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User-Friendly Modeling:
Introduction, Pros & Cons

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June 6, 2013
Ctr for TB Research
Annual Meeting

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Protecting Health, Saving Lives—*Millions at a Time*

Background

Population Health Impact and Cost-Effectiveness of Tuberculosis Diagnosis with Xpert MTB/RIF: A Dynamic Simulation and Economic Evaluation

Nicolas A. Menzies^{1,2*}, Ted Cohen^{3,4}, Hsien-Ho Lin⁵, Megan Murray³, Joshua A. Salomon^{1,6}

- Choosing between different TB diagnostic tests/algorithms is a complex task.
- While we have data to inform this decision, those data are not synthesized in a readily-accessible fashion.
- Mathematical models have been constructed, but generally do not speak to actual decision-making.
 - For example, “Implementation of Xpert would avert 132,000 TB cases in southern Africa over 10 years...at a cost of US\$460 million”
 - Nice if you’re the Minister of Health of “southern Africa”...



Research Objective

To create a user-friendly modeling tool enabling decision-makers to compare TB diagnostic strategies as deployed within an epidemic representative of local epidemiological and conditions

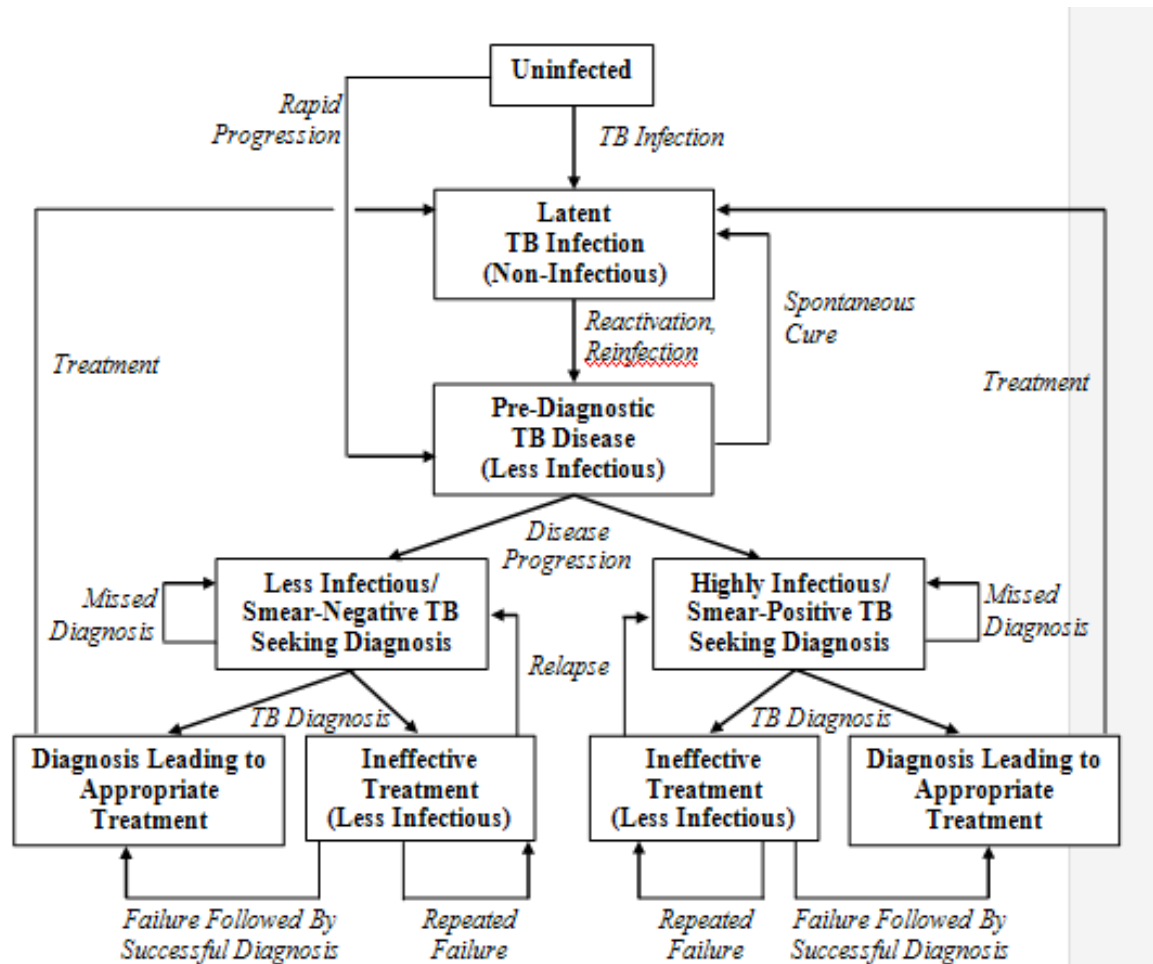


Methods

- Construct a steady-state TB epidemic using differential equations
 - In areas of low incidence or emerging MDR, allow for non-equilibrium dynamics to account for these trends
- Create a program that will generate this steady-state for 3 variables:
 - TB incidence
 - MDR-TB prevalence
 - HIV prevalence
- Add in costs of diagnosis and treatment
 - As a simple function of “cost of first-line therapy”



Underlying Model

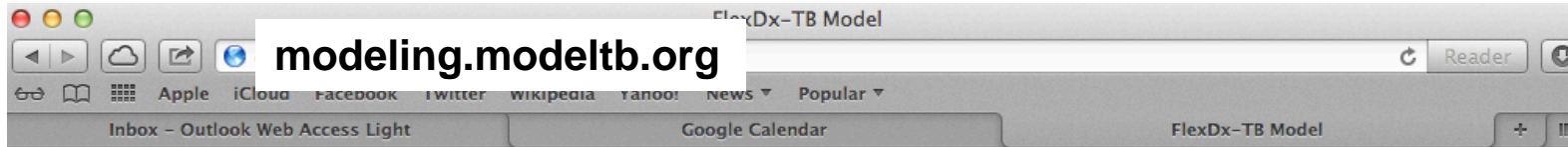


Diagnostic Options

- **Baseline:** smear + existing array of tests
- **Culture if Previously Treated:** baseline otherwise
- **Xpert for HIV-Positive Only:** “best case” assuming perfect knowledge of HIV status
- **Xpert if Smear-Positive:** MDR-TB strategy (e.g., India)
- **Xpert for All:** Treat RIF positive as MDR
- **Xpert for All, Culture Confirmation:** Confirm RIF w/ culture
- **MODS/TLA for All:** Slower but more sensitive than Xpert
- **Same-Day Microscopy:** Eliminate “initial default,” 2x costs
- **Same-Day Xpert:** Most expansive strategy



User Interface



Flex^D TB Model

A user-friendly, open-source transmission model of TB

ABOUT

MODEL INPUTS

- 1. Smear
- 2. Culture for retreatment
- 3. GeneXpert for HIV positive only
- 4. GeneXpert for smear positive only
- 5. GeneXpert for all
- 6. GeneXpert for all, culture confirmed
- 7. MODS/TLA
- 8. Same-day smear microscopy
- 9. Same-day GeneXpert
- 10. All

Target TB incidence, per 100,000 (baseline 250):

Target MDR-TB prevalence among new cases, % (baseline 3.7):

Target adult HIV prevalence, % (baseline 0.83):

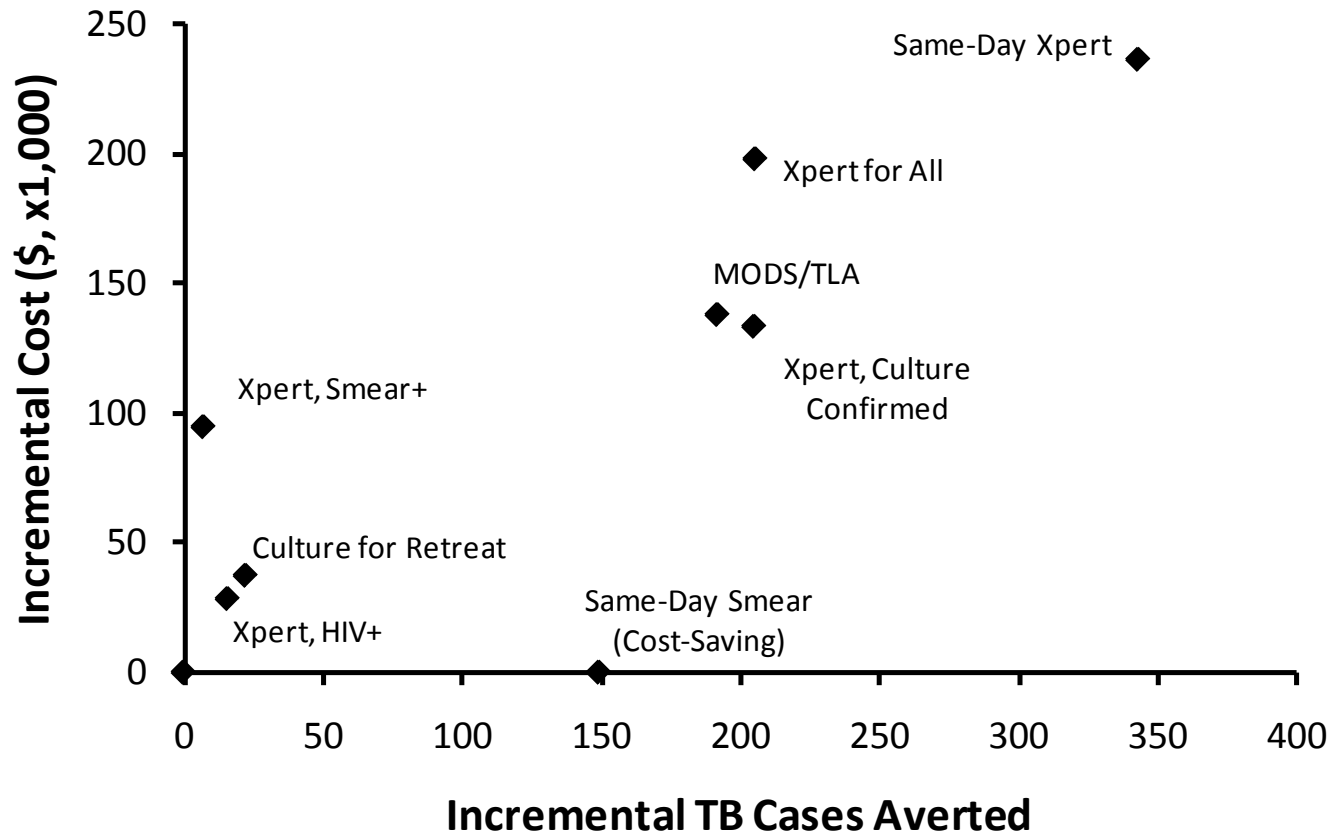
Cost to treat 1 patient with first-line drugs, \$ (baseline 500):

Brief Description of Diagnostic Strategies

Mouseover individual diagnostic strategies to see further details

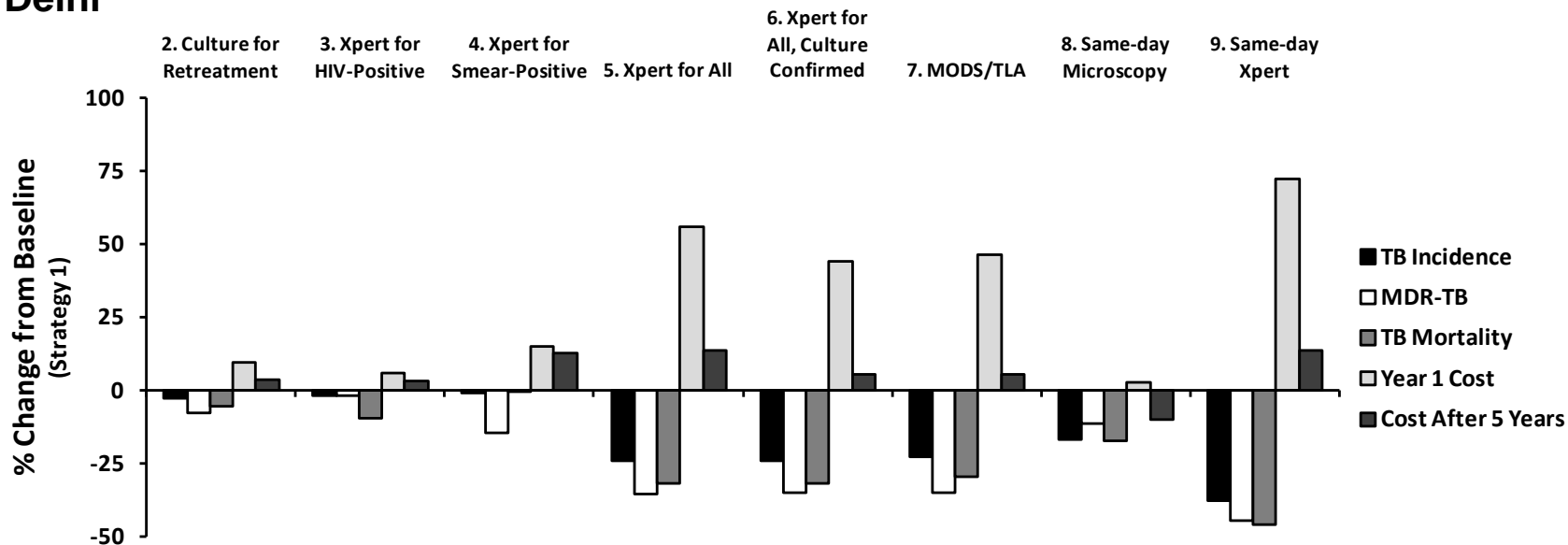


Model Output: "High Incidence" Scenario

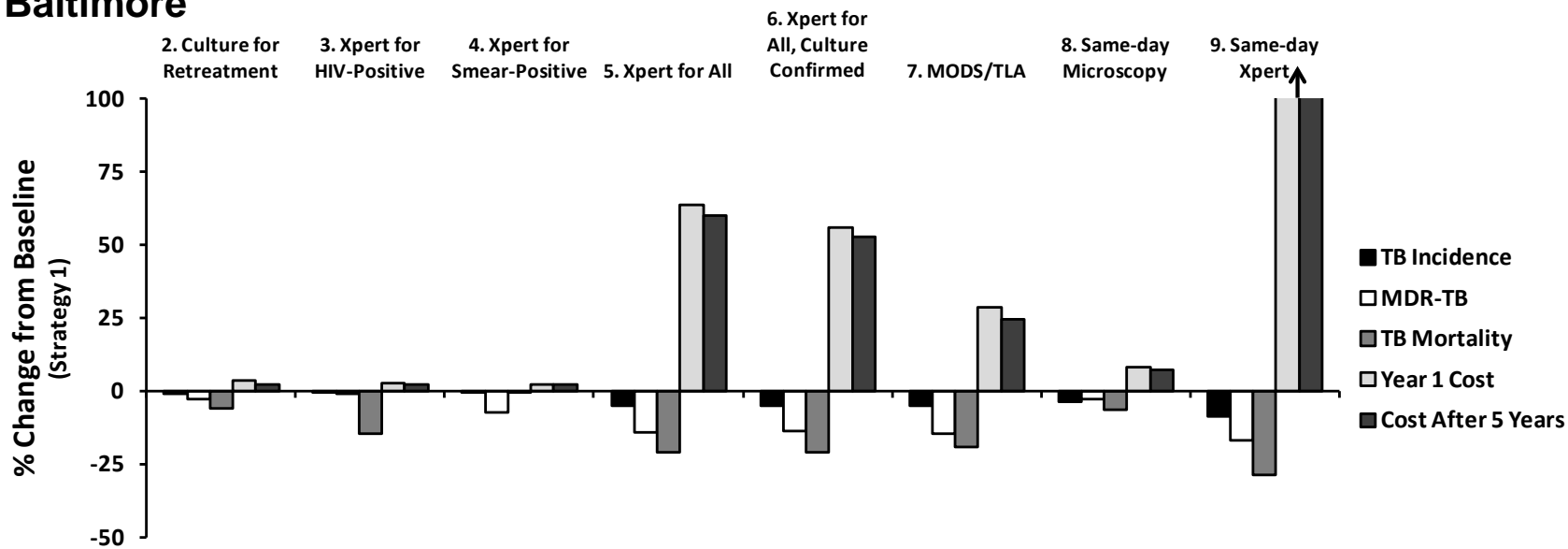


Comparing Settings

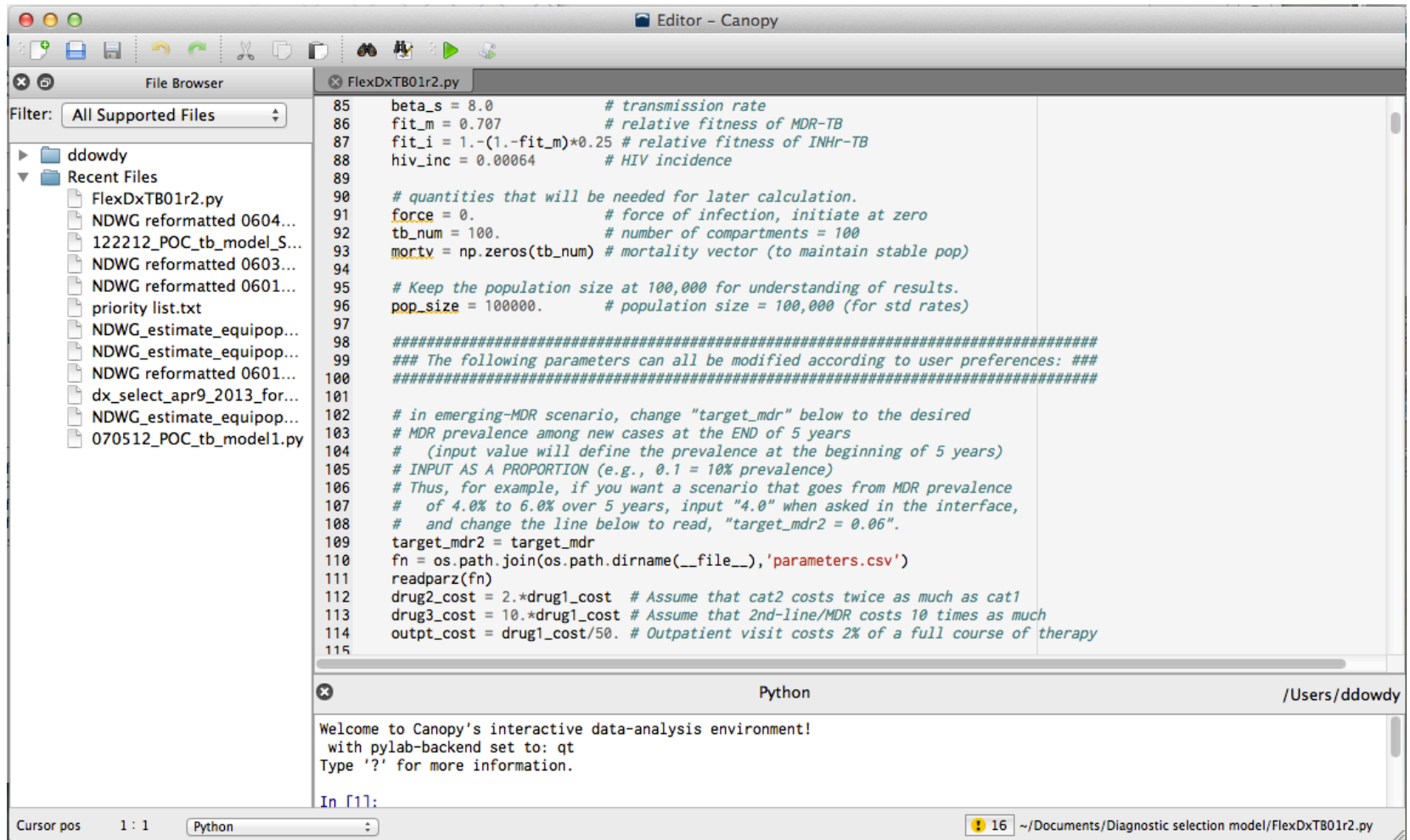
Delhi



Baltimore



Open-Source Program Available



The screenshot displays the Canopy IDE interface. On the left, a File Browser shows a directory structure with files like 'FlexDxTB01r2.py' and 'NDWG reformatted 0604...'. The main editor window shows the code for 'FlexDxTB01r2.py', which includes parameters for transmission rate, relative fitness, and population size, along with comments explaining the model's assumptions. Below the editor, a Python console window shows the welcome message and the start of an interactive session.

```
85 beta_s = 8.0 # transmission rate
86 fit_m = 0.707 # relative fitness of MDR-TB
87 fit_i = 1.-(1.-fit_m)*0.25 # relative fitness of INHr-TB
88 hiv_inc = 0.00064 # HIV incidence
89
90 # quantities that will be needed for later calculation.
91 force = 0. # force of infection, initiate at zero
92 tb_num = 100. # number of compartments = 100
93 mortv = np.zeros(tb_num) # mortality vector (to maintain stable pop)
94
95 # Keep the population size at 100,000 for understanding of results.
96 pop_size = 100000. # population size = 100,000 (for std rates)
97
98 #####
99 ### The following parameters can all be modified according to user preferences: ###
100 #####
101
102 # in emerging-MDR scenario, change "target_mdr" below to the desired
103 # MDR prevalence among new cases at the END of 5 years
104 # (input value will define the prevalence at the beginning of 5 years)
105 # INPUT AS A PROPORTION (e.g., 0.1 = 10% prevalence)
106 # Thus, for example, if you want a scenario that goes from MDR prevalence
107 # of 4.0% to 6.0% over 5 years, input "4.0" when asked in the interface,
108 # and change the line below to read, "target_mdr2 = 0.06".
109 target_mdr2 = target_mdr
110 fn = os.path.join(os.path.dirname(__file__), 'parameters.csv')
111 readparz(fn)
112 drug2_cost = 2.*drug1_cost # Assume that cat2 costs twice as much as cat1
113 drug3_cost = 10.*drug1_cost # Assume that 2nd-line/MDR costs 10 times as much
114 outpt_cost = drug1_cost/50. # Outpatient visit costs 2% of a full course of therapy
115
```

```
Python /Users/ddowdy
Welcome to Canopy's interactive data-analysis environment!
with pylab-backend set to: qt
Type '?' for more information.

In [1]:
```



Flexible Modeling Approach: Pros

- Allows decision-makers to create models that are relevant to their local situations
 - Only a handful of TB modelers in the world, thousands of settings
 - Where comparisons exist, this model seems to do well
- Provides insight by generating comparative scenarios
 - More useful to play and compare than come up with “one number”
 - For those with more modeling expertise, program is available
- Transparent conclusions
 - Very few additional assumptions behind the scenes
 - Simple model, simple results: can be understood!



Flexible Modeling Approach: Cons

- Arguably too simple
 - Real-world complexities (e.g., level of ART availability) not included
 - Though code is available, few will change it
- Target audience difficult to define
 - Local decision-makers will not know how to interpret
 - Expert modelers, given enough time, can do better for any one setting
- Is open-source modeling dangerous?
 - Very few people understand the implications of model modifications
 - Models may be constructed that are grossly inappropriate
- **This is the start of a conversation, not the end of it.**



Summary



- Global models are useful for publishing, but locally relevant models are needed for actual decision-making.
- A flexible, Web-based, user-friendly model can provide users across the globe access to tailored modeling results.
 - Free, open-source, modifiable platform
 - Web-based interface
 - Expanding to incorporate operational characteristics as well
- This strategy has great potential, but also important and controversial limitations.
 - Our philosophy: “If we don’t create it, we can’t have the conversation.”



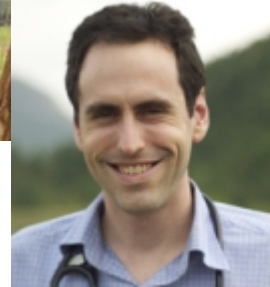
Feedback on Flexible Modeling

- What additional parameters would you like to control?
 - Operational data, natural history assumptions, etc.
- What additional interventions would you like to compare?
 - May need a different model structure for non-diagnostic interventions
- Is this a valuable approach, or a dangerous one?
 - Are we “playing with fire” by enabling individuals with little expertise in TB modeling to create estimates that may seem more “official”?
- What are the strengths and limitations of this approach?



Acknowledgments

- Pete Dodd, LSHTM
- Co-Authors
 - Jason Andrews, MGH
 - Bob Gilman, JHSPH
- Flexible TB Modeling Team
 - Jonathan Golub, JHU
 - Dick Chaisson, JHU
 - Madhu Pai, McGill
 - Adithya Cattamanchi, UCSF
- Funding
 - NIH, R21AI101152





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Modeling and Cost-Effectiveness:
Synthesis



Protecting Health, Saving Lives—*Millions at a Time*

Modeling: Summary Points

- **1. The purpose of modeling is to inform decision-making, not tell the future.**
- Models serve as the link between epi data (usually individual-level) and population-level decision-making.
 - Without a quantitative structure for this, the process is subjective.
- Projections of future impact are the means, not the end.
 - Decision-makers generally can't process model results without projections.
 - But an appropriate decision-making process involves the modelers discussing strengths and weaknesses of the approach.



Modeling: Summary Points

- **2. Modeling of TB is an uncertain business.**
- Much of our data is weak, and can strongly influence results.
 - For example, we estimate natural history from pre-chemotherapy era.
- Model structure introduces as much uncertainty as the parameters.
 - Example of including a “pre-clinical infectious” stage for diagnostics
- Uncertainty is difficult to convey appropriately.
 - Do you want a confidence interval that includes every possibility?
 - Is the goal to provide precise projections in the first place?



Modeling: Summary Points

- **3. Lessons from Models of TB Diagnostics**
- It's not just about sensitivity & specificity, but rather:
 - Duration of infectious period that can be averted
 - Existing quality of diagnosis
 - Healthcare system into which a diagnostic is deployed
 - Speed at which scale-up can occur
- Impact on mortality is likely greater than on incidence.
- To have transformative impact, diagnostics should be considered as part of a combined approach.



Modeling: Summary Points

- **4. Needs and Future Directions**
- Models of other diagnostic strategies, in other settings
 - DST, active case finding, pediatric/extrapulmonary, same-day dx, etc.
- Evaluation of more flexible approaches
 - In addition to “user-friendly” approach, there is also the “adaptive” approach
 - Need to balance importance of “global” findings with known local heterogeneity
- Better incorporation of health systems
 - Need more data



Cost-Effectiveness: Summary Points

- **1. Importance of Basic Economic Concepts**
- Opportunity costs, not financial costs
- Unit costs (fixed & variable) – not straightforward
- Discounting, inflation, currency conversion
 - \$1 is not always \$1
- Perspective of the analysis
 - Costs from one perspective may not be important from another



Cost-Effectiveness: Summary Points

- **1. Tenets of Cost-Effectiveness Analysis**
- Measure effectiveness in a fashion that allows for appropriate comparison.
 - Health utility (QALYs/DALYs) designed for this purpose
- Incremental analysis: always comparing interventions to something else



Cost-Effectiveness: Summary Points

- **2. Challenges of CEA for TB Diagnostics**
- TB treatment is so effective that even bad diagnostics can look very cost-effective.
- Assumptions that more sensitive diagnosis = more people treated and more lives saved may not be accurate.
- Difficult to incorporate transmission effects and impacts on the health system
 - Though we are improving in this regard



Cost-Effectiveness: Summary Points

- **3. CEA Case Studies**
- Triage testing: cost-effectiveness depends on cost, prevalence of TB among the population screened, and test characteristics
 - Can help to identify where a triage test can be implemented in the most cost-effective fashion
- Diagnostics for HIV-associated TB: cost-effectiveness is challenging.
 - Difficult to quantify clinical benefits
 - ART drives cost considerations
 - Need to consider affordability & budget impact, not just C-E.



Cost-Effectiveness: Summary Points

- **4. Integrating Cost-Effectiveness and Transmission into a Flexible Framework**
- Users want to be able to adapt results to their settings but may not have the expertise to use models appropriately.
- Transmission and economic models are increasingly being integrated, but the fields have traditionally been separate.
- User-friendly modeling as one approach, but not the solution to all problems
 - Need to develop a priority listing, given limited modeling resources

