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THE CENTER FOR TB RESEARCH JOHNS HOPKINS UNIVERSITY

User-Friendly Modeling: Introduction, Pros & Cons

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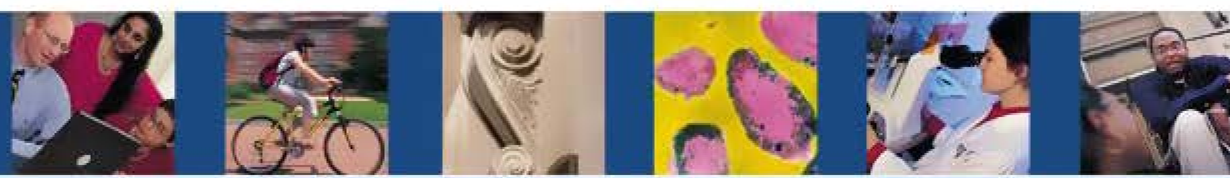


Protecting Health, Saving Lives—*Millions at a Time*

Background

OPEN ACCESS Freely available online PLOS MEDICINE

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 Lin[5], Megan Murray[3], 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”…

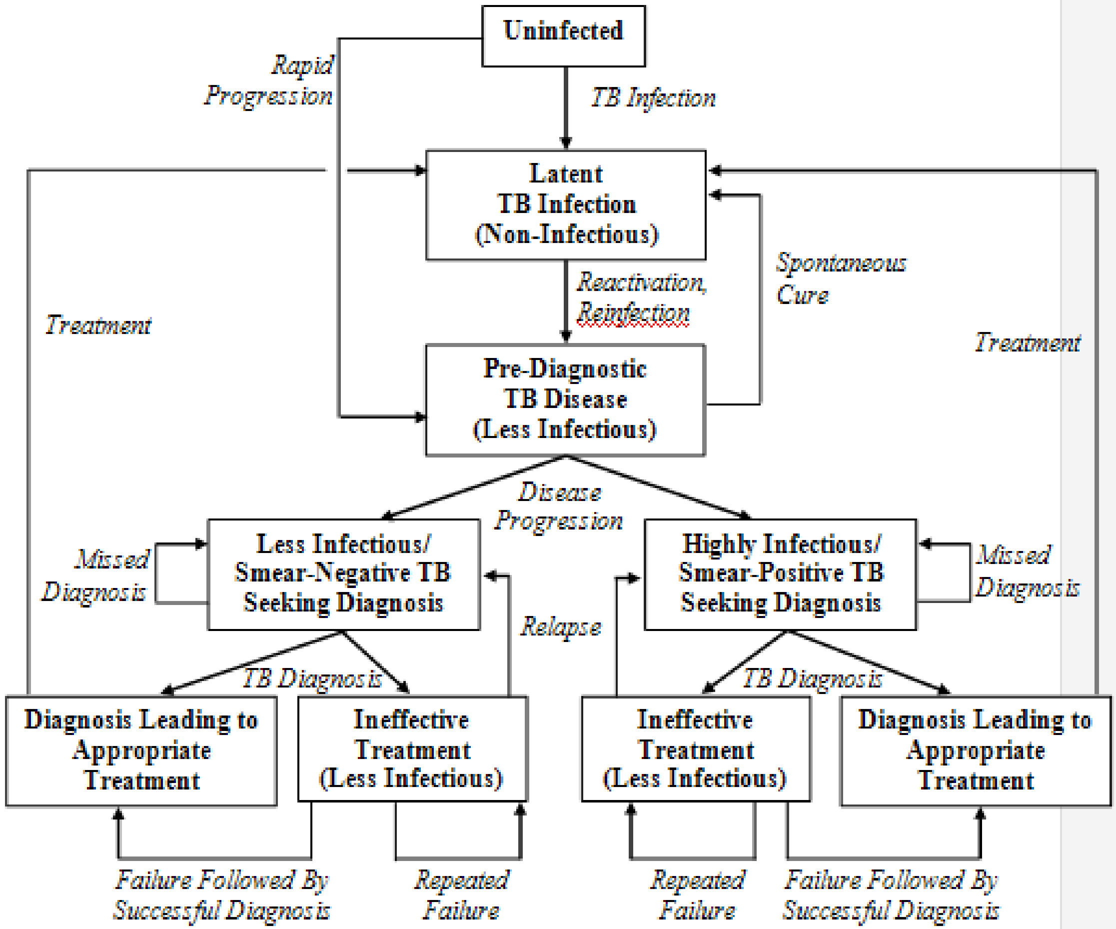
Research Objective

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”

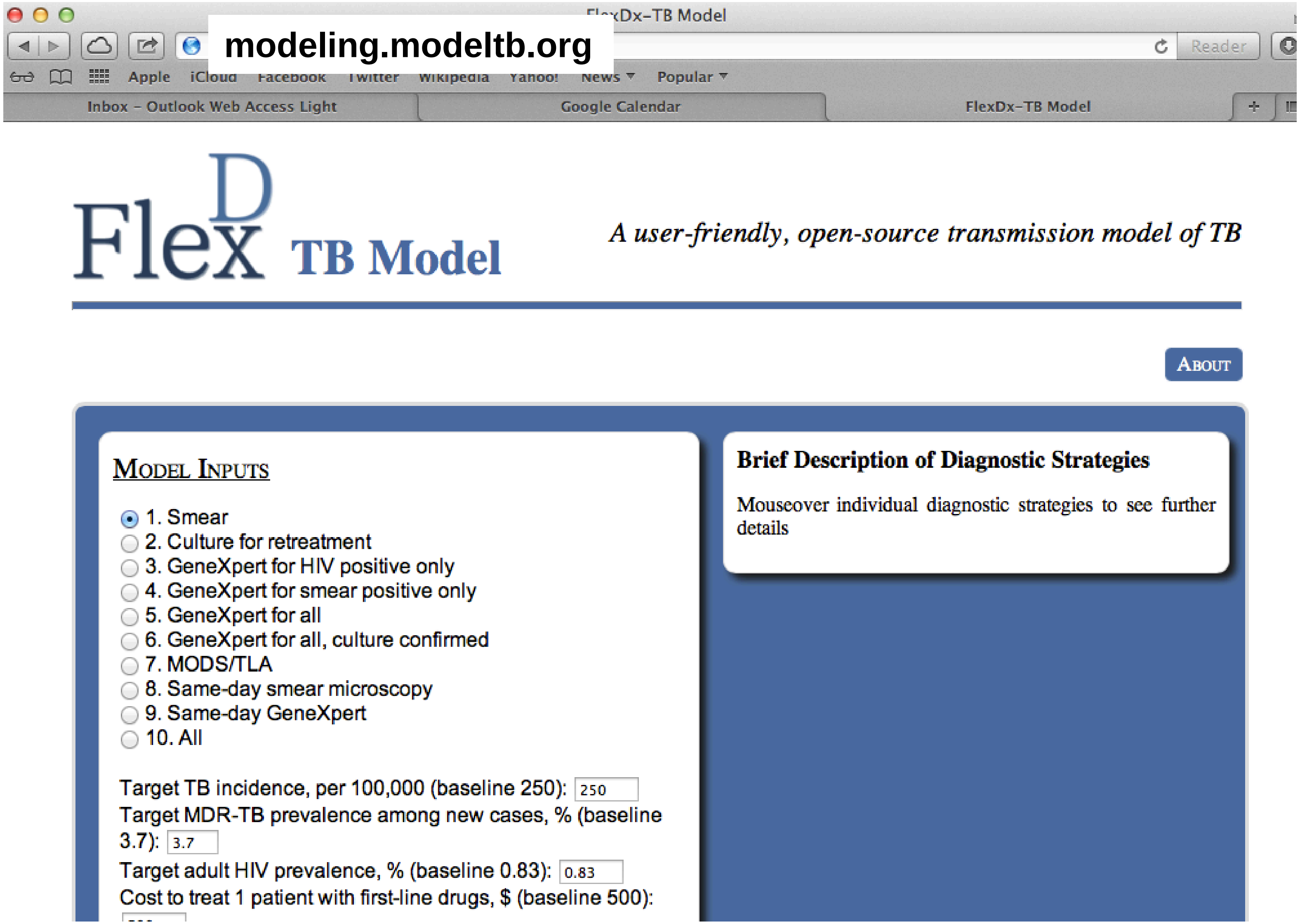
Underlying Model



Diagnostic Options

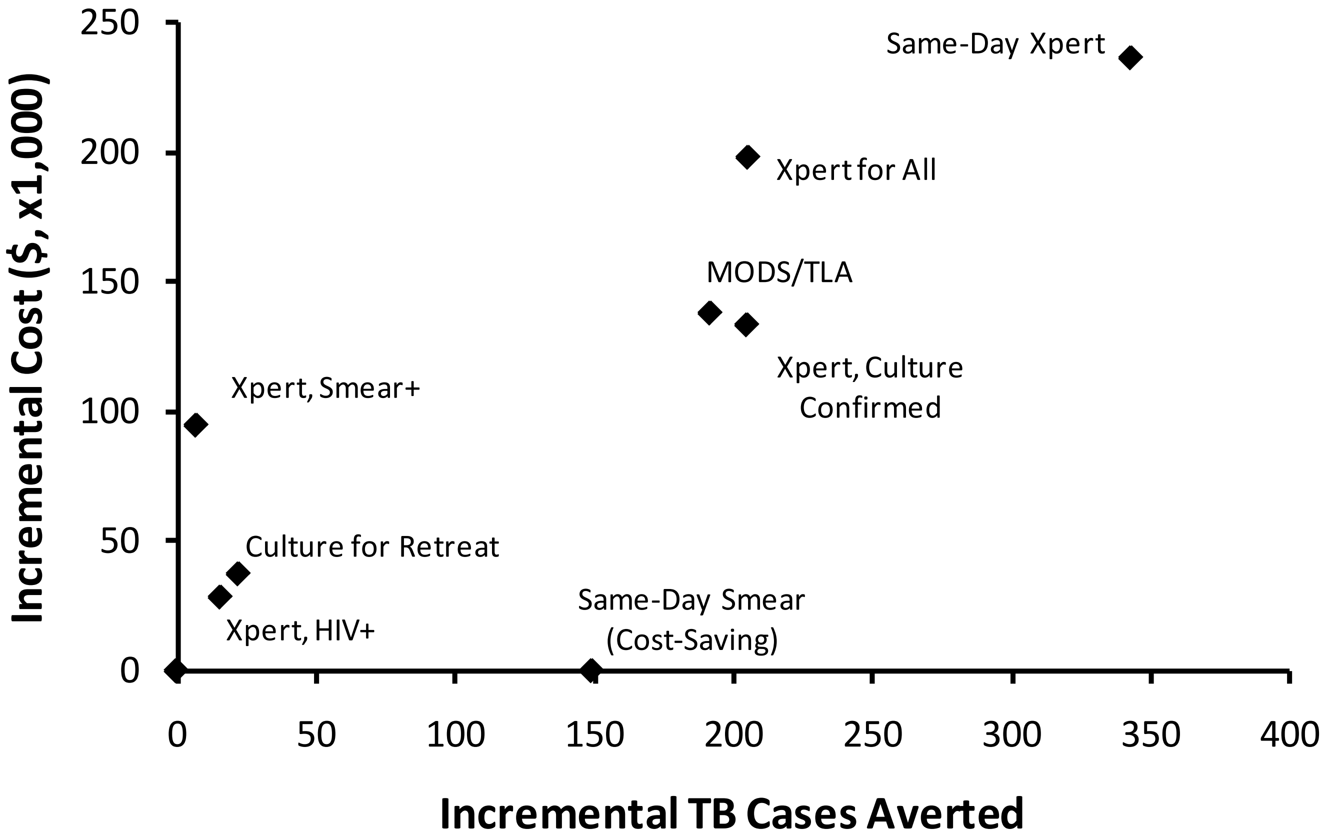
- **Baseline:** smear + existing array of tests
- **Culture if Previously Treated**: baseline otherwise
- **Xpert for HIV-Positive Only:** "best case" assuming perfect knowledge of HIV status
- **Xpert if Smear-Positive:** MDR-TB strategy (e.g., India)
- **Xpert for All:** Treat RIF positive as MDR
- **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



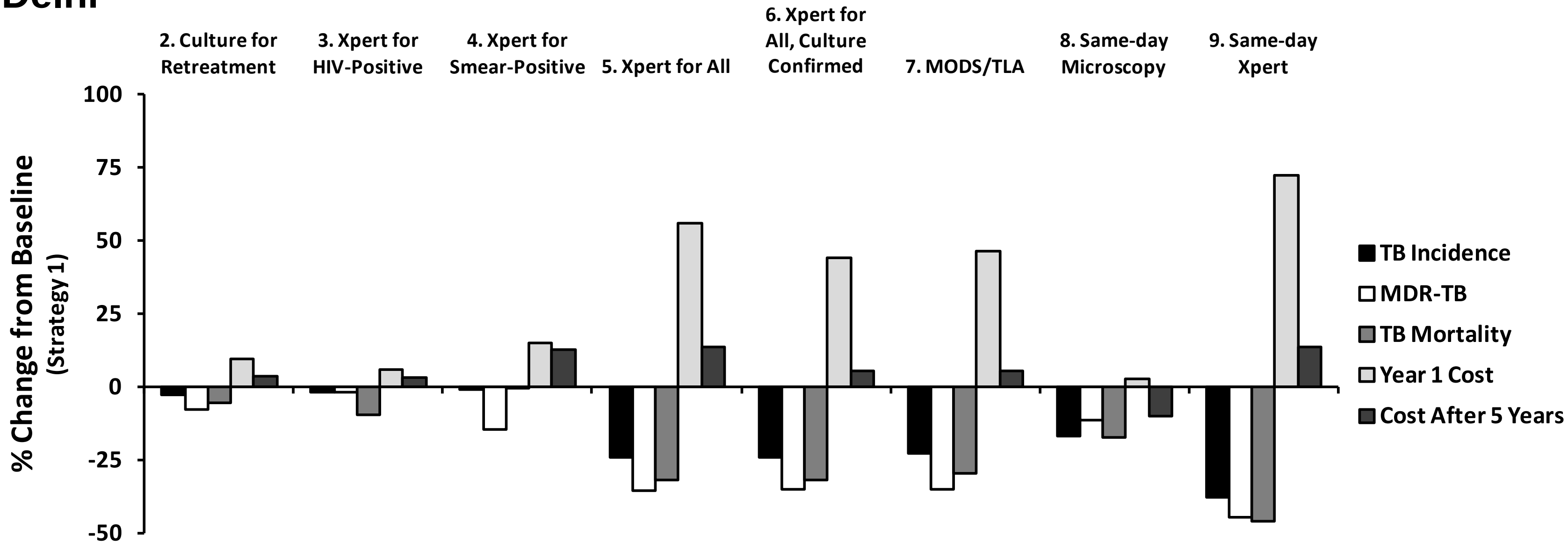
http://ec2-50-19-25-22.compute-1.amazonaws.com

Model Output: “High Incidence” Scenario

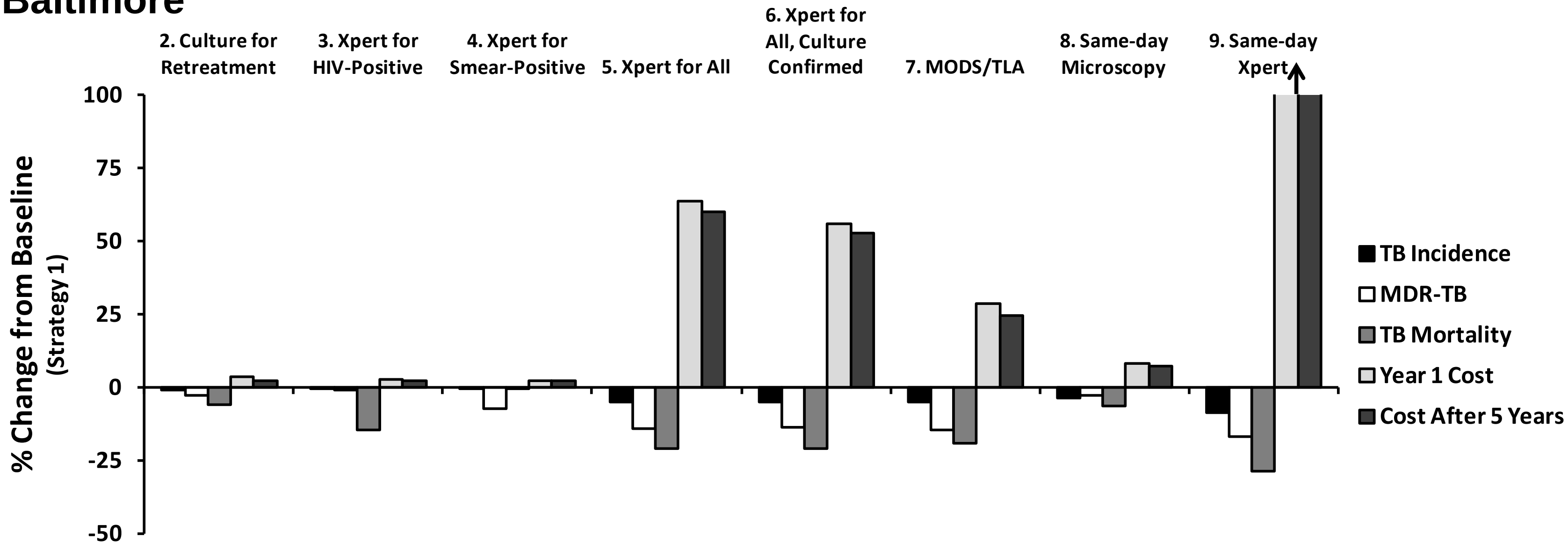


Comparing Settings

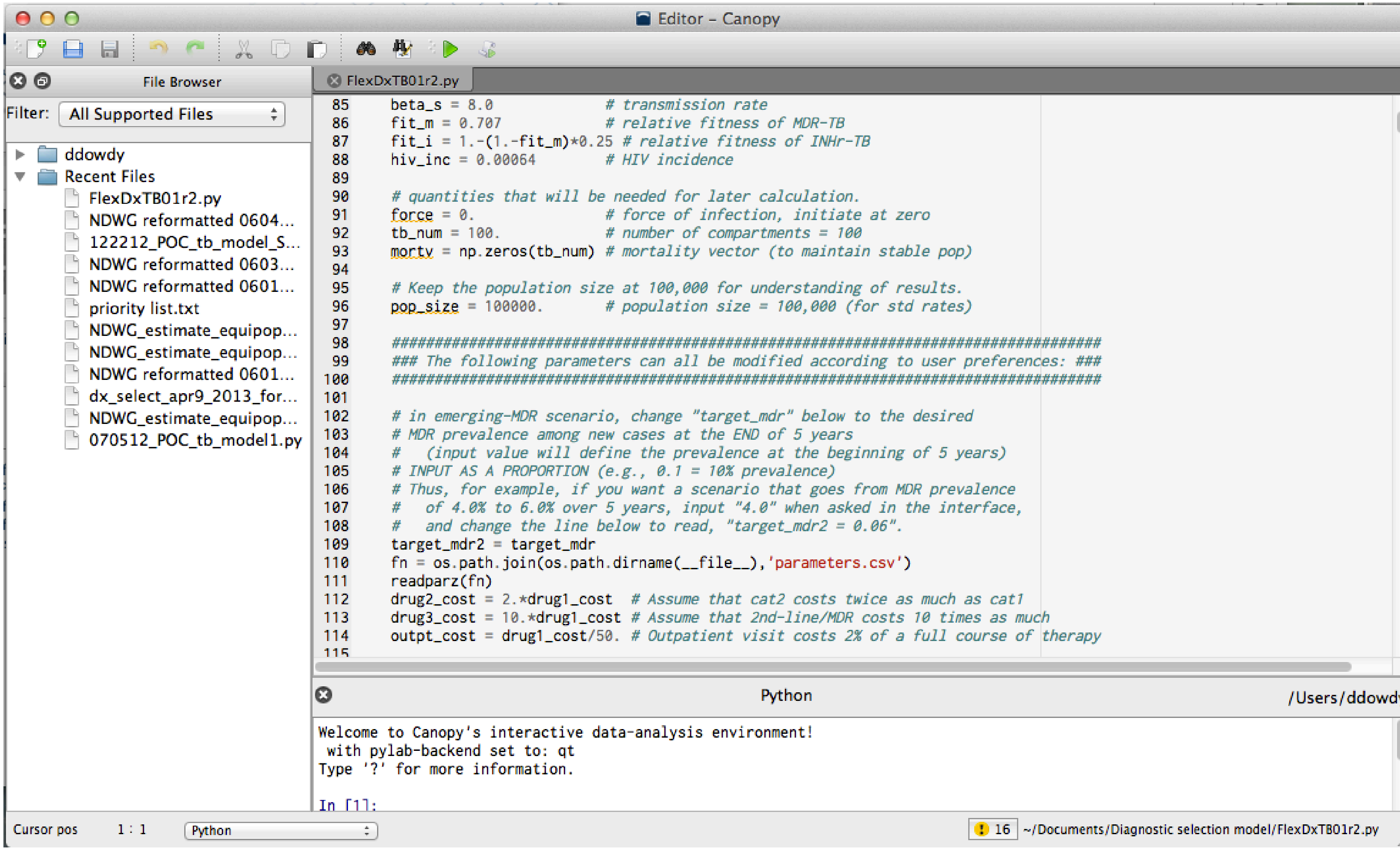
Delhi



Baltimore



Open-Source Program Available



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?

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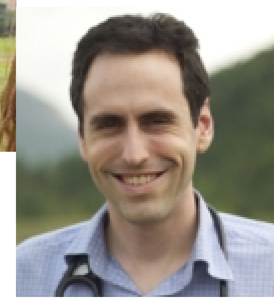
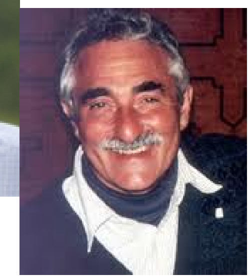



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Modeling and Cost-Effectiveness: Synthesis






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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