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RESEARCH ARTICLE

Mathematical Modeling of Tuberculosis Transmission Dynamics with Vaccination and Drug Resistance

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Abstract: The spread of tuberculosis, a disease that is communicable and caused by the Bacillus mycobacterium, is the main topic of this study. Vaccination and drug-resistant patients are the subjects of particular attention. Patients who are freshly infected with tuberculosis undergo an average treatment duration of 6–8 months; however, for those who are multidrug resistant, the treatment can extend up to 2.5 years. Despite decades of study, widespread use of a vaccine, and an apparent push by the WHO to promote a single global management strategy in recent years, tuberculosis continues to be the second most prevalent infectious killer, following COVID-19. In 2021, experts estimate that 10.6 million people worldwide contracted tuberculosis, either latently or actively. Using a mathematical model, we performed an investigation to investigate the dynamics of tuberculosis transmission in humans. We conducted sensitivity analysis on the model to identify the primary parameters impacting the disease's propagation and establish the fundamental reproduction number. The analysis's findings can inform the proposal of effective intervention techniques. The research looked at the tuberculosis endemic equilibrium point and assessed the stability on a local and global scale related to the disease-free equilibrium point. We examined the effects of the transmission rate on the backward bifurcation of the model. Global stable endemic equilibrium coexists with stable disease-free equilibrium (DFE). It has been demonstrated that vaccine efficacy and a small percentage of the population who receive vaccinations contribute equally to reducing the burden of disease. The drug-resistant group is a bigger concern than the infected group, which shows that health workers and government agencies need to be extra careful to keep an eye on this silent source of tuberculosis transmission. Based on the numerical simulation, it can be demonstrated that, if vaccination coverage and efficacy are both quite high, it is possible to effectively control tuberculosis in a population by using an imperfect vaccination. Health professionals and government organizations should monitor this covert method of tuberculosis transmission, as these findings indicate that the group resistant to drugs poses a greater threat than those who are afflicted.

Keywords: Tuberculosis, Drug-resistance, Bifurcation, Equilibria, Bi-quadratic polynomial.

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Introduction

The infectious disease tuberculosis (TB) is caused by the Mycobacterium tuberculosis bacteria, that primarily impacts the lungs and other respiratory organs [10,15]. But it can also cause damage to various organs, including the lymphatic system, kidneys, spine, brain, and central nervous system [17,21,28]. A persistent cough that occasionally produces sputum or blood, fatigue, weight loss, fever and persistent night sweats lasting three weeks or longer are some of the symptoms of active lung TB illness.

There were 1.6 million TB-related deaths globally in 2021, of which 187,000 were people with HIV/AIDS. After coronavirus, tuberculosis has emerged as the second most prevalent infectious disease-related cause of mortality, and the thirteenth most significant worldwide mortality cause. 10

million cases of TB were reported worldwide in 2021, with 9.4 million adult cases and 1.2 million paediatric cases [33]. There are large disparities in the number of people with TB and those who are freshly screened whereby in 2021, 4.2 million of the former group did not make it to a hospital [33]. Consequently, the number of individuals reported and screened for TB fell drastically in 2021, with 7.1 million compared to 6.4 million reported in 2019 [33]. Treatment of TB is necessary; hence, 74 million lives have been saved between 2000 and 2021 because of proper TB treatment. Drug-resistant TB (DR-TB) is also projected to become more prevalent between 2020 and 2021, with 450,000 new cases reported in 2021 [33].

Typically, there are three medical approaches for treating TB: preventative treatment for individuals with latent TB infections to avoid internal reactivation, curing active TB patients, and vaccination to decrease the spread of TB [19]. Currently, the most widely used and successful TB vaccine is Bacillus Calmette-Guerin (BCG). It has been found to be effective in protecting children, with a success rate of over 50% against lung TB and 80% against various forms of the disease [26].

The most important factor is that children don't transmit TB, only adults do [22]. Sadly, the BCG vaccine has demonstrated inconsistent protection against TB in adults. Drug-resistant TB is a severe problem in many developing countries, where treatment can be prolonged and costly [33]. In some developing nations, while treatment for TB may be available, it may not be entirely free. This can present a financial burden for some patients with TB, who may not be able to afford the full cost of treatment. Due to financial constraints, some patients with TB opt to receive treatment at home instead of staying in the hospital. Additionally, some patients who do not improve in the hospital choose to leave and continue their care at home [27].

However, multidrug-resistant TB (MDR-TB) can develop during TB treatment and, in rare cases, progress to extensive drug-resistant TB (XDR-TB). This is often a result of incorrect use of TB medicine, poor prescription choices, the patient's early termination of treatment or the usage of subpar medications. In spite of this, successful therapy for MDR-TB and XDR-TB is still possible, however it will require more time and effort. Treatment success rates for MDR-TB are currently 28% and 52%, respectively [33, 34].

Drug-resistant strains could pose a threat to the control of TB, according to [9], who developed a mathematical model that enabled drug-resistant strains to have similar relative fitness to drug-sensitive strains. According to their discoveries, to end drug-resistant TB epidemics, at least 70% of drug-resistant patients must be identified and treated [33]. In recent years, there has been widespread use of simple mathematical models with compartmental structure, referred to as SVI or SVIR models, in the investigation of the possible or actual effects of inadequate immunization. According to the paradigm, people can be classified as susceptible, immunized, infectious, or recovered [3,5,8,11].

The creation of TB prevention and control methods and the formulation of interim goals for intervention initiatives have benefited dramatically from mathematical models of the disease. Numerous mathematical studies on the dynamics of TB transmission have been accomplished [30,31]. [27] created and assessed a study on the best ways to prevent TB from spreading when treatment is insufficient and external re-infection occurs. In addition, they separated the infected group into two groups: inadequate therapy and external re-infection. They found that reducing the TB burden can be positively impacted by implementing a single control measure or a combination of multiple controls.

Taking into account both vaccinated and multidrug-resistant patients, [7] created a mathematical model to describe the mechanisms underlying the TB epidemic. Vaccination and quarantine classes were considered in their work. They obtained thresholds and equilibria of the system. They also obtained the model system's reproduction number, and stability analysis. After all, they performed a simulation and discovered that quarantining the multi-drug-resistant TB patients has achieved rapid recovery and almost tends to stop the transmission of the tuberculosis virus. By immunizing TB patients, they found that the vaccination would decrease the number of people with active TB. In order to investigate the effects of isolating patients with MDR-TB, [6] developed a compartmental deterministic mathematical model of TB. Their model system exhibits two equilibria that leads to backward bifurcation. By lowering the disease's occurrence, the numerical simulation that was performed shows how quarantine regulations can be used to handle MDR-TB cases in an efficient manner.

By immunising babies and treating those who are both latently and actively infected, [18] conducted research on the prevention of TB. The analysis of the stability of DFE's findings shows that TB is curable as long as measures are implemented to guarantee that the overall rate at which latently infected individuals get the disease is continuously lower than the outcome of complete contraction. When imperfect vaccination is involved, [13] developed a model known as SVEIL to explain the transmission of TB. The model considers that susceptible individuals can receive an imperfect vaccine, which loses its efficacy over time. Additionally, the model considers reinfection and treatment of individuals with active and latent tuberculosis at high risk. The findings indicate that the implementation of the imperfect vaccine in the model can significantly decrease the spread of TB.

With seven compartments—susceptible, vaccinated, exposed, undiagnosed infectious, diagnosed infected, treated, and recovered, [4] created a mathematical model of TB. Because of the backward bifurcation of their system, TB can no longer be prevented from spreading across the society by maintaining a basic reproduction number below one. The analysis of their studies revealed that implementing a vaccination program, diagnosis, and treatment can assist in managing the spread of tuberculosis. In addition, it has been shown that giving priority to diagnosis over treatment is important because diagnosis precedes treatment. Studies have shown that even if the vaccination rate for TB is low, ranging from 0-20%, TB would persist in the population. Therefore, to prevent TB from spreading within the population, a high rate of vaccination is necessary.

In the Democratic Republic of the Congo (DRC), [29] created a mathematical model that takes into account several elements and their impact on TB transmission. The model also examines the effects of these factors on the disease's long-term expansion. Their findings show that lost to follow-up and transmitted individuals pose a risk, but not as much as cases booming bacteria. According to their findings, latent/exposed cases that evolve more quickly are the cause of the short- and medium-term increases in TB incidence, whereas latent/exposed cases that evolve more slowly are the cause of the long-term incidence and maintenance of TB. However, as demonstrated in their studies, TB might be eliminated or drastically decreased in the DRC across the board under specific conditions. Lastly, they proposed that in order to successfully manage TB in the DRC, steps including contact monitoring, identifying people with latent symptoms, and treating them are required.

To look into how vaccinations affect the dynamics of TB in a particular community, [20] created a six-chambered deterministic model. Their findings suggest that the population-wide burden of TB can be reduced by reducing the frequency of contact between infected persons and by vaccinating vulnerable individuals at a higher rate with highly efficient vaccinations.

To create a deterministic model of the dynamics of TB transmission, three control strategies were implemented by [35]: immunisation, therapy for patients who are actively infected but do not have drug resistance, and treatment for those who are actively infected but do have drug resistance. With the Pontryagin maximal concept serving as the basis, they developed an optimality system to examine the impact of implementing any one of the three control methods on the dynamics of TB. The resulting system was then solved numerically. Furthermore, analyses of cost-effectiveness and efficiency were carried out to identify the best single, double, and triple therapies for stopping the spread of TB in underprivileged communities. According to their research, an intervention strategy that includes all necessary controls is the most efficient way to drastically minimize the spread of TB in the community, given the available resources. Finally, they suggested that in communities with limited resources, there are other approaches available for effectively managing the burden of TB. These include administering optimal vaccinations as a one-time intervention and combining optimal vaccinations with treatment control for individuals who are actively infected but do not have drug resistance.

In order to explain the research on optimum control to simulate a TB disease with exogenous reinfection, [14] used ordinary differential equations to create a mathematical model. Their primary objective is to decrease the infectious group in a community by decreasing the interaction between those who are exposed and those who can spread the infection. Control was used to prevent exogenous reinfection. Optimal control is also described using the Maximal principle of Pontryagin. The numerical findings showed that developing a rule that successfully prevents exogenous reinfection by sensitizing the latent people to infectious contact is feasible.

For the dynamics of TB transmission, [31] developed a deterministic mathematical model that took into account the effects of an imperfect vaccination as well as other exogenous variables like re-infection in those who had received treatment and exogenous re-infection. Based on their research, a subpar TB vaccination consistently prevents the transmission of infectious diseases among the

public. All things considered, the overall impact grows as efficacy and coverage rise. Also, Vaccine efficacy and steady-state vaccination coverage contribute to reducing disease burden. Their numerical simulation has demonstrated that the vaccine's efficiency and coverage are highly adequate; an imperfect vaccination can optimally control TB in a community. For the dynamics of TB transmission with reinfection, a mathematical model was created [32]. This study focused on the boundedness of the TB model incorporating reinfection and identified a biologically meaningful region for its solutions. Through mathematical analysis, the researchers established that the TB model with reinfection exhibits local and global asymptotic stability under specific conditions. when the reproductive number, at minimum, is less than one, the model is stable, leading to the disappearance of TB infection. Conversely, the model is stable when the reproductive number is bigger than 1 and TB infection persists. Numerical simulations corroborated the theoretical findings, revealing that higher reinfection rates elevate the force of infection, yet the infected population persists at equilibrium.

However, in their model, the authors of [32] did not include vaccinated individuals and individuals who develop drug resistance. One of the crucial elements in individuals' lives is still this factor. The provision of public health services played a role in decreasing the transmission of tuberculosis. In our proposed research, a mathematical model which captures the key compartments and parameters regarding TB is formulated. the objective of this work is to address a deficiency in the sources referred to by considering vaccinated individuals and individuals who are both presently infected and resistant to drugs. The main distinctions are the recovery of individuals with latent infections as a result of preventive treatment received, the inclusion of drug-resistant individuals on the spread of the disease and the treatment of TB patients with an ineffective vaccination. Furthermore, the exogeneous reinfection for the model system will be considered also.

Model Formulation

In this study, the entire population, $N(t)$, is separated into six compartments that are mutually exclusive: susceptible population $S(t)$, vaccinated population $V(t)$, latently infected population $E(t)$, actively infected individuals $I(t)$, infected population that developed drug resistance $I_R(t)$ and recovered population with temporary immunity$R(t)$.
Thus, $N(t) = S(t) + V(t) + E(t) + I(t) + I_R(t) + R(t)$

Model Equations

The model comprises a set of nonlinear ODES:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi + \phi V - \left(\frac{\beta(I+\rho I_R)}{N} + \omega + \mu\right)S \\
\frac{dV}{dt} &= \omega S - \left(\frac{\beta(1-\varepsilon)(I+\rho I_R)}{N} + \phi + \mu\right)V \\
\frac{dE}{dt} &= \frac{\beta(I+\rho I_R)S}{N} + \frac{\beta(1-\varepsilon)(I+\rho I_R)V}{N} + \frac{\beta\psi(I+\rho I_R)R}{N} - (\kappa+\alpha+\mu)E \\
\frac{dI}{dt} &= \kappa E - (\tau+\sigma+\delta_1+\mu)I \\
\frac{dI_R}{dt} &= \sigma I - (\eta+\delta_2+\mu)I_R \\
\frac{dR}{dt} &= \alpha E + \tau I + \eta I_R - \left(\frac{\beta\psi(I+\rho I_R)}{N} + \mu\right)R
\end{aligned}\right\} \quad (1)$$

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi + \phi V - (\lambda + \omega + \mu)S \\
\frac{dV}{dt} &= \omega S - (\lambda(1-\varepsilon) + \phi + \mu)V \\
\frac{dE}{dt} &= \lambda S + \lambda(1-\varepsilon)V + \lambda\psi R - (\kappa+\alpha+\mu)E \\
\frac{dI}{dt} &= \kappa E - (\tau+\sigma+\delta_1+\mu)I \\
\frac{dI_R}{dt} &= \sigma I - (\eta+\delta_2+\mu)I_R \\
\frac{dR}{dt} &= \alpha E + \tau I + \eta I_R - (\lambda\psi+\mu)R
\end{aligned}\right\} \quad (2)$$

Where $\lambda = \frac{\beta(I+\rho I_R)}{N}$

The starting values assigned to every state variable in the model are as follows:
$S(0) > 0, V(0) > 0, E(0) > 0, I(0) > 0, I_R(0) > 0, R(0) > 0.$

Table 1. The model's parameters and Variables

Parameter	Description	Value	Source
π	Rate of Recruitment	37684	Assumed
ψ	Rate of low immunity of recovered individuals	0.85	[31]
β	Transmission Rate	1.990	Assumed
κ	Rate of progression from exposed class to active infected class	0.350	[32]
ρ	A modification parameter associated with reduced infectiousness of Drug-resistance individuals as compared with Actively infected individuals.	0.8	Assumed
σ	Proportion of individuals that recovered due to treatment without drug resistance. So that $(1-\sigma)$ is the proportion of individuals that developed drug resistance. Therefore, $\tau\sigma$ represent the rate of recovery due to effective treatment and is the rate of treatment failure that resulted in drug resistance	0.02	Assumed
η	Rate of recovery of Drug-resistance individuals to recovered class due to another different drug(s) been taken	0.2	Assumed
τ	Rate of treatment by Infected individuals (I)	0.8	[32]
δ_1	The death rate due to primary infectious TB individuals	0.06	Assumed
δ_2	Disease-induced death rate because of resistance to the drug	0.19	[35]
μ	Natural death rate	0.01	Assumed
ε	Vaccine efficacy	0.2	[31]
α	Rate of recovery of Exposed individuals to recovered class due to body immune response.	0.21	[32]
ϕ	Rate of vaccine waning	0.1	[31]
ω	Vaccination coverage	0.98	[31]

The TB model's clinical Assumptions

The model's fundamental biological assumptions are as follows:

1. A constant recruitment rate into susceptible compartment at the rate π [31].
2. There is homogenous mixing among the populace such that everyone is equally likely to be infected in case of effective contact.
3. Different strains are not distinguished.

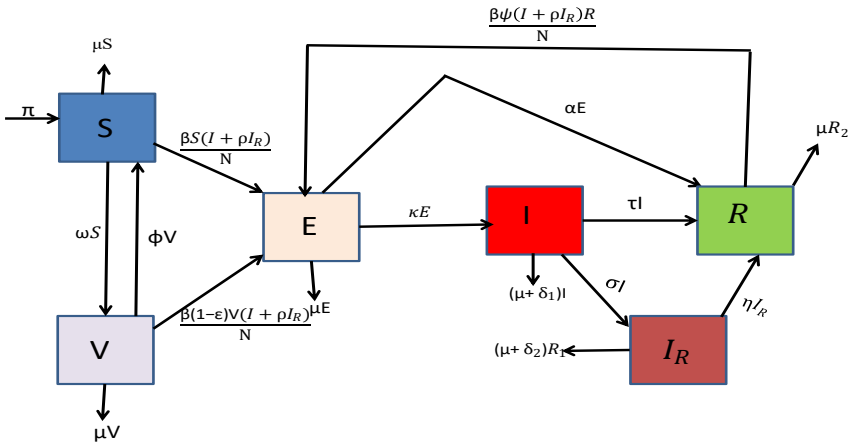


Figure 1. Flow Diagram of the tuberculosis model

The model variables and parameters are presented in Table 1 and the flow diagram is depicted in Figure 1. The susceptible compartment grows at a constant rate of π when more people enter the population through immigration or birth, whereas each compartment shrinks at a rate of μ. When the BCG vaccination is administered, people from susceptible populations are transferred at a rate of ω into the immunized population. But with time, the vaccine's protection diminishes at a rate equal to ϕ. The illness spreads at a rate of $\frac{\beta(I+\rho I_R)}{N}$. among those who are susceptible. The model assumes the vaccination to be less than 100% effective. Therefore, vaccinated people in this compartment can get the disease through contact with the Infected individuals, but less frequently $\varepsilon$where $0 \leq \varepsilon \leq 1$. At a rate of κ, the exposed people advance to the class that is actively infected and recover at the rate α due to preventive treatment received. Infected individuals recovered at the rate $\tau\sigma$, reduced as a related mortality a rate δ_1 and progressed to drug-resistance class due to failure to complete an entire course of TB treatment at the $\tau(1-\sigma)$. It is assumed that drug-resistance individuals continue to make contracted with other population members; It does not affect the dynamics of how the disease spreads. Drug-resistance individuals recovered at the rate η and decreased due to TB-induced death at the δ_2 Lastly, the recovered people may become infected again due to low immunity; but with a lower level at the rate ψ.

Basic Properties of the Model

The essential features of the TB model are examined in this section. Considering the mathematical presentation in equation set (1), which illustrates the fluctuations in various segments of the populations, its epidemiological significance lies in ensuring that every state variable stays positive throughout time $t > 0$. To clarify, the solutions derived from (1), given initial data with positive values, will consistently maintain positivity for all time values greater than zero. It is important to emphasize that because the model encapsulates the interplay between populations, it is assumed that every model parameter has non-negative values. Consequently, the ensuring outcome is as follows:

Existence and Uniqueness

Theorem 1

Let denote the region $|t-t_0| \leq p$ and $\|t-t_0\| \leq q$ where $y=(y_1,y_2,y_3,\ldots,y_n)$ and $y_0=(y_{0,1},y_{0,2},y_{0,3},\ldots,y_{0,n})$. Suppose that$f(t,y)$ satisfies Lipchitz condition $\|f(t,y_1)-f(t,y_2)\| \leq \|y_1-y_2\|$. where the pair (t,y_1) and (t,y_2) belong to d and k is a positive constant [1]. Thus, we consider the following lemma.

Lemma 1

Let d denote the region$0 \leq N \leq k$ then system (1) has a unique solution.

Proof: Let $y_1=S, y_2=V, y_3=E, y_4=I, y_5=I_R, y_6=R$ and $\lambda=\frac{\beta(I+\rho I_R)}{N}$

Alsof_1,f_2,f_3,f_4,f_5,f_6 be respectively the equations in (3).

Our objective is to demonstrated that $\frac{\partial f_i}{\kappa} i,j=1,2,3,4,5,6$ is bounded and continuous in d.

$$\left.\begin{aligned} f_1 &= \pi+\phi y_2-\left(\tfrac{\beta(y_4+\rho y_5)}{N}+\omega+\mu\right)y_1,\\ f_2 &= \omega y_1-\left(\tfrac{\beta(1-\varepsilon)(y_4+\rho y_5)}{N}+\phi+\mu\right)y_2,\\ f_3 &= \tfrac{\beta(y_4+\rho y_5)y_1}{N}+\tfrac{\beta(1-\varepsilon)(y_4+\rho y_5)y_2}{N}+\tfrac{\beta\psi(y_4+\rho y_5)y_6}{N}-(\kappa+\alpha+\mu)y_3,\\ f_4 &= \kappa y_3-(\tau+\sigma+\delta_1+\mu)y_4,\\ f_5 &= \sigma y_4-(\eta+\delta_2+\mu)y_5,\\ f_6 &= \alpha y_3+\tau y_4+\eta y_5-\left(\tfrac{\beta\psi(y_4+\rho y_5)}{N}+\mu\right)y_6. \end{aligned}\right\} \quad (3)$$

Now, from (3)

$$\left|\frac{\partial f_1}{\partial y_1}\right|=\left|-\left(\frac{\beta(y_4+\rho y_5)}{N}+\omega+\mu\right)\right|<\infty, \left|\frac{\partial f_1}{\partial y_2}\right|=|\phi|<\infty, \left|\frac{\partial f_1}{\partial y_4}\right|=\left|-\left(\frac{\beta y_1}{N}\right)\right|<\infty, \left|\frac{\partial f_1}{\partial y_5}\right|=\left|-\left(\frac{\beta\rho y_1}{N}\right)\right|<\infty,$$

$$\left|\frac{\partial f_1}{\partial y_3}\right|=\left|\frac{\partial f_1}{\partial y_6}\right|=0<\infty.$$

Similar forf_3,f_4,f_5 and f_6. Therefore, the partial derivatives for the model equations (1) exist for all the equations and are unique.

Positivity of the Solution

To ensure the epidemiological realism of the TB infection model systems (1), it is imperative to demonstrate that every state variable stays positive throughout time.

Theorem 2. Let the initial data be $\{(S(t),V(t),E(t),I(t),I_R(t),R(t)) \geq 0\} \in \Gamma$. Then, the solution set $(S(t),V(t),E(t),I(t),I_R(t),R(t)) \in \Gamma$ of the model systems (1) is non-negative for all $t > 0$.
Proof. As stated in the study of [1], considering the non-linear systems of equation (1), we take the first equation.

$$\frac{dS}{dt} = \pi + \phi V - \left(\frac{\beta(I + \rho I_R)}{N} + \omega + \mu\right) S$$

We have
$\frac{dS}{dt} \geq \left(\frac{\beta(I+\rho I_R)}{N} + \omega + \mu\right) S$
Integrating the above equation, by separation of variables, we have

$$\frac{dS}{S} \geq -\left(\frac{\beta(I + \rho I_R)}{N} + \omega + \mu\right) dt$$
$$\int \frac{dS}{S} \geq -\int \left(\frac{\beta(I + \rho I_R)}{N} + \omega + \mu\right) dt$$
$$ln\, S \geq -\left(\frac{\beta(I + \rho I_R)}{N} + \omega + \mu\right) t + C_1$$

Taking the exponential of both sides, we have

$$exp^{ln\, S} \geq exp^{-\left(\frac{\beta(I+\rho I_R)}{N}+\omega+\mu\right)t}$$
$$S(t) \geq exp^{-\left(\frac{\beta(I+\rho I_R)}{N}+\omega+\mu\right)t}.exp^{C_1}$$

at $t \to 0$

$$S(0) = exp^{C_1}$$

From above

$$S(t) \geq S(0)exp^{-\left(\frac{\beta(I+\rho I_R)}{N}+\omega+\mu\right)t}$$

At $t \to \infty$

$$S(t) \geq 0$$

In a similar vein, $V(t) \geq 0, E(t) \geq 0, I(t) \geq 0, I_R(t) \geq 0, R(t) \geq 0$ has also been proven. Because of this, therefore, the disease is uniformly persistent for every positive solution.

Invariant Region

Theorem 3: Given the initial conditions, let (S,V,E,I,I_R,R) be the solution of model (1) and biological feasible region given by the set $\Theta \in R_+^6$, where;

$$\Theta = \left\{(S,V,E,I,I_R,R) \in R_+^6 : N(t) \leq \frac{\pi}{\mu}\right\} \quad (4)$$

Proof
The sum of all the model systems' equations (1):

$$\frac{dN(t)}{dt} = \frac{dS(t)}{dt} + \frac{dV(t)}{dt} + \frac{dE(t)}{dt} + \frac{dI(t)}{dt} + \frac{dI_R(t)}{dt} + \frac{dR(t)}{dt} \quad (5)$$

The definition of the population's overall change is

$$\frac{dN}{dt} = \pi - \mu(S + V + E + I + I_R + R) - (\delta_1 I + \delta_2 I_R)$$

Which gives

$$\frac{dN}{dt} \leq \pi - \mu N \quad (6)$$

The comparison theorem presented in [7] can be used to demonstrate that

$$N(t) \leq \frac{\pi}{\mu}(1 - e^{-\mu t}) + N(0)e^{-\mu t} \quad (7)$$

Adopting the theorem of Birkhoff-Rota, we note that, if $N(0) < \frac{\pi}{\mu}$, then$N \to \frac{\pi}{\mu}$ asymptotically as $t \to \infty$ in equation (7) and the total population $N \to \frac{\pi}{\mu}$, which means that $0 \leq N \leq \frac{\pi}{\mu}$. Consequently, both mathematically and epidemiologically, the fundamental model is well articulated. Therefore, studying the dynamics of the foundational model suffices.

Mathematical Analysis of the Model

By locating steady-state solutions, we conduct a comprehensive analysis of model (1) in this section. In doing so, it involves confirming the existence of two equilibrium states: the TB-free equilibrium, which is the state in which TB incidence is zero, and the endemic state, in which the illness is prevalent. In addition, we assess the stability of these equilibria at both local and global levels. Moreover, we explore the type of bifurcation demonstrated by the model.

Tuberculosis Disease Free Equilibrium (TDFE)

The Tuberculosis Disease-Free Equilibrium (TDFE) $E_\Delta$represents a population's steady-state condition in which no infection cases exist. In the absence of tuberculosis, we established, $E = I = I_R = 0$, as adopted by [1,2,30]. From equation (1),

$$S^* = \frac{\pi(\phi+\mu)}{\mu(\omega+\phi+\mu)} \text{and } V^* = \frac{\pi\omega}{\mu(\omega+\phi+\mu)}. \quad (8)$$

Thus, the disease-free equilibrium (DFE) condition E_Δ for tuberculosis is given by:

$$E_\Delta = \left(\frac{\pi(\phi+\mu)}{\mu(\omega+\phi+\mu)}, \frac{\pi\omega}{\mu(\omega+\phi+\mu)}, 0,0,0,0\right). \quad (9)$$

Effective Reproduction Number

The effective reproduction number, or R_{eff}, according to Diekman ***et al***., is a measure of how many secondary infections a primary infected person really causes over the course of their whole infectious period. We employed the following generation's matrix technique, which was put into practice by [35]. In order to determine the effective reproduction number R_{eff}, one must first determine the transition terms' matrix (V) and the new infection terms' matrix (F). The matrices F and V can be found using the coefficients of E, I, and I_R in equation (1). Making use of the model equations (1), we took the afflicted class into account.

$$\left.\begin{aligned} \frac{dE}{dt} &= \frac{\beta(I+\rho I_R)S}{N} + \frac{\beta(1-\varepsilon)(I+\rho I_R)V}{N} + \frac{\beta(1-\psi)(I+\rho I_R)R}{N} - (\kappa+\alpha+\mu)E, \\ \frac{dI}{dt} &= \kappa E - (\tau+\sigma+\delta_1+\mu)I, \\ \frac{dI_R}{dt} &= \sigma I - (\eta+\delta_2+\mu)I_R. \end{aligned}\right\} \quad (10)$$

$$F = \begin{bmatrix} 0 & a_1 & a_2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \text{and } V^{-1} = \begin{bmatrix} \frac{1}{B_1} & 0 & 0 \\ \frac{\kappa}{B_1B_2} & \frac{1}{B_2} & 0 \\ \frac{\kappa\sigma}{B_1B_2B_3} & \frac{\sigma}{B_2B_3} & \frac{1}{B_3} \end{bmatrix},$$

where

$$a_1 = \frac{\beta(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)},$$
$$a_2 = \frac{\beta\rho(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)},$$
$$B_1 = (\kappa+\alpha+\mu),$$
$$B_2 = (\tau+\sigma+\delta_1+\mu),$$
$$B_3 = (\eta+\delta_2+\mu).$$

Therefore,

$$R_{eff} = \frac{\beta\kappa(\phi+\mu+(1-\varepsilon)\omega)(\eta+\delta_2+\mu+\sigma\rho)}{(\omega+\phi+\mu)(\kappa+\alpha+\mu)(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)}. \quad (11)$$

Local Stability of TDFE

The proposed model system's Jacobian, $J(E_\Delta)$, is utilized to demonstrate the disease's local stability [30].

Theorem 4: When $R_{eff} < 1$, the system (1)'s disease-free equilibrium is locally asymptotically stable.

Proof: At $J(E_\Delta)$, the Jacobian of system (1) is examined in order to demonstrate the local stability of the system, and it is provided by:

$$J(E_\Delta) = \begin{bmatrix} -(\omega+\mu) & \phi & 0 & -\frac{\beta(\phi+\mu)}{(\omega+\phi+\mu)} & -\frac{\beta\rho(\phi+\mu)}{(\omega+\phi+\mu)} & 0 \\ \omega & -(\phi+\mu) & 0 & -\frac{\beta(1-\varepsilon)\omega}{(\omega+\phi+\mu)} & -\frac{\beta\rho(1-\varepsilon)\omega}{(\omega+\phi+\mu)} & 0 \\ 0 & 0 & -(\kappa+\alpha+\mu) & \frac{\beta(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)} & \frac{\beta\rho(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)} & 0 \\ 0 & 0 & \kappa & -(\tau+\sigma+\delta_1+\mu) & 0 & 0 \\ 0 & 0 & 0 & \sigma & -(\eta+\delta_2+\mu) & 0 \\ 0 & 0 & \alpha & \tau & \eta & -\mu \end{bmatrix},$$

$$= \begin{bmatrix} -d_1 & \phi & 0 & -d_4 & -d_8 & 0 \\ \omega & -d_2 & 0 & -d_5 & -d_9 & 0 \\ 0 & 0 & -d_3 & d_6 & d_{10} & 0 \\ 0 & 0 & \kappa & -d_7 & 0 & 0 \\ 0 & 0 & 0 & \sigma & -d_{11} & 0 \\ 0 & 0 & \alpha & \tau & \eta & -\mu \end{bmatrix}, \quad (12)$$

where

$$d_1 = (\omega+\mu), d_2 = (\phi+\mu), d_3 = (\kappa+\alpha+\mu), d_4 = \frac{\beta(\phi+\mu)}{(\omega+\phi+\mu)}, d_5 = \frac{\beta(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)},$$
$$d_6 = \frac{\beta(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)}, d_7 = (\tau+\sigma+\delta_1+\mu), d_8 = \frac{\beta\rho(\phi+\mu)}{(\omega+\phi+\mu)}, d_9 = \frac{\beta\rho(1-\varepsilon)\omega}{(\omega+\phi+\mu)},$$

$d_{10} = \frac{\beta\rho(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)}, d_{11} = (\eta+\delta_2+\mu).$

Using trace and determinant method as employed by [30], we have

$tr = -(d_1+d_2+d_3+d_7+d_{11}+\mu)$and $det = \mu(d_1d_2-\omega\phi)\big(d_3d_7d_{11}-\kappa(d_6d_{11}+\sigma d_{10})\big)$,

$$det = \mu^2(\omega+\phi+\mu)\left((\kappa+\alpha+\mu)(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)\left(1-\frac{\beta\kappa(\phi+\mu+(1-\varepsilon)\omega)(\eta+\delta_2+\mu+\rho\sigma)}{(\omega+\phi+\mu)(\kappa+\alpha+\mu)(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)}\right)\right),$$

$$det = \mu^2(\omega+\phi+\mu)(\kappa+\alpha+\mu)(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)\big(1-R_{eff}\big).$$

Based on the findings in [21], We can conclude that the DFE point's local asymptotic stability is proven.

Sensitivity Analysis

Infectious disease epidemiology aims to be better understood through mathematical modelling of the disease. It can be used to understand how bacteria or viruses spread throughout a population, according to [25]. Therefore, the output of the model needs to be able to shed light on the dynamics of the illness. One technique for providing this kind of crucial information is sensitivity analysis (SA). To evaluate the degree of correlation among the model parameters, we conducted a sensitivity analysis in this section. In addition to educating public health and policymakers, this will help us comprehend how each parameter influences the threshold quantity and enable them to prioritize an intervention approach aimed at halting the disease's spread. For each of the parameters T, Using the formula in [23, 24], we can find the normalized forward sensitivity index $\Gamma_T^{R_0}$ on the reproduction number R as $\Gamma_T^{R_0} = \frac{\partial R_0}{\partial T} X \frac{T}{R_0}$. With the use of the method previously mentioned and the parameter values that Table 1 displays. Table 2 displays the corresponding sensitivity index values. To further illustrate the numerical outcome of the sensitivity indices, we present a bar plot in Figure 2. The threshold quantity of the disease will directly rise in response to any positive index from the sensitivity analysis and vice versa; conversely, any negative index will result in a decrease in the threshold quantity and vice versa. According to Table 2, a rise in the parameters $\beta, \kappa, \sigma, \rho, \phi$ and ε positive values is linked to an increase in the spread of TB. The spread of tuberculosis is also correlated with a decline in the negative values of the

parameters $\delta_1, \delta_2, \eta, \tau, \omega, \alpha$ and μ. The sensitivity index's largest negative value is the rate of natural death. The findings shed light on control methods that are effective in reducing TB's population spread. For instance, the transition from exposed to actively infected κ has a positive index (+0.8092), which suggests that a 1% increase (or reduction) in κvalue will result in a 1% increase (or decrease) in the number of reproductions. Additionally, the natural death index α has a negative index of -0.8014, which means that a 1% change in α value will result in a 1% change in the number of reproductions.

The TB sensitivity analysis results, in summary, demonstrate the efficacy of any control methods that reduce the risk of transmission and the time it takes for a community to transition from exposure to active infection. Vaccination and therapy are two examples of this type of control mechanism, and they can be promoted through educational initiatives.

$$\left.\begin{aligned}
\Gamma_{\beta}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \beta} X \frac{\beta}{R_{eff}} = 1,\\
\Gamma_{\kappa}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \kappa} X \frac{\kappa}{R_{eff}} = \frac{(\alpha+\mu)}{(\kappa+\alpha+\mu)},\\
\Gamma_{\phi}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \rho} X \frac{\rho}{R_{eff}} = \frac{\varepsilon\omega\phi}{(\omega+\phi+\mu)(\phi+\mu+(1-\varepsilon)\omega)},\\
\Gamma_{\mu}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \mu} X \frac{\mu}{R_{eff}} = \frac{\mu\left(d_1 B_1 B_2 B_3(\rho\sigma+\delta_2+\eta+2\mu+\phi+(1-\varepsilon)\omega)\right)-\Pi}{(\phi+\mu+(1-\varepsilon)\omega)(\rho\sigma+\delta_2+\eta+\mu)},\\
\Gamma_{\varepsilon}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \varepsilon} X \frac{\varepsilon}{R_{eff}} = -\frac{\omega\varepsilon}{(\phi+\mu+(1-\varepsilon)\omega)},\\
\Gamma_{\omega}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \omega} X \frac{\omega}{R_{eff}} = -\frac{\omega\varepsilon(\mu+\phi)}{(\omega+\phi+\mu)(-\mu+(\varepsilon-1)\omega-\phi)},\\
\Gamma_{\eta}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \eta} X \frac{\eta}{R_{eff}} = -\frac{\rho\eta\sigma}{(\eta+\delta_2+\mu)(\rho\sigma+\eta+\delta_2+\mu)},\\
\Gamma_{\delta_2}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \delta_2} X \frac{\delta_2}{R_{eff}} = -\frac{\sigma\rho\delta_2}{(\eta+\delta_2+\mu)(\rho\sigma+\eta+\delta_2+\mu)},\\
\Gamma_{\sigma}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \sigma} X \frac{\sigma}{R_{eff}} = \frac{((\delta_1+\mu+\tau)\rho-\mu-\eta-\delta_2)\sigma}{(\tau+\sigma+\delta_1+\mu)(\rho\sigma+\eta+\delta_2+\mu)},\\
\Gamma_{\rho}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \rho} X \frac{\rho}{R_{eff}} = \frac{\rho\sigma}{(\rho\sigma+\eta+\delta_2+\mu)},\\
\Gamma_{\alpha}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \alpha} X \frac{\alpha}{R_{eff}} = -\frac{\alpha}{(\kappa+\alpha+\mu)},\\
\Gamma_{\tau}^{R_{eff}} &= \frac{\partial R_{eff}}{\partial \tau} X \frac{\tau}{R_{eff}} = -\frac{\tau}{(\tau+\sigma+\delta_1+\mu)},\\
\Gamma_{\delta_1}^{R_{eff}} m &= \frac{\partial R_{eff}}{\partial \delta_1} X \frac{\delta_1}{R_{eff}} = -\frac{\delta_1}{(\tau+\sigma+\delta_1+\mu)},
\end{aligned}\right\} \quad (13)$$

where

$$\begin{aligned}
\Pi &= (\phi+\mu+(1-\varepsilon)\omega)(\eta+\delta_2+\mu+\sigma\rho)(B_1B_2B_3 + d_1B_2B_3 + d_1B_1B_2 + d_1B_1B_3),\\
d_1 &= (\omega+\phi+\mu),\\
B_1 &= (\kappa+\alpha+\mu),\\
B_2 &= (\tau+\sigma+\delta_1+\mu),\\
B_3 &= (\eta+\delta_2+\mu).
\end{aligned}$$

Table 2. Normalized reproduction number sensitivity index

Parameter	Description	Sensitivity index	Sign
β	Transmission rate	1	+ve
κ	Rate of progression from exposed class to active infected class	0.8092	+ve
ϕ	Rate of vaccine wanning	0.0204	+ve
σ	Proportion of individuals that recovered due to treatment without drug resistance. So that $(1-\sigma)$ is the proportion of individuals that developed drug resistance. Therefore, $\tau\sigma$ represent the rate of recovery due to effective treatment and is the rate of treatment failure that resulted in drug resistance	0.0617	+ve
ρ	A modification parameter associated with reduced infectiousness of Drug-resistance individuals as compared with Actively infected individuals	0.0711	+ve
μ	Natural death rate	-0.0087	-ve
δ_1	The death rate due to actively infected TB individuals	-0.2827	-ve
δ_2	Disease-induced death rate because of resistance to the drug	-0.0344	-ve
ε	Rate of vaccine inefficacy	-0.2212	-ve
ω	Vaccination coverage	-0.0208	-ve
η	Rate of recovery of Drug-resistance individuals to recovered class due to another different drug(s) been taken	-0.0363	-ve
α	Rate of progression of exposed into recovered compartment	-0.8014	-ve
τ	Rate of treatment by Infected individuals (I)	-0.7069	-ve

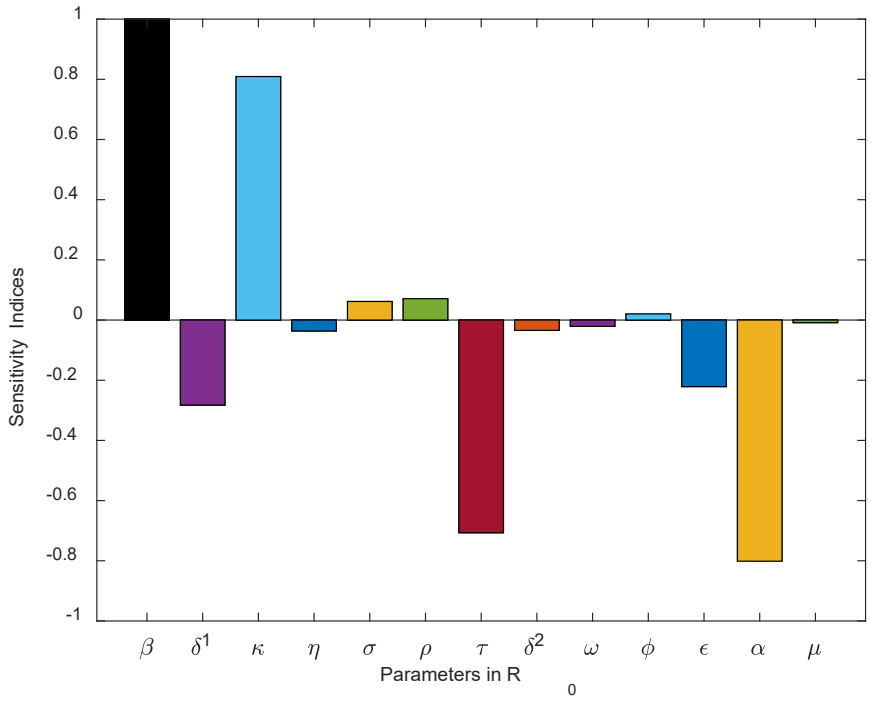


Figure 2. Sensitivity Indices of the tuberculosis reproduction number

Threshold Analysis and Impact of Vaccine

Given our doubts about the efficacy of the TB vaccine, it's important to determine if its widespread use in a population can be reliably ensured. The key consideration here is whether the consistent and reliable administration of the vaccine can be guaranteed to a large group of people. By looking

at the percentage of the population that received the vaccine in a steady state, assessing how the immunization affects the spread of the illness can be done qualitatively.
Let

$$\eta_{\Delta} = \frac{V^*}{N^*}.$$

η_{Δ} can be considered as a variable that determines R_{eff}, therefore.

$$R_{eff} = R_{eff}(\eta_{\Delta}) = R_0\left(1 - \varepsilon\frac{\omega}{(\omega+\phi+\mu)}\right) = R_0(1 - \varepsilon\eta_{\Delta}). \quad (14)$$

Observing that $R_{eff} \leq R_0$, with equivalence only if $\omega = 0(i.e, \eta_{\Delta} = 0)$ or $\varepsilon = 0$. That is to say, in other words, even though the vaccine may not work effectively, it's important to note that a decrease in the spread of the disease will occur as the rate of infection decreases. With$\omega > 0$ and $\varepsilon > 0$, the impact of illness would be reduced. Thus, the requirement for η_{Δ} is equally crucial and sufficient for control, just as $R_{eff} \leq 1$, which is a necessary and adequate condition for disease elimination, is an indispensable and suitable requirement.

$$\eta_{\Delta} \geq \frac{1}{\varepsilon}\left(1 - \frac{1}{R_0}\right) = \eta_{eff}. \quad (15)$$

The result can be achieved by combining the information from Section 4.3 with Theorem 4.
Lemma 2: If $\eta_{\Delta} > \eta_{eff}$, TB can be eliminated from the population.
We use the same idea as that derived in [10,12] for the fraction vaccinated at equilibrium point η_{Δ}.. Figure 3 provides a graphic representation of the critical value, η, as a function of E for a range of values. In order to reduce the value of R to less than one and hence control the disease, equation (15) shows that the vaccinated fraction (FV) and vaccine efficacy (ε) both play important roles in the decrease of R_{eff}. Both of these variables must be high. It is also possible to confirm inequality (15) as $\eta_{\Delta}\varepsilon \geq \left(1 - \frac{1}{R_0}\right)$
Regarding the vaccination rate, one may apply inequality (15). This is accomplished by first realizing that Equation (14)'s centre representation might be a diminishing function of ω; hence, it is constrained by allowing ω to have no bound. When we adopt the limit as ω gets closer to infinity, we observe that this expression is always more significant than $(1 - \omega)R_0$. No vaccination level can subsequently make R_{eff} smaller than one if $(1 - \omega)R_0 \geq 1$, at that time. Likewise, if $(1 - \omega)R_0 < 1$, at that time, the condition

$$\omega \geq \frac{\mu(R_0 - 1)}{1-(1-\omega)R_{eff}} = \omega_0 \quad (16)$$

gives $R_{eff} \leq 1$. This condition clearly presupposes that $R_0 > 1$. If $R_0 \leq 1$, then vaccination is not necessary for disease control. (by Section 4.2 and Theorem 3 and the proof that $R_{eff} \leq R_0$). By (16), it is easy to see that $R_{eff} \leq 1$. if $\omega \geq \omega_0$ and $R_{eff} > 1$ if $\omega < \omega_0$. Therefore, we obtained the following results:
Lemma 2. If $(1 - \omega)R_0 < 1$, and $\omega \geq \omega_0$ then TB will be eradicated from the population. If$(1 - \omega)R_0 \geq 1$, at that point, no measure of vaccination will prevent a TB epidemic in the population.

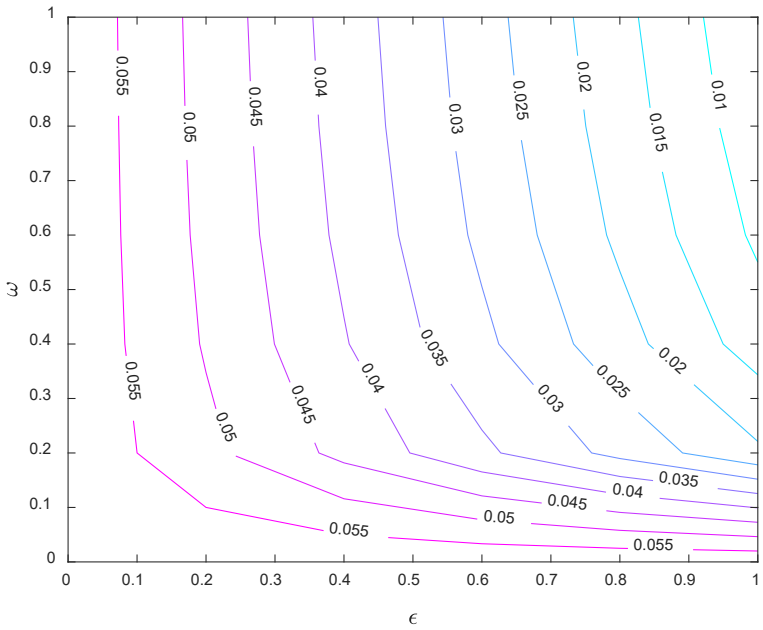


Figure 3. A contour plot of as a function of vaccinated persons at steady-state and vaccine efficacy is displayed in the simulation of the system model (1). Table 2 provides the parameter values that were used

In Figure 3, the effective threshold R_{eff} is plotted as a function of vaccine efficacy ε and the fraction of people vaccinated at a steady-state. The contours demonstrate a significant drop in effective basic reproduction number R for the set of parameters employed in these simulations as vaccination efficiency (ε) and the fraction of vaccinated persons (ω) increase. Notably, in order to attain $R_{eff} < 1$, high efficacy and vaccination coverage are required for the population to be adequately controlled for the disease.

Global Stability of TDFE

The disease-free equilibrium of model (1) under [30] condition is examined in this study to determine its global asymptotic stability.

Lemma: Consider a model system written in the form

$$\left.\begin{aligned}\frac{dX}{dt} &= F(X,Z),\\ \frac{dZ}{dt} &= G(X,Z), (X,0) = 0,\end{aligned}\right\} \tag{17}$$

where $X = (S, V, R())$ and $Z = (E, I, I_R)$with the components of $X \in \mathbb{R}^3$denoting the uninfected population and the components of $Z \in \mathbb{R}^3$ denoting infected population.

The disease-free equilibrium is now denoted as

$$E_{\Delta} = (X^{\Delta}, 0),$$

where

$$X^{\Delta} = \left(\frac{\pi(\phi+\mu)}{\mu(\omega+\phi+\mu)}, \frac{\pi\omega}{\mu(\omega+\phi+\mu)}, 0\right).$$

The following conditions must hold to guarantee a global asymptotic stability. Assume that,

H_1: $\frac{dX}{dt} = F(X,0)$, X^{Δ} is globally asymptotically stable.

H_2: $G(X,Z) = PZ - \hat{G}(X,Z), \hat{G}(X,Z) \geq 0$, for$(X,Z) \in \Omega$,

where $P = D_z G(X^{\Delta}, 0)$ is an M-matrix (the off-diagonal elements of $P$are non-negative) and Ω is the region where the model makes biological sense, Then, E^{Δ} is globally asymptotically stable provided that $R_{eff} < 1$.

Theorem 5

The DFE of model (1) is globally asymptotically stable provided that $R_{\Delta} < 1$.

Proof:
We need to show that the conditions (H_1) and (H_2) hold when $R_\Delta < 1$.
From our model (1), (2) and (6) we have, for the uninfected population.

$$F(X,0) = \begin{pmatrix} \pi + \phi V - (\lambda + \omega + \mu)S \\ \omega S - (\lambda\varepsilon + \phi + \mu)V \\ \alpha E + \tau I + \eta I_m - (\lambda\psi + \mu)R \end{pmatrix}. \tag{18}$$

From the above equation, we have

$$X^\Delta = \left(\frac{\pi(\phi+\mu)}{\mu(\omega+\phi+\mu)}, \frac{\pi\omega}{\mu(\omega+\phi+\mu)}, 0\right)$$

is globally asymptotically stable. This can be proved below, thus,

$$S(t) = \frac{\pi+\phi V}{\mu(\omega+\phi+\mu)} + \left(S(0) - \frac{\pi+\phi V}{\mu(\omega+\phi+\mu)}\right)e^{-(\omega+\phi+\mu)t},$$
$$V(t) = \frac{\pi\omega}{\mu(\omega+\phi+\mu)} + + \left(V(0) - \frac{\pi\omega}{\mu(\omega+\phi+\mu)}\right)e^{-(\omega+\phi+\mu)t},$$
$$R(t) = R(0)e^{-\mu t}.$$

As $t \to \infty, S(t) \to \frac{\pi+\phi V}{(\omega+\mu)}\, S \to \frac{\pi+\phi V}{\mu(\omega+\phi+\mu)}, V \to \frac{\pi\omega}{\mu(\omega+\phi+\mu)}, R \to 0$

Convergence of $X^\Delta$is therefore global inΩ. This implies $X^\Delta = \left(\frac{\pi(\phi+\mu)}{\mu(\omega+\phi+\mu)}, \frac{\pi\omega}{\mu(\omega+\phi+\mu)}, 0\right)$ is globally asymptotically stable and satisfiedH_1.

Thus, using the second condition of the theorem

H_2:$\hat{G}(X,Z) = PZ - G(X,Z), \hat{G}(X,Z) \geq 0for(X,Z) \in \Omega$. Therefore, $\hat{G}(X,Z) = PZ - G(X,Z), \hat{G}(X,Z) \geq 0$. Where P is an $n_\circ \times n_\circ$matrix, Z is a column vector and $G(X,Z)$ is a column vector formed from the infectious classes, recall that:

$$G(X,Z) = \begin{pmatrix} G_1(X,Z) \\ G_2(X,Z) \\ G_3(X,Z) \end{pmatrix} = \begin{pmatrix} \frac{\beta(I+\rho I_R)S}{N} + \frac{\beta(1-\varepsilon)(I+\rho I_R)V}{N} + \frac{\beta\psi(I+\rho I_R)R}{N} - (\kappa+\alpha+\mu)E \\ \kappa E - (\tau+\sigma+\delta_1+\mu)I \\ \sigma I - (\eta+\delta_2+\mu)I_R \end{pmatrix}.$$

Let's now compute A

$$P = \begin{pmatrix} -(\kappa+\alpha+\mu) & \frac{\beta(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)} & \frac{\beta\rho(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)} \\ \kappa & -(\tau+\sigma+\delta_1+\mu) & 0 \\ 0 & \sigma & -(\eta+\delta_2+\mu) \end{pmatrix},$$

and

$$Z = \begin{pmatrix} E \\ I \\ I_R \end{pmatrix}.$$

Therefore,

$$PZ = \begin{pmatrix} -(\kappa+\alpha+\mu)E + \frac{\beta(\phi+\mu+(1-\varepsilon)\omega)(I+\rho I_R)}{(\omega+\phi+\mu)} \\ \kappa E - (\tau+\sigma+\delta_1+\mu)I \\ \sigma I - (\eta+\delta_2+\mu)I_R \end{pmatrix}. \tag{19}$$

The use of $\hat{G}(X,Z) = PZ - G(X,Z)$, results

H_2 is not met since $\hat{G}_1(X,Z), \hat{G}_2(X,Z), \hat{G}_3(X,Z)$ does not equal zero or be bigger than zero. Therefore, when $R_{eff} < 1$, the equation system might not be globally asymptotically stable. This indicates that the equation system may display the phenomenon of a forward or backward bifurcation that extends to the area where $R_{eff} < 1$.

Endemic Equilibrium Point (EEP)

Lemma 3. The tuberculosis model has a unique endemic equilibrium if and only if $R_{eff} > 1$.

Proof. When we compute the endemic equilibrium point, we get,

$$\left.\begin{aligned} S^* &= \frac{\pi(\varepsilon\lambda+A_3)}{(\varepsilon\lambda^2+A_1\lambda+A_2)},\\ V^* &= \frac{\pi\omega}{(\varepsilon\lambda^2+A_1\lambda+A_2)}\\ E^* &= \frac{A_4(m_9\lambda^3+m_{10}\lambda^2+m_{11}\lambda)}{\kappa(m_5\lambda^3+m_6\lambda^2+m_7\lambda+m_8)},\\ I^* &= \frac{(m_9\lambda^3+m_{10}\lambda^2+m_{11}\lambda)}{(m_5\lambda^3+m_6\lambda^2+m_7\lambda+m_8)},\\ I_R^* &= \frac{\sigma(m_9\lambda^3+m_{10}\lambda^2+m_{11}\lambda)}{A_5(m_5\lambda^3+m_6\lambda^2+m_7\lambda+m_8)},\\ R* &= \frac{G_1(m_9\lambda^3+m_{10}\lambda^2+m_{11}\lambda)}{(G_2\lambda+G_3)(m_5\lambda^3+m_6\lambda^2+m_7\lambda+m_8)}, \end{aligned}\right\} \tag{20}$$

where:

$$\begin{aligned} \lambda &= \frac{\beta(I+\rho I_R)}{N}, & m_4 &= \pi(A_8 + A_1\omega),\\ A_1 &= (1-\varepsilon), & m_5 &= A_1m_1,\\ A_2 &= \psi, & m_6 &= A_1m_2 + A_6m_1,\\ A_3 &= (\kappa+\alpha+\mu), & m_7 &= A_6m_2 + A_7m_1,\\ A_4 &= (\tau+\sigma+\delta_1+\mu), & m_8 &= A_7m_2,\\ A_5 &= (\eta+\delta_2+\mu), & m_9 &= \kappa G_2m_3,\\ A_6 &= (\mu A_1 + \omega A_1 + \mu + \phi), & m_{10} &= \kappa G_2m_4 + \kappa G_3m_3,\\ A_7 &= \mu(\mu+\phi+\omega), & m_{11} &= \kappa G_3m_4,\\ A_8 &= (\phi+\mu), & m_{12} &= (A_8+\omega),\\ G_1 &= A_4A_5\alpha + A_5\kappa\tau + \eta\sigma\kappa, & P_1 &= \sigma G_2,\\ G_2 &= A_2A_5\kappa, & P_2 &= \sigma G_3 + G_1A_5,\\ G_3 &= A_5\kappa\mu, & P_3 &= A_4A_5G_2 + G_2A_5\kappa,\\ m_1 &= A_3A_4G_2 - A_2G_1\kappa, & P_4 &= A_5G_3(A_4+\kappa),\\ m_2 &= A_3A_4G_3, & P_5 &= P_3 + P_1\kappa,\\ m_3 &= A_1\pi, & P_6 &= P_4 + P_2\kappa,\\ F(\Pi) &= \Pi_6\lambda^6 + \Pi_5\lambda^5 + \Pi_4\lambda^4 + \Pi_3\lambda^3 + \Pi_2\lambda^2 + \Pi_1 + \Pi_0, \end{aligned} \tag{21}$$

where

$$\Pi_6 = A_1m_9P_5$$

$$\Pi_5 = \pi\kappa A_1A_5G_2m_5 + A_1P_5m_{10} + A_1P_6m_9 + A_6P_5m_9 - \beta\kappa(A_5+\sigma\rho)A_1G_2m_9$$

$$\Pi_4 = \pi\kappa A_1A_5G_2m_6 + \pi\kappa A_1A_5G_3m_5 + \pi\kappa A_5G_2m_5m_{12} + A_1P_5m_{11} + A_1P_6m_{10} + A_6P_5m_9 + A_6P_6m_9 + A_7P_5m_9 - \beta\kappa(A_5+\sigma\rho)(A_1G_2m_{10} + A_1G_3m_9 + A_6G_2m_9),$$

$$\Pi_3 = \pi\kappa A_1A_5G_2m_7 + \pi\kappa A_1A_5G_3m_6 + \pi\kappa A_5G_2m_6m_{12} + \pi\kappa A_5G_3m_5m_{12} + A_1m_{11}P_6 + A_6m_{11}P_5 + A_6m_{10}P_6 + A_7m_{10}P_5 + A_7m_9P_6 - \beta\kappa(A_5+\rho\sigma)(A_1G_2m_{11} + A_1G_3m_{10} + A_6G_2m_{10} + A_6G_3m_9 + A_7G_2m_9),$$

$$\Pi_2 = \pi\kappa A_1A_5G_2m_8 + \pi\kappa A_1A_5G_3m_7 + \pi\kappa A_5G_2m_7m_{12} + \pi\kappa A_5G_3m_6m_{12} + A_6m_{11}P_6 + A_5m_{11}P_5 + A_7m_{10}P_6 - \beta\kappa(A_5+\sigma\rho)(A_1G_3m_{11} + A_6G_2m_{11} + A_6G_3m_{10} + A_7G_2m_{10} + A_7G_3m_9),$$

$$\Pi_1 = \pi\kappa A_1A_5G_3m_8 + \pi\kappa A_5G_2m_8m_{12} + \pi\kappa A_5G_3m_7m_{12} + G_3m_7m_{12} + A_7m_{11}P_6 - \beta\kappa(A_5+\sigma\rho)(A_6G_3m_{11} + A_7G_2m_{11} + A_7G_3m_{10}),$$

$$\Pi_0 = \pi\kappa A_7G_3^2(A_3A_4A_5(A_8+\omega))(1-R_{eff}).$$

It can easily be seen from the above equation that $\Pi_6 > 0$ (since all the model parameters are non-negative). Further, $\Pi_0 < 0$ whenever $R_{eff} < 0$. Thus, the number of possible positive real roots of the polynomial (19) can have depends on the signs of $\Pi_5, \Pi_4, \Pi_3, \Pi_2$ and Π_1. Therefore, adopting [16] the left side of (19) by $f(x)$. Note that $\lim_{x\to\infty} f(x) = +\infty$ and $f(x) = \Pi_0 < 0$ if $R_{eff} > 1$, thus, system (19) has a positive equilibrium E_Δ.

Bifurcation Analysis

The probability of the backward bifurcation phenomena in the model system (1) is shown by the presence of numerous TB persistence equilibria E_Δ for $R_{eff} < 1$. According to epidemiology, $R_{eff} < 1$ is insufficient to determine whether tuberculosis would persist; rather, it is dependent upon the size of the starting population at the time $R_{eff} < 1$ Our objective is to examine the existence of backward

bifurcation in system (1) and establish a threshold for its occurrence. We use the noteworthy findings of [30] to accomplish this.
To put it another way, we redesign our system (1) as follows:

$$\frac{dy}{dx} = f(x) \tag{22}$$

Where $x = (x_1, x_2, x_3, x_4, x_5, x_6)^T$ and $f = (f_1, f_2, f_3, f_4, f_5, f_6)^T$. We further modify the variable be setting $S = x_1, V = x_2, E = x_3, I = x_4, I_R = x_5, R = x_6$. Hence, following the above transformation, the transformed model (1) is given as

$$F(x) = \begin{pmatrix} \pi + \phi x_2 - \left(\frac{\beta(x_4 + \rho x_5)}{N} + \omega + \mu\right)x_1 \\ \omega x_1 - \left(\frac{\beta(1-\varepsilon)(x_4 + \rho x_5)}{N} + \phi + \mu\right)x_2 \\ \frac{\beta(x_4 + \rho x_5)x_1}{N} + \frac{\beta(1-\varepsilon)(x_4 + \rho x_5)x_2}{N} + \frac{\beta\psi(x_4 + \rho x_5)x_6}{N} - (\kappa + \alpha + \mu)x_3 \\ \kappa x_3 - (\tau + \sigma + \delta_1 + \mu)x_4 \\ \sigma x_4 - (\eta + \delta_2 + \mu)x_5 \\ \alpha x_3 + \tau x_4 + \eta x_5 - \left(\frac{\beta\psi(x_4 + \rho x_5)}{N} + \mu\right)x_6 \end{pmatrix} = \begin{pmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \\ f_5 \\ f_6 \end{pmatrix}$$

The Jacobian of the transformed system (1) at the *DFE* is given by:

$$J(E_{vac}) = \begin{bmatrix} -(\omega+\mu) & \phi & 0 & -\frac{\beta(\phi+\mu)}{(\omega+\phi+\mu)} & -\frac{\beta\rho(\phi+\mu)}{(\omega+\phi+\mu)} & 0 \\ \omega & -(\phi+\mu) & 0 & -\frac{\beta(1-\varepsilon)\omega}{(\omega+\phi+\mu)} & -\frac{\beta\rho(1-\varepsilon)\omega}{(\omega+\phi+\mu)} & 0 \\ 0 & 0 & -(\kappa+\alpha+\mu) & \frac{\beta(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)} & \frac{\beta\rho(\phi+\mu+(1-\varepsilon)\omega)}{(\omega+\phi+\mu)} & 0 \\ 0 & 0 & \kappa & -(\tau+\sigma+\delta_1+\mu) & 0 & 0 \\ 0 & 0 & 0 & \sigma & -(\eta+\delta_2+\mu) & 0 \\ 0 & 0 & \alpha & \tau & \eta & -\mu \end{bmatrix} \tag{23}$$

The Jacobian matrix (22) has a right eigenvector (associated with the zero eigenvalues) given by

$w = (w_1, w_2, w_3, w_4, w_5, w_6)^T$, where

$$w = \begin{pmatrix} \frac{\beta\kappa(\eta+\delta_2+\mu+\sigma\rho)\{\rho\mu(\omega+\phi+\mu)((1-\varepsilon)-(\phi+\mu)^2)-((1-\varepsilon)(\omega+\mu)(\phi+\mu))\}w_3}{\mu(\omega+\phi+\mu)(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)}, \frac{\beta\kappa\omega(\eta+\delta_2+\mu+\sigma\rho)\{(\phi+\mu)+(\omega+\mu)(1-\varepsilon)\}w_3}{\mu(\omega+\phi+\mu)(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)} \\ w_3, \frac{\kappa w_3}{(\tau+\sigma+\delta_1+\mu)}, \frac{\kappa\sigma w_3}{(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)}, \frac{(\alpha(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)+\tau\kappa(\eta+\delta_2+\mu)+\eta\sigma\kappa)w_3}{\mu(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)}. \end{pmatrix}$$

Similarly, the Jacobian matrix (22) has a left eigenvector (associated with the zero eigenvalues) given by

$v = (v_1, v_2, v_3, v_4, v_5, v_6)^T$, where $v = \left(0,0, v_3, \frac{(\kappa+\alpha+\mu)v_3}{\kappa}, \frac{\beta\rho(\phi+\mu+(1-\varepsilon)\omega)v_3}{(\omega+\phi+\mu)(\eta+\delta_2+\mu)}, 0\right)$

Bifurcation coefficients a and b computation. By calculating the corresponding non-zero partial derivative of bifurcation coefficients a and b, one can ascertain the direction of the bifurcation at $R_{eff} = 1$.

$a = \sum_{k,i,j=1}^{6} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0)$ and $a = \sum_{k,i=1}^{6} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \beta}(0,0)$,
which are determined to be

$$a = \left(\frac{V_3 W_3 \beta\mu\gamma_1}{\pi^2(\omega+\phi+\mu)^2(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)}\right) > 0,$$
$$b = \left(\frac{V_3 W_3 (1+\rho)\gamma_2}{\pi(\omega+\phi+\mu)^2(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)}\right) > 0,$$

where

$$\gamma_1 = [(1+\rho)(v_2 - v_1) + \mu(\omega+\phi+\mu)^2(\eta+\delta_2+\mu)\left(\frac{\pi}{\mu}(A_1+A_2) - 2\right)\kappa + \mu(\omega+\phi+\mu)^2\left(\frac{\pi}{\mu}(A_1+A_2)(1+2\rho) - 2\rho\right)\kappa\sigma],$$

$$\gamma_2 = [v_1 + \mu(\omega+\phi+\mu)^2(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu) + \kappa\mu(\omega+\phi+\mu)^2(\eta+\delta_2+\mu) + \kappa\sigma\mu(\omega+\phi+\mu)^2 +$$

$(\alpha(\tau+\sigma+\delta_1+\mu)(\eta+\delta_2+\mu)+\tau\kappa(\eta+\delta_2+\mu)+\eta\kappa\sigma-\upsilon_2)]$,

$\upsilon_1=\beta\kappa(\eta+\delta_2+\mu+\sigma\rho)[\rho\mu(\omega+\phi+\mu)(1-\varepsilon)-(\phi+\mu^2)-(1-\varepsilon)(\phi+\mu)(\omega+\mu)]$,

$\upsilon_2=\beta\kappa\omega(\eta+\delta_2+\mu+\sigma\rho)\big((\phi+\mu)+(\omega+\mu)(1-\varepsilon)\big)$,

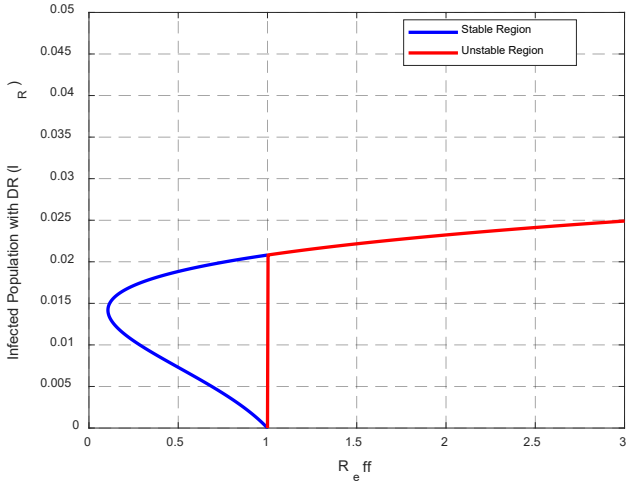


Figure 4. The bifurcation diagram of force of infection against R_{eff} which illustrates a backward bifurcation for the system model

Our system only undergoes backward bifurcation at $\beta=\beta^{\otimes}$, when both a and b are positive at $(E_{\Delta},\beta^{\otimes})$, as demonstrated by the result displayed in [15]. It is evident that b is constantly positive. Therefore, the condition of a's positivity provides the cutoff point for the backward bifurcation phenomena.

Global Stability of the Endemic Equilibrium

Theorem 6: If$R_{eff}>1$, the endemic equilibrium$E_{\Delta}$of the model is globally asymptotically stable.

$$L(S^*,V^*,E^*,I^*,I_R^*,R^*)=\left(S-S^*-S^*\,ln\frac{S^*}{S}\right)+\left(V-V^*-V^*\,ln\frac{V^*}{V}\right)+\left(E-E^*-E^*\,ln\frac{E^*}{E}\right)+\left(I-I^*-I^*\,ln\frac{I^*}{I}\right)+\left(I_R^*-I_R^*-I_R^*\,ln\frac{I_R^*}{I_R^*}\right)+\left(R-R^*-R^*\,ln\frac{R^*}{R}\right).$$

Differentiating L with respect to t produced

$$\frac{dL}{dt}=\frac{(S-S^*)}{S}\frac{dS}{dt}+\frac{(V-V^*)}{V}\frac{dV}{dt}+\frac{(E-E^*)}{E}\frac{dE}{dt}+\frac{(I-I^*)}{I}\frac{dI}{dt}+\frac{(I_R-I_R^*)}{I_R}\frac{dI_R}{dt}+\frac{(R-R^*)}{R}\frac{dR}{dt}.$$

Substitute the values of Substitute the values of $\frac{dS}{dt},\frac{dV}{dt},\frac{dE}{dt},\frac{dI}{dt},\frac{dI_R}{dt}$ and $\frac{dR}{dt}$ into $\frac{dL}{dt}$ and then simplify to get

$$\frac{dL}{dt}=\frac{(S-S^*)}{S}(\pi+\phi V-(\lambda+\omega+\mu)S)+\frac{(V-V^*)}{V}\big(\omega S-\big((1-\varepsilon)\lambda+\phi+\mu\big)V\big)+\frac{(E-E^*)}{E}(\lambda S+(1-\varepsilon)\lambda V+\psi\lambda R-(\kappa+\alpha+\mu)E)+\frac{(I-I^*)}{I}(\kappa E-(\tau+\sigma+\delta_1+\mu)I)+\frac{(I_R-I_R^*)}{I_R}(\sigma I-(\eta+\delta_2+\mu)I)+\frac{(R-R^*)}{R}(\alpha E+\tau I+\eta I_R-(\psi\lambda+\mu)R),$$

$$\frac{dL}{dt}=\left(1-\frac{S^*}{S}\right)(\pi+\phi V-(\lambda+\omega+\mu)S)+\left(1-\frac{V^*}{V}\right)\big(\omega S-\big((1-\varepsilon)\lambda+\phi+\mu\big)V\big)+\left(1-\frac{E^*}{E}\right)(\lambda S+(1-\varepsilon)\lambda V+\psi\lambda R-(\kappa+\alpha+\mu)E)+\left(1-\frac{I^*}{I}\right)(\kappa E-(\tau+\sigma+\delta_1+\mu)I)+\left(1-\frac{I_R^*}{I_R}\right)(\sigma I-(\eta+\delta_2+\mu)I)+\left(1-\frac{R^*}{R}\right)(\alpha E+\tau I+\eta I_R-(\psi\lambda+\mu)R),$$

$$\frac{dL}{dt}=\pi+\phi V-\lambda S-\omega S-\mu S-\frac{S^*}{S}\pi\pm\frac{S^*}{S}\phi V+\frac{S^*}{S}(\lambda+\omega+\mu)S+\omega S-(1-\varepsilon)\lambda V-\phi V-\mu V-\frac{V^*}{V}\omega S+\frac{V^*}{V}\big((1-\varepsilon)\lambda+\phi+\mu\big)V+\lambda S+(1-\varepsilon)\lambda V+\psi\lambda R-\kappa E-\alpha E-\mu E-\frac{E^*}{E}\lambda S-\frac{E^*}{E}(1-\varepsilon)\lambda V-\frac{E^*}{E}\psi\lambda R+\frac{E^*}{E}(\kappa+\alpha+\mu)E+$$

$$\kappa E - \tau I - \sigma I - \delta_1 - \mu I - \frac{I^*}{I}\kappa E + \frac{I^*}{I}(\tau + \sigma + \delta_1 + \mu)I + \sigma I - \eta I - \delta_2 I - \mu I - \frac{I_R^*}{I_R}\sigma I + \frac{I_R^*}{I_R}(\eta + \delta_2 + \mu)I +$$
$$\alpha E + \tau I + \eta I_R - \psi\lambda R - \mu R - \frac{R^*}{R}\alpha E - \frac{R^*}{R}\tau I - \frac{R^*}{R}\eta I_R + \frac{R^*}{R}((\psi\lambda + \mu)R,$$
$$\frac{dL}{dt} = \pi + \frac{S^*}{S}(\lambda + \omega + \mu)S + \frac{V^*}{V}\big((1-\varepsilon)\lambda + \phi + \mu\big)V + \frac{E^*}{E}(\kappa + \alpha + \mu)E + \frac{I^*}{I}(\tau + \sigma + \delta_1 + \mu)I + \frac{I_R^*}{I_R}(\eta + \delta_2 + \mu)I +$$
$$\frac{R^*}{R}(\psi\lambda + \mu)R$$
$$-\mu S - \frac{S^*}{S}\pi - \frac{S^*}{S}\phi V - \mu V - \frac{V^*}{V}\omega S - \mu E - \frac{E^*}{E}\lambda S - \frac{E^*}{E}(1-\varepsilon)\lambda V - \frac{E^*}{E}\psi\lambda R - \delta_1 I - \mu I - \frac{I^*}{I}\kappa E - \delta_2 I_R - \mu I_R - \frac{I_R^*}{I_R}\sigma I +$$
$$-\psi\lambda R - \mu R - \frac{R^*}{R}\alpha E - \frac{R^*}{R}\tau I - \frac{R^*}{R}\eta I_R,$$

$$\frac{dL}{dt} = \begin{pmatrix} \pi + \frac{S^*}{S}(\lambda + \omega + \mu)S + \frac{V^*}{V}\big((1-\varepsilon)\lambda + \phi + \mu\big)V + \frac{E^*}{E}(\kappa + \alpha + \mu)E + \frac{I^*}{I}(\tau + \sigma + \delta_1 + \mu)I + \frac{I_R^*}{I_R}(\eta + \delta_2 + \mu)I + \\ \frac{R^*}{R}(\psi\lambda + \mu)R \end{pmatrix}$$
$$- \begin{pmatrix} \mu S - \frac{S^*}{S}\pi - \frac{S^*}{S}\phi V - \mu V - \frac{V^*}{V}\omega S - \mu E - \frac{E^*}{E}\lambda S - \frac{E^*}{E}(1-\varepsilon)\lambda V - \frac{E^*}{E}\psi\lambda R - \delta_1 I - \mu I - \frac{I^*}{I}\kappa E - \delta_2 I_R - \mu I_R - \frac{I_R^*}{I_R}\sigma I \\ -\psi\lambda R - \mu R - \frac{R^*}{R}\alpha E - \frac{R^*}{R}\tau I - \frac{R^*}{R}\eta I_R \end{pmatrix},$$

$$\frac{dL}{dt} = \mathbb{Z}_1 - \mathbb{Z}_2.$$

where

$$\mathbb{Z}_1 = \pi + \frac{S^*}{S}(\lambda + \omega + \mu)S + \frac{V^*}{V}\big((1-\varepsilon)\lambda + \phi + \mu\big)V + \frac{E^*}{E}(\kappa + \alpha + \mu)E + \frac{I^*}{I}(\tau + \sigma + \delta_1 + \mu)I + \frac{I_R^*}{I_R}(\eta + \delta_2 + \mu)I +$$
$$\frac{R^*}{R}(\psi\lambda + \mu)R,$$
$$\mathbb{Z}_2 = \mu S - \frac{S^*}{S}\pi - \frac{S^*}{S}\phi V - \mu V - \frac{V^*}{V}\omega S - \mu E - \frac{E^*}{E}\lambda S - \frac{E^*}{E}(1-\varepsilon)\lambda V - \frac{E^*}{E}\psi\lambda R - \delta_1 I - \mu I - \frac{I^*}{I}\kappa E - \delta_2 I_R - \mu I_R - \frac{I_R^*}{I_R}\sigma I - \psi\lambda R - \mu R - \frac{R^*}{R}\alpha E - \frac{R^*}{R}\tau I - \frac{R^*}{R}\eta I_R,$$
$$\frac{dL}{dt} = \mathbb{Z}_1 - \mathbb{Z}_2.$$

$\frac{dL}{dt} \leq 0$ if $\mathbb{Z}_1 < \mathbb{Z}_2$

$\frac{dL}{dt} = 0$ if and only if $S = S^*, V = V^*, E = E^*, I = I^*, I^* = I_R^*, R = R^*$.

Consequently, the singleton set E_Δ^* in $\left\{(S^*, V^*, E^*, I^*, I_R^*, R^*) \in \Omega : \frac{dL}{dt} = 0\right\}$ has the greatest invariant impact invariant set. where E_Δ^* represents the system's endemic equilibrium (1). Consequently, if $\mathbb{Z}_1$ is less than $\mathbb{Z}_2$, then E_Δ^* is implied to be globally asymptotically stable by Lasalle's Invariant principle.

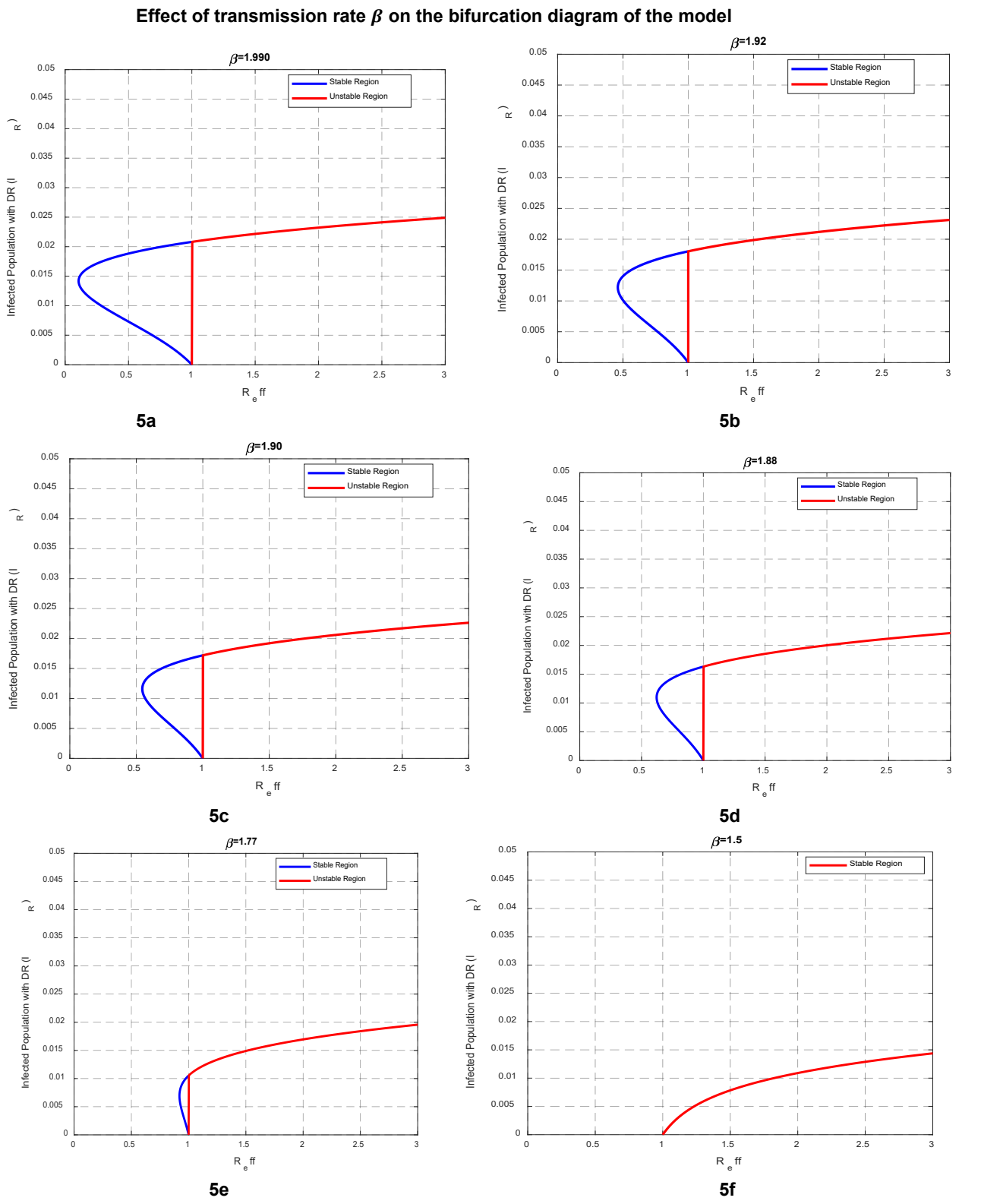


Figure 5a-5f. The system model (1)'s backward bifurcation diagram illustrates many behavioral patterns. Different values of β are employed in a clockwise direction as the bifurcation parameter β varies from the top left: $\beta = 1.990, \beta = 1.92, \beta = 1.90, \beta = 1.88, \beta = 1.77,$ and $\beta = 1.5,$ while the values of the other parameters are constant:$\mu = 0.01, \eta = 0.2, \delta_1 = 0.06, \delta_2 = 0.19, \kappa = 0.350, \alpha = 0.21, \rho = 0.8, \pi = 37684, \phi = 0.1, \psi = 0.85, \tau = 0.8, \omega = 0.98, \sigma = 0.02$and $\varepsilon = 0.2$. The endemic equilibrium point is represented by the symbol EEP, and the disease-free equilibrium point is represented by the symbol DFE

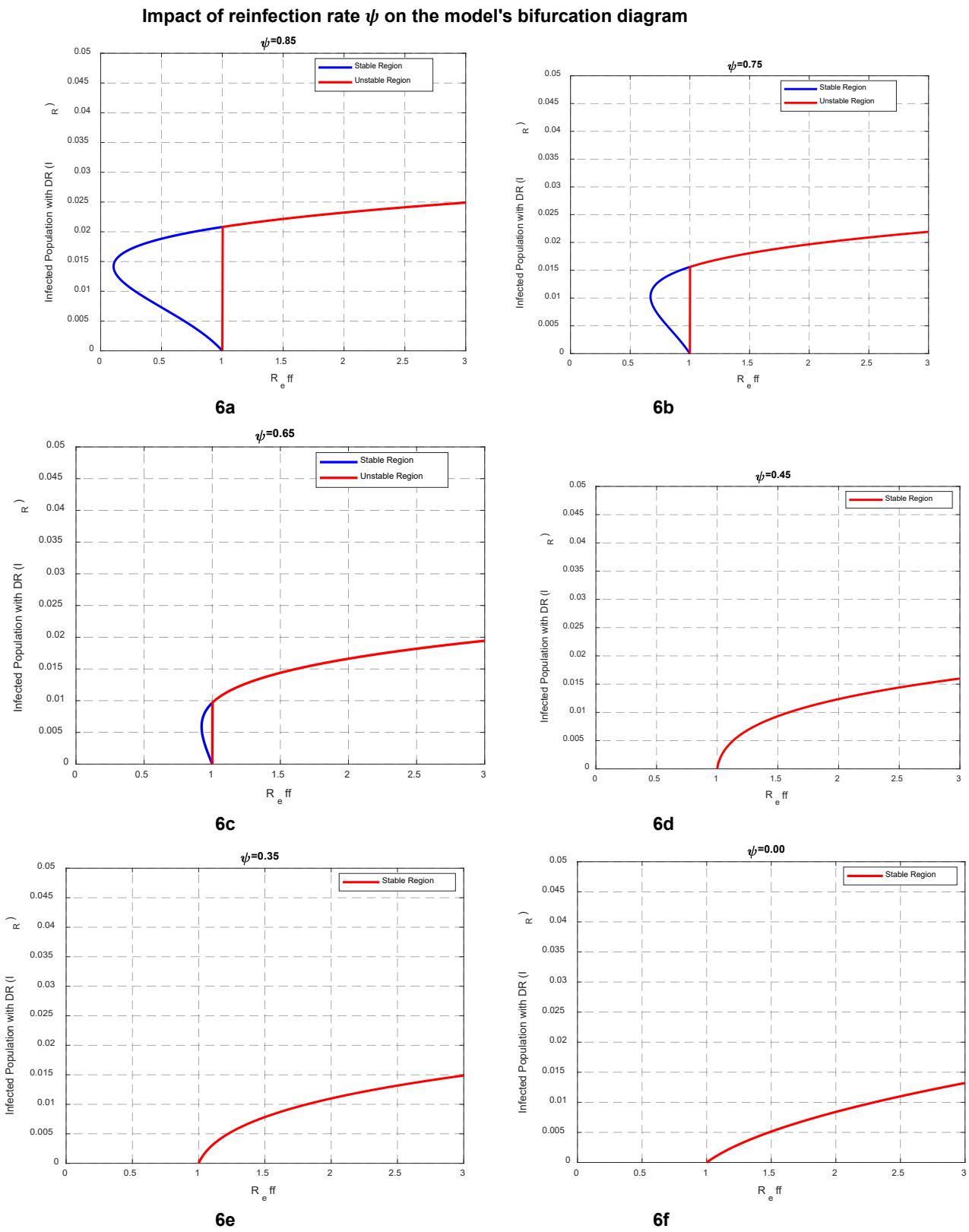
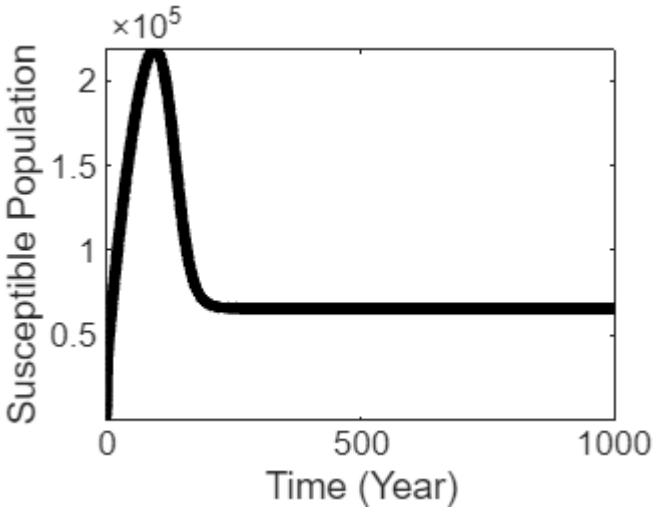
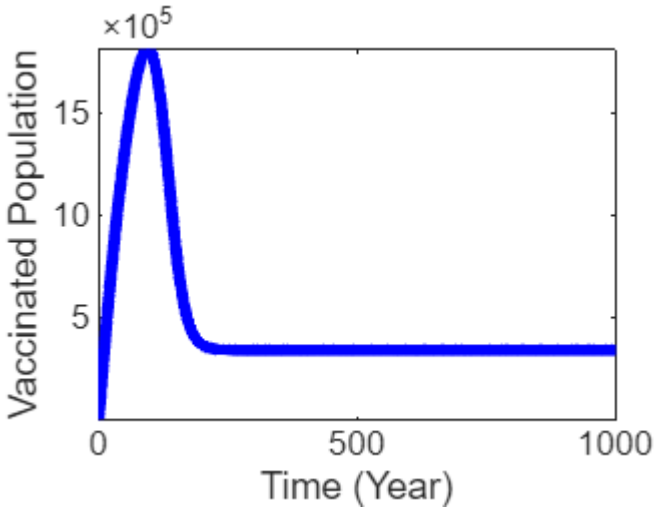


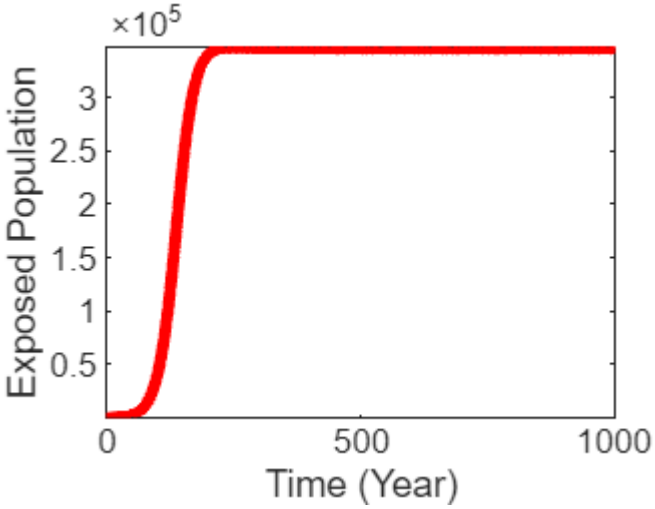
Figure 6a-6f. The system model (1)'s backward bifurcation diagram illustrates many behavioral patterns. In a clockwise path, various values of ψ are utilized as the bifurcation parameter ω varies from the top left:: $\psi = 0.85, \psi = 0.75, \psi = 0.65, \psi = 0.45, \psi = 0.35,$ and $\psi = 0.00,$ while the values of the other parameters are constant: $\mu = 0.01, \eta = 0.2, \delta_1 = 0.06, \delta_2 = 0.19, \kappa = 0.35, \alpha = 0.21, \rho = 0.8, \pi = 37684, \phi = 0.1, \beta = 1.990, \tau = 0.8, \omega = 0.98, \sigma = 0.02$and $\varepsilon = 0.2$



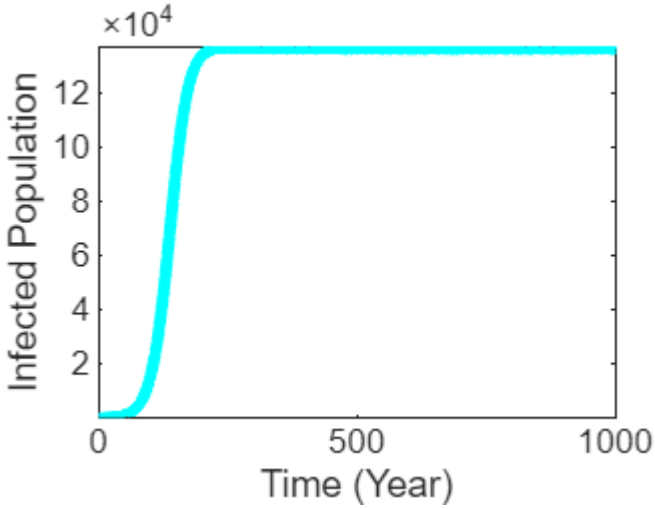
a) Susceptible Individual



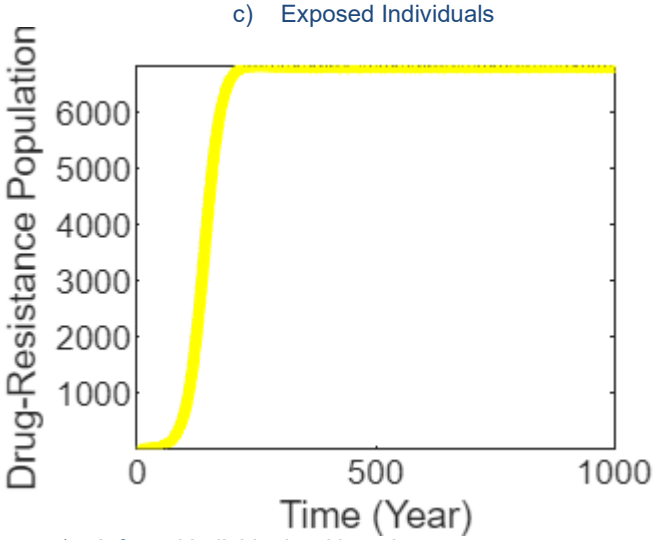
b) Vaccinated Individuals



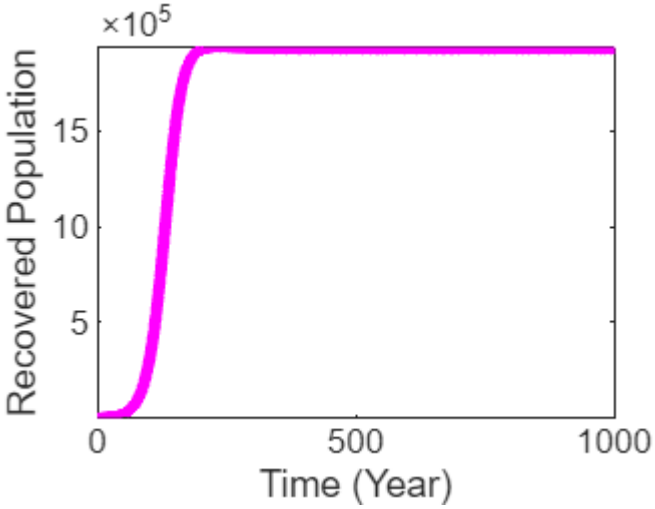
c) Exposed Individuals



d) Infected Individuals without resistance



e) Infected individuals with resistance



f) Recovered individuals without resistance

Figure 7 (a)-(f). Simulation result of S, V, E, I, and R as a function of time using parameter values as stated in Table 1

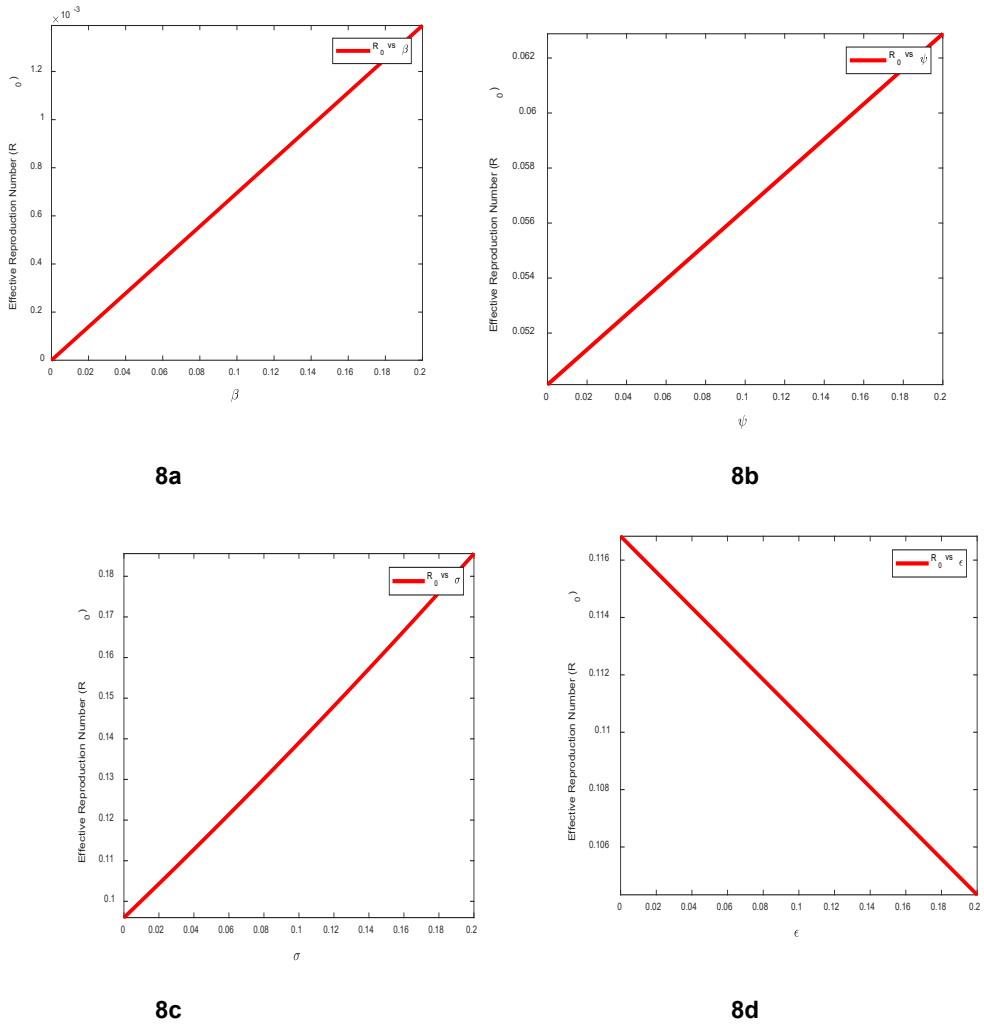


Figure 8. The relationship between (**a**) β (**b**) ψ (**c**)σ (d) ε and the effective reproduction numberR_{eff}

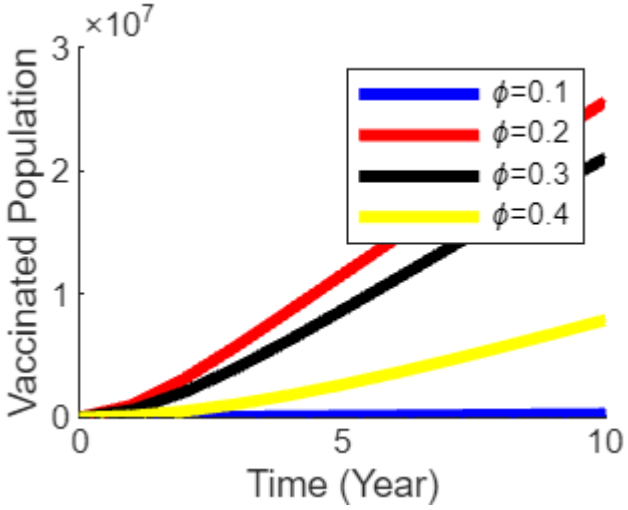


Figure 9. The effect of vaccine wanning on vaccinated individuals over time

Discussion

To investigate how TB spreads, we created a deterministic $SVEII_RRE$ model. Our model's findings show that the model was built correctly from an epidemiological and mathematical perspective, with positive and bounded solutions. We looked into, calculated, and assessed the equilibrium point's stability in addition to determining the basic reproduction number. Our findings show that when $R_0 < 1$ is formed, the equilibrium point where TB illness is absent is globally asymptotically stable. A bifurcation study was performed on the model using the Centre manifold theory, which revealed a backward bifurcation at $R_0 = 1$, this implies that when $R_0 < 1$, both a stable EE and a TB DFE co-exist. The occurrence of the model's backward bifurcation predicts that bringing down the basic reproduction number to less than one alone cannot lead to the extinction of the disease. The second phase of the analysis entailed assessing the sensitivity of the fundamental reproduction number's attributes. Positive sensitivity was observed for the transmission rate β, the modification parameters associated with drug-resistance individuals ρ, and the pace at which exposed people develop actively infectiousness κ, Rate of vaccine wanning ϕ, and Progression rate of actively infected individuals without drug resistance into actively infected with drug resistance class σ. The basic reproduction number will increase as these parameters are increased. Therefore, to eradicate TB, reducing the values of these parameters is necessary. On the other hand, the rate at which actively infectious individuals are recovered τ, the rates of natural mortality μ, TB disease-related deaths due to actively infections without resistance δ_1, the rate of drug-resistance δ_2, rate of vaccine inefficacy ε, vaccination coverage ω, Rate of progression of exposed into recovered compartment $\alpha$and the recovery rate of drug-resistance η exhibited negative sensitivity. The basic reproduction number will decrease if the values of these parameters are increased. In the third part of the analysis, the scaling factor of the transmission parameter was changed from 1.990 to 1.5. The corresponding results are presented in Figure 5. It is evident that when the transmission parameter values increase, the bifurcation diagram demonstrates backward bifurcation. When the value is equal to or less than 1.5, the model shows forward bifurcation, demonstrating that reducing the fundamental reproduction number to below one can eradicate the infection. However, between these values, eradicating the disease becomes impossible. In addition, the scaling factor of the reinfection parameter was modified from 0.85 to 0.00, and the outcomes are shown in Figure 6. These figures indicate that as the values of the reinfection parameter decrease, the bifurcation diagram exhibits a forward ward bifurcation.

From Figure 7(a), Due to the influx of new members into the society, we saw an exponential increase in the number of susceptible individuals. From Figure 7(b), we observed that the population of vaccinated individuals increased exponentially and later stabilize. Latently infected individuals rise gradually, as shown in Figure 7(c), failing treatment efficacy. From Figure 7(d), we observe that the population of actively infectious individuals without resistance increased exponentially and dropped drastically to a steady point because of treatment efficacy. In Figure 7(e), it was observed that the population of drug-resistant individuals increased exponentially and later decreased to some certain level because of treatment efficacy. Figure 7(f) shows that the population of recovered individuals also increased exponentially over time and later decreased slightly because both primary infectious individuals and individuals with drug resistance recovered as a result of proper treatment.

Table 2 shows the link between $R_{eff}, \beta, \psi, \sigma$ and ε, the effective reproduction numbers. The relationship between R_{eff} and the transmission rate β is shown to be linear in Figure 8(a–c). Figure 8a shows us that R_{eff} rises as β, ψ and σ. grow. This indicates that the rates of reinfection, transmission, and progression to treatment resistance classes all significantly contribute to the spread of tuberculosis infection. R_{eff} and ε connection is shown in Figure 8d. Figure 8d makes it very evident that R_{eff} rises as ε falls. From a biological perspective, this indicates that immunizations significantly influence the dynamics of tuberculosis disease, Figure 9. This indicates that the rates of vaccine wanning significantly contributes to the spread of tuberculosis infection

Conclusions

To obtain understanding of the dynamic behavior of an infection with tuberculosis, we constructed a deterministic numerical model and examined how treatment resistance and imperfect vaccination affect the dynamics of the spread of TB infections. By applying the next-generation matrix technique, the recommended system's effective reproduction number was discovered. The backward bifurcation phenomena were demonstrated to exist by the application of centre manifold theory in depth model research, in which a stable disease-free equilibrium coexists with a stable endemic equilibrium, with the restriction that $R_{eff} < 1$. With six mutually exclusive compartments that represent the dynamics

of tuberculosis, the proposed model demonstrated a disease-free equilibrium that was locally asymptotically stable, provided that a particular epidemiological threshold quantity, known as the effective reproduction number (R_{eff}), , was less than unity. There was a backward bifurcation in the model system (1), indicating that even while the basic epidemiological criteria of $R_{eff} < 1$ is met, the illness may still exist in the population and that effective control of tuberculosis (TB) spread is still necessary. An imperfect vaccination is predicted by the investigated $SVEII_RRE$ model to lessen the burden of disease and benefit the population's epidemiology, despite the fact that its overall impact increased as vaccination rates and efficacy increased. This is because it has been recognized that the use of an imperfect vaccine can occasionally have a negative impact on the population. To attain herd immunity, a fixed fraction of persons (η_4) was determined to get vaccinations at steady state. A population's tuberculosis can be efficiently controlled by utilizing an imperfect vaccine, as demonstrated by the system model's simulation (1). This occurs as a result of the vaccine's exceptionally high effectiveness. To summarize, this paper's main conclusions showed that the TB model, which took into account treatment resistance and an incomplete vaccination, showed signs of backward bifurcation. The findings of our investigation indicated that there are two ways to stop this occurrence. To prevent the hazardous range, it is first necessary to lower the effective reproductive number below the sub-threshold R_0 [R_0, 1]. Furthermore, it is recommended to raise the immunization rate within the specified range of values. The immunization rate is therefore very important. From the standpoint of disease prevention campaigns, public policymakers ought to take into account the subsequent two matters: First, make an effort to avoid the risky backward situation, in which illness endemicity may persist even in cases where the effective reproductive number (i.e., the classic threshold value) is smaller than unity. They might take action at this point by continuing to vaccinate susceptible people at a relatively modest rate. In this case, the TB model with an imperfect vaccination suggests that disease control can proceed along the conventional route of lowering the effective reproduction number (R_{eff}) to less than unity. If the reversible scenario cannot be avoided, then public policy makers ought to proceed with great caution, thus tuberculosis can become endemic even if its effective reproduction number remains below unity. The TB model indicated that the R_{eff} in this case needed to be lowered below the R_{eff} sub-threshold. If R_{eff} is lowered by the planning of educational initiatives that can affect public members' individual behaviors, which can operate to correctly limit disease contact and, consequently, future disease transmission, this goal can be accomplished. Future research can alter the model to include other dynamics that affect the transmission of tuberculosis infection. To reduce or completely eradicate tuberculosis infection, for example, some model assumptions can be loosened, or alternative strategies can be implemented. Assessments of cost-effectiveness, sensitivity, optimal control, and childhood vaccination can potentially yield additional insights into the dynamics of the TB model.

Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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