Mathematical modeling: a very quick intro

Madhukar Pai

McGill University, Montreal

I am not a modeler, but have been part of modeling studies

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PLOS | MEDICINE

The Importance of Implementation Strategy in Scaling Up Xpert MTB/RIF for Diagnosis of Tuberculosis in the Indian Health-Care System: A Transmission Model

Henrik Salje[1], Jason R. Andrews[2¤], Sarang Deo[3], Srinath Satyanarayana[4,5], Amanda Y. Sun[6], Madhukar Pai[4,5,7*], David W. Dowdy[1,8*]

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PLOS MEDICINE

Serological Testing Versus Other Strategies for Diagnosis of Active Tuberculosis in India: A Cost-Effectiveness Analysis

David W. Dowdy[1], Karen R. Steingart[2], Madhukar Pai[3*]

PLOS | ONE

RESEARCH ARTICLE

Xpert® MTB/RIF for the Diagnosis of Tuberculosis in a Remote Arctic Setting: Impact on Cost and Time to Treatment Initiation

Olivia Oxlade[1,2], Jordan Sugarman[1], Gonzalo G. Alvarez[3,4], Madhukar Pai[1,2], Kevin Schwartzman[1,2*]

American Journal of Epidemiology
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Advance Access publication: October 7, 2013

Practice of Epidemiology

Modeling the Impact of Alternative Strategies for Rapid Molecular Diagnosis of Tuberculosis in Southeast Asia

Amanda Y. Sun, Madhukar Pai, Henrik Salje, Srinath Satyanarayana, Sarang Deo, and David W. Dowdy*

The potential impact of health service disruptions on the burden of malaria:

a modelling analysis for countries in sub-Saharan Africa

Stop TB Partnership

Developed by Stop TB Partnership in collaboration with Imperial College, Avenir Health, Johns Hopkins University and USAID.

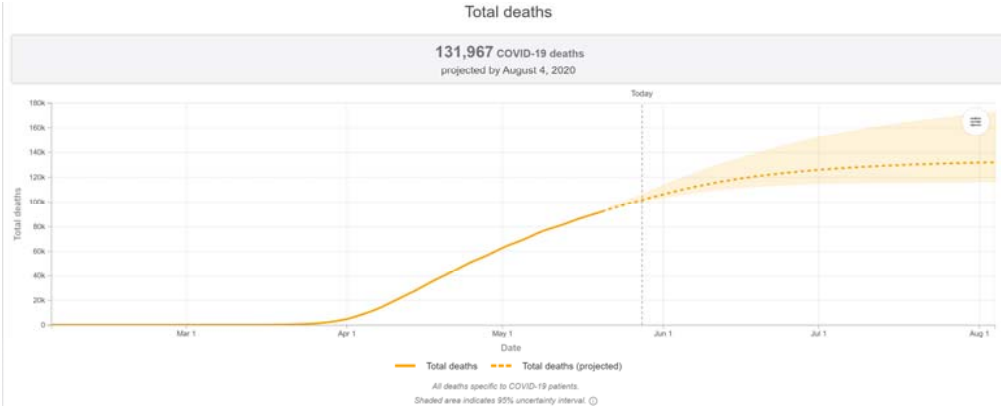
THE POTENTIAL IMPACT OF THE COVID-19 RESPONSE ON TUBERCULOSIS IN HIGH-BURDEN COUNTRIES: A MODELLING ANALYSIS

16 March 2020 *Imperial College COVID-19 Response Team*

Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand

Neil M Ferguson, Daniel Laydon, Gemma Nedjati-Gilani, Natsuko Imai, Kylie Ainslie, Marc Baguelin, Sangeeta Bhatia, Adhiratha Boonyasiri, Zulma Cucunubá, Gina Cuomo-Dannenburg, Amy Dighe, Ilaria Dorigatti, Han Fu, Katy Gaythorpe, Will Green, Arran Hamlet, Wes Hinsley, Lucy C Okell, Sabine van Elsland, Hayley Thompson, Robert Verity, Erik Volz, Haowei Wang, Yuanrong Wang, Patrick GT Walker, Caroline Walters, Peter Winskill, Charles Whittaker, Christl A Donnelly, Steven Riley, Azra C Ghani.

On behalf of the Imperial College COVID-19 Response Team



Flood of Covid-19 modeling analyses

Models as a scaffold or thinking framework

- Models are **not** designed to predict the future, nor to represent the full complexity of the world.
  - Simpler is often better, as only models that are sufficiently simple can be useful to the average decision-maker.

- Rather, models provide a decision-making framework that is:
  - Systematic
  - Data-driven
  - Transparent
  - Comprehensible
  - Reproducible
  - Able to describe uncertainty and key data needs

Slide courtesy: David Dowdy, Johns Hopkins U

A Modeling Exercise

- Consider two diagnostic tests for TB:
  - Test 1: 50% sensitive, but can be used to screen the population once per year (in addition to self-presentation)
  - Test 2: 90% sensitive, but requires patients to self-present
- A few basic assumptions:
  - Duration of TB disease before self-presentation = 1 year
  - Number of secondary transmissions per infectious person-year = 10
  - Proportion of secondary transmissions that result in active TB = 20%
    - 1 new case of active TB every 6 months
  - Mortality of TB without screening at the end of year 1:
    - 20% if detected
    - 100% if not detected
- Which test is better?

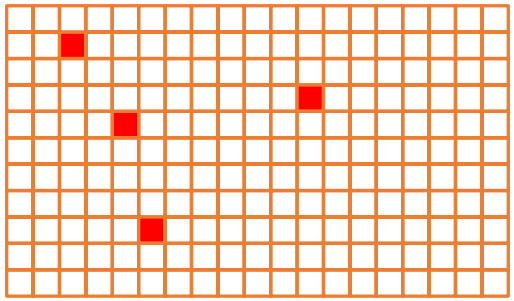
Slide courtesy: David Dowdy, Johns Hopkins U

The Simple Approach…

- Evaluate a cohort of 100 people

Outcome	Test 1	Test 2
Screened	50	0
Diagnosed after 1 year Survive Die	25 20 5	90 72 18
Undiagnosed = dead	25	10
Total Alive	**70**	**72**
Total Dead	**30**	**28**

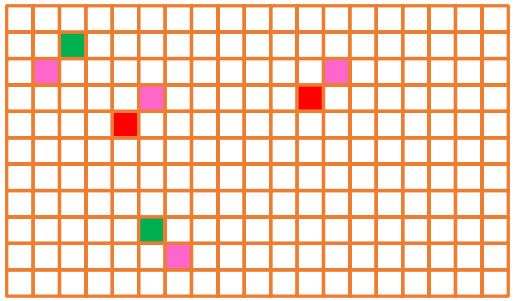
What If We're Interested in the Population?



4 TB cases in a community with test 1

Slide courtesy: David Dowdy, Johns Hopkins U

Population Dynamics



Diagnosed

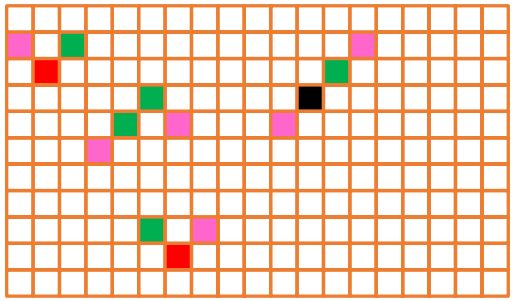
Old Active

New Active

At 6 Months: 6 Active Cases

Slide courtesy: David Dowdy, Johns Hopkins U

Population Dynamics



Diagnosed

Old Active

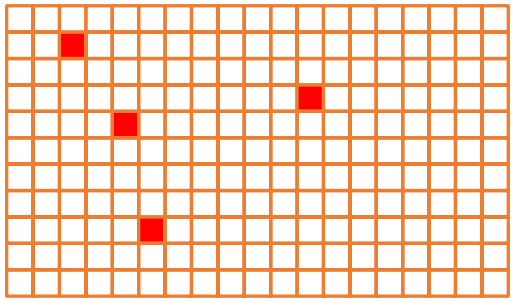
New Active

Dead

At 12 Months: 8 Active Cases

Slide courtesy: David Dowdy, Johns Hopkins U

Alternative Population Dynamics



Diagnosed

Old Active

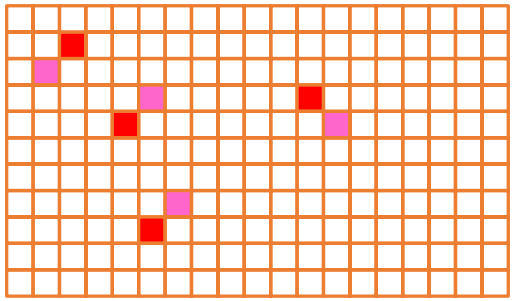
New Active

Dead

What about test 2?

Slide courtesy: David Dowdy, Johns Hopkins U

Alternative Population Dynamics



Diagnosed

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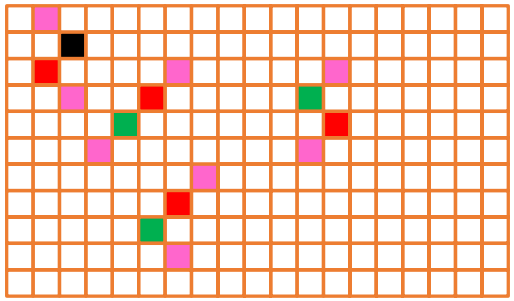
6 Months: 8 Active Cases

Slide courtesy: David Dowdy, Johns Hopkins U

Alternative Population Dynamics



Diagnosed

Old Active

New Active

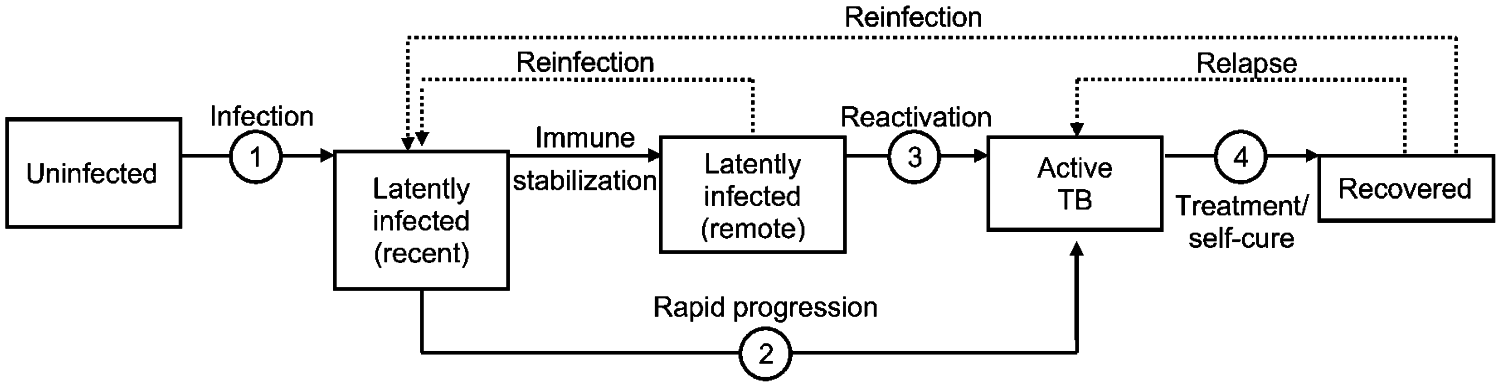
Dead

12 Months: 12 Active Cases!

Slide courtesy: David Dowdy, Johns Hopkins U

This is a compartmental or SIR model

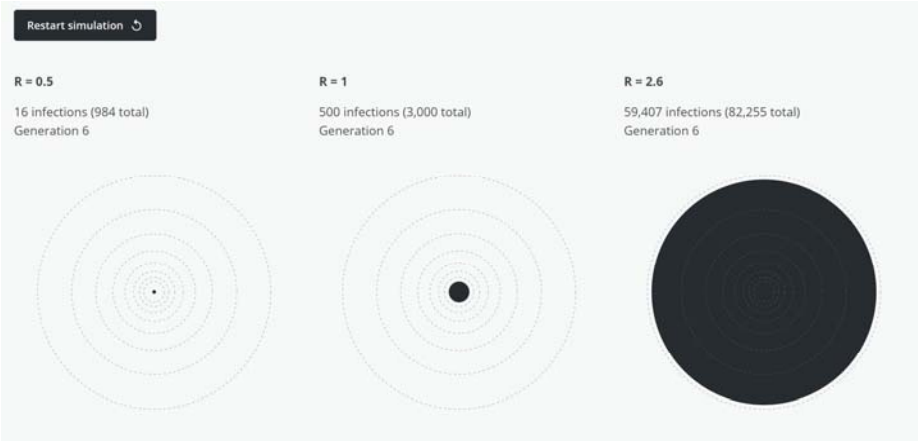
SIR (Susceptible, Infectious, or Recovered)



- Re-calculate the population every few days
- As the size of the active TB compartment grows, the rate of infection grows
- Allows for real-time evaluation of population-level effects on transmission

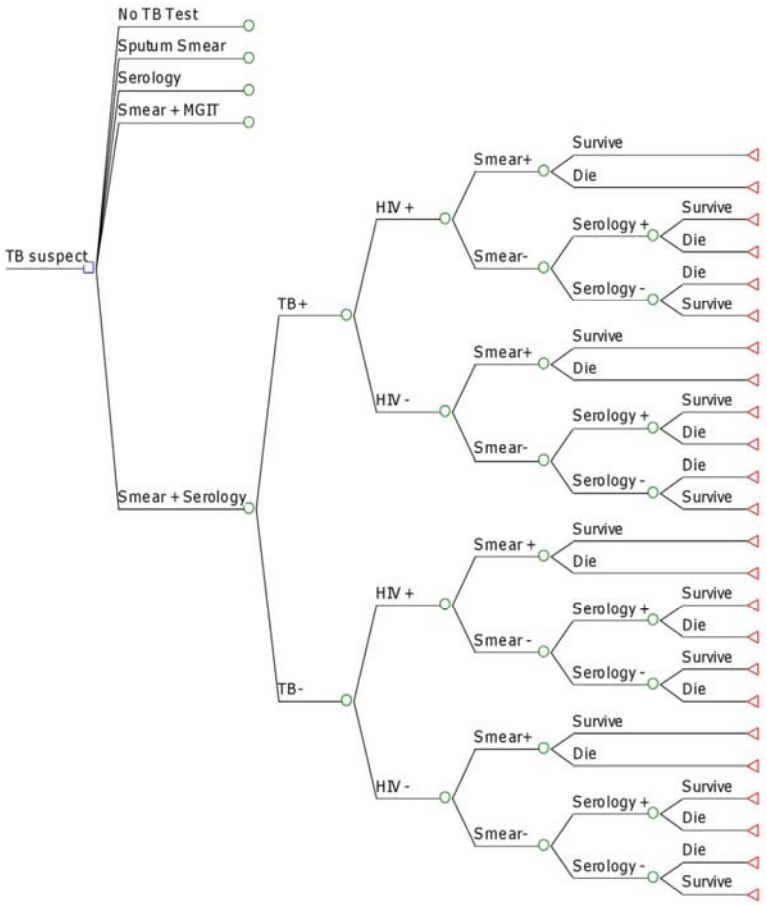
Slide courtesy: David Dowdy, Johns Hopkins U

Dowdy, Cohen, Dye. IJTLD 2013



https://newsinteractives.cbc.ca/coronavirusr0/

This is a decision analysis model



Dowdy et al. PLoS Med 2011

All good models must

- Describe the setting & population
- Limit to a certain time horizon
- Describe and quantify all the assumptions and justify them
- Provide projections with uncertainty ranges
- Do sensitivity analyses by varying the assumptions
- Discuss limitations of the model
- Publish the code and data used for others to verify

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Wrong but Useful — What Covid-19 Epidemiologic Models Can and Cannot Tell Us

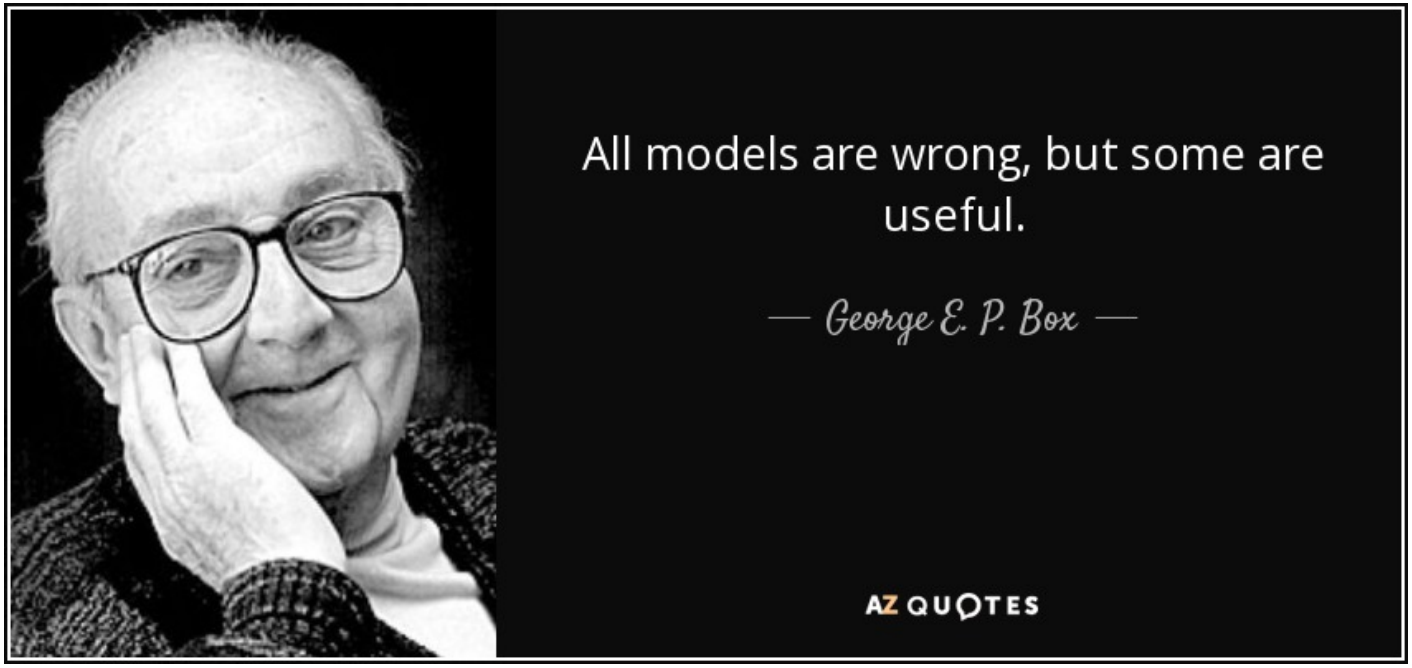
Inga Holmdahl, S.M., and Caroline Buckee, D.Phil.

Five Questions to Ask about Model Results.

1. What is the purpose and time frame of this model? For example, is it a purely statistical model intended to provide short-term forecasts or a mechanistic model investigating future scenarios? These two types of models have different limitations.
2. What are the basic model assumptions? What is being assumed about immunity and asymptomatic transmission, for example? How are contact parameters included?
3. How is uncertainty being displayed? For statistical models, how are confidence intervals calculated and displayed? Uncertainty should increase as we move into the future. For mechanistic models, what parameters are being varied? Reliable modeling descriptions will usually include a table of parameter ranges — check to see whether those ranges make sense.
4. If the model is fitted to data, which data are used? Models fitted to confirmed Covid-19 cases are unlikely to be reliable. Models fitted to hospitalization or death data may be more reliable, but their reliability will depend on the setting.
5. Is the model general, or does it reflect a particular context? If the latter, is the spatial scale — national, regional, or local — appropriate for the modeling questions being asked and are the assumptions relevant for the setting? Population density will play an important role in determining model appropriateness, for example, and contact-rate parameters are likely to be context-specific.

What makes Covid-19 modeling challenging?

- New disease – everyone is learning
- R0 is not static
- Testing rates are changing
- Natural protective immunity: unclear
- % of population infected: unclear
- Case fatality: highly variable
- Do asymptomatic people infect others?
- Duration of infectiousness?
- Do children transmit infection?
- How many people come into contact with a case?
- Are there ‘super-spreaders’?
- Lockdowns, restrictions & other interventions keep changing
- Human behaviour!!!!


All models are wrong, but some are useful.
— George E. P. Box —
AZ QUOTES

We should not have crazy expectations!