An Introduction to Tuberculosis Disease Modeling

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What will TB disease incidence in South Africa look like over the next 10 years?

Current WHO estimates

What factors will drive future trends?
Roadmap

1. Overview of dynamic TB models
   – What are they good for?
   – What data goes into a model?

2. Constructing the canonical TB transmission model
   – How do we structure the model
   – Example: Deriving Styblo’s rule

3. Model fitting and analysis
   – Calibration
   – Validation
Dynamic TB models

Properties

- Explains risk in a dynamic population
  - Infection
  - Disease
  - Death
- Models both transmission and pathogenesis over time
- Models demographic processes: birth and non-TB deaths
- Mechanistic in nature
  - Diagnostics and treatment
  - Human behavior (eg. care seeking)

Uses

- Quantifying the impact of changes in TB epidemiology on TB burden and transmission
  - Changes in demographics
  - Changes in health systems
    - Treatment
    - Diagnostic algorithms
  - Changing prevalence of individual risk factors
- Quantifying cost-effectiveness of interventions
How to visualize a dynamic transmission model

- Simplest: SI Model
  - $S$: susceptible
  - $I$: infected

- Population in one of two states, $N = S + I$
- Newly infected individuals move from $S$ to $I$
How do we compute the dynamics?

- Consider a total population of 1000 of which 10 have active disease
- $\frac{\beta}{N} = 10$ per 1000 per year
- What is the state at time $\Delta t = 1$ year

\[
S_0 = 990 \\
I_0 = 10
\]

\[
I(\Delta t) = I_0 + \Delta t \times \left( \frac{\beta}{N_0} \right) S_0 I_0
\]

\[
= 10 + 1 \times \left( \frac{10}{1000} \right) \times 990 \times 10 = 109
\]
Does this simple model reflect TB epidemiology?

What are we missing?

- Births ($\sigma$)
- Non-TB deaths ($\mu$)
- TB deaths ($\gamma$)
Latency

- Potentially long **Latent** non-infectious period \( \frac{1}{\rho} \)

\[
\begin{align*}
S & \quad \beta \frac{SI}{N} \quad L \\
L & \quad \rho \quad I \\
I & \quad \gamma
\end{align*}
\]

* Omitting the non-TB dynamics, i.e. births and non-TB deaths
Primary disease (fast progressors)

- Potentially long **Latent** non-infectious period ($\frac{1}{\rho}$)
- In certain fraction ($f$), high risk of active disease after initial infection ($\rho_{fast}$)
Cure without treatment

- In certain fraction (r) disease will resolve even without treatment

\[
\frac{\beta}{N} SI f \quad L_{\text{fast}} \quad \rho_{\text{fast}} \\
1-f \quad L_{\text{slow}} \quad \rho_{\text{slow}} \\
(1 - r)\gamma \\
\gamma \\
r\gamma \\
\]
Incorporating health care systems

\[ d_s \eta \]

\( \gamma \)

\( d_s \) – diagnostic sensitivity

\( \eta \) – rate symptomatic individuals seek care
Example: Deriving the Styblo Rule

- Styblo rule: In a population of 100,000 an annual incidence of 50 smear positive cases will generate an annual risk of infection (ARI) of 1%.

1. Where does this rule come from? How do assumptions affect its derivation?
2. What are potential pitfalls of this rule of thumb?

Dr. Karel Styblo

Courtesy Wikipedia.org
Deriving Styblo’s Rule of Thumb

Assumptions

– Smear positive case generates 10 infections per year (in a population of 100k)
– Average duration of active disease is 2 years
– System is in dynamic equilibrium

\[ V_{eq} = \frac{\text{in}}{\text{out}} \]

• \( V \rightarrow V_{eq} \) “eventually”
Deriving Styblo’s Rule of Thumb

• Dynamic equilibrium
  
  \[
  \frac{50}{\text{yr}} \quad \text{Smear-positive} \quad \frac{1}{2 \text{ yr}}
  \]

  \[
  \text{Smear}_{eq} = \frac{\text{in}}{\text{out}} = 100
  \]

• Annual risk of infection:
  
  – New infections = \( \left( \frac{\beta}{N} \right) \times \text{Smear}_{eq} = \frac{10}{100000} \times 100 = 0.01 = 1\% \)

• How could this “rule of thumb” model be violated?
  
  – Treatment cuts down duration
  
  – HIV, other risk factors
Calibration and validation

• Some parameters are difficult to measure directly
  – Infectiousness
  – Care seeking rates (passive case detection)

• Calibration:
  – Infer these parameters by fitting to population level data
  – Disease incidence and mortality

• Validation:
  – Does fitted model make sense?
  – Ideally use data different from calibration
  – Compare to smear-positives from prevalence survey in the same population
Complexity increases, models based on same principles

- Individual-based models
- Metapopulation models (multiple groups)
- Compartmental models (single population)

- Best fit to WHO South Africa data from IDM individual based model (EMOD-TB)
- Freely available on github (www.idmod.org)
Summary

• We constructed the canonical dynamic TB transmission model

• Dynamic models used to predict
  – Future TB burden
  – Impact of programmatic changes
  – Cost effectiveness (eg. DALYs averted)

• Models are closely linked to data
  – Epidemiological
  – Demographic
  – Health systems

• The modeling process involves both calibration and validation
Thank You