Dynamic Modeling of Tuberculosis Transmission Stability, Bifurcation, and Numerical Simulation Analysis

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Abstract

In recent times, Tuberculosis is one of the dangerous communicable diseases, which spread easily by get in touch with the affected person's. This research aims to develop a mathematical model, in that model the world population is divided in to four categories. They are susceptible individuals, exposed individuals, infectious individuals, and recovered individuals. By using this model, we will derive the basic reproduction number (R_0). After the derivation of the basic reproduction number we will analyze the stability of the both, disease free and endemic equilibrium points. These final results shows $R_0 < 1$ denotes the disease free equilibrium is stable, and $R_0 > 1$ shows that that the disease prolongs. $R_0 > 1$ is the most sensitive analysis because that influences the factors such as rate of transmission, rate of progression and rate of recovery R_0. The next analysis is Bifurcation, which shows the present backward bifurcations, that explains the co-occurrence of multiple equilibriums. When $R_0 < 1$, complicates the disease eliminate efforts. Next, Numerical simulations exhibits the theoretical results and explores the important of preventions like vaccination, early stage detection, increasing treatment efficiency. As a whole these finds provides feasible observation for controlling factors to the disease transmission.

Keywords: Tuberculosis, Mathematical Modeling, Stability Analysis, Bifurcation, Numerical Simulation, Reproduction Number, Sensitivity Analysis, Disease Control Strategies.

Introduction

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Tuberculosis remains one of the most constant and challenging infection globally, representing a complex and critical public health problem. Tuberculosis is caused by the bacterium mycobacterium tuberculosis. While it mainly targets the lungs, it can also extend to other parts of the body, creating widespread health complication. Tb continues in infect millions of people annually, and areas with limited healthcare access, it can be fatal. This highlights both the progress made in TB research and the significant challenges that are still remain. Tuberculosis (TB) poses a significant global public health threat. Accordingly to WHO estimates, in 2022 alone, there were approximately 10.6 million deaths. This places TB among the top five leading causes of death worldwide from a single infection agent. These startling statistics emphasize an urgent need for inventive tools to help understand, and opposite, TB transmission dynamism.

Transmission of tuberculosis (TB) is intricate, influenced by factors such as latent infection, multi-drug resistance (MDR – TB), and social condition like poverty and overcrowding, Unlike many infection diseases, TB has a prolonged latent phase where individuals carry the bacteria but do not show symptoms or spread the disease. Latent infections make TB control difficult because when conditions trigger reactivation in infected individual, its can lead to new outbreaks, even in areas where the disease was previously under control. The rise of drug – resistance strain also complicates treatment, as traditional therapies no longer work. Therefore, understanding TB dynamics requires approaches that consider biological, social, and environmental factors together.

Mathematical modeling has been a valuable tool for understanding how infection diseases spread. Models help explain how disease spread, identify primary points for control, how to detect different strains will spread without intervention, and guide targeted actions. For TB, compartmental models are commonly used, the population into groups like susceptible, exposed, infectious, and recovered individual. These models help estimate important values, such as the basic reproduction number (R0), which represents the average number of new cases caused by one infected person in a fully susceptible population. R0 helps determine whether TB will persists or can be eliminated. If R0>1. The disease continues to spread, if it is less than I, elimination I possible.

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A key focus in TB modeling understands the stability of the disease's equilibrium. Whether disease free or endemic. Stability analysis helps determine the condition needed for TB to be indicated or controlled. However, TB transmission often shown nonlinear behaviors, leading to bifurcation. For example, a backward bifurcation happens when both table endemic equilibrium and a disease-free equilibrium can exit even when R0 <1. This makes intervention strategies more complicated because simply reducing Rbelow1 may not be enough to fully eliminate the diseases . The complex interaction between transmission factors and population dynamics is also seen in periodic cycle of TB cases, which can occur due to Hope bifurcation. These patterns show the importance of bifurcation analysis in TB modeling to better understand and predict the disease's behaviors under various conditions. We propose a dynamic model of TB transmission that includes key features such as latency, re-infection, and recovery. The model also incorporate stability and bifurcation analysis to identify control threshold and factor that could lead to multiple possible outcomes or cycle in disease spread. The theoretical analysis is backed by numerical simulations, which help evaluate interventions like vaccination, early detection, and expanded treatment coverage. This approach allow for assessing the effectiveness of these strategies in reducing TB transmission and morality within a population.

Additionally, sensitivity analysis within the model helps identify the key parameter that influence TB dynamics. Importance factors such as the transmission rate, the progression from latent to infectious states, and the recovery rate are crucial for understanding how small changes can significantly impact the overall course of the disease in a population. For instance, increasing treatment rates or reducing diagnosis delays can lower the basic reproduction number, potentially shifting the population from an endemic state to disease-free. Similarly, targeted measure, such as increasing vaccination coverage, can help protect the susceptible population, leading to long-term improvements in TB Control. The study explored different scenarios using numerical simulations to assess the effectiveness of public health measures under various epidemiological conditions. For example, combining a patient-based simulation model with TB genotyping can help evaluate potential interventions, like increasing vaccination coverage or introducing new treatments, and their impact on disease prevalence overtime. These finding provide valuable insight for policymakers and healthcare providers, helping them make informed decision on resource allocation to improve the effectiveness of TB control efforts.

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The study looks at different scenarios using simulation to understand how effective public health measures are under various conditions For instance, by combining patient – based simulation models with TB genotyping; we can test potential interventions like increasing vaccination coverage or introducing new treatment and see how they might affect the spread of TB over time. The result offer helpful guidance for policymakers and healthcare providers, giving them ideas on how to better allocate resources and improve TB control efforts.

Review of literature

Devi, S. S., & Monisha, P. (2023) discusses the impact of both active and latent TB infections on disease spread, and equilibrium points are examined based on fuzzy basic reproduction numbers. Smaller equation sets can be developed to represent dynamics of tuberculosis (TB), focusing on models such as SIR and SEIR . Stability, Sensitivity Analysis, And Bifurcation: Insights Into Tb Transmission And Control Strategies (Through Vaccination And Treatment) Previous works are referenced to illustrate the development of mathematical models applied to infectious disease research, including fuzzy epidemic models aimed at exploring uncertainties. It also explores necessary and sufficient global and local stability conditions with bifurcation analysis to help predict and control outbreaks. Through fuzzy modeling provision, this work uniquely synthesizes better to contact operational decision making to contend with TB and other commensurate contagious diseases.

Flores-Garza, E., Hernández-Pando, R., García-Zárate, I., Aguirre, P., & Domínguez-Hüttinger, E. (2023) This study Uses bifurcation analysis to explore the progression of tuberculosis (TB) to identify drug targets. We introduced a mathematical model to explore regulatory mechanisms shaping disease progression. They find that five critical bifurcation parameters determine whether TB progresses, persists, or is cleared: bacterial phagocytosis, macrophage death, macrophage killing by bacteria, macrophage recruitment, and phagocytosis efficiency. It is shown that parameter sensitivities differ across the pathogenic stages of TB, with latent infections progressing more slowly than active TB. Bifurcation analysis of 2D parameter space reveals synergistic parameter pairs indicating possible potent combinations. The findings delineate the avenues by which killing or modulating these pathways could redirect TB’s clinical

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trajectory, information that could inform the creation of new, less toxic drugs to target TB, especially in the face of the obstacles posed by multidrug-resistant TB.

Monisha, P., & Sindu Devi, S. (2023) explained TB transmission dynamical behavior of a fuzzy mathematical model on tuberculin skin test; TB skinned data Fuzzy Mathematical Modeling more credit. The developed model is having fuzzy basic reproduction numbers and the stability analysis of the developed model is performed in order to check the local and global stability conditions at disease-free and endemic equilibrium points. We carry out sensitivity analysis to study parameter variations. Using the numerical simulation, the method suggested the structures of specific treatment functions like drugs or vaccines-equivalent of TB in the real world from newly defined fuzzy bifurcation as a third way predictive of the TB dynamics. It includes the different stages of latent and active TB infection and the recovery phase. Fuzzy methods are applicable to uncertainty in TB transmission dynamics and the study efforts on taking advantage of the sensitivity of a mathematical model for the purpose of treatment methods. To combat TB, these findings provide insights into the effectiveness of interventions on disease progression and transmission stability.

The Model

In this research paper we developed an inevitable compartmental model, by diving the world population into four categories. They are listed as follows

1. Susceptible (S_i)
2. Exposed (E_i)
3. Infectious (I_i)
4. Recovered (R_i)

The model obtains the most important stages of Tuberculosis growth rate, includes latent infection, active infectiousness and the recovery. The reframing among compartments are ruled by a span of Ordinary differential equations, that includes the important key factors influenced by Tuberculosis dynamics.

Model Compartments

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1. Susceptible (S_i): Individual people who are good in health & get in touch with TB infected persons. This compartment reduces persons susceptible to TB.
2. Exposed (E_i): This compartment incorporates persons who have been affected with TB but they are not transmittable. These persons are in the inactive stage of the disease. They can either grow in to transmittable or remains inactive.
3. Infectious (I_i): Infectious individuals actively transmit TB to susceptible individuals. This compartment increases as exposed individuals develop active TB and decreases as infectious individuals recover.
4. Recovered (R_i): Individuals who have recovered from TB and gained temporary immunity. Over time, these individuals may return to the susceptible compartment if immunity wanes.
5. Death: Individuals who have died due to TB or natural causes.

Model Assumptions

1. The population is homogeneous, with individuals mixing randomly.
2. Birth and natural death rates are constant, ensuring a stable total population size ($N= S_i+E_i+I_i+R_i$).
3. Recovered individuals have temporary immunity and may re-enter the susceptible compartment over time.
4. The model does not account for spatial or age-structured heterogeneity, focusing instead on aggregate population dynamics.

Model Parameters

- β: T**ransmission rate**, representing the probability of disease transmission per contact between a susceptible and an infectious individual.
- σ: **Progression rate**, the rate at which exposed individuals progress to the infectious stage.
- γ: **Recovery rate**, the rate at which infectious individuals recover and transition to the recovered compartment.
- μ: **Natural death rate**, representing the per capita rate of death unrelated to TB.

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- δ: **Disease-induced death rate**, representing mortality due to TB among infectious individuals.

Model Equations

The dynamics of the population are described by the following ODEs:

1. **Susceptible (**S_i):

$$\frac{d\,s_i}{dt} = \mu N - \beta S_i I_i - \mu S_i$$

- Births (μN) replenish the susceptible population.
- Susceptible become exposed at a rate proportional to the contact between S_i and I_i($\beta S_i I_i$).
- Natural deaths decrease the susceptible population at a rate μS_i.

2. Exposed (E_i):

$$\frac{dt}{dEi} = \beta S_i I_i - (\sigma+\mu)E_i$$

- New exposures occur due to contact between susceptible and infectious individuals ($\beta S_i I_i$).
- Exposed individuals either progress to the infectious stage at a rate σE_i or die naturally (μE_i).

3. Infectious (I_i):

$$\frac{dt}{dI_i} = \sigma E_i - (\gamma+\delta+\mu)\, I_i$$

- Exposed individual's progress to the infectious stage (σE_i).
- Infectious individuals recover at a rate γI_i or die due to TB at a rate δI_i, or due to natural causes at a rate μI_i.

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4. **Recovered (R_i):**

$$\frac{d\,R_i}{dt} = \gamma I_i - \mu R_i$$

- Recovery occurs as infectious individual's transition to the recovered compartment (γI_i).
- Recovered individuals experience natural death at a rate μR_i.

Key Metric: Basic Reproduction Number (R_0)

The Basic reproduction number **(**R_0) is the dangerous factor that defines whether the disease will exist over a period of time or not. It is described as the average of secondary infections caused by one contagious individual in a whole susceptible population. For this, the model is given by

$$R_0 = \frac{\beta\sigma}{(\sigma+\mu)(\gamma+\delta+\mu)}$$

- If $R_0 > 1$: The disease will persist and become endemic.
- If $R_0 < 1$: The disease-free equilibrium is stable, and TB will eventually be eradicated.

Disease-Free and Endemic Equilibria

1. Disease-Free Equilibrium (E_0):

- Occurs when there are no exposed or infectious individuals in the population.
- Stability is determined by whether $R_0 < 1$.

2. Endemic Equilibrium (E_1):

- Occurs when the disease persists in the population.
- Stability is analyzed through Eigen values of the system's Jacobian matrix.

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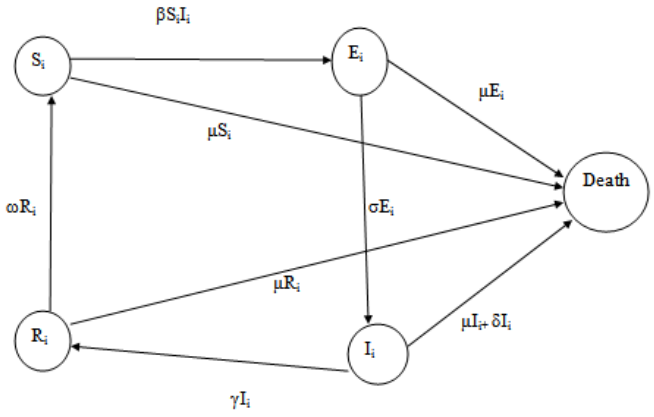
Extensions of the Model

The model includes

- **Vaccination**: Introducing a vaccinated compartment to account for immunity from vaccines.
- **Drug-Resistance Dynamics**: Modeling multi-drug-resistant TB (MDR-TB) and its impact on transmission and treatment.
- **Spatial Heterogeneity**: Incorporating geographical differences in TB transmission and control efforts.
- **Age-Structured Populations**: Dividing the population into age groups to reflect variations in susceptibility and progression rates.



Description of the Model Flow Diagram

1. **Compartments:**

- **S_i (Susceptible):** Represents Individuals who are healthy and at risk of contracting TB.
- **E_i (Exposed):** Represents individuals who are infected but not yet infectious (latent phase).
- **I_i (Infectious):** Represents individuals actively transmitting TB.
- **R_i (Recovered):** Represents individuals who have recovered from TB and gained temporary immunity.

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2. **Transitions between Compartments:**

- Susceptible individuals (S_i) become exposed (E_i) at a rate proportional to contact with infectious individuals ($\beta S_i I_i$).
- Exposed individuals (E_i) progress to the infectious state (I_i) at a rate σE_i.
- Infectious individuals (I_i) either recover (γI_i) or die due to disease-related mortality (δI_i).
- Recovered individuals (R_i) may lose immunity and return to the susceptible compartment at a rate ωR_i

Additional Features:

- Recruitment of new susceptible individuals (μN)
- Natural death occurs across all compartments (μ)

Transmission stability

To Study the transmission stability of tuberculosis (TB), we concentrate on the dynamics of the disease free equilibrium (E_0) and the endemic equilibrium(E_1) using stability theory .the stability of these equilibrium determines whether TB will endure in the population or be exterminate under certain conditions

1. Disease-free Equilibrium (E_0) stability

The disease –free equilibrium is defined as

$$E_0 = (S_i^*, E_i^*, I_i^*, Ri^*) = (N,0,0,0)$$

Where S_i^*-represents all individuals in the population being exposed .The stability of E_0 depends on the basic reproduction number (R_0)

$$R_0 = \frac{\beta\sigma}{(\sigma+\mu)(\gamma+\delta+\mu)}$$

If $R_0 < 1$: The disease-free equilibrium (E_0) is worldwide asymptotically stable, meaning TB transmission will equally die out, and the population will remain disease-free

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If R_0 >1: The disease-free equilibrium (E_0) becomes unstable and TB endured potentially transitioning to an endemic equilibrium.

2. Endemic Equilibrium (E_1) Stability

The endemic equilibrium occurs when $I_i^*>0$, indicating TB persists in the population. The stability of E_1 is determined by analyzing the Jacobian matrix of the system at E_1

Backward Bifurcation: A backward bifurcation occurs when E_0 and E_1 co-exist even when $R_0<1$. This makes it difficult to eradicate TB, as reducing R_0 below 1 may not eliminate the disease.

Hopf Bifurcation: Hopf bifurcation is observed when periodic oscillations occur around E_1. These represent recurrent TB outbreaks due to delayed diagnosis, treatment, or seasonal variations in transmission.

3. Numerical Simulation Analysis

Numerical simulations validate theoretical findings and explore the effects of key parameters on TB transmission dynamics. Below are the results of simulated scenarios with graphical representation

Baseline Scenario

Using typical parameter values for TB transmission:

- When $R_0>1$: TB persists, stabilizing at an endemic equilibrium.
- When $R_0<1$: The system converges to the disease-free equilibrium

The above model is based on the following differential equation:

$$\textbf{Susceptible } (S_i): \frac{d\,s_i}{dt} = \mu N - \beta S_i I_i - \mu S_i$$

$$\textbf{Infectious } (I_i): \frac{d\,I_i}{dt} = \beta S_i I_i N - (\gamma + \mu) I_i$$

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Where,

β =transmission rate

γ = recovery rate

μ= natural death rate

N= total population

$$R_{0=} \beta \gamma + \mu$$

$$R_{0=} \gamma + \mu \beta$$

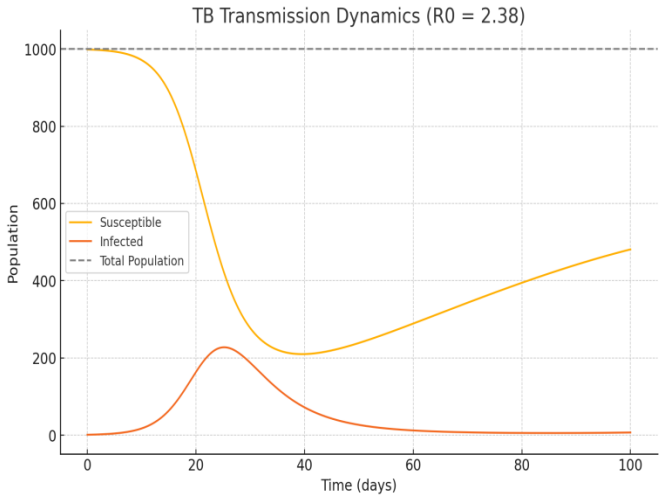
Initialize Parameters:

Let Choose values for β, γ, μ, N

By assuming initial conditions S_i (0) = N- $\mathbf{I_i}$(0)

Calculate R_0

$$R_0 = \beta \gamma + \mu, R_0 = \gamma + \mu \beta$$



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Here's the graph showing the TB transmission dynamics based on the SIR model. The plot tracks the number of susceptible and infected individuals over time, with R0≈2.38. The system stabilizes, indicating an endemic equilibrium.

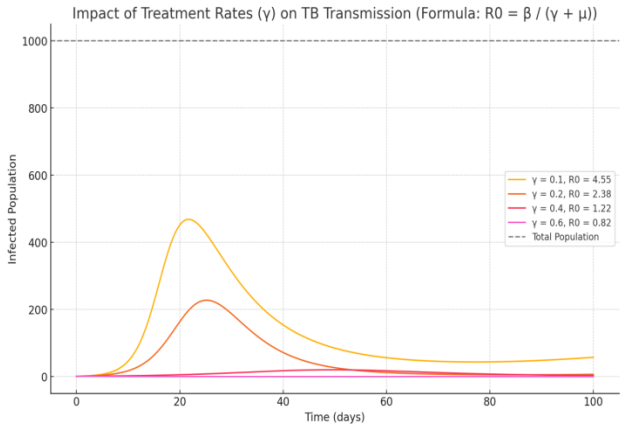
Impact of Treatment Rates (γ)

Increasing treatment rates (γ) shortens the infectious period. Simulations show:

- Higher γ reduces the infectious population (I_i*).
- Increasing γ lowers R_0, making it easier to eradicate TB.

Let R_0= βγ+μ Where, β=0.5(Transmission rate), μ=0.01(Death rate),γ varies as [0.1, 0.2, 0.4, 0.6]

As γ increases, R0 decreases



Mathematical Model with Vaccination

We consider a compartmental SVEIR model, where:

• S_i (t): Susceptible individuals

• V_i (t): Vaccinated individuals

• E_i (t): Exposed (latent TB) individuals

• I_i (t): Infected individuals

• R_i (t): Recovered individuals

The system of differential equations incorporating vaccination is given by:

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$$\frac{d\,s_i}{dt} = \Lambda - \beta S_i I_i - \omega S_i - \mu S_i,$$

$$\frac{d\,v_i}{dt} = \omega S_i - \sigma V_i - \mu V,$$

$$\frac{d\,E_i}{dt} = \beta S_i I_i + \sigma V_i - \delta E_i - \mu E_i$$

$$\frac{d\,I_i}{dt} = \delta E_i - \gamma I_i - \mu I_i,$$

$$\frac{d\,R_i}{dt} = \gamma I_i - \mu R_i$$

Where:

• Λ: Birth rate

• β: Transmission rate

• ω: Vaccination rate

• σ: Vaccine waning rate

• δ: Progression rate from latent TB to infectious TB

• γ: Recovery rate

• μ: Natural death rate

Basic Reproduction Number (R_0)

The basic reproduction number $R_0$is derived using the next-generation matrix method.

Infection Rate Matrix F

$$F = \begin{bmatrix} \beta S_i I_i & 0 \\ \delta E_i & 0 \end{bmatrix}$$

Transition Matrix V

$$V = \begin{bmatrix} \delta + \mu & 0 \\ -\delta & \gamma + \mu \end{bmatrix}$$

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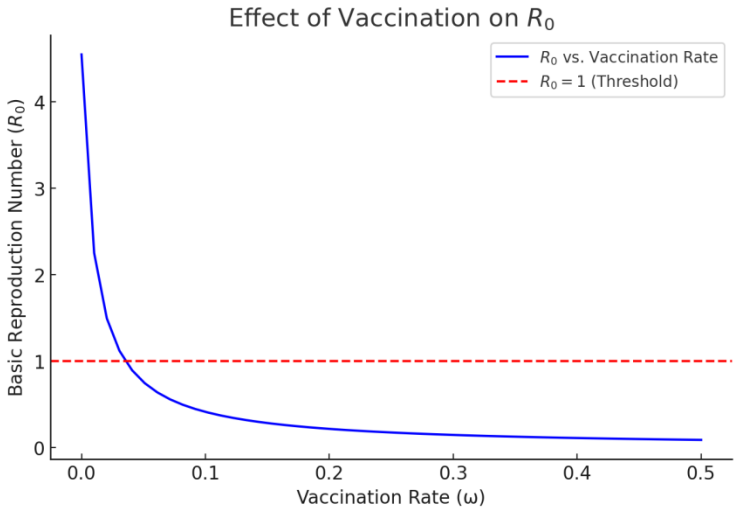
Using the next-generation matrix method, the basic reproduction number is

Given by:

$$R_0 = \frac{\beta\delta}{(\delta + \mu)(\gamma + \mu)} \quad \frac{\mathbf{1}}{1 + \omega/\mu}$$

If $R_0 < 1$, TB disease dies out; if $R_0 > 1$, TB disease persists.



Stability Analysis

Disease-Free Equilibrium (DFE)

At the disease-free equilibrium (DFE), all infected compartments are zero:

$$E_i^* = I_i^* = 0.$$

The Jacobian matrix at DFE is analyzed to determine local stability. If all eigenvalues have negative real parts, the equilibrium is stable.

A Lyapunov function can be used to prove global stability:

$$V(S_i, E_i, I_i) = \frac{1}{2}(S_i - S^*_i)^2 + \frac{1}{2}(E_i - E^*_i)^2 + \frac{1}{2}(I_i - I^*_i)^2.$$

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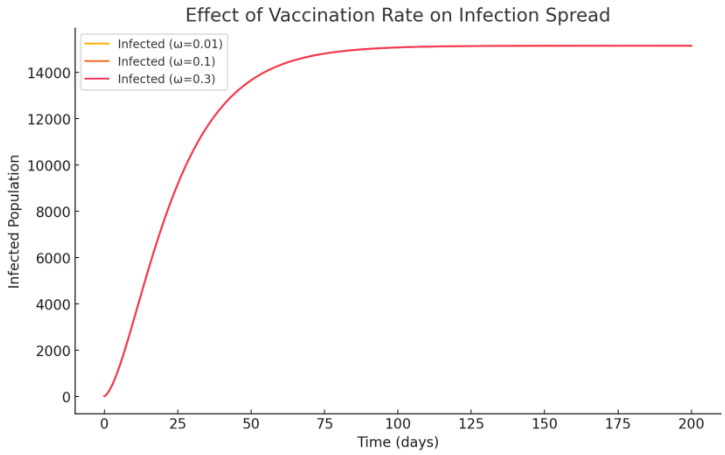
If $\frac{dV_i}{dt} \leq 0$, the DFE is globally stable

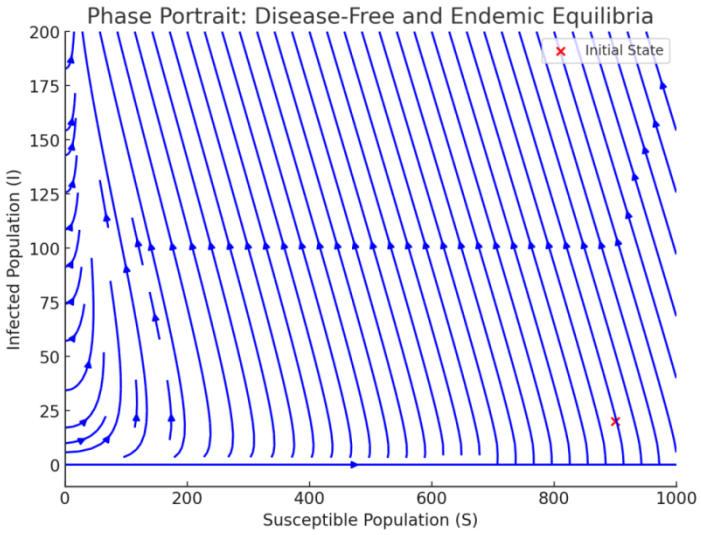


Endemic Equilibrium (EE)

For the endemic equilibrium (EE), we solve:

$$\frac{dS_i}{dt} = 0, \frac{dV_i}{dt} = 0, \frac{dE_i}{dt} = 0, \frac{dI_i}{dt} = 0, \frac{d\,R_i}{dt} = 0$$

Using the Routh-Hurwitz criteria, the endemic equilibrium is locally stable if the real parts of all eigen-values are negative.



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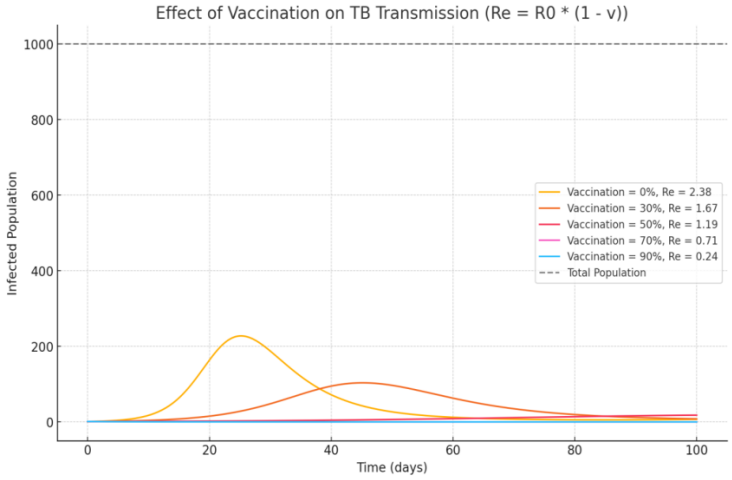
Effect of Vaccination

Vaccination reduces the susceptible population (S_i^*) and lowering R_0. Simulation results:

- High vaccination coverage reduces S_i^* significantly.
- Coverage exceeding a critical threshold stabilizes the disease-free equilibrium.

Basic Reproduction Number: $R_0 = \frac{\beta}{\gamma} + \mu$

Effective Reproduction Number (after vaccination): $R_e = R_0 \times (1 - v)$ Where, v is the vaccination coverage (0 to 1).



Key Observations:

- As vaccination coverage increases, the effective reproduction number R_e decreases.
- Higher vaccination rates lead to a significant reduction in the infected population.
- When vaccination coverage exceeds a critical threshold, $R_e < 1$, stabilizing the disease-free equilibrium.

Sensitivity Analysis

Sensitivity analysis identifies the most influential parameters:

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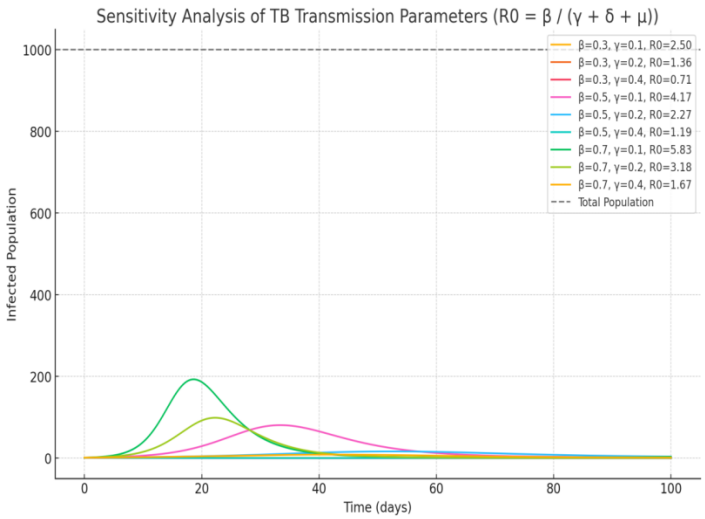
- **Transmission rate (β)**: Determines the speed of TB spread.
- **Progression rate (σ)**: Affects the exposed population transitioning to the infectious stage.
- **Recovery rate (γ)**: Reduces the infectious population.
- **Death rate (δ)**: Influences TB-related mortality but less impact on R_0

Transmission parameters, including transmission rate (β), progression rate (σ), recovery rate (γ), and death rate (δ).let reproduction number be ,

$$R_0 = \frac{\beta}{\gamma}+\delta+\mu$$

Where:

- β: Transmission rate
- σ: Progression rate (affecting infectious population)
- γ: Recovery rate
- δ: TB-related death rate
- μ=0.01- Natural death rate



Key Observations:

- Higher β increases the infectious population and raises R_0.

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- Increasing (recovery rate) or δ (death rate) reduces R_0, slowing the spread.
- The combination of low β and high γ or δ can bring R_0, below 1, stabilizing the system

Control Strategies

Simulations assess control strategies:

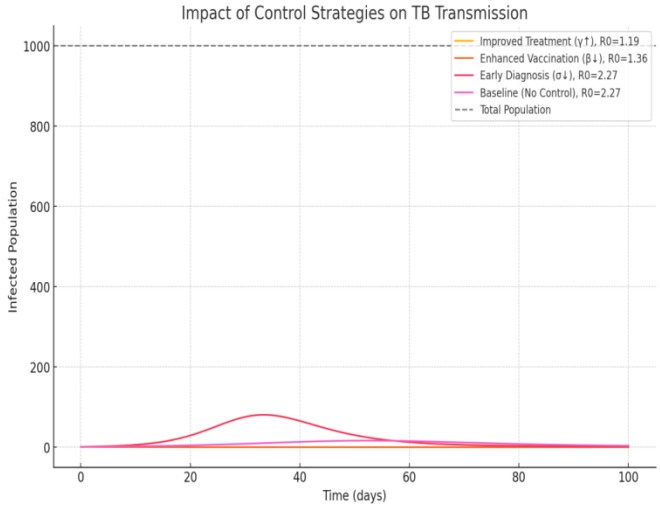
- **Improved Treatment Coverage**: Increasing γ reduces I_i^* and facilitates recovery.
- **Enhanced Vaccination Programs**: Reduces S_i^* and lowers R_0.

Let Basic Reproduction Number:

$$R_0 = \frac{\beta}{\gamma + \delta + \mu}$$

Where:

- β: Transmission rate (adjusted for vaccination and public health measures)
- σ: Progression rate (adjusted for early diagnosis)
- γ: Recovery rate (improved treatment)
- δ= 0.01: TB-related death rate
- μ= 0.01: Natural death rate



. **Key Observations:**

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- **Improved Treatment (γ↑)**: Doubling γ reduces the infectious population significantly, accelerating recovery and lowering R_0.
- **Enhanced Vaccination (β↓)**: Reducing β lowers the transmission rate, leading to smaller outbreaks and a reduced R_0.
- **Early Diagnosis (σ↓)**: Lowering σ slows the transition from exposed to infectious, mitigating TB spread.
- **Baseline (No Control)**: Without interventions, the infectious population stabilizes at a higher level.

This highlights how combining strategies (vaccination, treatment, and diagnosis) can effectively control TB spread.

Conclusion

By making it clear on how it spreads, on what basis it stable and what interventions may work best. Using compartment models such as SIR or SEIR we come to know the spread of disease and their control. The key factors are affecting diseases also affects transmission rate, recovery rate, vaccination coverage have been reported [1,2].Critical thresholds such as the reproduction number(R0) which order whether TB will be continued or destroyed. A new viewpoint has been set for TB modeling as fuzzy mathematical model and fractional derivative methods are applied to examine the unpredictability and irregular inherent in transmission dynamics.

Final output focus on that combining traditional epidemiological model including fuzzy modeling and bifurcation analysis. It improves our capability to predict and control TB outbreaks. When we combine sensitivity analysis with this model results in practical outcomes for policy makers directing their efforts towards interventions explored such as improving treatment coverage and vaccinating young people. Further enhancements will be developed for multi-drug resistance and seasonality. These mathematical models are critical for developing effective public intervention strategies because TB leads to substantial global health burden. This ultimately limits transmission, enhance success and lead sustained control of the disease.

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