*
  - Current approach: take range given by source of burden estimates. If unavailable, use default +/- 25% of point estimate

Benchmarks 3

Country-specific economic benchmarks

Rationale: Country-specific economic benchmarks

- These benchmarks describe **country-specific features of TB program resource utilization**
- Evidence available to benchmark econ aspects of modelling currently weak, but improving. Focus on those inputs/outputs where evidence currently stronger, but even these still require some interpretation

Current benchmarks

	Description
B3.1	Total **TB spending** (health service costs, including diagnostics, treatment (first line and MDR), program support and management costs) for the most recent year* ** Benchmark **only** applies to modelling applications designed to inform program budget estimates*
B3.2	**Unit cost** per person month of first line **treatment*** ** Benchmark applies if country has previously reported in GHCC or WHO World TB Report*

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Feedback from initial review

- The care cascade and TB spending don’t match completely
- Why is the second benchmark restricted to 1st line treatment? Should we add additional cost categories?

Ease of reporting responses

Benchmark Description	Model already produces this value	Model doesn't currently produce		
		Easy to add	Difficult to add	Impossible to add
Total **TB spending** (health service costs, including diagnostics, treatment (first line and MDR), program support and management costs) for the most recent year	XX	XX	X	
Unit cost per person month of first line **treatment**	XX	X	XX	

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Discussion points

- *How do we benchmark cost inputs and resource need estimates given current scarcity of econ evidence?*
- *How do we make sure benchmarks only apply to those analyses for which they are relevant?*
- *Should the focus be on reporting data sources, methods (for including costs/ economic evaluation methods/ uncertainty)?*

Benchmarks 4

Additional standard outputs

Rationale: Additional standard outputs

- Outputs describe features of TB epidemiology and program performance for which **no benchmark** is provided, but which are useful for interpreting model assumptions and results
- Include metrics for features of TB epidemiology for which empirical data not typically collected in high-burden settings, as well as metrics for the TB treatment cascade

Current metrics

	Description
	Epidemiology
B4.1	Percentage of total population infected with latent *M.tb* infection (**LTBI**), in most recent year (%)
B4.2	Percent of incident TB cases due to **recent infection** (*M.tb* infection or reinfection within the last 2 years), in most recent year (%)
B4.3	Annual **rate of *M.tb* infection** for uninfected individuals, in most recent year (per 100 person-years)
B4.4	Average **number of new *M.tb* infections/reinfections** produced **by an infectious case**, in most recent year.
B4.5	Average **duration** of an episode of **active TB** (ie to death, self-cure, or treatment initiation), in most recent year.

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Current metrics

	Description
	Care cascade
B4.6	Percent of all incident TB cases that access healthcare and **initiate diagnosis**, for current year
B4.7	Percent of TB cases that initiate diagnosis who receive a **positive TB diagnosis**, for current year (ie 100 minus percentage false negative or not completing diagnostic algorithm)
B4.8	Percent of diagnosed TB cases that **initiate treatment**, for current year (ie 100 minus percent lost before treatment initiation)
B4.9	Percent of TB cases initiating treatment that **complete the regimen**, for current year (ie 100 minus percent died or discontinued)
B4.10	Percent of TB cases completing treatment that are **cured**, for current year

Possible additional metrics

	Description
	Percent of all diagnosed TB cases **false-positive**

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Feedback from initial review

- Epi indicators:
  - Definition of recent infection (2 years) different from definitions in general epi benchmarks (5 years)
  - Some outcomes difficult to report for ODE models?
- Care cascade indicators:
  - Should these indicators include the private sector?

Ease of reporting responses

Benchmark Description	Model already produces this value	Model doesn't currently produce		
		Easy to add	Difficult to add	Impossible to add
Epidemiology				
Percentage of total population infected with latent *M.tb* infection (**LTBI**), in most recent year (%)	XXXXX			
Percent of incident TB cases due to **recent infection** (*M.tb* infection or reinfection within the last 2 years), in most recent year (%)	X	XXXX		
Annual **rate of *M.tb* infection** for uninfected individuals, in most recent year (per 100 person-years)	XXXXX			
Average **number of new *M.tb* infections/reinfections** produced **by an infectious case**, in most recent year.	XX	XXX		

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Ease of reporting responses (cont.)

Benchmark Description	Model already produces this value	Model doesn't currently produce		
		Easy to add	Difficult to add	Impossible to add
Average **duration** of an episode of **active TB** (ie to death, self-cure, or treatment initiation), in most recent year.	XX	XXX		
Care Cascade				
Percent of all incident TB cases that access healthcare and **initiate diagnosis**, for current year	XXXX	X		
Percent of TB cases that initiate diagnosis who receive a **positive TB diagnosis**, for current year (ie 100 minus percentage false negative or not completing diagnostic algorithm)	XX	XXX		

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Ease of reporting responses (cont.)

Benchmark Description	Model already produces this value	Model doesn't currently produce		
		Easy to add	Difficult to add	Impossible to add
Percent of diagnosed TB cases that **initiate treatment**, for current year (ie 100 minus percent lost before treatment initiation)	XXX	XX		
Percent of TB cases initiating treatment that **complete the regimen**, for current year (ie 100 minus percent died or discontinued)	XXXXX			
Percent of TB cases completing treatment that are **cured**, for current year	XXXXX			

Discussion points

- *How much flexibility should there be around how models calculate a given metric?*
  - Current approach: models to calculate as they see fit.
- *Are these the most important aspects of TB health services to report/compare?*
- *How should the private sector be considered in cascade indicators?*

Reporting template

Rationale: Reporting Template

- A standardized framework to ensure that relevant information is communicated to appropriate parties, allowing for easy review and synthesis of applications as well as assessment of the benchmarks

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Current template

ESSENTIAL INFORMATION

RT1. EVALUATION QUESTION

RT1.1 What was the primary research question?
RT1.2 What policy alternatives were compared?
RT1.3 What outcomes were used to summarise health or epi effects of policy alternatives?
RT1.4 What outcomes were used to summarise economic effects of policy alternatives?
RT1.5 Over what time period/point were results estimated for?
RT1.6 How were optimal policies chosen?

RT2. MODELLING PROCESS

RT2.1 Which stakeholders participated?
RT2.2 What activities were undertaken to support local capacity building?
RT2.3 Did you seek or receive independent review?
RT2.4 Were there any conflicts of interest?
RT2.5 Is there a report or publication that provides technical details?

Current template

RT3. MODELLING RESULTS

RT3.1 Were results consistent with modelling benchmarks?
RT3.2 If there were deviations, how should these be interpreted?
RT3.3 Were other steps taken to validate the model?
RT3.4 What were the main findings and policy recommendations of the modelling?
RT3.5 What sensitivity analyses were conducted, and what conclusions were drawn from these for policy recommendations?
RT3.6 Did policy scenarios involve a substantial improvement in program coverage, quality or effectiveness?

RT4. LIMITATIONS & DATA NEEDS

RT4.1 What are major uncertainties/assumptions?
RT4.2 What are major threats to success of the novel policies examined?
RT4.3 What is the most urgent or important research needed to confirm these findings?

RT5. NEXT STEPS

RT5.1 Have these modelling results been accepted/endorsed by the requesting organization?
RT5.2 What policy decisions were informed by this modelling?

Feedback from initial review

- There needs to be clarity on the audience and purpose
- A number of sections require significant additional work
- Difficult to manage openness and honesty
- Difficult to consider continuous interaction & long-term outputs

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Discussion points

- *Does this meet the need of funders?*
  - *Who should mandate this template & review?*
  - *How could this fit into a modelling application process?*
- *Does sensitivity of the reports affect their wider distribution?*
- *How best should we reduce unnecessary reporting burden?*
- *How should we report on economic approaches?*
- *How should we report on the impact of interventions*

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Review process

Rationale: Review Process

- To facilitate external review of modelling applications, linking experts with requests to review

Proposed approach

RP1.INITIATION PHASE

- **RP1.1** Repository of potential reviewers established
- **RP1.2** Potential reviewers contacted
- **RP1.3** List of reviewers interested and able to provide review hosted on the TB MAC website with access open to institutional and close collaborators, country expertise, intervention/activity expertise

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Proposed approach

RP2. REVIEW PROCESS

- **RP2.1** Review requests submitted on TB MAC website, including summary information
  - -- Suggested reviewers
  - -- Required timeline
  - -- Country/region modelled
  - -- Modelling TA organisation
  - -- Funding source
  - -- Programme areas informed
  - -- Decision process informed
- **RP2.2** Review summary information sent to suggested reviewer(s) for decision, CoI disclosed
- **RP2.3** Open review process conducted during modelling application (unless inappropriate)
- **RP2.4** Review included in final report

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Feedback from initial review

- There needs to be clarity on the audience and purpose
- We could consider inclusion of non-TB modeller reviewers

Discussion points

- *When should external review happen (during modelling application, after modelling application)?*
- *Who should mandate this process?*
- *How should the review be finalised?*
- *What should the role of TB MAC be?*
- *How should we avoid CoI as part of external review?*

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