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## Letter to Editor

# Unravelling the web of tuberculosis: Mathematical models to decode and defeat tuberculosis transmission complexity

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## ABSTRACT

In the transmission of infectious illnesses like tuberculosis, mathematical models are crucial in public health. The fundamental paradigm is compartmental modelling, which classifies people into categories such as susceptible, latent, active, and recovered. Extensions and variations in this model can be utilized to capture intricate details. To research TB transmission dynamics, structural models including age-structured, agent-based, stochastic, SEIR, spatial, drug-resistant, vaccination, contact tracking, and treatment models are employed. Populations are divided into age groups by age-structured models, intricate interactions are shown by agent-based models, disease outbreaks are simulated by stochastic models, social networks are considered by SEIR models, and treatment success rates are considered by treatment models. Real-world mathematical simulations of TB transmission in public health settings offer useful tools for comprehending TB dynamics, making decisions, allocating resources, and assisting in the reduction and eradication of tuberculosis.

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## 1. Introduction

Mathematical models are important tools in public health to study the transmission dynamics of infectious diseases like tuberculosis (TB). These models help the researchers and public health officials to understand how actually TB spreads through populations and evaluate the necessity impact of interventions to be done.

The basic model for transmission of tuberculosis can be represented using compartmental modelling. In this model, individuals are divided into different compartments based on their disease status.

## 2. Compartments Used In TB Transmission Models Are:

1. *Susceptible (S)*: Individuals who are not infected with TB but are susceptible or at risk of getting infected.
2. *Latent TB (LTB)*: Individuals who have been infected with TB but are not contagious and do not show symptoms.
3. *Active TB (ATB)*: Individuals who have active TB disease, are contagious, and who exhibit signs & symptoms.
4. *Recovered (R)*: Individuals who have recovered from active TB and are no longer considered contagious and they may have acquired immunity.

The disease transmission dynamics in this simple model can be described by a system of differential equations. Here's a basic set of differential equations:

$$\text{Change in Susceptible: } dS/dt = -\beta * S * (ATB + \epsilon * LTB)$$

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1.  $\beta$  represents the transmission rate (how easily TB spreads from an active case to a susceptible individual).
2.  $\varepsilon$  represents the rate at which latent TB individuals progress to active TB

*Change in Latent TB:*  $dLTB/dt = \beta * S * (ATB + \varepsilon * LTB) - \alpha * LTB$

- $\alpha$  Represents the rate at which latent TB individuals become active cases

*Change in Active TB:*  $dATB/dt = \alpha * LTB - \gamma * ATB$

$\gamma$  Represents the recovery rate (how quickly individuals recover from active TB)

*Change in Recovered:*  $dR/dt = \gamma * ATB$

Individuals in the active TB compartment recover and move to the recovered compartment.

This is a basic model and numerous variations and extensions are possible to capture more complex aspects of TB transmission such as different age structure, treatment dynamics, drug resistance, and population mobility.<sup>1</sup>

### 3. Different Structured Models to Understand Dynamics of TB Transmission

1. *Age-Structured Models:* The transmission of TB varies with age and age-structured models can divide the population into different age groups for better capture of this variation. Different age groups can have different contact rates, vaccination rates and response to treatment which affect the dynamics of TB transmission.
2. *Agent based models:* Here individual agents (representing people) interact with each other within a simulated environment. These models capture complex interactions and behaviours that have an influence on TB transmission
3. *SEIR (Susceptible Exposed Infected Recovered Models) :* In addition to the compartments for Susceptible (S), Latent TB (E or LTB), Active TB (I or ATB) and Recovered (R) more complex models may include an Exposed compartment (E) to represent individuals who have recently been infected with TB but are not yet infectious. SEIR models allow for a more detailed representation of the disease progression. Many TB models include an exposed (E) compartment to account for the latent period during which individuals have been infected but are not yet infectious. This allows for a more detailed representation of disease progression.<sup>2</sup>
4. *Network Models:* TB transmission occurs within social networks or in communities. Network models represent individuals as nodes with their interactions as edges in a network. This model can be used to study the spread of TB in specific populations, such as in households or schools

5. *Stochastic Models:* The transmission of the disease in real-world is inherently stochastic. Stochastic models include randomness by incorporation of probability distributions into the model thereby allowing the simulation of the disease outbreaks and the estimation of uncertainty of occurrence.
6. *Spatial Models:* There is geographical variation in TB transmission. These models divide the population into spatial compartments and they consider the movement of the individuals between them. These models help to study how inter and intra-regional spread of TB occur
7. *Vaccination Models:* Mathematical models are used to assess the potential impact of TB vaccines on TB transmission. These models can help optimize vaccination strategies to control the disease
8. *Drug-Resistant TB Models:* TB can develop resistance to antibiotics. Models that account for drug resistance can help study the emergence and spread of drug-resistant TB strains and evaluate the impact of treatment regimens.
9. *Contact Tracing Models:* Contact tracing is a key public health strategy for controlling TB. Models to guide contact tracing efforts, predict the risk of transmission among the contacts and prioritize different interventional measures can be implemented to reduce the burden.
10. *Treatment Models:* Various models of TB treatment dynamics consider factors like treatment initiation, adherence and completion rates. These are essential for assessing the effectiveness of TB treatment programs and to identify various strategies so as to improve treatment outcomes.
11. *Epidemiological Data Fitting:* Mathematical models are often fitted to epidemiological data on relevant variables like TB incidence and prevalence. This process estimates model parameters and assesses how approximately the model aligns with observed data.
12. *The SIR Model for TB Transmission:* A classic epidemiological model is the Susceptible-Infectious-Recovered (SIR) model, which can be adapted for estimating TB transmission. This model divides the population into compartments of susceptible individuals, infectious individuals (those with active TB) and recovered individuals. Variations of the SIR model can incorporate latent TB infection and age structure to better represent TB dynamics.

3.1. *Here are some key purposes that mathematical models can serve in the context of TB transmission dynamics*

1. Quantifying Transmission Dynamics
2. Predicting Future Trends
3. Evaluating Interventions
4. Identifying High-Risk Groups

5. Optimizing Control Strategies for reducing TB incidence and mortality
6. Understanding Drug Resistance
7. Informing Policy Decisions about resource allocation and program planning
8. Simulating Outbreak Scenarios to assess the likelihood of outbreaks
9. Exploring Hypothetical Scenarios
10. Data Integration for providing a coherent framework

### 3.2. Example of a mathematical model (e.g., agent based model) to reduce the complexity in transmission of tuberculosis in real field settings in public health.

In this model, individuals are represented as agents with specific characteristics and behaviours.<sup>3</sup> The model operates in discrete time steps and simulates interactions and disease dynamics among these agents.

## 4. Key Features and Components

1. *Individual Characteristics:* Each agent has unique attributes such as age, gender, household size, socioeconomic status, TB infection status (susceptible, latent, active), and treatment history.

2. *Spatial Representation:* The model includes a spatial component that takes into account geographical locations, population density, and movement patterns. It can simulate the spread of TB within and between different communities or regions.

3. *Disease Progression:* Agents transition between different TB states (susceptible, latent, active, recovered) based on age-specific risks, exposure to infectious individuals, and treatment history. Disease progression can follow a more realistic pattern, considering factors like reinfection and co-infections (e.g., HIV and diabetes).

4. *Transmission Dynamics:* The model incorporates realistic TB transmission dynamics taking into account factors such as household contacts, community interactions and workplace-based exposure. Transmission rates can be adjusted based on local conditions, environmental factors, and behaviors.

5. *Healthcare System:* The model includes elements of the healthcare system like diagnosis, initiation of treatment, drug adherence, and treatment completion. It can also simulate the impact of healthcare access and quality on TB control.

6. *Interventions:* Interventions like contact tracing, active case finding, different vaccination campaigns and treatment can be implemented and their effects can be assessed within the model. These interventions can be targeted to specific population groups or geographic areas.

7. *Scenarios and Sensitivity Analysis:* It can also be used to explore various scenarios, assess the impact of different interventions, and conduct sensitivity analyses to identify key drivers of TB transmission in the specific public health setting.

## 5. Conclusion

The use of mathematical models in real-field settings of TB transmission in public health offers a powerful set of tools to enhance our understanding of TB dynamics, inform decision-making, optimize resource allocation and ultimately to contribute in the reduction and elimination of tuberculosis as a public health threat. These models are valuable tools in the fight against this global health challenge. The introduction of mathematical models to study the TB transmission has profound implications for public health. It empowers public health authorities to make informed decisions, design effective interventions and work together towards the ultimate goal of reducing and eventually eliminating tuberculosis.

## 6. Source of Funding

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## 7. Conflict of Interest

None.

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