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Mathematical Analysis of a Tuberculosis model incorporating vaccination, treatment and re-infection

Abstract

Tuberculosis (TB) remains to be a major global health challenge with complex dynamics influenced by various factors including transmission, vaccination, treatment and re-infection. In this paper, we formulate and analyze a mathematical model of TB transmission that incorporates vaccination, treatment and re-infection. The equilibrium points exist. The basic reproduction number $\mathcal{R}_0$ of the model was established. Both local and global stability analyses of the equilibrium points were conducted. In contrast to the endemic equilibrium, which displays a local and global stable state anytime $\mathcal{R}_0 > 1$, the disease-free equilibrium is locally and globally stable when $\mathcal{R}_0 < 1$. The system undergoes a forward bifurcation when $\mathcal{R}_0 = 1$. The graphical solutions illustrated that incorporating vaccination, treatment and re-infection in a TB transmission model is pivotal in determining the correct thresholds for controlling and finally curbing this disease in the population.

Keywords: Tuberculosis, Stability analysis, Bifurcation analysis

2010 Mathematics Subject Classification: 53C25; 83C05; 57N16

1 Introduction

The bacteria *Mycobacterium tuberculosis* is the cause of the infectious illness tuberculosis (TB). Although the lungs are the main organ affected, other organs such as the kidneys, brain, spine, and skin may also be impacted. TB bacteria can live in the body without showing symptoms and this can be referred to as latent TB infection.Latent TB patients can get ill with active TB at any time (3; 6). A severe cough, chest pain, coughing up blood, exhaustion, weight loss, lack of appetite, chills, and fever are all signs of active tuberculosis. People who are exposed or have a close physical proximity to those with TB disease have a higher risk of developing active TB disease once infected. TB infection and spread can be prevented through screening those at high risk, early detection and treatment of TB cases and vaccination with the Bacillus Calmette-Guerin (BCG) vaccine (8). TB is usually treated with antibiotics such as isoniazid, rifampin, pyrazinamide, ethambutol and streptomycin.(7).

TB continues to be the world's biggest cause of death, especially in low- and middle-income nations (9). In 2023, an estimated 10.8 million people worldwide contracted tuberculosis (TB) (6), which led to an estimated 1.25 million fatalities, including 167 000 HIV-positive individuals (7). Several mathematical models have been developed in order to address this issue. Oshinubi *et al* (12) formulated a mathematical modelling of TB Outbreak in East African Country (Rwanda and Burundi) incorporating Vaccination and Treatment. According to the model study, the prevalence and impact of tuberculosis on the human population can be decreased by expanding access to vaccine and, in particular, treatment for those who are afflicted.

Ojo *et al* (10) developed a mathematical model for control of tuberculosis epidemiology. The analysis of the model imply that the disease-free equilibrium is locally asymptotically stable whenever the basic reproduction number $\mathcal{R}_0 < 1$. Additionally, the endemic equilibrium's stability was investigated, and the prerequisites for backward bifurcation's existence were determined. The findings indicate that the burden of tuberculosis in the population can be decreased by decreasing effective contact with an infected individual and increasing the vaccination rate of susceptible persons with high vaccine efficacy. Despite the efforts of these research studies, TB has continued to persist in the human population. Therefore, a mathematical analysis on the TB transmission incorporating vaccination, treatment and re-infection is relevant to effectively manage and combat this disease.

The subsequent sections of this paper are organized as follows; the model is formulated in section 2. It is analysed in section 3 where the equilibrium points are evaluated, the basic reproduction number is derived, the stability analyses are conducted and the bifurcation analysis is also demonstrated. The model is verified and validated numerically in section 4. Finally, the study concludes by discussing the results and giving recommendations based on its findings.

2 Model Formulation

The Susceptible (S(t), Vaccinated (V(t), Exposed (E(t), Infectious (I(t), Treated (T(t) and Recovered individuals (R(t)) comprise the compartments into which the model divides the human population N(t). $N(t) = S(t) + V(t) + E(t) + I(t) + T(t) + R(t)$ is the formula for the entire population.
The study based on the following assumptions;

(i) The population is homogeneous as all individuals have an equal probability of coming into contact with infectious individuals and being vaccinated or treated.

(ii) There is partial immunity as vaccination results to a lower but non-zero risk of developing Tuberculosis.

The recruiting rate, which is presumed to be by birth, is Λ. The symbol representing the force of infection is βSI. Through interaction with infectious TB class, the immunized individuals can contract the disease at a rate of $(1-\alpha)$; hence, the infection force for protected individuals is $\beta(1-\alpha)VI$. The vaccination rate is determined by the parameter ρ, while the vaccination wane rate is represented by η. All of the compartments have the natural death rate μ. The movement of exposed individuals into infecious class is at the rate τ. Meanwhile, the disease-induced death rate is ϵ whereas ϕ represents the treatment rate. The movement rate from the treated class is represented by ω and γ represents the treatment failure rate. The rate $\gamma\ \omega$ is assumed to be the proportion of treated individuals moving into infectious TB class and the rest $(1-\gamma)\omega$, those who moved to exposed TB compartment due to the treatment failure. Parameter ν represents the recovery rate of treated individuals. The rate of re-infection is given as θ. The dynamics described above can be represented by the following system

of ordinary differential equations ;

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda + \eta V - \beta SI - (\rho + \mu - \theta)S, \\
\frac{dV}{dt} &= \rho S - \beta(1-\alpha)VI - (\eta + \mu)V, \\
\frac{dE}{dt} &= \beta SI + \beta(1-\alpha)VI + (1-\gamma)\omega T - (\tau + \mu)E, \\
\frac{dI}{dt} &= \tau E + \gamma\omega T - (\mu + \epsilon + \phi)I, \\
\frac{dT}{dt} &= \phi I - (\mu + \nu + \omega)T, \\
\frac{dR}{dt} &= \nu T - (\mu + \theta)R. \qquad (2.1)
\end{aligned}$$

2.1 Invariant region

Theorem 2.1. (Boundness) All solutions of the system of equations (2.1) will lie in the region Γ = [(S, V, E, I, T, R) $\in \mathbb{R}^6_+$: 0 $\leq$ S+V+E+I+T+R $\leq \frac{\Lambda}{\mu}$] for all positive values S(o), V(o), E(o), I(o), T(o), R(o) $\in \mathbb{R}^6_+$

Proof. Consider N(t) = [(S(t), V(t), E(t), I(t), T(t), R(t)) $\in \mathbb{R}^6_+$: 0$\leq$ S + V + E + I + T + R $\leq \frac{\Lambda}{\mu}$]
Now, taking the time derivative of N.
$\frac{dN}{dt}$ = Λ - μ[S + V + E + I + T + R]

$$\frac{dN}{dt} = \Lambda - \mu N$$
$$\frac{dN}{dt} \leq \Lambda - \mu N$$

$$\frac{dN}{dt} + \mu N \leq \Lambda \qquad (2.2)$$

Integrating equation (2.2) by the integrating factor then;

$$N(t) \leq \frac{\Lambda}{\mu} + Ce^{-\mu t} \qquad (2.3)$$

At t = 0, N(0) - $\frac{\Lambda}{\mu}$ = C
It follows that;

$$N \leq \frac{\Lambda}{\mu} + \Big[N(0) - \frac{\Lambda}{\mu}\Big]e^{-\mu t} \qquad (2.4)$$

Thus, as t $\to \infty$;

$$\lim_{t\to\infty} N \leq \frac{\Lambda}{\mu}$$

$$0 \leq N(t) \leq \frac{\Lambda}{\mu} \qquad (2.5)$$

The population is bounded for t $\geq$ 0 as it can't grow beyond $\frac{\Lambda}{\mu}$.
Thus, all the solutions of the system of equations (2.1) enter and remain in the region Γ □

Theorem 2.2. All solutions [(S, V, E, I, T, R)] of the system of equations (2.1) starting in $(S_o, V_o, E_o, I_o, T_o, R_o)$ $\in \mathbb{R}^6_+$ remain positive $\forall$ t $>$ 0 in the feasible region Γ

Proof. From the system of equations (2.1), picking on S(t), then

$$\frac{dS}{dt} = \Lambda + \eta V - (\beta I + \rho + \mu - \theta)S. \tag{2.6}$$

Separating the variables;

$$\frac{dS}{S} \geq -(\beta I + \rho + \mu - \theta)dt \tag{2.7}$$

Integrating equation (2.7) gives;

$$\ln S(t) \geq -(\beta I + \rho + \mu - \theta)t + \ln C. \tag{2.8}$$

At t = 0; $\ln$ S(0) = $\ln$ C $\Rightarrow$ S(0) = C
Thus, $\ln$ S(t) $\geq$ -($\beta I + \rho + \mu - \theta$)t + $\ln$ S(0)
Which can be simplified as;

$$S(t) \geq S(0)e^{-(\beta I+\rho+\mu-\theta)t} \tag{2.9}$$

Thus, S(t) $\geq$ 0 $\forall$ t $\geq$ 0.
Performing the similar process to the other equations of system (2.1), then;

$$\begin{aligned} V(t) &\geq V(0)e^{-(\beta(1-\alpha)I+\eta+\mu))t} \\ E(t) &\geq E(0)e^{-(\mu+\tau)t} \\ I(t) &\geq I(0)e^{-(\mu+\epsilon+\phi)t} \\ T(t) &\geq T(0)e^{-(\mu+\nu+\omega)t} \\ R(t) &\geq R(0)e^{-(\mu+\theta)t} \end{aligned}$$

Therefore, all the solutions of the systen of equations (2.1) remained postive in the feasible bounded region Γ □

3 Model Analysis

3.1 Disease-Free Equilibrium point

The Disease-free equilibrium point denoted as E^o is defined as a steady-state solution for which there is no disease or infection in the population (11). To obtain the disease-free equilibrium point, the system of equations (2.1) is equated to zero and seek for solution of S, V, E, I, T, R. The variables E, I, T and R are set to zero since there are no infections and then obtain E^o of the model of the system of equations (2.1) as;
E^o = S(t)^o, V(t)^o, E(t)^o, I(t)^o, T(t)^o, R(t)^o =($\frac{(\eta+\mu)\Lambda}{(\rho+\mu-\theta)(\eta+\mu)-\eta\rho}$, $\frac{\rho\Lambda}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho}$,0, 0, 0, 0)

3.2 Endemic Equilibrium point

Endemic equilibrium denoted as E^* can be defined as a steady-state solution for which there exist a constant occurrence of diseases within the population (11). To obtain the endemic equilibrium point, system of equations (2.1) is equated to zero and its solutions obtained. The solutions are denoted by

E* and are given as follows;

$$\begin{aligned} S(t)^* &= \frac{(\beta(1-\alpha)I^*+\eta+\mu)}{\rho}\cdot\frac{\rho\Lambda}{(\beta(1-\alpha)I^*+\mu)(\beta I^*+\rho+\mu-\theta)-\rho\eta)}, \\ V(t)^* &= \frac{\rho\Lambda}{(\beta(1-\alpha)I^*+\eta+\mu)(\beta I^*+\rho+\mu-\theta)-\rho\eta)}, \\ E(t)^* &= \frac{1}{\tau}\left(\mu+\epsilon+\Phi-\frac{\gamma\omega\Phi}{\mu+\nu+\omega}\right)I^*, \\ T(t)^* &= \frac{\Phi}{\mu+\nu+\omega}I^*, \\ R(t)^* &= \frac{\nu\Phi}{(\mu+\theta)(\mu+\nu+\omega)}I^*. \end{aligned} \tag{3.1}$$

3.3 The basic reproduction number

The basic reproduction number denoted as $\mathcal{R}_0$ is defined as the number of secondary infections produced by one primary case in a completely susceptible population during his or her entire infectious period (4). The disease's persistence or extinction in the population is determined by this threshold value. The method of the next generation matrix approach described in Van (13) was used to determine the $\mathcal{R}_0$.
From the system of equations (2.1), the associated matrices are;

$$f = \begin{bmatrix} \beta SI+\beta(1-\alpha)VI \\ 0 \end{bmatrix} \tag{3.2}$$

and

$$v = \begin{bmatrix} (\tau+\mu)E \\ -\tau E+(\mu+\epsilon+\phi)I \end{bmatrix} \tag{3.3}$$

Differentiating f and v with respect to E and I respectively, then;

$$F = \begin{bmatrix} 0 & \beta S^0+\beta(1-\alpha)V^0 \\ 0 & 0 \end{bmatrix} \tag{3.4}$$

and

$$V = \begin{bmatrix} \tau+\mu & 0 \\ -\tau & \mu+\epsilon+\phi \end{bmatrix} \tag{3.5}$$

Substituting the values of S^o and V^o respectively into the matrix of F;

$$F = \begin{bmatrix} 0 & \beta\frac{(\eta+\mu)\Lambda}{(\rho+\mu-\theta)(\eta+\mu)-\eta\rho}+\beta(1-\alpha)\frac{\rho\Lambda}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho} \\ 0 & 0 \end{bmatrix} \tag{3.6}$$

The inverse of V was computed and obtained as follows;

$$V^{-1} = \begin{bmatrix} \frac{1}{\tau+\mu} & 0 \\ \frac{\tau}{(\tau+\mu)(\mu+\epsilon+\phi)} & \frac{1}{\mu+\epsilon+\phi} \end{bmatrix} \tag{3.7}$$

Hence,

$$FV^{-1} = \frac{1}{\mu+\epsilon+\phi}\begin{bmatrix} \frac{\Lambda\beta\tau((\eta+\mu)+(1-\alpha)\rho)}{(\rho+\mu-\theta)(\eta+\mu)-\eta\rho} & \frac{\Lambda\beta((\eta+\mu)+(1-\alpha)\rho)}{((\rho+\mu-\theta)(\eta+\mu)-\eta\rho)(\tau+\mu)} \\ 0 & 0 \end{bmatrix} \tag{3.8}$$

$\mathcal{R}_0$ = $\rho(M)$, is the spectral radius of the matrix FV^{-1}
Therefore,

$$\mathcal{R}_0 = \frac{\Lambda\beta\tau((\eta+\mu)+(1-\alpha)\rho)}{((\rho+\mu-\theta)(\eta+\mu)-\eta\rho)(\mu+\epsilon+\phi)} \tag{3.9}$$

3.4 Local Stability of the Disease-Free Equilibrium (DFE)

The equilibrium point's stability is correlated with the model's basic reproduction number $\mathcal{R}_0$.

Theorem 3.1. The disease-free equilibrium point E^o = ($\frac{(\eta+\mu)\Lambda}{(\rho+\mu-\theta)(\eta+\mu)-\eta\rho}$, $\frac{\rho\Lambda}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho}$,0, 0, 0, 0) of the system of equations (2.1) is locally asymptotically stable when $\mathcal{R}_0 < 1$ and unstable when $\mathcal{R}_0 > 1$ for any t $\geq$ 0

Proof. The Jacobian matrix of the system of equations (2.1) was given by;

$$J = \begin{bmatrix} -\beta I^0 - d & \eta & 0 & -\beta S^0 & 0 & 0 \\ \rho & -\psi I^0 - (\eta+\mu) & 0 & -\psi V^0 & 0 & 0 \\ \beta I & \psi I^0 & -(\tau+\mu) & \beta S^0 + \psi V^0 & \delta\omega & 0 \\ 0 & 0 & \tau & -(\mu+\epsilon+\phi) & \gamma\omega & 0 \\ 0 & 0 & 0 & \phi & -(\mu+\nu+\omega) & 0 \\ 0 & 0 & 0 & 0 & \nu & -e \end{bmatrix} \tag{3.10}$$

where d = ($\rho+\mu-\theta$), e = ($\mu+\theta$), $\beta(1-\alpha)=\psi$ and $(1-\gamma)$ = δ
Analyzing matrix (3.10) at the DFE, E^o [S(t)^o, V(t)^o, E(t)^o, I(t)^o, T(t)^o, R(t)^o] = ($\frac{(\eta+\mu)\Lambda}{(\rho+\mu-\theta)(\eta+\mu)-\eta\rho}$, $\frac{\rho\Lambda}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho}$,0, 0, 0, 0) then

$$J_{DFE} = \begin{bmatrix} -d & \eta & 0 & -\beta\frac{(\eta+\mu)\Lambda}{(\rho+\mu-\theta)(\eta+\mu)-\eta\rho} & 0 & 0 \\ \rho & -(\eta+\mu) & 0 & -\psi\frac{\rho\Lambda}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho} & 0 & 0 \\ 0 & 0 & -(\tau+\mu) & \frac{\beta((\eta+\mu)\Lambda))+\psi(\rho\Lambda)}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho} & \delta\omega & 0 \\ 0 & 0 & \tau & -(\mu+\epsilon+\phi) & \gamma\omega & 0 \\ 0 & 0 & 0 & \phi & -(\mu+\nu+\omega) & 0 \\ 0 & 0 & 0 & 0 & \nu & -e \end{bmatrix} \tag{3.11}$$

where d = ($\rho+\mu-\theta$), e = ($\mu+\theta$), $\beta(1-\alpha)$ = ψ and $(1-\gamma)$ = δ
Splitting the J_{DFE} since the matrix is block lower-triangular, its eigenvalues are the union of the eigenvalues of three main diagonal blocks, then the reduced matrices are analysed as follows;

(i) The uninfected subsystem block (S,V): a 2×2 matrix whose eigenvalues are computed as follows;

$$A_u = \begin{bmatrix} -d & \eta \\ \rho & -(\eta+\mu) \end{bmatrix} \tag{3.12}$$

The characteristic equation of matrix (3.12) is obtained by finding its determinant as follows;

$$\begin{vmatrix} -d-\lambda & \eta \\ \rho & -(\eta+\mu)-\lambda \end{vmatrix} = 0 \tag{3.13}$$

The polynomial can be given as

$$\lambda^2 + (d+\eta+\mu)\lambda + d(\eta+\mu) - \eta\rho = 0.$$

All eigenvalues are negative if and only if $d(\eta+\mu) > \eta\rho$ as shown;

$$\lambda = \frac{-(d+\eta+\mu) \pm \sqrt{(d+\eta+\mu)^2 - 4[d(\eta+\mu)-\eta\rho]}}{2} \tag{3.14}$$

(ii) The recovered compartment R
Consider;

$$\dot{R} = -eR,$$

hence the eigenvalue is

$$\lambda = -e < 0$$

(iii) The Infected subsystem (E, I, T)
The critical block governing infection dynamics is;

$$A_i = \begin{bmatrix} -(\tau+\mu) & \frac{\beta((\eta+\mu)\Lambda))+\psi(\rho\Lambda)}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho} & \delta\omega \\ \tau & -(\mu+\epsilon+\phi) & \gamma\omega \\ 0 & \phi & -(\mu+\nu+\omega) \end{bmatrix} \tag{3.15}$$

Matrix (3.15) yields:

$$tr(A_i) = -\big[\tau + 3\mu + \epsilon + \phi + \nu + \omega\big]. \tag{3.16}$$

which is negative.

$$\begin{aligned} det(A_i) = \big[-(\tau+\mu)\big]\Big[(-(\mu+\epsilon+\phi)(-(\mu+\nu+\omega) - \phi\gamma\omega\Big] - \\ \frac{\beta((\eta+\mu)\Lambda)) + \psi(\rho\Lambda)}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho} \cdot \tau\Big[-(\mu+\nu+\omega)\Big] + \delta\omega\tau\phi = 0 \end{aligned} \tag{3.17}$$

which is positive if

$$\begin{aligned} \Big[\delta\omega\tau\phi + \Big(\frac{\beta((\eta+\mu)\Lambda)) + \psi(\rho\Lambda)}{(\eta+\mu-\theta)(\eta+\mu)-\eta\rho}\Big) \cdot \tau(\mu+\nu+\omega)\Big] > \\ (\tau+\mu)\Big[(\mu+\epsilon+\phi)(\mu+\nu+\omega) - \phi\gamma\omega\Big] \end{aligned} \tag{3.18}$$

Therefore; for $\mathcal{R}_0 < 1$, All eigenvalues are negative implying that the DFE is locally asymptotically stable and unstable otherwise. □

3.5 Local Stability of the Endemic Equilibrium point

Theorem 3.2. The Endemic Equilibrium point E^* of the system of equations (2.1) is locally asymptotically stable whenever $\mathcal{R}_0 > 1$

Proof. The jaobian matrix of the system of equations (2.1) at the endemic equilibrium point E* = ($\frac{(\beta(1-\alpha)I^*+\eta+\mu)}{\rho}.\frac{\rho\Lambda}{(\beta(1-\alpha)I^*+\mu)(\beta I^*+\rho+\mu-\theta)-\rho\eta}$, $\frac{\rho\Lambda}{(\beta(1-\alpha)I^*+\eta+\mu)(\beta I^*+\rho+\mu-\theta)-\rho\eta}$, $\frac{1}{\tau}\left(\mu+\epsilon+\Phi-\frac{\gamma\omega\Phi}{\mu+\gamma+\omega}\right)I^*$, $\frac{\Phi}{\mu+\gamma+\omega}I^*$, $\frac{\nu\Phi}{(\mu+\theta)(\mu+\gamma+\omega}I^*$) was given by;

$$J_{EE}=\begin{bmatrix} -\beta I^*-d & \eta & 0 & -\beta S^* & 0 & 0 \\ \rho & -\psi I^*-g & 0 & -\psi V^* & 0 & 0 \\ \beta I^* & \psi I^* & -(\tau+\mu) & \beta S^*+\psi V^* & \delta\omega & 0 \\ 0 & 0 & \tau & -(\mu+\epsilon+\phi) & \gamma\omega & 0 \\ 0 & 0 & 0 & \phi & -(\mu+\nu+\omega) & 0 \\ 0 & 0 & 0 & 0 & \nu & -e \end{bmatrix} \tag{3.19}$$

where d = $(\rho+\mu-\theta)$, e = $(\mu+\theta)$, g = $(\eta+\mu)$, $\beta(1-\alpha)=\psi$ and $(1-\gamma)=\delta$
Since J_{EE} is block lower-triangular, two eigenvalues are directly obtained from the bottom-right 2×2 block:

$$\lambda_5=-(\mu+\nu+\omega), \qquad \lambda_6=-(\mu+\theta),$$

which are always negative for positive parameter values.
The stability of E^* thus depends only on the eigenvalues of the 4×4 subsystem.
Let

$$A=\begin{bmatrix} -\beta I^*-d & \eta & 0 & -\beta S^* \\ \rho & -\beta(1-\alpha)I^*-(\eta+\mu) & 0 & -\beta(1-\alpha)V^* \\ \beta I^* & \beta(1-\alpha)I^* & -(\tau+\mu) & \beta S^*+\beta(1-\alpha)V^* \\ 0 & 0 & \tau & -e \end{bmatrix} \tag{3.20}$$

From matrix (3.20)
$\mathrm{trace}(A)$

$$=-(\beta I^*+\rho+\mu-\theta)+-(\beta(1-\alpha)I^*+\eta+\mu)+-(\tau+\mu)+-(\mu+\epsilon+\phi) \tag{3.21}$$

$$=-[4\mu+\rho+\eta+\tau+\epsilon+\phi-\theta+\beta I^*(2-\alpha)] \tag{3.22}$$

The determinant of A can be computed as follows;

$$A \quad =(\mu+\epsilon+\phi)\det\begin{bmatrix} \beta I^*+\rho+\mu-\theta & -\eta & 0 \\ -\rho & \beta(1-\alpha)I^*+\eta+\mu & 0 \\ -\beta I^* & -\beta(1-\alpha)I^* & \tau+\mu \end{bmatrix}$$

$$+\tau\det\begin{bmatrix} \beta I^*+\rho+\mu-\theta & -\eta & \beta S^* \\ -\rho & \beta(1-\alpha)I^*+\eta+\mu & \beta(1-\alpha)V^* \\ -\beta I^* & -\beta(1-\alpha)I^* & -(\beta S^*+\beta(1-\alpha)V^*) \end{bmatrix} \tag{3.23}$$

Hence, the determinant of A can be given as

$$\begin{aligned} det(A)=(\mu+\epsilon+\phi)(\tau+\mu)\Big[&\beta^2(1-\alpha)I^{*2}+\beta I^* \\ &(\eta+\mu)+(\rho+\mu-\theta)\beta(1-\alpha)I*+(\rho+\mu-\theta)(\eta+\mu)-\eta\rho\Big] \\ -\tau\Big[&(\beta I^*+\rho+\mu-\theta)(\beta(1-\alpha)I^*+\eta+\mu)(\beta S^*+\beta(1-\alpha)V^*) \\ &-(\beta I^*+\rho+\mu-\theta)\beta^2(1-\alpha)^2I^*V^*-\eta\rho(\beta S^*+\beta(1-\alpha)V^* \\ &-\eta\beta^2(1-\alpha)I^*V^*-\rho\beta^2(1-\alpha)I^*S^*-\beta^2I^*S^*(\beta(1-\alpha)I^*+\eta+\mu)\Big]. \end{aligned} \tag{3.24}$$

From expression (3.24):

$$det(A) > 0$$

Provided that

$$(\mu + \epsilon + \phi)(\tau + \mu)\Omega > \tau\kappa$$

where

$$\Omega = \beta^2(1-\alpha)I^{*2} + \beta I^*(\eta + \mu) + (\rho + \mu - \theta)\beta(1-\alpha)I * +(\rho + \mu - \theta)(\eta + \mu) - \eta\rho.$$

and

$$\begin{aligned}\kappa = (\beta I^* + \rho + \mu - \theta)(\beta(1-\alpha)I^* + \eta + \mu)(\beta S^* + \beta(1-\alpha)V^*) \\ -(\beta I^* + \rho + \mu - \theta)\beta^2(1-\alpha)^2 I^* V^* - \eta\rho(\beta S^* + \beta(1-\alpha)V^* \\ -\eta\beta^2(1-\alpha)I^* V^* - \rho\beta^2(1-\alpha)I^* S^* - \beta^2 I^* S^*(\beta(1-\alpha)I^* + \eta + \mu)\end{aligned}$$

E* is locally asymptotically stable for the specified parameter values as confirmed by the fact that all eigenvalues have negative real portions. When $\mathcal{R}_0 > 1$, the Endemic Equilibrium is present and locally asymptotically stable. This suggests that the system will eventually return to the endemic equilibrium after small perturbations around the endemic state fade. □

3.6 Global Stability Analysis of the Disease-Free Equilibrium

The technicque by Castillo *et al* (2) is used to analyse the global stability.

Theorem 3.3. The DFE is globally asymptotically stable in the feasible region Γ whenever $\mathcal{R}_0 < 1$.

Proof. The model is partitioned as:

$$\frac{dX}{dt} = F(X, 0), \quad \frac{dY}{dt} = B(X, Y).$$

3.6.1 Dynamics of uninfected subsystem:

when Y = 0, the subsystem

$$\frac{dX}{dt} = F(X, 0)$$

$$\begin{aligned}\frac{dS}{dt} &= \Lambda + \eta V - (\rho + \mu - \theta)S, \\ \frac{dV}{dt} &= \rho S - (\eta + \mu)V, \\ \frac{dR}{dt} &= -(\mu + \theta)R. \end{aligned} \tag{3.25}$$

The system is linear, with recruitment, vaccination, loss of immunity and natural death terms only. This system can be written in matrix form as:

$$\frac{dX}{dt} = AX + b$$

$$A = \begin{bmatrix} -d & \eta & 0 \\ \rho & -(\eta + \mu) & 0 \\ 0 & 0 & -e \end{bmatrix} \tag{3.26}$$

and

$$b = \begin{bmatrix} \Lambda \\ 0 \\ 0 \end{bmatrix} \tag{3.27}$$

where d = $\rho + \mu - \theta$ and e = $\mu + \theta$. At equilibrium, setting:

$$0 = AX_0 + b.$$

This yields the following system of equations:

$$\begin{aligned} -dS_0 + \eta V_0 + \Lambda &= 0, \\ \rho S_0 - (\eta + \mu)V_0 &= 0, \\ -eR_0 &= 0. \end{aligned} \tag{3.28}$$

Based on the system of equations' third equation (3.28), it follows that:

$$R_0 = 0. \tag{3.29}$$

From the second equation in the system of equations (3.28), solving for V_0 gives:

$$V_0 = \frac{\rho}{\eta + \mu} S_0. \tag{3.30}$$

Substituting equation (3.30) into the first equation in the system of equations (3.28) yields:

$$-dS_0 + \eta \left(\frac{\rho}{\eta + \mu} S_0 \right) + \Lambda = 0.$$

Thus:

$$S_0 = \frac{\Lambda(\eta + \mu)}{(\rho + \mu - \theta)(\eta + \mu) - \eta\rho}. \tag{3.31}$$

Finally, substituting back for V_0:

$$V_0 = \frac{\rho}{\eta + \mu} S_0 = \frac{\rho\Lambda}{(\rho + \mu - \theta)(\eta + \mu) - \eta\rho}. \tag{3.32}$$

Therefore, the unique steady state are in equations (3.29), (3.31) and (3.32) respectively. Since matrix A is triangular with strictly negative diagonal entries $-(\rho + \mu - \theta)$, $-(\eta + \mu)$, and $-(\mu + \theta)$, all its eigenvalues have negative real parts. Consequently, any solution of the uninfected subsystem converges to this unique disease-free equilibrium, proving global asymptotic stability of the uninfected subsystem in absence of infection. Therefore, the subsystem admits a unique global asmptotic stable steady state.

3.6.2 Dynamics of Infected subsystem:

The infected subsystem can be written as:

$$\frac{dY}{dt} = AY - B(X, Y),$$

Where A is an M- matrix with nonnegative off-diagonal elements.

$$\begin{aligned} \frac{dE}{dt} &= \beta SI + \psi VI + \delta\omega T - (\tau + \mu)E, \\ \frac{dI}{dt} &= \tau E + \gamma\omega T - (\mu + \epsilon + \phi)I, \\ \frac{dT}{dt} &= \varphi I - (\mu + \nu + \omega)T. \end{aligned} \tag{3.33}$$

Writing the system of equations (3.33) in matrix form;

$$A = \begin{bmatrix} -(\tau+\mu) & 0 & \delta\omega \\ \tau & -(\mu+\epsilon+\phi) & \gamma\omega \\ 0 & \varphi & -(\mu+\gamma+\omega) \end{bmatrix} \tag{3.34}$$

and

$$B(X,Y) = \begin{bmatrix} (\beta SI + \psi VI) \\ 0 \\ 0 \end{bmatrix} \tag{3.35}$$

Matrix A describes the linear transitions among infected compartments and has negative diagonal entries:

$$-(\tau+\mu), \quad -(\mu+\epsilon+\varphi), \quad -(\mu+\gamma+\omega).$$

These ensures that in absence of new infections, any perturbation decays exponentially to zero.
Observe that $B(X,Y)$ is nonnegative $\forall\, Y \geq 0$.
With $\psi = \beta(1-\alpha)$, and $0 \leq \alpha < 1$, this implies that $0 \leq \psi \leq \beta$.

$$b_1 = \beta SI + \psi VI.$$

Since $\beta > 0$, $S \geq 0$, $V \geq 0$, $I \geq 0$, and $\psi \geq 0$, each term satisfies:

$$\beta SI \geq 0, \quad \psi VI \geq 0.$$

Therefore:

$$b_1 \geq 0.$$

$$b_2 = 0, b_3 = 0.$$

Clearly nonnegative. Thus, $\forall Y \geq 0$:

$$B(X,Y) \geq 0.$$

Next $B(X,0) = 0$ for $Y = 0$.

$$B(X,Y) = \begin{bmatrix} (\beta SI + \psi VI) \\ 0 \\ 0 \end{bmatrix} \tag{3.36}$$

If $Y = 0$, then in particular:

$$I = 0.$$

$$b_1 = \beta S \cdot 0 + \psi V \cdot 0 = 0.$$

$$b_2 = 0.$$

and

$$b_3 = 0.$$

$$B(X,Y) = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix} \tag{3.37}$$

This confirms that in absence of infection, no new infections are generated.
Since $B(X,Y)$ is nonnegative and vanishes when $Y = 0$, the unforced dynamics always decay:

$$\frac{dY}{dt} \leq AY.$$

Consequently, the linear part A is stable and the system has no endemic equilibrium in the infected subsystem when $\mathcal{R}_0 < 1$.
By comparison theorem and standard arguments in monotone dynamical systems as outlined in (1) this implies:

$$\lim_{t\to\infty} Y(t) = 0.$$

Indeed, the spectral radius of the next-generation matrix satisfies:

$$\rho(FV^{-1}) = \mathcal{R}_0 < 1.$$

Therefore, any initial infection will eventually vanish, and the infected subsystem converges to the disease-free state when $\mathcal{R}_0 < 1$.
Thus, the DFE is globally asymptotically stable in the feasible region Γ whenever $\mathcal{R}_0 < 1$. □

3.7 Global Stability Analysis of the Endemic Equilibrium

Theorem 3.4. The endemic equilibrium point is globally asymptotically stable in the feasible region Γ whenever $\mathcal{R}_0 > 1$.

Proof. The model is partitioned as:

$$\frac{dX}{dt} = F(X,Y), \quad \frac{dY}{dt} = G(X,Y).$$

3.7.1 Global stability of the uninfected subsystem (C1)

Setting $E = I = T = 0)$, the uninfected subsystem becomes;

$$\begin{aligned} \frac{dS}{dt} &= \Lambda + \eta V - (\rho + \mu - \theta)S, \\ \frac{dV}{dt} &= \rho S - (\eta + \mu)V, \\ \frac{dR}{dt} &= 0. \end{aligned} \tag{3.38}$$

Analyzing the subsystem of equations (3.38) at (S, V) as

$$\begin{aligned} \frac{dS}{dt} &= \Lambda + \eta V - \kappa S, \\ \frac{dV}{dt} &= \rho S - \lambda V. \end{aligned} \tag{3.39}$$

where $\kappa = \rho + \mu - \theta$ and $\lambda = \eta + \mu$.
Setting the derivatives in system (3.39) to zero:

$$\begin{aligned} 0 &= \Lambda + \eta V - \kappa S, \\ 0 &= \rho S - \lambda V. \end{aligned} \tag{3.40}$$

Since $\frac{dR}{dt} = 0$ in absence of infection, R remains constant.
Solving for the steady state:

$$\begin{aligned} V^* &= \frac{\rho}{\lambda} S^*, \\ S^* &= \frac{\Lambda}{\kappa - \frac{\eta\rho}{\lambda}}. \end{aligned} \tag{3.41}$$

Provided that $\kappa > \frac{\eta\rho}{\lambda}$
The Jacobian matrix is:

$$\begin{bmatrix} -\kappa & \eta \\ \rho & -\lambda \end{bmatrix} \tag{3.42}$$

with the characteristic equation:

$$\lambda^2 + (\kappa + \lambda)\lambda + (\kappa\lambda - \eta\rho) = 0.$$

The roots have negative real parts if:

$$\text{Tr}(J) = -\kappa - \lambda < 0, \quad \det(J) = \kappa\lambda - \eta\rho > 0.$$

As a result, the system is linear and bounded, thus the equilibrium (S^*, V^*) is locally asymptotically stable. Therefore, this equilibrium is also globally asymptotially stable in the domain Γ.

3.7.2 Global stability of the infected subsystem (C2)

The infected subsystem is:

$$\begin{aligned} \frac{dE}{dt} &= \beta SI + \psi VI + \delta\omega T - (\tau + \mu)E, \\ \frac{dI}{dt} &= \tau E + \gamma\omega T - (\mu + \epsilon + \phi)I, \\ \frac{dT}{dt} &= \varphi I - (\mu + \nu + \omega)T. \end{aligned} \tag{3.43}$$

Define:

$$\hat{G}(X, Y) = G(X, Y) - G(X, 0).$$

Jacobian of $\hat{G}(X, Y)$ with respect to $Y = (E, I, T)$ is:

$$\begin{bmatrix} -(\tau + \mu) & \beta S + \psi V & \delta\omega \\ \tau & -(\mu + \epsilon + \phi) & \gamma\omega \\ 0 & \varphi & -(\mu + \gamma + \omega) \end{bmatrix} \tag{3.44}$$

From matrix (3.44) it's observed that the off-diagonal entries are all non-negative. Hence, matrix (3.44) can be termed as a metzler matrix.
System (3.43) is irreducible as by examining the flow of influence among E, I, T, the interaction graph contains the cycle

$$E \to I \to T \to E,$$

and also the direct edge $T \to I$. Finally, system (3.43) is verified to be cooperative as the elements in the off-digonal position are clearly positive. Since conditions (C1) and (C2) are satisfied, then the endemic equilibrium

$$E^* = (S^*, V^*, E^*, I^*, T^*, R^*)$$

of the tuberculosis model is globally asymptotically stable in the feasible region Γ. □

3.8 Bifurcation Analysis

In bifurcation analysis, the infected equations are split into a linear term and a nonlinear remainder. Thereby, applying the Center Manifold Theorem, the infected subsystem;

$\frac{dY}{dt}$ = AY + f(Y,β)
Near the DFE, the dominant infected subsystem is:

$$\begin{aligned}\frac{dE}{dt} &= \beta SI + \psi V I + \delta\omega T - (\tau+\mu)E \\ \frac{dI}{dt} &= \tau E - (\mu+\epsilon+\phi)I + \gamma\omega T \\ \frac{dT}{dt} &= \phi I - (\mu+\nu+\omega)T. \end{aligned} \tag{3.45}$$

$$A = \begin{bmatrix} -(\tau+\mu) & F & \delta\omega \\ \tau & -(\mu+\epsilon+\phi) & \gamma\omega \\ 0 & \phi & -(\mu+\nu+\omega) \end{bmatrix} \tag{3.46}$$

where F = $\beta\ S_0$ + $\psi\ V_0$. From the model, f_1 = $[\beta(S-S_0)+\psi(V-V_0)]I$ and f_2 = f_3 = 0 Therefore,

$$a = \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_1}{\partial y_i \partial y_j}(0,0), \quad b = \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_1}{\partial y_i \partial \beta}(0,0),$$

Hence

$$a = v_1 w_I w_I \frac{\partial^2 f_1}{\partial I^2} = v_1 w_2 w_2(-2\beta c) \quad b = v_1 w_I \frac{\partial^2 f_1}{\partial I \partial \beta} = v_1 w_2 S_0$$

Computing:

$$a = -2\beta c v_1 w_2 w_2 < 0, \quad b = v_1 w_2 S_0 > 0.$$

Since $a < 0$ and $b > 0$, this confirmed a forward bifurcation at $\mathcal{R}_0$ = 1. Increasing the transmission rate increases infection. Thus, the endemic equilibrium appears smoothly when $\mathcal{R}_0 > 1$. Therefore, the bifurcation analysis indicated that the control strategies should focus on ensuring that $\mathcal{R}_0$ remains below one to guarantee disease eradication. In addition, the possibility of re-infection and imperfect vaccination makes this threshold parameter to remain sensitive to variations in vaccination and treatment compliance.

4 Numerical Simulation

The parameter values used in the simulations were mainly derived from (1; 5; 6; 10). The other values Λ = 10, μ = 0.0079, α = 0.6, ϵ = 0.02, η = 0.03 and θ = 0.005 were used.
Three scenarios based on the value of $\mathcal{R}_0$ and other five control strategy scenarios were considered in order to examine the system's response under different transmission intensities:

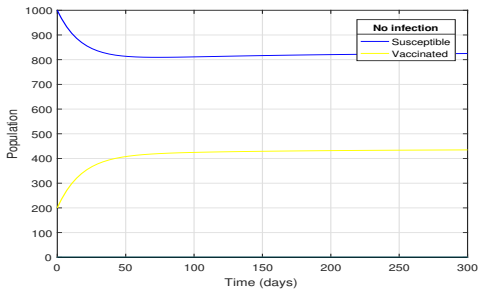

Figure 1 for ($\beta = 0.0001$)

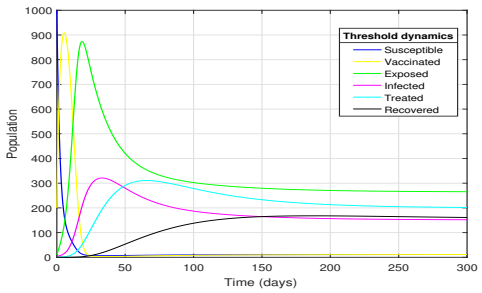

Figure 2 for ($\beta = 0.0034$)

From Figure 1, the number of susceptible individuals drops initially as people get protected as a result of vaccination. The population in the susceptible sub-group stabilizes with time as shown by

the curve. Meanwhile, the vaccinated individuals increases in number but this settles as time goes by. Therefore, for $\mathcal{R}_0 < 1$, the disease-free equilibrium is locally and globally asymptotically stable as there are no of infections. Figure 2 implies that the susceptible individuals decreases initially as people get vaccinated. They get exposed and later become infected. The infectious compartment peaks gradually and then levelizes at a constant rate. The treated individuals increases in number as infectious individuals receive treatment but then stabilizes. There is a steady rise in recoveries as people recover as a result of treatment. Thus, for $\mathcal{R}_0 = 1$, the system undergoes a transcritical bifurcation. As $\mathcal{R}_0$ crosses one, the stability of the disease-free equilibrium changes suggesting that the disease does not die out immediately. This is because the system reaches a steady state which reflects the critical threshold at which the infection neither fully disappears nor grows exponentially.

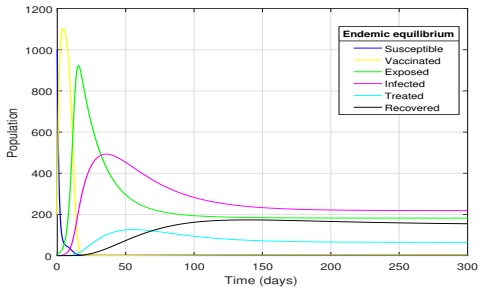

Figure 3 (for $\beta = 0.01$)

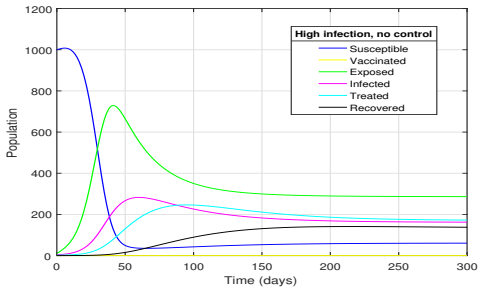

Figure 4

From figure 3, the population in susceptible class declines rapidly as more individuals are exposed after vaccination. Nevertheless, these individuals get infected so quickly due to higher contact rate and then settles at a higher epidemic level. There is also a steady rise in recoveries as people get treated but this stabilizes with time. Hence, for $\mathcal{R}_0 > 1$, the disease persists in the population and settles at an endemic equilibrium. Figure 4 entails that with no vaccination being considered as a control strategy, the number of people in susceptible compartment decreases and then those individuals move direclty into the exposed class. The exposed individuals also decreases in number as they move into the infected class. These people are treated and this increases the number of recoveries over time. The recovered individuals do not increase significantly due to absence of vaccination which is a control strategy that offers protection.

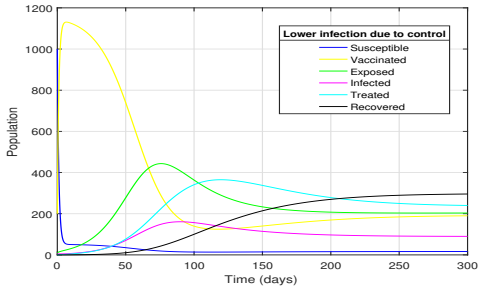

Figure 5 (α = 0.6, γ = 0.7)

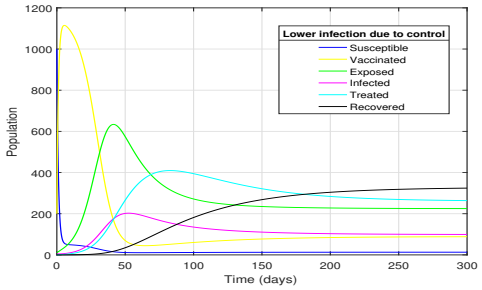

Figure 6 (α = 0.1, γ = 0.7)

From figure 5 considers high vaccine efficacy and treatment default rate in place, the recovered individuals tend to increase in number as shown by the rising curve. On the other hand, the number of infections lowers with time due to effective vaccination and treatment success rates implying the importance of the two control strategies. Figure 6 shows lower vaccine efficacy which suggests that the protection of the recovered individuals is at risk. This implys that treatment success rate alone is not enough as this leads to the rise of the number of infectious individuals compared to those in the vaccinated compartment.

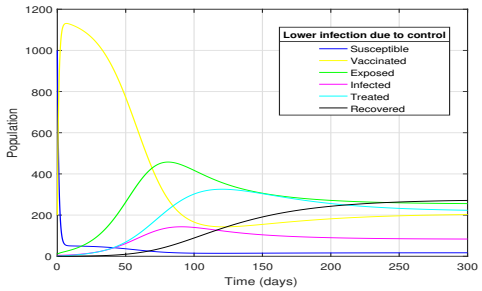

Figure 7 (α = 0.6, γ = 0.1)

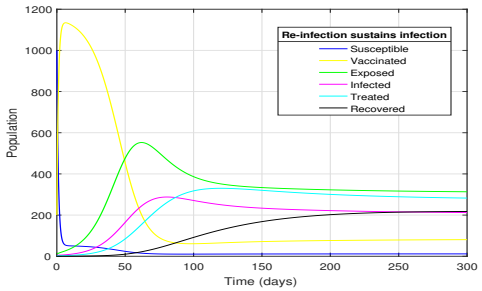

Figure 8

From figure 7, it's evident that the number of recovered individuals drops significantly as result of imperfect treatment. Therefore, both vaccination and treatment have to be effective in order to guarantee a stable rise in the number of recoveries. Figure 8 shows the impact of re-infection being considered with the other factors simultaneously. Re-infection reduces the number of recoveries thus leading to an increase in the number of exposed and subsequently the infected individuals.

5 Conclusion

This study examined the dynamics of tuberculosis (TB) transmission in a community using a deterministic model that was formulated and examined. It was demonstrated that every solution to the system of equations (2.1) remained positive in the feasible region Γ and the boundness suggested that the model is both biologically relevant and well posed. The endemic equilibrium (EE) and the disease-free equilibrium (DFE) were the model's equilibrium points. The basic reproduction number $\mathcal{R}_0$ was obtained with the help of the next-generation matrix technique. In contrast to $\mathcal{R}_0 > 1$, which implied that a single primary case could result in multiple secondary infections and thus the persistence of the epidemic in the population, $\mathcal{R}_0 < 1$ suggested that a single primary case could result in fewer than one secondary infection and the absence of the disease.

The eigenvalues of the Jacobian matrix assessed at each equilibrium were used to assess the stability analysis. The disease-free equilibrium point denoted as E^0 was shown to be locally and globally asymptotically stable whenever $\mathcal{R}_0 < 1$ and unstable otherwise. Conversely, the endemic equilibrium exhibits both a local and global asymptotic stable state whenever $\mathcal{R}_0 > 1$ implying that the disease persists in the population. In addition, a bifurcation analysis was conducted and the analysis demonstrated that the system undergoes a forward bifurcation at $\mathcal{R}_0 = 1$ indicating that when $\mathcal{R}_0$ crosses one, the DFE loses stability and an endemic equilibrium emerges smoothly. Finally, numerical simulations were performed and the results revealed that reducing transmission and increasing vaccination and treatment efficacy significantly contribute to lowering the number of infectious individuals and suppressing TB transmission. In addition, the simulations implied that understanding the role of re-infection is very vital as it significantly influences the transmission dynamics of this disease. These insights highlight the importance of sustained public health efforts to keep $\mathcal{R}_0$ below one and ultimately eliminate TB.

6 Recommendation

(i) The model recommends enhancement of vaccination coverage hence ensuring high vaccine effectiveness which can substantially reduce the susceptible population, lowering the overall risk of infection.

(ii) Ongoing education and awareness campaigns are vital to encourage early detection, treatment compliance and preventive measures.

(iii) Focusing on stochastic modeling which can easily capture random fluctuations in TB transmission, especially in small populations or places with low incidence.

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Competing Interests

The authors declare that no competing interests exists.

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